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Well-Defined Palladium N-Heterocyclic Carbene Complexes: Direct C−H Bond Arylation of Heteroarenes

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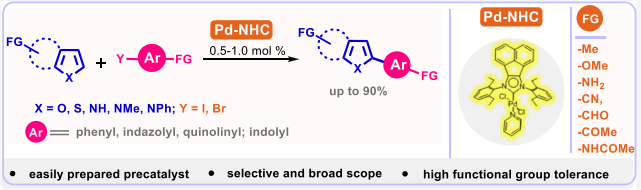
ABSTRACT: A series of palladium N-heterocyclic carbene (NHC) complexes of type *trans*-{(NHC)$PdCl_2L$} (L = C_5H_5N, 3-ClC_5H_4N, and PPh_3) (**3**−**5**) have been developed as efficient precatalysts for direct C−H bond arylation of various heteroarenes. In particular, an in situ generated new NHC ligand derived from {1,3-di-(2,6-diethylphenyl)acenaphtho[1,2-*d*] imidazolium} chloride (**2**) is used for the stabilization of the palladium metal center. Among the screened palladium precatalysts (**3**−**5**), the most active PEPPSI themed complex (**3**) was successfully employed toward direct C−H bond arylation of various heteroarenes and aryl bromides. A range of functional groups on aryl bromides as well as on heteroarenes sustained throughout the standard reaction conditions for easy access of various arylated heterocyclic compounds. Significantly, the utility of the protocol was demonstrated by the effective synthesis of a precursor of raloxifene, a selective estrogen receptor modulator.



INTRODUCTION

Arylated heteroarenes are constructive units for several important natural products, pharmaceuticals, and functional materials.[1−3] Primarily, thiophene-,[4−6] indole-,[7−9] and furan[10−12]-derived motifs are present in a variety of drugs and other bioactive organic molecules. The high utility of these molecules always demands the development of new alternative paths to access the arylated heterocycles and became an exciting area in organic chemistry.[13] Recently, the focus has been shifted toward the development of convenient, efficient, and time-dominant C−C bond formation methods.[14−20] In this order, direct C−H bond arylation emerged as an alternative approach over the traditional cross-coupling reactions as it does not require the preparation of organometallic reagents, which avoid the formation of quantitative metal waste (Figure 1).[21−24]

The last few decades were dedicated to ligand designing for improving the catalytic efficiency of palladium complexes for direct C−H bond arylation reaction.[25−28] Notably, extensive studies on bulky and electron-rich phosphine ligands have been carried out over the past few years. In addition, various phosphine-free nitrogen-based ligands, for example, 1,10-phenanthroline,[29,30] bipyridyl,[31−33] bulky diamine,[34,35] and others,[36] were used to increase the palladium catalytic efficiency for this type of conversion. However, the efficacy of the reported protocols was limited because of high catalytic loading, very high reaction temperature (up to 150 °C), and long reaction time.[37−39] Therefore, there is a need to design an efficient and structurally characterized catalytic system, which can make these reactions more user-friendly.

Parallelly, the development of N-heterocyclic carbene (NHC) ligands achieved an extensive portfolio in chemical

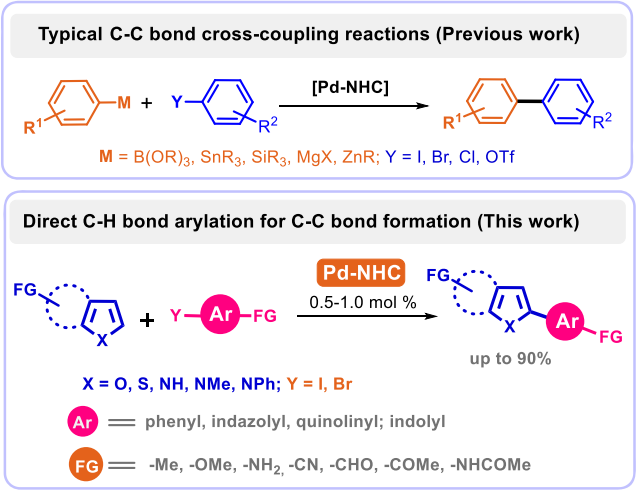


Figure 1. Pd−NHC-catalyzed cross-coupling reactions.

catalysis.[40−48] The great success of these classes of wonder ligands lies in their easily tunable steric and electronic properties, which play an essential role in catalysis.[49−53] Pd−NHC complexes were found to be extremely successful precatalysts for C−C and C−N bond formation via cross-

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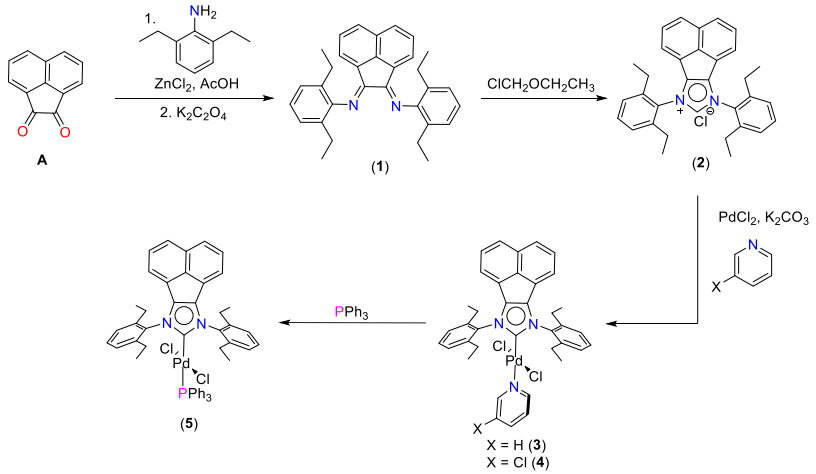
Scheme 1. Synthesis of Pd−NHC Complexes of Acenaphthoimidazoline-2-ylidene-Derived NHC Ligand



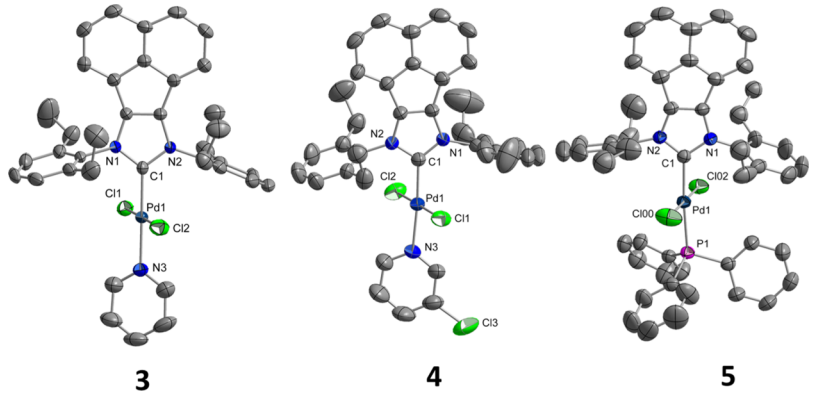


Figure 2. Molecular structures of complexes **3**, **4**, and **5** showing 50% probability ellipsoids; hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and angles (°) for **3**: Pd1−C1 1.971(3), Pd1−N3 2.106(3), Pd1−Cl1 2.295(1), Pd1−Cl2 2.287(1), C1−Pd1−N3 179.4(3), Cl1−Pd1−Cl2 178.0(5), and N1−C1−N2 105.5(2). **4**: Pd1−C1 1.968(3), Pd1−N3 2.091(3), Pd1−Cl1 2.298(1), Pd1−Cl2 2.301(1), C1−Pd1−N3 175.3(3), Cl1−Pd1−Cl2 176.7(1), and N1−C1−N2 106.1(3). **5**: Pd1−C1 2.036(2), Pd1−P1 2.317(1), Pd1−Cl00 2.279(1), Pd1−Cl02 2.296(1), C1−Pd1−P1 175.3(3), Cl00−Pd1−Cl02 179.6(3), N1−C1−N2 105.8(2).

coupling reactions.[54−58] In particular, pyridine-enhanced precatalyst preparation, stabilization, and initiation (PEPPSI)-themed and mixed NHC-/phosphine-derived Pd−NHC complexes have emerged as highly active precatalysts in terms of their low catalyst loading and broad applications.[55,56,59] Seminal reports by Shao *et al.*,[60−62] Özdemir *et al.*,[63−66] and others[67,68] represent the high catalytic efficiency of [PdX_2(NHC)(imidazole)], [PdX_2[$(NHC)_2$]], and *trans*-[PdX_2(NHC)(pyridine)] type palladium complexes in C−H bond arylation of various heteroarenes. Recently, we explored the C−H bond amination of arenes[69−71] and are further interested to explore the scope of NHCs in direct C−H bond arylation of heteroarenes.[10,72,73] In the present study, we chose to explore the potential of Pd−NHC complexes in more challenging and competitively less studied direct C−H bond arylating C−C bond formation reactions. In this article, we have reported a series of Pd−NHC complexes (**3**−**5**) based on a bis(imino)acenaphthene-derived new NHC ligand. The scope of various heteroarenes is explored with the most efficient catalyst **3** and 4-bromobenzonitrile as an arylating substrate.

RESULTS AND DISCUSSION

The imidazolium NHC ligand precursor (**2**) has been prepared from *N*,*N*′-(acenaphthylene-1,2-diylidene)bis(2,6-diethylaniline) using a modified literature procedure.[74] Ganter *et al.* described that the heteronuclear ^1J(C−H) coupling constant in azolium salts could provide an estimate on the σ-donor property of the corresponding NHCs.[75] Recently, Szostak and co-workers also extended this method for various commonly used azolium salts and ranked the σ-donor efficiency of the respective NHCs.[76] A larger coupling constant would indicate a lower σ-donor strength of the parent NHCs because of the increased s-orbital character of the C−H bond. The ^1J(C−H) coupling constant for salt **2** (227.28 Hz) was obtained from ^{13}C satellites of the acidic C2−H proton observed in ^{1}H NMR spectra. This value was found to be larger than that of IPr·HCl (223.70 Hz) and IMes·HCl (225.20 Hz).[76] It indicates toward less σ-donor ability of novel carbene ligand as compared to the famous IPr and IMes NHC ligands. Two PEPPSI-themed palladium complexes (**3**) and (**4**) were obtained by the reaction of imidazolium ligand precursor (**2**) in the presence of $PdCl_2$, K_2CO_3 as a base and pyridine or 3-chloropyridine as a solvent, respectively (Scheme 1). Finally, the mixed NHC/phosphine Pd−NHC complex (**5**) was synthesized by replacing the labile pyridine ligand of the complex (**3**) with

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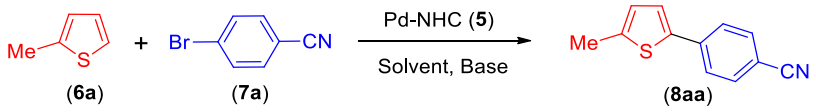
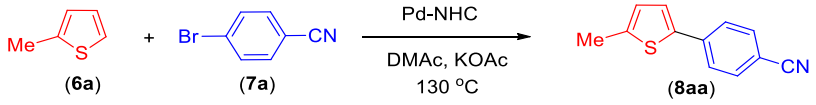
Table 1. Optimization of Reaction Conditions[a]



s. no.	Cat. (mol %)	time (h)	temp (°C)	solvent	base	conv.[b]
1	2.5	18	130	DMAc	NaOAc	71
2	2.5	18	130	DMAc	AgOAc	NR
3	2.5	18	130	DMAc	NH_4OAc	NR
4	2.5	18	130	DMAc	K^{t}BuO	NP[d]
5	2.5	18	130	DMAc	Cs_2CO_3	NP[d]
6	2.5	18	130	DMAc	K_3PO_4	NP[d]
7	2.5	18	130	DMAc	Na_2CO_3	51
8	2.5	18	130	DMAc	K_2CO_3	100
9	1.0	24	130	DMAc	K_2CO_3	100
10	1.0	3	130	DMAc	KOAc	100
11	2.5	18	90	DMAc	K_2CO_3	29
12	**1.0**	**2**	**130**	**DMAc**	**KOAc**	**100/89**[c]
13		2	130	DMAc	KOAc	NR
14	1.0	2	130	DMF	KOAc	71
15	1.0	2	130	DMSO	KOAc	29
16	1.0	2	130	toluene	KOAc	NR
17	1.0	2	130	DME	KOAc	13
18	1.0	2	130	dioxane	KOAc	5

[a]Reaction conditions: 2-methyl thiophene **6a** (0.6 mmol, 2 equiv), 4-bromobenzonitrile **7a** (0.3 mmol, 1 equiv), base (0.9 mmol, 3 equiv), and Pd−NHC **5** (*x* mol %) heated at *t* °C in a screw cap sealed tube under nitrogen atmosphere. [b]Conversion by GC. [c]Isolated yield. [d]Undefined product observed.

Table 2. Screening of Pd−NHC Complexes[a]



s. no.	Pd−NHC	catalyst (mol %)	time (h)	conversion[b]/yield[c]
1	(**3**)	1	1	100/92
2	(**4**)	1	1	100/91
3	(**5**)	1	1	84/-
4	(**5**)	1	2	100/89
5	(**3**)	**0.5**	**2**	**100/90**
6	(**4**)	0.5	2	74/60
7	Pd-PEPPSI-IPr	0.5	2	61/-
8	[d]$Pd(OAc)_2$	0.5	2	60/-

[a]Reaction conditions: 2-methyl thiophene **6a** (0.6 mmol, 2 equiv), 4-bromobenzonitrile **7a** (0.3 mmol, 1 equiv), KOAc (0.9 mmol, 3 equiv), and Pd−NHC (0.003 mmol, 1 mol % or 0.0015, 0.5 mol % mmol) heated at 130 °C in a screw cap sealed tube under nitrogen atmosphere. [b]Conversion by GC. [c]Yield isolated yield, DMAc = *N*,*N*-dimethylacetamide. [d]Reaction conditions (**6a** = 1.2 mmol, **7a** = 0.6 mmol, and KOAc = 1.8 mmol).

PPh_3 at room temperature. All the three palladium complexes (**3**−**5**) were structurally characterized by X-ray diffraction studies (Figure 2 and Table S2). As expected, Pd−NHC complexes (**3**−**5**) having a square-planar geometry around the central palladium atom and two chloride ligands occupied the remaining positions (Scheme 1).

The catalytic efficiency of Pd−NHC complexes (**3**−**5**) was examined in the catalytic C−H arylation of 2−methyl thiophene (**6a**). Significantly, all the three Pd−NHC complexes (**3**−**5**) were found to be active precatalysts for the C−H arylation reaction of 2-methyl thiophene (**6a**) and 4-bromobenzonitrile (**7a**) at 130 °C under standard reaction conditions. The mixed NHC/phosphine complex (**5**) has been chosen for optimization studies and the reaction progress was analyzed by gas chromatography−mass spectrometry (GC-GCMS).

The reaction of 2−methyl thiophene (**6a**) and 4-bromobenzonitrile (**7a**) yielded 71% conversion of **7a** by using 3.0 equiv of NaOAc as a base and 2.5 mol % catalyst **5** at 130 °C temperature in 18 h (Table 1, entry 1). No conversion was observed while using AgOAc or NH_4OAc (Table 1, entries 2 and 3), and the undefined product was formed by using K^{t}BuO, Cs_2CO_3, and K_3PO_4 as a base under similar reaction conditions (Table 1, entries 4−6). In the presence of Na_2CO_3, the catalyst was found to be moderately active with 51% conversion (Table 1, entry 7). The complete conversion of 4-bromobenzonitrile (**7a**) was achieved by using K_2CO_3 as a base in the presence of 2.5 mol % precatalyst (**5**) in 18 h (Table 1, entry 8). However, on reducing the catalyst loading

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from 2.5 mol % to 1 mol %, the reaction time was increased up to 24 h for achieving the complete conversion (Table 1, entry 9). Last, KOAc was found to be the most suitable base for the catalytic C−H arylation reaction of **6a** and **7a** at 130 °C temperature (Table 1, entries 10 and 11). The precatalyst **5** was efficient enough to complete the reaction within 2 h in the presence of KOAc and afforded the isolated product in 89% yield (Table 1, entry 12). There was no reaction in the absence of a catalyst (Table 1, entry 13), and solvents other than DMAc were not suitable for the given transformations (Table 1, entries 14−18).

After having the optimized reaction condition in hand, we have performed the screening of synthesized Pd−NHC complexes for this reaction. PEPPSI-themed catalysts **3** and **4** were found to be more active under standard reaction conditions and yielded the complete conversion of **7a** in 1 h while loading 1 mol % catalyst (Table 2, entries 1−2). Catalyst **5** was found to be comparatively less efficient, which yielded only 84% conversion in 1 h and takes 2 h for completing the reaction (Table 2, entries 3−4). The most active catalyst (**3**) completes the reaction within 2 h, using 0.5 mol % catalyst loading (Table 2, entry 5). However, under this catalyst loading, catalyst **4** was unable to complete the reaction (Table 2, entry 6). Pd-PEPPSI-IPr was much less efficient than catalyst **3** under the identical reaction conditions and yielded 61% product conversion (Table 2, entry 7). Probably, the introduction of bulky acenaphthyl backbone in **3**−**5** would facilitate the stabilization of catalytically active Pd(0) species as compared to less-hindered Pd-PEPPSI-IPr, which has hydrogen atoms on the backbone.[67,77] $Pd(OAc)_2$ was also found catalytically less efficient under the given reaction conditions and afforded only 60% product as calculated by GC-GCMS (Table 2, entry 8). The superior activity of two PEPPSI-themed Pd−NHC complexes **3** and **4** makes us interested in comparing the reaction kinetics under low catalyst loading conditions (Figures 3 and 4).

As shown in Figure 3, catalyst **3** was found to be the most active precatalyst, which can give a 100% conversion with 0.5% catalyst loading in 2 h. The reaction time increases up to 4 h, with 0.1 mol % catalyst loading, while catalyst **4** was found comparatively less efficient under these observations. The

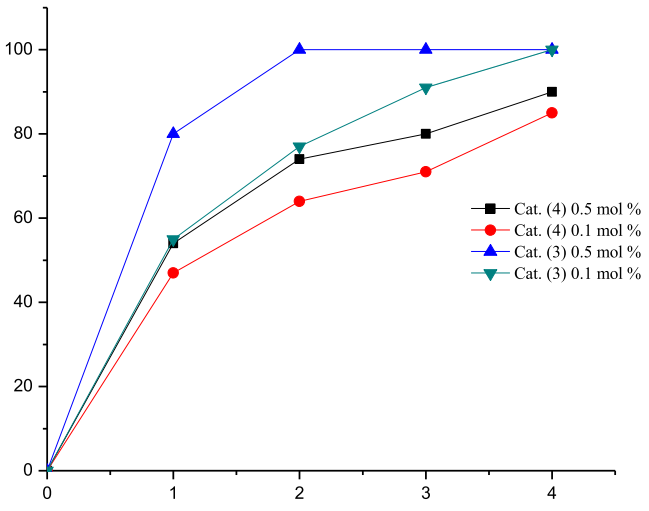

Figure 3. Comparison of the reaction progress of 2-methyl thiophene **6a** and 4-bromobenzonitrile **7a** by 0.1 and 0.5% catalyst loading of PEPPSI-themed complexes (**3**) and (**4**).

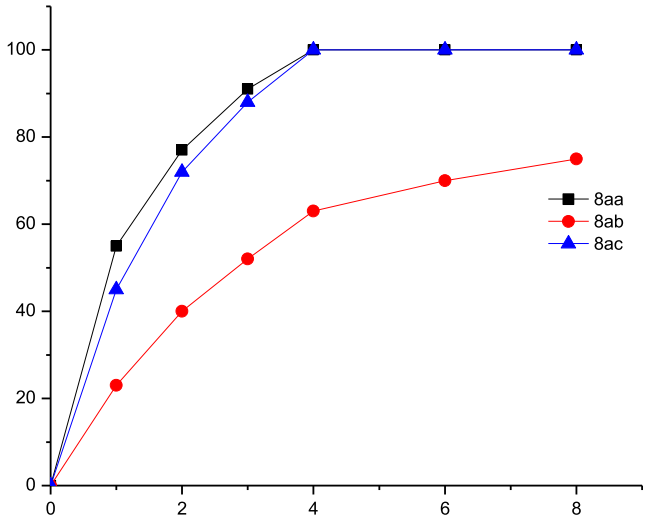

Figure 4. Reaction progress of 2-methyl thiophene and *para* (**8aa**)-, *meta* (**8ab**)-, and *ortho* (**8ac**)-substituted bromobenzonitrile by 0.1% catalyst loading of PEPPSI-themed complex (**3**).

electronic and steric influences of the CN group in the arylating substrate **7** was observed by conducting the reaction of 2-methyl thiophene (**6a**) with differently −CN-substituted bromobenzene as 4-bromobenzonitrile (**7a**), 3-bromobenzonitrile (**7b**), and 2-bromobenzonitrile (**7c**) with 0.1 mol % loading of the most active catalyst **3** under the standard reaction conditions (Figure 4). The electron-withdrawing CN group increases the reactivity of ortho- and para-substituted bromobenzene because of the −R effect. However, 2-bromobenzonitrile (**7c**) was found marginally slower reactive and can be explained by the steric fact. 3-Bromobenzonitrile (**7b**) was found to be least reactive and unable to give complete conversion even after 8 h under 0.1% catalyst loading.

In the view of time-efficient reaction conditions, the substrate scope of various aryl bromides was explored with 0.5 mol % catalyst loading and using 2-methyl thiophene (**6a**) as a heteroarene under standard reaction conditions. Activated aryl bromides, containing −CN and −CHO groups at ortho and para positions **7a**, **7c**, and **7g**, were more active and provide respective products in good yields (Scheme 2, **8aa**, **8ac**, and **8ag**) within 2−3 h. −OMe and $-NHCOCH_3$ groups at para position, that is, **7e** and **7h**, decreased the reactivity of aryl bromides and the reaction time increased up to 6−12 h. The products (**8ae** and **8ah**) were obtained in 81 and 60% yields, respectively, while using 1 mol % catalyst. −OMe at meta position **7d** was comparatively active and produced 78% yield in 4 h (**8ad**). Bromobenzene **7f** and *para* phenyl bromobenzene **7i** afforded the respective products (**8ai** and **8af**) in 69 and 77% yields, respectively, in 6 h. We did not get product using chlorobenzene as the arylating reagent under reaction conditions, while iodobenzene yielded only 52% yield of product **8af**, and GC-GCMS indicated the formation of homocoupled biphenyl as a side product. 6-Bromo-1-methyl-1*H*-indazole **7j** and 7-bromo-4-chloroquinoline **7k** reacted slowly and afforded the desired products (**8aj** and **8ak**) in 12 h. Finally, 5-bromo-1-methyl-1*H*-indole **7l** was also found to be suitable and afforded 29% yield of product in 12 h by using 1 mol % of most active catalyst **3**.

The substrate scope for heteroarenes was elaborated with 4-bromobenzonitrile (**7a**) as an arylating precursor under

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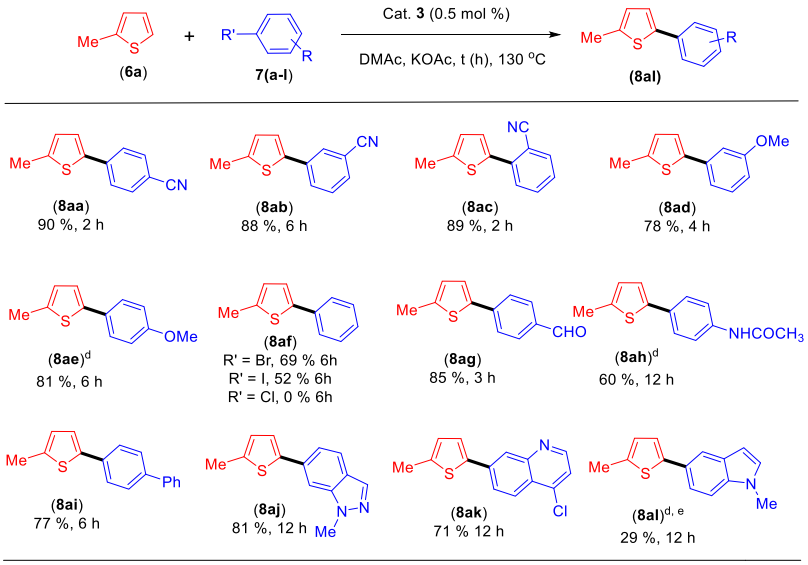
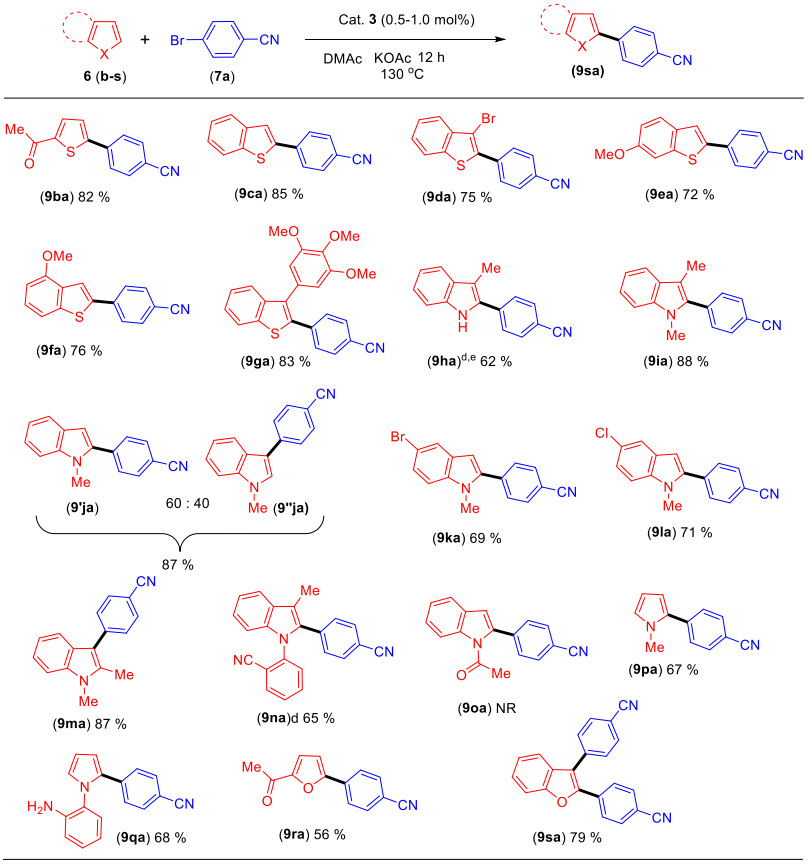
Scheme 2. Scope of Haloarenes for C−H Arylation Reaction of 2−Methyl Thiophene[a]



[a]Reaction conditions: 2-methyl thiophene **6a** (1.0 mmol, 2 equiv), aryl bromides (aryl halide for entry **8af**) (0.5 mmol, 1 equiv), KOAc (3 mmol, 3 equiv), and Pd−NHC (0.0025, 0.5 mol % mmol) heated at 130 °C in a screw cap sealed tube under nitrogen atmosphere, [d]0.005 mmol, 1 mol % Pd−NHC, yield = isolated yield, and [e]GC conversion.

Scheme 3. Scope of Heteroarenes for C−H Arylation Reaction[a]



[a]Reaction conditions: heteroarene (1.0 mmol, 2 equiv), aryl bromide **7a** (0.5 mmol, 1 equiv), KOAc (3 mmol, 3 equiv), and Pd−NHC (0.0025 mmol, 0.5 mol % mmol) heated at 130 °C in a screw cap sealed tube under nitrogen atmosphere, [d]0.005 mmol, 1 mol % Pd−NHC, yield = isolated yield, [e]GC conversion. DMAc = *N*,*N*-dimethylacetamide, and reaction time not optimized.

optimized reaction conditions. Significantly, various thiophene-, pyrrole-, indole-, and furan-derived heteroarenes are suitable under standard reaction conditions and afforded the corresponding products in moderate to good yield (Scheme 3).

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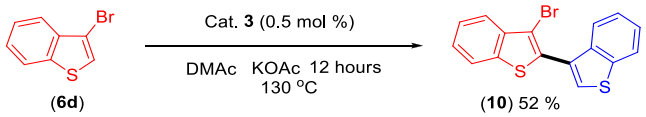
In particular, thiophene-derived heteroarenes such as 2-acetyl thiophene **6b**, benzo[*b*]thiophene **6c**, 3-bromobenzo[*b*]-thiophene **6d**, 6-methoxybenzo[*b*]thiophene **6e**, 4-methoxybenzo[*b*]thiophene **6f**, and even more satirically hindered 3-(3,4,5-trimethoxyphenyl)benzo[*b*]thiophene **6g** efficiently react to afford the respective products (**9ba**−**9ga**) in good yields (72−85%).

After the successful implementation of our Pd−NHC catalyst on thiophene-derived heteroarenes, we became interested in another important class of heterocycles, that is, indoles, which are also important building blocks of various important biologically active organic molecules. Many substituted indoles, for example, 3-methylindole **6h**, 1,3-dimethylindole **6i**, 1-methylindole **6j**, 5-bromo-1-methylindole **7l**, 5-chloro-1-methylindole **6l**, and 2-(3-methyl-1*H*-indol-1-yl)benzonitrile **6n** have been examined toward the C−H arylation reaction catalyzed by Pd−NHC complex **3**. 1,3-Dimethylindole **6i** yielded 88% product (**9ia**) under optimized reaction conditions while 3-methylindole **6h** afforded 62% product (**9ha**) yield even after 1 mol % of catalyst loading. 1-Methylindole **6j** yielded two products corresponding to C2−H and C3−H activation and found more selective for C2−H activation, as products were obtained in 60:40 ratio, respectively (**9′ja** & **9″ja**). It is noteworthy that 5-bromo-1-methylindole **7l** and 5-chloro-1-methylindole **6l** afforded predominantly C2−H-activated products (**9ka** and **9la**) in 69% and 71% yield, respectively. However, a less amount of C3−H-activated product can be identified by GC-GCMS. 2-(3-methyl-1*H*-indol-1-yl)benzonitrile **6n** yielded the corresponding products in 65% (**9na**) and 1-acetylindole **6o** remained unreacted in the standard reaction condition (**9oa**).

We have also extended the application of our Pd−NHC catalyst toward C−H activation of pyrroles. 1-Methylpyrrole **6p** and 2-(1*H*-pyrrol-1-yl) aniline **6n** were reacted well with 4-bromobenzonitrile (**7a**) to afford the corresponding arylated product (**9pa** and **9qa**) in good yields. 2-Acetyl furan yielded the respective C−H arylated product (**9ra**) in moderate yield. Quite interestingly, benzo[*b*]furan reacted to afford the predominantly double C−H-activated product **9sa** in 79% yield. 3-Bromobenzo[*b*]thiophene also behaved as a hetero-arylating agent and afforded a self hetero-arylated product, namely, 3-bromo-2,3′-bibenzo[*b*]thiophene (**10**) in 52% yield (Scheme 4).

Scheme 4. Self-Heteroarylation by C−H Activation of 3-Bromobenzo[*b*]thiophene



Furthermore, the bis(hetero)benzene **11**(**a**−**d**) type organic framework was constructed using dibromo benzene as an arylating agent, and the strategy is applicable for various heteroarenes. In particular, 2-methylthiophene **6a** and 1-methylpyrrole **6p** reacted with 1,3- and 1,4-dibromobenzene **7m** and **7n** to afford desired products in good yield by using 1 mol % of catalyst **3** and under optimized reaction conditions (Scheme 5).

Additionally, we have extended our synthetic methodology for catalytic double C−H arylation of unsubstituted furan **6t** and 1-methylpyrrole **6p**. Significantly, C−H-activated arylation observed selectively at C2 and C5 positions (Scheme 6). 4-Bromobenzonitrile (**7a**) reacted with respective heteroarenes to provide corresponding bis-arylated products **12 a**−**b** in moderate yield (55−79%). Notably, we obtained dominant or exclusively *α*-arylated products during arylation of a library of heteroarenes, which indicate that the catalytic cycle followed the concerted metalation−deprotonation mechanism.[27,78]

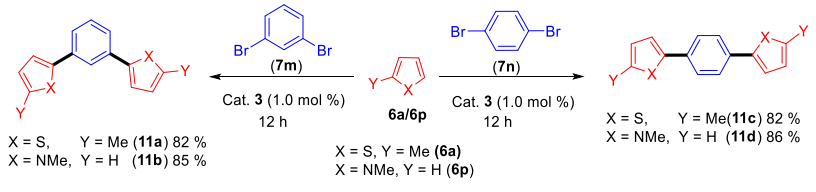
The competitive experiment studies may provide a deep understanding of heteroarene reactivity. The results are summarized in Scheme 7. 2-Methyl thiophene **6a** was found to be more reactive toward the C−H arylation reaction with 4-bromobenzonitrile **7a** as compared to the 2-acetyl thiophene **6b** (Scheme 7a) and 1,3-dimethylindole **6i** (Scheme 7b). 1,3-Dimethylindole **6i** has shown far better reactivity as compared to 3-methylindole **6h** (Scheme 7c). 1,3-Dimethylindole **6i** and 1,2-dimethylindole **6m** reacted similarly, and an equal amount of C3- and C2-activated product was observed by GC (Scheme 7d).

Last, we demonstrated the application of catalyst **3** in the synthesis of 6-methoxy-2-(4-methoxyphenyl)benzo[*b*]-thiophene (**13**), which is a key intermediate for the total synthesis of bioactive raloxifene[79] and known as a selective estrogen receptor modulator (Scheme 8). 6-Methoxybenzo-[*b*]thiophene **6e** reacted with 1-bromo-4-methoxybenzene **7e** with 1 mol % of catalyst to afford 67% of the desired compound (**13**) under standard reaction conditions. Similarly, the practical utility of the method as a synthetic tool is highlighted by the gram-scale synthesis of compound **8aa** in good (85%) yield. A comparison of precatalyst **3** has been made with some literature-reported precatalysts which are utilized for C−H arylation reaction of heteroarenes (Supporting Information Table S1). However, a fair comparison is not possible because of using different reaction conditions, arylating substrates, and temperature in various reports. Nevertheless, it resulted that precatalyst **3** afforded the arylated heteroarenes in a time-efficient way, without the requirement of any external additive, and with a decent catalyst loading.

CONCLUSIONS

The new structurally characterized Pd−NHC complexes (**3**−**5**) are active precatalysts for the C−H arylation of 2-methyl thiophene by using 4-bromobenzonitrile under optimized reaction conditions. PEPPSI-themed Pd−NHC complex (**3**) and (**4**) were found to be a better precatalyst than mixed

Scheme 5. Synthesis of Bis(hetero)benzene-Type Framework by Using Dibromo Benzene



https://dx.doi.org/10.1021/acs.joc.0c02024
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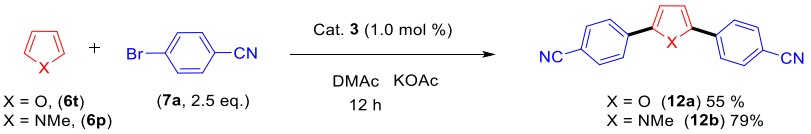
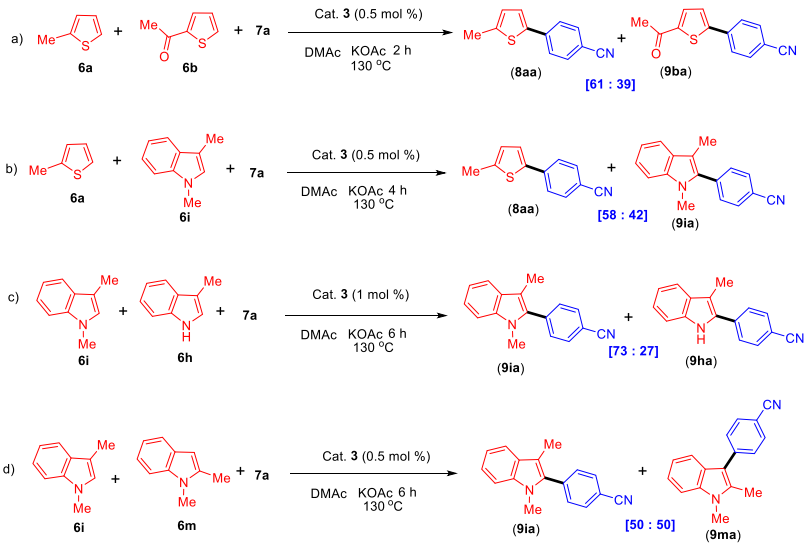
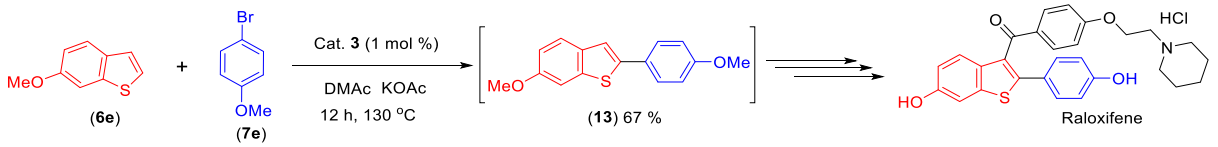
Scheme 6. C2 and C5 Activation of Heteroarenes



Scheme 7. Competitive Experiment Studies



Scheme 8. Synthesis of Intermediate Compound (13) by Direct C−H Arylation Reaction



NHC/phosphine complex (**5**), which again shows the superiority of these classes of NHC-derived, easily prepared, and demanding precatalysts. The aryl bromides were found to be a better choice of the arylating agent as compared to aryl iodides and aryl chlorides. The substrate scope of aryl bromide and heteroarenes elaborated with the most active precatalyst complex (**3**), which concluded that the reaction conditions sustain with various substituents on both the reactants. Competitive experimental studies suggest that the reactivity of heteroarenes follows the order thiophene > *N*-methylated indole > 1*H* indole in standard reaction conditions. Catalyst (**3**) was used to obtain an organic intermediate (**13**), which is a building block for a selective estrogen receptor modulator known as raloxifene. This is projecting its potential in the application for synthesis of natural products and other biologically active molecules, where the C−C bond formation reaction can be achieved in reduced steps and less metal waste manner by the C−H arylation reaction. Overall, the study keeps the NHC promise to behave as an efficient ligand in the world of chemical catalysis.

EXPERIMENTAL SECTION

General Information and Method. ^{1}H NMR (400 MHz) and $^{13}C\{^{1}H\}$NMR (100 MHz) spectra were recorded in $CDCl_3$ and $(CD_3)_2SO$. Chemical shifts for protons and carbons are reported in ppm from tetramethylsilane and are referenced to the carbon resonance of the solvent. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and dd = doublet of doublet), coupling constants in Hertz, and integration. The Pd-PEPPSI-IPr complex was prepared by the literature-reported procedure.[80] High-resolution mass spectra were recorded on a q-TOF electrospray mass spectrometer. X-ray diffraction data for compounds **3**, **4**, and **5** were collected on an Oxford Diffraction XCALIBUR diffractometer using graphite-monochromatic Mo Kα radiation (λ = 0.71073 Å). Crystal data collection and refinement parameters are summarized in Table S2. The structures were solved by direct methods using SHELXS-97and refined with SHELXL-2014 using Olex2. The non-hydrogen atoms were refined anisotropically, whereas the hydrogen atoms were fixed at the calculated positions with isotropic thermal parameters. TLC analysis was performed on commercially prepared 60 F_{254} silica gel plates and visualized by either UV irradiation or by staining with I_2. All purchased chemicals were used as received. Aromatic carbon signals were assigned as (Ar−C) in the $^{13}C\{^{1}H\}$NMR spectrum of respective compounds. The preheated oil bath has been used as a heating source for the reactions performed at higher than room temperature.

*Synthesis of N,N′-(Acenaphthylene-1,2-diylidene)bis(2,6-diethylaniline) (**1**).* Acenaphthenequinone (6.00 g, 33.0 mmol), 2,6-diethylaniline (10.3 g, 69.2 mmol), and $ZnCl_2$ (4.50 g, 33.0 mmol) were suspended in glacial acetic acid (*ca.* 100 mL). The mixture was refluxed for 2 h and then cooled to room temperature, during which a red-colored precipitate was observed. The precipitate was filtered and washed with water, followed by diethyl ether. The precipitate was dried under vacuum and further suspended in dichloromethane (*ca.*

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300 mL). A solution of potassium oxalate (12.1 g, 66.0 mmol) in 30 mL of H_2O was added to the suspension and stirred vigorously for 45 min. A white precipitate of zinc oxalate was observed in the aqueous phase during this period. The organic layer was separated, washed with water (*ca.* 3 × 40 mL), and dried over anhydrous sodium sulfate. Finely, the organic layer was filtered and vacuum-dried to afford the product as an orange solid (12.4 g, 85%). ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ 7.88 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_{12}\underline{H}_6$), 7.37 (t, 2H, $^3J_{HH}$ = 8 Hz, $C_{10}\underline{H}_{13}$), 7.22−7.15 (m, 6H, $C_{12}\underline{H}_6$ & $C_{10}\underline{H}_{13}$), 6.68 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_{12}\underline{H}_6$), 2.81−2.54 (m, 4H, $C\underline{H}_2CH_3$ of $C_{10}\underline{H}_{13}$), 2.50−2.42 (m, 4H, $C\underline{H}_2CH_3$ of $C_{10}\underline{H}_{13}$), 1.11 (t, 12H, $^3J_{HH}$ = 8 Hz, $CH_2C\underline{H}_3$ of $C_{10}\underline{H}_{13}$), $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 160.7 ($\underline{C}$═N), 148.5, 140.6, 131.0, 130.7, 129.6, 128.8, 128.1, 126.4, 123.9, 122.9 (Ar−C), 24.7 ($\underline{C}H_2CH_3$), 13.9 ($CH_2\underline{C}H_3$). HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $[C_{32}H_{33}N_2]$, 445.2662; found, 445.2599. (Unable to get satisfactory CHN results after multiple attempts.)

*Synthesis of 1,3-Bis(2,6-diethylaniline)acenaphthylenyl-4,5-imidazolium Chloride (**2**).* *N*,*N*′-(Acenaphthylene-1,2-diylidene)bis(2,6-diethylaniline) (**1**) (0.800 g, 1.80 mmol) and chloromethyl ethyl ether (*ca.* 5 mL) were added to a thick-walled sealed tube and then the reaction mixture was allowed to stir overnight at 90 °C. A brown-colored suspension was separated from a clear red solution during this period. The reaction mixture was cooled to ambient temperature and diethyl ether (*ca.* 20 mL) was added into it. After that, the resulting yellow precipitate was filtered off, washed with diethyl ether (*ca.* 60 mL), and dried under vacuum to afford a yellow solid (0.731 g, 82%). ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ 11.9 (s, 1H, NC$\underline{H}$N), 8.01 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_{12}\underline{H}_6$), 7.63−7.56 (m, 4H, $C_{12}\underline{H}_6$ & $C_{10}\underline{H}_{13}$), 7.42 (d, 4H, $^3J_{HH}$ = 8 Hz, $C_{10}\underline{H}_{13}$), 7.24 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_{12}\underline{H}_6$), 2.74−2.57 (m, 8H, $C\underline{H}_2CH_3$ of $C_{10}\underline{H}_{13}$), 1.19 (t, 12H, $^3J_{HH}$ = 8 Hz, $CH_2C\underline{H}_3$ of $C_{10}\underline{H}_{13}$), $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 141.8 (N$\underline{C}$HN), 140.1, 137.1, 131.8, 130.9, 130.5, 130.4, 129.9, 128.2, 127.7, 123.1, 123.0 (Ar−C), 24.5 ($\underline{C}H_2CH_3$), 14.5 ($CH_2\underline{C}H_3$). HRMS (ESI-TOF): 457.2632 $[M - Cl]^+$ calcd for $[C_{33}H_{33}N_2]$, 457.2638; found, 457.2632. Anal. Calcd for $C_{33}H_{33}ClN_2{\cdot}2H_2O$: C, 74.91; H, 7.05; N, 5.29. Found: C, 75.28; H, 6.32; N, 5.90%.

*Synthesis of [{1,3-Bis(2,6-diethylaniline)acenaphthylenyl-4,5-imidazolium-2-ylidene}PdCl$_2$-(pyridine)] (**3**).* A mixture of NHC·HCl (**2**) (0.200 g, 0.406 mmol), $PdCl_2$ (0.072 g, 0.406 mmol), and K_2CO_3 (0.224 g, 1.62 mmol) was refluxed in pyridine (*ca.* 5 mL) for 16 h. Then, the reaction mixture was cooled to room temperature, diluted with ethyl acetate (*ca.* 150 mL), and then washed with an aqueous $CuSO_4$ solution (*ca.* 3 × 70 mL) and water (*ca.* 70 mL). The organic layer was separated, dried over Na_2SO_4, and finally vacuum-dried to afford the product as a yellow solid (0.215 g, 74%). Single crystals were obtained by slow evaporation of concentrated acetonitrile solutions. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ 8.52−8.49 (m, 2H, $C_5\underline{H}_5$), 7.75 (d, 2H, J_{HH} = 8 Hz, $C_{12}\underline{H}_6$), 7.58 (t, 2H, $^3J_{HH}$ = 8 Hz, $C_{10}\underline{H}_{13}$), 7.57−7.53 (m, 1H, $C_5\underline{H}_5$), 7.42 (d, 4H, $^3J_{HH}$ = 8 Hz, $C_{10}\underline{H}_{13}$), 7.41−7.37 (m 2H, $C_{12}\underline{H}_6$), 7.10 (d, 2H, $^3J_{HH}$ = 7 Hz, $C_5\underline{H}_5$), 6.96 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_{12}\underline{H}_6$), 3.09−2.99 (m, 4H, $C\underline{H}_2CH_3$ of $C_{10}\underline{H}_{13}$), 2.85−2.75 (m, 4H, $C\underline{H}_2CH_3$ of $C_{10}\underline{H}_{13}$), 1.15 (t, 12H, $^3J_{HH}$ = 8 Hz, $CH_2C\underline{H}_3$ of $C_{10}\underline{H}_{13}$), $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 158.8 (Pd−N$\underline{C}$N), 151.5, 142.0, 139.2, 137.4, 135.1, 130.1, 128.0, 127.6, 126.3, 125.8, 123.9, 121.0 (Ar−C), 24.8 ($\underline{C}H_2CH_3$), 14.2 ($CH_2\underline{C}H_3$). Anal. Calcd for $C_{38}H_{37}Cl_2N_3Pd$: C, 64.01; H, 5.23; N, 5.89. Found: C, 63.84; H, 5.06; N, 6.15%.

*Synthesis of [{1,3-Bis(2,6-diethylaniline)acenaphthylenyl-4,5-imidazolium-2-ylidene}PdCl$_2$-(3-chloropyridine)] (**4**).* A mixture of NHC·HCl (**2**) (0.300 g, 0.610 mmol), $PdCl_2$ (0.108 g, 0.610 mmol), and K_2CO_3 (0.338 g, 2.45 mmol) was stirred at 90 °C in 3-chloropyridine (*ca.* 3 mL) for 24 h. After that, 3-chloropyridine was removed by vacuum distillation to afford a crude product as a brown solid. The crude product was purified by column chromatography using petroleum ether/EtOAc (90:10 v/v) to afford a yellow solid (0.257 g, 56%). Single crystals were obtained by slow evaporation of concentrated acetonitrile solutions. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ 8.57 (s, 1H, $C_5\underline{H}_4Cl$), 8.47 (d, 1H, J_{HH} = 5 Hz, $C_5\underline{H}_4Cl$), 7.75 (d, 2H, J_{HH} = 8 Hz, $C_{12}\underline{H}_6$), 7.58 (t, 2H, $^3J_{HH}$ = 8 Hz, $C_{10}\underline{H}_{13}$), 7.57−7.53 (m, 1H, $C_5\underline{H}_4Cl$), 7.43 (d, 4H, $^3J_{HH}$ = 8 Hz, $C_{10}\underline{H}_{13}$), 7.41−7.37 (m 2H, $C_{12}\underline{H}_6$), 7.09−7.05 (m, 1H, $C_5\underline{H}_4Cl$), 6.96 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_{12}\underline{H}_6$), 3.08−2.98 (m, 4H, $C\underline{H}_2CH_3$ of $C_{10}\underline{H}_{13}$), 2.84−2.73 (m, 4H, $C\underline{H}_2CH_3$ of $C_{10}\underline{H}_{13}$), 1.15 (t, 12H, $^3J_{HH}$ = 8 Hz, $CH_2C\underline{H}_3$ of $C_{10}\underline{H}_{13}$), $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 158.8 (Pd−N$\underline{C}$N), 151.5, 142.1, 139.5, 137.4, 135.3, 130.1, 128.0, 127.6, 126.3, 123.9, 121.0 (Ar−C), 24.8 ($\underline{C}H_2CH_3$), 14.2. Anal. Calcd for $C_{38}H_{36}Cl_3N_3Pd$: C, 61.06; H, 4.85; N, 5.62. Found: C, 60.59; H, 4.58; N, 5.76%.

*Synthesis of [{1,3-Bis(2,6-diethylaniline)acenaphthylenyl-4,5-imidazolium-2-ylidene}PdCl$_2$-(PPh$_3$)] (**5**).* A mixture of palladium complex (**3**) (0.100 g, 0.140 mmol) and PPh_3 (0.036 g, 0.140 mmol) was stirred in CH_2Cl_2 (*ca.* 20 mL) at room temperature for 3 h. The solvent was removed under vacuum to afford the crude product as a yellow solid. The crude product was recrystallized from CH_3CN to afford the product as a yellow solid (0.112 g, 89%). Single crystals were obtained by slow evaporation of concentrated acetonitrile solutions. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ 7.73 (d, 2H, J_{HH} = 8 Hz, $C_{12}\underline{H}_6$), 7.61 (t, 2H, $^3J_{HH}$ = 8 Hz, $C_{10}\underline{H}_{13}$), 7.42 (d, 4H, $^3J_{HH}$ = 8 Hz, $C_{10}\underline{H}_{13}$), 7.41−7.20 (m 17H, $C_{12}\underline{H}_6$ & $C_{18}\underline{H}_{15}P$), 6.99 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_{12}\underline{H}_6$), 3.03−2.92 (m, 4H, $C\underline{H}_2CH_3$ of $C_{10}\underline{H}_{13}$), 2.88−2.79 (m, 4H, $C\underline{H}_2CH_3$ of $C_{10}\underline{H}_{13}$), 1.09 (t, 12H, $^3J_{HH}$ = 8 Hz, $CH_2C\underline{H}_3$ of $C_{10}\underline{H}_{13}$), $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 176.5 (Pd−N$\underline{C}$N), 142.1, 139.0, 138.9, 135.5, 135.0, 134.9, 130.7, 130.2, 129.7, 129.6, 129.6, 127.8, 127.7, 127.6, 126.1, 126.0, 120.9 (Ar−C), 24.7 ($\underline{C}H_2CH_3$), 14.0 ($CH_2\underline{C}H_3$). Anal. Calcd for $C_{51}H_{47}Cl_2N_2PPd$: C, 68.35; H, 5.29; N, 3.13. Found: C, 67.87; H, 5.22; N, 3.20%.

General Procedure for Reaction Optimization, Catalyst Screening, and Kinetic Studies. 2-methyl thiophene **6a** (0.6 mmol, 2 equiv), bromobenzonitrile **7a** (or **7b** or **7c**) (0.3 mmol, 1 equiv), base (0.9 mmol, 3 equiv), and Pd−NHC (*x* mol %) were transferred to a screw cap sealed tube under nitrogen atmosphere. The solvent (*ca.* 2 mL) was added and the sealed tube was heated at 130 °C for the respective time. The reaction mixture was cooled to ambient temperature and an aliquot was taken out with the help of a micropipette under the nitrogen atmosphere. The aliquot was diluted with ethyl acetate and analyzed by GC-GCMS.

General Procedure for Schemes 2 and 3. Heteroarene (1.0 mmol, 2 equiv), aryl halide (0.5 mmol, 1 equiv), base (3 mmol, 3 equiv), and Pd−NHC (**3**) (0.5−1.0 mol %) were transferred to the screw cap sealed tube under nitrogen atmosphere. DMAc (*ca.* 3 mL) was added *via* a syringe, and the sealed tube was heated at 130 °C for the respective time. The reaction mixture was cooled to ambient temperature, diluted with ethyl acetate (*ca.* 60 mL), and then washed with water (*ca.* 3 × 15 mL). The organic layer was separated, dried over Na_2SO_4, and finally vacuum-dried to afford the crude product. The crude product was purified by column chromatography using hexane/EtOAc.

General Procedure for Scheme 5. Heteroarene (1.5 mmol, 3 equiv), dibromobenzene (0.5 mmol, 1 equiv), base (4.0 mmol, 4 equiv), and Pd−NHC (**3**) (1.0 mol %) were transferred to the screw cap sealed tube under nitrogen atmosphere. DMAc (*ca.* 3 mL) was added *via* a syringe and the sealed tube was at 130 °C for 12 h.

General Procedure for Scheme 6. Heteroarene (0.5 mmol, 1 equiv), dibromobenzene (1.25 mmol, 2.5 equiv), base (3.0 mmol, 3 equiv), and Pd−NHC (**3**) (1.0 mol %) were transferred to the screw cap sealed tube under nitrogen atmosphere. DMAc (*ca.* 3 mL) was added *via* a syringe and the sealed tube was heated at 130 °C for 12 h.

General Procedure for Competitive Experiment Studies. Heteroarenes (0.6 mmol each), 4-bromobenzonitrile **7a** (0.3 mmol, 1 equiv), base (1.2 mmol, 4 equiv), and Pd−NHC (*x* mol %) were transferred to the screw cap sealed tube under nitrogen atmosphere. DMAc (*ca.* 2 mL) was added and the sealed tube was heated at 130 °C for the respective time. The reaction mixture was cooled to ambient temperature and an aliquot was taken out with the help of a micropipette under nitrogen atmosphere. The aliquot was diluted with ethyl acetate and analyzed by GC-GCMS.

*4-(5-Methylthiophen-2-yl)benzonitrile (**8aa**).* The crude product was purified by column chromatography (hexane/EtOAc = 98/02) to

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afford 8aa as a white solid (90 mg, 90%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ 7.61 (br, 4H, $C_6\underline{H}_4$), 7.22 (d, 1H, $^3J_{HH}$ = 4 Hz, $C_5\underline{H}_5S$), 6.77 (d, 1H, $^3J_{HH}$ = 4 Hz, $C_5\underline{H}_5S$), 2.53 (s, 3H, $C\underline{H}_3$ of $C_5\underline{H}_5S$), $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 142.2, 139.6, 138.9, 132.6, 126.8, 125.5, 125.1 (Ar−C), 118.9 ($\underline{C}\equiv N$), 109.9 (Ar−C), 15.5 ($\underline{C}H_3$). HRMS (ESI-TOF): $[M + H]^+$ calcd for $[C_{12}H_{10}NS]$, 200.0528; found, 200.0516.

*3-(5-Methylthiophen-2-yl)benzonitrile (**8ab**).* The crude product was purified by column chromatography (hexane/EtOAc = 98/02) to afford **8ab** as a white solid (88 mg, 88%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ 7.77 (s, 1H, $C_6\underline{H}_4$), 7.77 (d, 1H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.47 (d, 1H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.41 (t, 1H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.13 (d, 1H, $^3J_{HH}$ = 4 Hz, $C_5\underline{H}_5S$), 6.73 (d, 1H, $^3J_{HH}$ = 4 Hz, $C_5\underline{H}_5S$), 2.50 (s, 3H, $C\underline{H}_3$ of $C_5\underline{H}_5S$), $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 141.2, 139.0, 135.8, 130.0, 1129.5, 129.4, 128.5, 126.5, 124.3 (Ar−C), 118.6 ($\underline{C}\equiv N$), 112.9 (Ar−C), 15.4 ($\underline{C}H_3$). HRMS (ESI-TOF): $[M + H]^+$ calcd for $[C_{12}H_{10}NS]$, 200.0528; found, 200.0516.

*2-(5-Methylthiophen-2-yl)benzonitrile (**8ac**).* The crude product was purified by column chromatography (hexane/EtOAc = 98/02) to afford **8ac** as a white solid (89 mg, 89%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ 7.62 (d, 1H, $^3J_{HH}$ = 8 Hz,$C_6\underline{H}_4$), 7.50 (s, 1H, $C_6\underline{H}_4$), 7.49−7.48 (m, 1H, $C_6\underline{H}_4$), 7.39 (d, 1H, $^3J_{HH}$ = 4 Hz, $C_5\underline{H}_5S$), 7.28−7.24 (m, 1H, $C_6\underline{H}_4$), 6.75 (d, 1H, $^3J_{HH}$ = 4 Hz, $C_5\underline{H}_5S$), 2.47 (s, 3H, $C\underline{H}_3$ of $C_5\underline{H}_5S$), $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 142.1, 137.5, 136.8, 134.1, 132.7, 129.0, 127.4, 126.9, 126.4 (Ar−C), 118.9 ($\underline{C}\equiv N$), 109.1 (Ar−C), 15.2 ($\underline{C}H_3$). HRMS (ESI-TOF): $[M + H]^+$ calcd for $[C_{12}H_{10}NS]$, 200.0528; found, 200.0516.

*2-(3-Methoxyphenyl)-5-methylthiophene (**8ad**).* The crude product was purified by column chromatography (hexane/EtOAc = 98/02) to afford **8ad** as a white solid (79 mg, 78%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ 7.33 (t, 1H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.22 (d, 1H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.18 (d, 1H, $^3J_{HH}$ = 4 Hz, $C_5\underline{H}_5S$), 7.17 (s, 1H, $C_6\underline{H}_4$), 6.87 (dd, 1H, $^3J_{HH}$ = 8 Hz, 1H, $^4J_{HH}$ = 1 Hz, $C_6\underline{H}_4$), 6.79−6.78 (m, 1H, $C_5\underline{H}_5S$), 3.88 (s, 3H, $OC\underline{H}_3$), 2.56 (s, 3H, $C\underline{H}_3$ of $C_5\underline{H}_5S$), $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 159.8, 141.7, 139.5, 135.9, 129.7, 126.1, 123.0, 118.0, 112.3, 111.0 (Ar−C), 55.0 ($O\underline{C}H_3$), 15.3 ($\underline{C}H_3$). HRMS (ESI-TOF): $[M + H]^+$ calcd for $[C_{12}H_{13}OS]$, 206.0682; found, 206.0665.

*2-(4-Methoxyphenyl)-5-methylthiophene (**8ae**).* The crude product was purified by column chromatography (hexane/EtOAc = 98/02) to afford **8ae** as a white solid (82 mg, 81%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ 7.48 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 6.98 (d, 1H, $^3J_{HH}$ = 4 Hz, $C_5\underline{H}_5S$), 6.89 (d, 1H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 6.70−6.79 (m, 1H, $C_5\underline{H}_5S$), 3.82 (s, 3H, $OC\underline{H}_3$), 2.50 (s, 3H, $C\underline{H}_3$ of $C_5\underline{H}_5S$), $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 158.8, 141.9, 138.4, 127.6, 126.7, 126.0, 1218, 114.2 (Ar−C), 55.3 ($O\underline{C}H_3$), 15.4 ($\underline{C}H_3$). HRMS (ESI-TOF): $[M + H]^+$ calcd for $[C_{12}H_{13}OS]$, 206.0682; found, 206.0665.

*2-Methyl-5-phenylthiophene (**8af**).* The crude product was purified by column chromatography (hexane/EtOAc = 98/02) to afford **8af** as a white solid (66 mg, 69%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ 7.58 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_5$), 7.37 (t, 2H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_5$), 7.26 (t, 1H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_5$), 7.13 (d, 1H, $^3J_{HH}$ = 4 Hz, $C_5\underline{H}_5S$), 6.75−6.73 (m, 1H, $C_5\underline{H}_5S$), 2.53 (s, 3H, $C\underline{H}_3$ of $C_5\underline{H}_5S$), $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 142.1, 139.6, 138.9, 132.6, 126.8, 125.5, 125.1, 118.9, 109.9 (Ar−C), 15.5 ($\underline{C}H_3$). HRMS (ESI-TOF): $[M + H]^+$ calcd for $[C_{11}H_{11}S]$, 175.0576; found, 175.0564.

*4-(5-Methylthiophen-2-yl)benzaldehyde (**8ag**).* The crude product was purified by column chromatography (hexane/EtOAc = 95/05) to afford **8ag** as a white solid (86 mg, 85%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ 9.97 (s, 1H, $C\underline{H}O$), 7.84 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.68 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.26 (d, 1H, $^3J_{HH}$ = 4 Hz, $C_5\underline{H}_5S$), 6.78 (d, 1H, $^3J_{HH}$ = 4 Hz, $C_5\underline{H}_5S$), 2.53 (s, 3H, $C\underline{H}_3$ of $C_5\underline{H}_5S$), $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 191.5 ($\underline{C}HO$), 142.1, 140.4, 140.2, 134.7, 130.4, 126.9, 126.7, 125.4, 125.2 (Ar−C), 15.6 ($\underline{C}H_3$). HRMS (ESI-TOF): $[M + H]^+$ calcd for $[C_{12}H_{11}OS]$, 203.0525; found, 203.0514.

*N-(4-(5-Methylthiophen-2yl)phenyl)acetamide (**8ah**).* The crude product was purified by column chromatography (hexane/EtOAc = 85/15) to afford **8ah** as a white solid (69 mg, 60%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ 7.86 (br, 1H, $N\underline{H}COCH_3$), 7.41−7.35 (m, 4H, $^3J_{HH}$ $C_6\underline{H}_4$), 6.94 (d, 1H, $^3J_{HH}$ = 4 Hz, $C_5\underline{H}_5S$), 6.61 (d, 1H, $^3J_{HH}$ = 4 Hz, $C_5\underline{H}_5S$), 2.40 (s, 3H, $C\underline{H}_3$ of $C_5\underline{H}_5S$), 2.07 (s, 3H, $NHCOC\underline{H}_3$),$^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 168.7 ($\underline{C}OCH_3$), 141.3, 139.1, 136.8, 131.8, 130.8, 126.1, 125.8, 122.4, 120.3 (Ar−C), 24.4 ($\underline{C}H_3$)., 15.4 ($\underline{C}H_3$). HRMS (ESI-TOF): $[M + H]^+$ calcd for $[C_{13}H_{13}NOS]$, 232.0791; found, 232.0778.

*2-([1,1′-Biphenyl]-4-yl)-5-methylthiophene (**8ai**).* The crude product was purified by column chromatography (hexane/EtOAc = 95/05) to afford **8ai** as a white solid (96 mg, 77%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ 7.72−7.66 (m, 6H, $C_6\underline{H}_4$ & $C_6\underline{H}_5$), 7.53 (t, 1H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_5$), 7.43 (t, 1H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_5$), 7.23 (d, 1H, $^3J_{HH}$ = 4 Hz, $C_5\underline{H}_5S$), 6.84−6.82 (m, 1H, $C_5\underline{H}_5S$), 2.60 (s, 3H, $C\underline{H}_3$ of $C_5\underline{H}_5S$), $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 141.5, 140.5, 139.7, 139.6, 133.7, 128.8, 127.4, 127.3, 126.8, 126.3, 125.8, 122.9 (Ar−C), 15.5 ($\underline{C}H_3$). HRMS (ESI-TOF): $[M + H]^+$ calcd for $[C_{17}H_{15}S]$, 251.0889; found, 251.0913.

*1-Methyl-6-(5-methylthiophen-2-yl)-1H-indazole (**8aj**).* The crude product was purified by column chromatography (hexane/EtOAc = 90/10) to afford **8aj** as a white solid (92 mg, 81%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): 7.94 (s, 1H, $C_8\underline{H}_7N_2$), 7.67 (d, 1H, $^3J_{HH}$ = 8 Hz, $C_8\underline{H}_7N_2$), 7.50 (s, 1H, $C_8\underline{H}_7N_2$), 7.38 (d, 1H, $^3J_{HH}$ = 8 Hz, $C_8\underline{H}_7N_2$), 7.19 (d, 1H, $^3J_{HH}$ = 3 Hz, $C_5\underline{H}_5S$), 6.76 (d, 1H, $^3J_{HH}$ = 3 Hz, $C_5\underline{H}_5S$), 4.08 (s, 1H, $C\underline{H}_3$ of $C_8\underline{H}_7N_2$), 2.53 (s, 3H, $C\underline{H}_3$ of $C_5\underline{H}_5S$), $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 142.3, 140.6, 140.1, 133.2, 132.9, 126.5, 123.8, 123.3, 121.5, 119.6, 105.2 (Ar−C), 35.7 ($\underline{C}H_3$), 15.7 ($\underline{C}H_3$). HRMS (ESI-TOF): $[M + H]^+$ calcd for $[C_{13}H_{13}N_2S]$, 229.0794; found, 229.0805.

*4-Chloro-7-(5-methylthiophen-2-yl)quinoline (**8ak**).* The crude product was purified by column chromatography (hexane/EtOAc = 90/10) to afford **8ak** as a white solid (92 mg, 71%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): 8.71 (br, 1H,, $C_9\underline{H}_5ClN$), 8.21 (s, 1H, $C_9\underline{H}_5ClN$), 8.12 (d, 1H, $^3J_{HH}$ = 8 Hz,, $C_9\underline{H}_5ClN$), 7.79 (d, 1H, $^3J_{HH}$ = 8 Hz,, $C_9\underline{H}_5ClN$), 7.37 (d, 1H, $^3J_{HH}$ = 6 Hz,, $C_9\underline{H}_5ClN$), 7.29 (d, 1H, $^3J_{HH}$ = 4 Hz, $C_5\underline{H}_5S$), 6.76 (d, 1H, $^3J_{HH}$ = 4 Hz, $C_5\underline{H}_5S$), 2.51 (s, 3H, $C\underline{H}_3$ of $C_5\underline{H}_5S$), $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 150.3, 149.4, 142.4, 141.5, 140.3, 136.6, 126.6, 125.5, 125.3, 124.7, 124.5, 124.4, 120.6 (Ar−C), 15.5 ($\underline{C}H_3$). HRMS (ESI-TOF): $[M + H]^+$ calcd for $[C_{14}H_{11}ClNS]$, 260.0295; found, 260.0310.

*4-(5-Acetylthiophen-2-yl)benzonitrile (**9ba**).* The crude product was purified by column chromatography (hexane/EtOAc = 95/05) to afford **9ba** as a white solid (93 mg, 82%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): 7.72−7.70 (m, 2H, $C_6\underline{H}_4$), 7.67−7.65 (m, 3H, $C_6\underline{H}_4$ & $C_6\underline{H}_5OS$), 7.39 (d, 1H, $^3J_{HH}$ = 4 Hz, $C_6\underline{H}_5OS$), 2.56 (s, 3H, $C\underline{H}_3$ of $C_6\underline{H}_5OS$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 190.4 ($\underline{C}OCH_3$), 149.5, 144.9, 137.4, 133.3; 132.8, 127.8, 126.5, 125.7, 118.3, 112.1 (Ar−C), 26.6 ($\underline{C}H_3$). HRMS (ESI-TOF): $[M + H]^+$ calcd for $[C_{13}H_{10}NOS]$, 228.0478; found, 228.0492.

*4-(Benzo[b]thiophen-2-yl)benzonitrile (**9ca**).* The crude product was purified by column chromatography (hexane/EtOAc = 95/05) to afford **9ca** as a white solid (99 mg, 85%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): 7.83 (d, 1H, $^3J_{HH}$ = 8 Hz, $C_8\underline{H}_5S$), 7.80 (d, 1H, $^3J_{HH}$ = 8 Hz, $C_8\underline{H}_5S$), 7.76 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.60 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.63 (s, 1H, $C_8\underline{H}_5S$), 7.40−7.34 (m, 2H, $C_8\underline{H}_5S$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 141.6, 140.2, 139.9, 138.5, 132.7, 126.7, 125.3, 124.9, 124.1, 122.3, 121.7 (Ar−C), 118.6 ($\underline{C}\equiv N$), 111.3 (Ar−C). HRMS (ESI-TOF): $[M + H]^+$ calcd for $[C_{15}H_{10}NS]$, 236.0528; found, 236.0518.

*4-(3-Bromobenzo[b]thiophen-2-yl)benzonitrile (**9da**).* The crude product was purified by column chromatography (hexane/EtOAc = 95/05) to afford **9da** as a white solid (117 mg, 75%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): 7.89 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.83 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_8\underline{H}_4SBr$), 7.40 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.83 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.57−7.43 (m, 2H, $C_8\underline{H}_4SBr$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 138.9, 137.7, 137.6, 135.6, 132.3, 130.1, 126.2, 125.6, 124.0, 122.3 (Ar−C), 118.5 ($\underline{C}\equiv N$), 112.2, 106.6

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(Ar−C). HRMS (ESI-TOF): [M + H]$^+$ calcd for [$C_{15}H_9BrNS$], 313.9634; found, 313.9654.

*4-(6-Methoxybenzo[b]thiophen-2-yl)benzonitrile (**9ea**).* The crude product was purified by column chromatography (hexane/EtOAc = 90/10) to afford **9ea** as a white solid (95 mg, 72%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): 7.66−7.57 (m, 5H, $C_6\underline{H}_4$ & $C_8\underline{H}_4S$), 7.48 (s, 1H, $C_8\underline{H}_4S$), 7.28 (s, 1H, $C_8\underline{H}_4S$), 6.98−6.95 (m, 1H, $C_8\underline{H}_4S$), 3.84 (s, 3H, $OC\underline{H}_3$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 158.1, 141.5, 138.8, 134.2, 132.5, 126.1, 124.8, 121.3 (Ar−C), 118.7 ($\underline{C}\equiv N$), 115.1, 110.6, 104.6 (Ar−C), 55.5 ($O\underline{C}H_3$). HRMS (ESI-TOF): [M + H]$^+$ calcd for [$C_{16}H_{12}NOS$], 266.0634; found, 266.0628.

*4-(4-Methoxybenzo[b]thiophen-2-yl)benzonitrile (**9fa**).* The crude product was purified by column chromatography (hexane/EtOAc = 90/10) to afford **9fa** as a white solid (100 mg, 76%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): 7.48 (s, 1H, $C_8\underline{H}_4S$), 7.68 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.58 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.36 (d, 1H, $^3J_{HH}$ = 8 Hz, $C_8\underline{H}_4S$), 7.26 (t, 1H, $^3J_{HH}$ = 8 Hz, $C_8\underline{H}_4S$), 6.71 (d, 1H, $^3J_{HH}$ = 8 Hz, $C_8\underline{H}_4S$), 3.93 (s, 3H, $OC\underline{H}_3$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 155.2, 141.3, 139.8, 138.6, 132.5, 131.1, 126.5, 118.7, 118.5, 114.6, 110.8, 104.4 (Ar−C), 55.4 ($O\underline{C}H_3$). HRMS (ESI-TOF): [M + H]$^+$ calcd for [$C_{16}H_{12}NOS$], 266.0634; found, 266.0628.

*4-(3-(3,4,5-Trimethoxyphenyl)benzo[b]thiophen-2-yl)-benzonitrile (**9ga**).* The crude product was purified by column chromatography (hexane/EtOAc = 85/15) to afford **9ga** as a white solid (166 mg, 83%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): 7.86 (d, 1H, $^3J_{HH}$ = 8 Hz, $C_8\underline{H}_4S$), 7.68 (d, 1H, $^3J_{HH}$ = 8 Hz, $C_8\underline{H}_4S$), 7.52 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.42 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.40−7.37 (m, 2H, $C_8\underline{H}_4S$), 6.51 (s, 2H, $C_6\underline{H}_2$), 3.92 (s, 3H, $OC\underline{H}_3$), 3.73 (s, 6H, $OC\underline{H}_3$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 153.5, 140.3, 138.7, 137.6, 136.5, 135.0, 131.9, 129.9, 129.6, 127.6, 125.3, 124.8, 123.6, 122.0 (Ar−C), 118.4 ($\underline{C}\equiv N$), 110.8, 107.0 (Ar−C), 60.8 ($O\underline{C}H_3$), 55.9 ($O\underline{C}H_3$). HRMS (ESI-TOF): [M + H]$^+$ calcd for [$C_{24}H_{20}NO_3S$], 402.1158; found, 402.1166.

*4-(1,3-Dimethyl-1H-indol-2-yl)benzonitrile (**9ia**).* The crude product was purified by column chromatography (hexane/EtOAc = 95/05) to afford **9ia** as a white solid (108 mg, 88%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): 7.80 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.66 (d, 1H, $^3J_{HH}$ = 8 Hz, $C_8\underline{H}_4N$), 7.54 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.39 (d, 1H, $^3J_{HH}$ = 8 Hz, $C_8\underline{H}_4N$), 7.34 (t, 1H, $^3J_{HH}$ = 8 Hz, $C_8\underline{H}_4N$), 7.22 (t, 1H, $^3J_{HH}$ = 8 Hz, $C_8\underline{H}_4N$), 3.66 (s, 3H, $C\underline{H}_3$), 2.35 (s, 3H, $C\underline{H}_3$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 137.7, 136.8, 135.4, 132.0, 130.9, 128.2, 122.7, 119.5, 119.1 (Ar−C), 118.7 (C≡N), 111.1, 110.3, 109.4 (Ar−C), 31.1 ($\underline{C}H_3$), 9.35 ($\underline{C}H_3$). HRMS (ESI-TOF): [M + H]$^+$ calcd for [$C_{17}H_{15}N_2$], 247.1230; found, 247.1219.

*4-(1-Methyl-1H-indol-2-yl)benzonitrile (**9′ja**).* The crude product was purified by column chromatography (hexane/EtOAc = 95/05) to afford **9′ja** as a white solid (60 mg, 60%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): 7.78 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.68 (d, 1H, $^3J_{HH}$ = 8 Hz, $C_8\underline{H}_5N$), 7.66 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.42 (d, 1H, $^3J_{HH}$ = 8 Hz, $C_8\underline{H}_5N$), 7.33 (t, 1H, $^3J_{HH}$ = 8 Hz, $C_8\underline{H}_5N$), 7.22 (t, 1H, $^3J_{HH}$ = 8 Hz, $C_8\underline{H}_5N$), 6.69 (s, 1H, $C_8\underline{H}_5N$), 3.81 (s, 3H, $C\underline{H}_3$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 139.5, 139.2, 137.5, 132.5, 129.7,127.9, 122.9, 121.1, 120.6 (Ar−C), 118.9 ($\underline{C}\equiv N$), 111.4, 110.0, 103.7 (Ar−C), 31.7 ($\underline{C}H_3$). HRMS (ESI-TOF): [M + H]$^+$ calcd for [$C_{17}H_{15}N_2$], 247.1230; found, 247.1219.

*4-(1-Methyl-1H-indol-3-yl)benzonitrile (**9″ja**).* The crude product was purified by column chromatography (hexane/EtOAc = 90/10) to afford **9″ja** as a white solid (41 mg, 40%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): 7.96 (d, 1H, $^3J_{HH}$ = 6 Hz, $C_8\underline{H}_5N$), 7.73 (d, 4H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.44−7.29 (m, 4H, $C_8\underline{H}_5N$), 3.89 (s, 3H, $C\underline{H}_3$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 140.8, 137.8, 133.0, 132.7, 128.1, 128.0, 127.2, 125.7, 122.7, 120.9, 119.7 (Ar−C), 119.7 ($\underline{C}\equiv N$), 115.0, 110.1, 108.5 (Ar−C), 33.3 ($\underline{C}H_3$). HRMS (ESI-TOF): [M + H]$^+$ calcd for [$C_{16}H_{13}N_2$], 233.1073; found, 233.1052.

*4-(5-Bromo-1-methyl-1H-indol-2-yl)benzonitrile (**9ka**).* The crude product was purified by column chromatography (hexane/EtOAc = 90/10) to afford **9ka** as a white solid (107 mg, 69%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): 8.00 (s, 1H, $C_8\underline{H}_4NBr$), 7.68 (s, 4H, $C_6\underline{H}_4$), 7.38 (d, 1H, $^3J_{HH}$ = 8 Hz, $C_8\underline{H}_4NBr$), 7.31 (s, 1H, $C_8\underline{H}_4NBr$), 7.24 (d, 1H, $^3J_{HH}$ = 8 Hz, $C_8\underline{H}_4NBr$), 3.84 (s, 3H, $C\underline{H}_3$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 139.8, 136.3, 132.6, 128.7, 127.1, 125.4, 122.1 (Ar−C), 119.2 ($\underline{C}\equiv N$), 114.5, 114.2, 111.4, 108.8 (Ar−C), 33.2 ($\underline{C}H_3$). HRMS (ESI-TOF): [M + H]$^+$ calcd for [$C_{16}H_{12}BrN_2$], 311.0178; found, 311.0182.

*4-(5-Chloro-1-methyl-1H-indol-2-yl)benzonitrile (**9la**).* The crude product was purified by column chromatography (hexane/EtOAc = 90/10) to afford **9la** as a white solid (94 mg, 71%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): 7.82 (s, 1H, $C_8\underline{H}_4NCl$), 7.74 (d, 1H, $^3J_{HH}$ = 8 Hz, $C_8\underline{H}_4NCl$), 7.66 (s, 4H, $C_6\underline{H}_4$), 7.32 (s, 1H, $C_8\underline{H}_4NCl$), 7.24 (d, 1H, $^3J_{HH}$ = 8 Hz, $C_8\underline{H}_4NCl$), 3.82 (s, 3H, $C\underline{H}_3$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 143.4, 139.8, 135.9, 132.8, 128.9, 126.9, 126.6, 122.8(Ar−C), 119.0 ($\underline{C}\equiv N$), 114.5, 110.9, 108.7 (Ar−C), 33.2 ($\underline{C}H_3$). HRMS (ESI-TOF): [M + H]$^+$ calcd for [$C_{16}H_{12}ClN_2$], 267.0684; found, 267.0674.

*4-(1,2-Dimethyl-1H-indol-3-yl)benzonitrile (**9ma**).* The crude product was purified by column chromatography (hexane/EtOAc = 90/10) to afford **9ma** as a white solid (106 mg, 87%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): 7.71 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.63 (d, 1H, $^3J_{HH}$ = 8 Hz, $C_8\underline{H}_4N$), 7.57 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.34 (d, 1H, $^3J_{HH}$ = 8 Hz, $C_8\underline{H}_4N$), 7.23 (t, 1H, $^3J_{HH}$ = 8 Hz, $C_8\underline{H}_4N$), 7.15 (t, 1H, $^3J_{HH}$ = 8 Hz, $C_8\underline{H}_4N$), 3.75 (s, 3H, $C\underline{H}_3$), 2.50 (s, 3H, $C\underline{H}_3$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 141.2, 136.9, 134.6, 132.4, 129.9, 126.4, 121.8, 120.5, 119.5 (Ar−C), 118.3 ($\underline{C}\equiv N$), 112.7, 109.2, 108.8 (Ar−C), 29.9 ($\underline{C}H_3$), 11.3 ($\underline{C}H_3$). HRMS (ESI-TOF): [M + H]$^+$ calcd for [$C_{17}H_{15}N_2$], 247.1230; found, 247.1228.

*2-(2-(4-Cyanophenyl)-3-methyl-1H-indol-1yl)benzonitrile (**9na**).* The crude product was purified by column chromatography (hexane/EtOAc = 90/10) to afford **9na** as a white solid (108 mg, 65%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): 7.69−7.64 (m, 3H, $C_6\underline{H}_4$), 7.56 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.46−7.43 (m, 1H, $C_8\underline{H}_4N$), 7.37−7.33 (m, 3H, $C_8\underline{H}_4N$ & $C_6\underline{H}_4$), 7.27−7.25 (m, 2H, $C_8\underline{H}_4N$ & $C_6\underline{H}_4$), 7.11−7.09 (m, 2H, $C_8\underline{H}_4N$), 2.43 (s, 3H, $C\underline{H}_3$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 141.1, 138.2, 136.0, 135.0, 134.0, 133.8, 131.8, 130.8, 129.9, 129.3, 128.2, 124.0, 121.2, 119.7 (Ar−C), 118.6 ($\underline{C}\equiv N$), 115.9, 114.2, 112.7, 110.8, 110.1 (Ar−C). HRMS (ESI-TOF): [M + H]$^+$ calcd for [$C_{23}H_{16}N_3$], 334.1339; found, 334.1324.

*4-(1-Methyl-1H-pyrrol-2-yl)benzonitrile (**9pa**).* The crude product was purified by column chromatography (hexane/EtOAc = 98/02) to afford **9pa** as a white solid (61 mg, 67%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): 7.65 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.50 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 6.79−6.78 (m, 1H, $C_4\underline{H}_3N$), 6.35 (dd, 1H, $^3J_{HH}$ = 4 Hz, $^4J_{HH}$ = 2 Hz, $C_4\underline{H}_3N$), 6.23 (dd, 1H, $^3J_{HH}$ = 4 Hz, $^4J_{HH}$ = 2 Hz, $C_4\underline{H}_3N$), 3.71 (s, 3H, $C\underline{H}_3$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 137.8, 132.9, 134.4, 128.4, 126.0 (Ar−C), 119.2 ($\underline{C}\equiv N$), 110.9, 109.7, 108.7 (Ar−C), 35.6 ($\underline{C}H_3$). HRMS (ESI-TOF): [M + H]$^+$ calcd for [$C_{12}H_{11}N_2$], 183.0917; found, 183.0917.

*4-(1-(2-Aminophenyl)-1H-pyrrol-2-yl)benzonitrile (**9qa**).* The crude product was purified by column chromatography (hexane/EtOAc = 85/15) to afford **9qa** as a white solid (88 mg, 68%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): 7.42 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.25 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.19 (t, 1H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.03 (d, 1H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 6.88−6.84 (m, 1H, $C_4\underline{H}_3N$), 6.77−6.72 (m, 2H, $C_6\underline{H}_4$), 6.63 (dd, 1H, $^3J_{HH}$ = 4 Hz, $^4J_{HH}$ = 2 Hz, $C_4\underline{H}_3N$), 6.42 (dd, 1H, $^3J_{HH}$ = 4 Hz, $^4J_{HH}$ = 2 Hz, $C_4\underline{H}_3N$), 3.62 (br, 2H, $N\underline{H}_2$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 143.1, 137.1, 133.0, 132.2, 131.9, 129.8, 128.6, 128.1, 127.1, 126.9, 126.4, 125.9, 119.3, 119.0 (Ar−C), 118.7 ($\underline{C}\equiv N$), 116.2, 111.7, 110.5, 109.2 (Ar−C). HRMS (ESI-TOF): [M + H]$^+$ calcd for [$C_{17}H_{14}N_3$], 260.1182; found, 260.1169.

*4-(5-Acetylfuran-2-yl)benzonitrile (**9ra**).* The crude product was purified by column chromatography (hexane/EtOAc = 95/05) to afford **9ra** as a white solid (59 mg, 56%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): 7.84 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.67 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.24 (br, 1H, $C_6\underline{H}_5O_2$), 6.90 (br, 1H, $C_6\underline{H}_5O_2$), 2.50 (s, 3H, $C\underline{H}_3$ of $C_6\underline{H}_5O_2$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 190.4 ($\underline{C}OCH_3$), 149.5, 144.9, 137.4, 133.4, 132.8, 127.8, 126.5, 125.7

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(Ar−C), 118.3 (C≡N) 112.1 (Ar−C), 26.6 ($\underline{C}H_3$). HRMS (ESI-TOF): $[M + H]^+$ calcd for $[C_{13}H_{10}NO_2]$, 212.0706; found, 212.0701.

*4,4′-(Benzofuran-2,3-diyl)dibenzonitrile (**9sa**).* The crude product was purified by column chromatography (hexane/EtOAc = 90/10) to afford **9sa** as a white solid (63 mg, 79%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): 7.79−7.78 (m, 2H, $C_8\underline{H}_4O$), 7.70−7.68 (m, 2H, $C_8\underline{H}_4O$ & $C_6\underline{H}_4$), 7.61−7.57 (m, 5H, $C_8\underline{H}_4O$ & $C_6\underline{H}_4$), 7.46−7.40 (m, 1H, $C_8\underline{H}_4O$ & $C_6\underline{H}_4$), 7.29−7.24 (m, 1H, $C_8\underline{H}_4O$), $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 141.6, 140.2, 139.9, 138.5, 132.7, 126.7, 125.3, 124.9, 124.1, 122.3, 121.7 (Ar−C), 118.6 ($\underline{C}$≡N), 111.3 (Ar−C). HRMS (ESI-TOF): $[M + H]^+$ calcd for $[C_{22}H_{13}N_2O]$, 321.1022; found, 321.1034.

*3-Bromo-2,3′-Bibenzo[b]thiophene (**10**).* The crude product was purified by column chromatography (hexane/EtOAc = 95/05) to afford **10** as a white solid (90 mg, 52%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): 7.91−7.88 (m, 3H, $C_8\underline{H}_4SBr$ & $C_8\underline{H}_5S$), 7.82−7.77 (m, 1H, $C_8\underline{H}_4SBr$ or $C_8\underline{H}_5S$), 7.72 (s, 1H, $C_8\underline{H}_5S$), 7.47−7.46 (m, 1H, $C_8\underline{H}_4SBr$ or $C_8\underline{H}_5S$), 7.42−7.37 (m, 3H, $C_8\underline{H}_4SBr$ & $C_8\underline{H}_5S$), $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 139.8, 138.5, 138.1, 137.7, 132.0, 128.5, 128.1, 125.6, 125.4, 125.3, 124.8, 124.5, 123.6, 123.5, 122.7, 122.2, 107.5 (Ar−C). HRMS (ESI-TOF): $[M + H]^+$ calcd for $[C_{16}H_{10}BrS_2]$, 344.9402; found, 344.9396.

*1,3-Bis(5-methylthiophen-2-yl)benzene (**11a**).* The crude product was purified by column chromatography (hexane/EtOAc = 98/02) to afford **11a** as a white solid (110 mg, 82%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ 7.82 (s, 1H, $C_6\underline{H}_4$), 7.50 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.41 (t, 1H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.23 (d, 1H, $^3J_{HH}$ = 1 Hz, $C_5\underline{H}_5S$), 7.82 (d, 1H, $^3J_{HH}$ = 1 Hz, $C_5\underline{H}_5S$), 2.60 (s, 6H, $C\underline{H}_3$ of $C_5\underline{H}_5S$), $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 141.6, 139.6, 135.2, 129.2, 126.2, 124.1, 123.2, 123.1, 122.5 (Ar−C), 15.4 ($\underline{C}H_3$). HRMS (ESI-TOF): $[M + H]^+$ calcd for $[C_{16}H_{15}S_2]$, 271.0610; found, 271.0591.

*1,3-Bis(1-methyl-1H-pyrrol-2-yl)benzene (**11b**).* The crude product was purified by column chromatography (hexane/EtOAc = 98/02) to afford **11b** as a white solid (100 mg, 85%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ 7.48−7.42 (m, 2H, $C_6\underline{H}_4$), 7.36 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.41 (t, 1H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 6.75 (br, 2H, $C_5\underline{H}_6N$), 6.28 (d, 2H, $^3J_{HH}$ = 4 Hz, $C_5\underline{H}_6N$), 6.24 (d, 2H, $^3J_{HH}$ = 4 Hz, $C_5\underline{H}_6N$), 3.72 (s, 6H, $C\underline{H}_3$ of $C_5\underline{H}_6N$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 134.3, 133.4, 128.6, 128.3, 126.9, 127.7, 108.8, 107.8 (Ar−C), 35.1 ($\underline{C}H_3$). HRMS (ESI-TOF): $[M + H]^+$ calcd for $[C_{16}H_{17}N_2]$, 237.1386; found, 237.1392.

*1,4-Bis(5-methylthiophen-2-yl)benzene (**11c**).* The crude product was purified by column chromatography (hexane/EtOAc = 98/02) to afford **11c** as a white solid (111 mg, 82%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ 7.51 (s, 4H, $C_6\underline{H}_4$), 7.10 (d, 2H, $^3J_{HH}$ = 1 Hz, $C_5\underline{H}_5S$), 6.72 (d, 2H, $^3J_{HH}$ = 1 Hz, $C_5\underline{H}_5S$), 2.50 (s, 6H, $C\underline{H}_3$ of $C_5\underline{H}_5S$), $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 141.6, 139.5, 133.3, 126.3, 125.7, 122.8, 122.7 (Ar−C), 29.7 ($\underline{C}H_3$). HRMS (ESI-TOF): $[M + H]^+$ calcd for $[C_{16}H_{15}S_2]$, 271.0610; found, 271.0591.

*1,4-Bis(1-methyl-1H-pyrrol-2-yl)benzene (**11d**).* The crude product was purified by column chromatography (hexane/EtOAc = 95/05) to afford **11d** as a white solid (101 mg, 86%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ 7.46 (s, 4H, $C_6\underline{H}_4$), 6.77 (br, 2H, $C_5\underline{H}_6N$), 6.30−6.29 (m, 2H, $C_5\underline{H}_6N$), 6.26−6.25 (m, 2H, $C_5\underline{H}_6N$), 3.75 (s, 6H, $C\underline{H}_3$ of $C_5\underline{H}_6N$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 134.4, 131.8, 128.6, 124.0, 108.9, 108.0 (Ar−C), 35.3 ($\underline{C}H_3$). HRMS (ESI-TOF): $[M + H]^+$ calcd for $[C_{16}H_{17}N_2]$, 237.1386; found, 237.1392.

*4,4′-(Furan-2,5-diyl)dibenzonitrile (**12a**).* The crude product was purified by column chromatography (hexane/EtOAc = 90/10) to afford **12a** as a white solid (74 mg, 55%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ 7.83 (d, 4H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.70 (d, 4H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 6.95 (br, 2H, $C_4\underline{H}_2O$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 153.0, 134.0, 132.9, 124.3 (Ar−C), 118.9 ($\underline{C}$≡N), 111.1, 110.8 (Ar−C). HRMS (ESI-TOF): $[M + H]^+$ calcd for $[C_{18}H_{11}N_2O]$, 271.0866; found, 271.0863.

*4,4′-(1-Methyl-1H-pyrrole-2,5 diyl)dibenzonitrile (**12b**).* The crude product was purified by column chromatography (hexane/EtOAc = 90/10) to afford **12b** as a white solid (112 mg, 79%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ 7.74 (d, 4H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.59 (d, 4H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 6.42 (br, 2H, $C_5\underline{H}_5N$), 3.68 (s, 6H, $C\underline{H}_3$ of $C_5\underline{H}_5N$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 137.3, 137.1, 132.6, 128.8 (Ar−C), 119.0 ($\underline{C}$≡N), 111.5, 110.5 (Ar−C), 35.1 ($\underline{C}H_3$). HRMS (ESI-TOF): $[M + H]^+$ calcd for $[C_{19}H_{14}N_3]$, 284.1182; found, 284.1162.

*6-Methoxy-2-(4-methoxyphenyl)benzo[b]thiophene (**13**).* The crude product was purified by column chromatography (hexane/EtOAc = 90/10) to afford **13** as a white solid (90 mg, 67%), ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): 7.53 (d, 1H, $^3J_{HH}$ = 8 Hz $C_8\underline{H}_4S$), 7.51 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 7.24 (s, 1H, $C_8\underline{H}_4S$), 7.21 (s, 1H, $C_8\underline{H}_4S$), 6.88 (d, 1H, $^3J_{HH}$ = 8 Hz $C_8\underline{H}_4S$), 7.85 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_6\underline{H}_4$), 3.79 (s, 3H, $OC\underline{H}_3$), 3.76 (s, 3H, $OC\underline{H}_3$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 158.4, 156.2, 140.5, 139.6, 133.9, 126.4, 126.2, 122.9, 116.7, 113.3, 103.9 (Ar−C), 54.6 ($O\underline{C}H_3$), 54.3 ($O\underline{C}H_3$). HRMS (ESI-TOF): $[M + H]^+$ calcd for $[C_{16}H_{15}O_2S]$, 271.0787; found, 271.0791.

*Gram-Scale Synthesis of 4-(5-Methylthiophen-2-yl)benzonitrile (**8aa**).* 1-Methyl thiophene **6a** (1.08 g, 11.1 mmol), 4-bromobenzonitrile **7a** (1.00 g, 5.55 mmol), KOAc (1.63 g, 16.6 mmol), and Pd−NHC (**3**) (0.020 g, 0.028 mmol, 0.5 mol %) were transferred to the Schlenk tube under nitrogen atmosphere and DMAc (*ca.* 20 mL) was added via a syringe. The Schlenk tube was closed using a glass stopper and a steel clamp, and the reaction mixture was heated at 130 °C for the 2 h. After this, the volatiles were removed under vacuum at 80 °C, and then the reaction mixture was cooled to ambient temperature. The residue was diluted with ethyl acetate (*ca.* 150 mL) and then washed with water (*ca.* 3 × 50 mL). The organic layer was separated, dried over Na_2SO_4, and finally vacuum-dried to afford the crude product. The crude product was purified by column chromatography using petroleum ether/EtOAc to afford a white solid (0.941 g, 85%).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02024.

Comparison table, NMR spectra, elemental analysis data (**2**−**5**), selected crystallographic data table (**3**−**5**), and selected GC-GCMS data (PDF)

Crystallographic data of 4 (CIF)

Crystallographic data of 3 (CIF)

Crystallographic data of 5 (CIF)

Accession Codes

CCDC **1887442**, **1887443**, and **1887444** contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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