JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

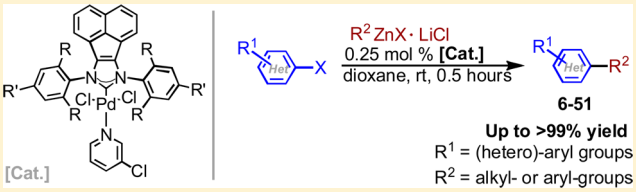
Mild Negishi Cross-Coupling Reactions Catalyzed by Acenaphthoimidazolylidene Palladium Complexes at Low Catalyst Loadings

Zelong Liu, Ningning Dong, Mizhi Xu, Zheming Sun, and Tao Tu*

Department of Chemistry, Fudan University, 220 Handan Road, Shanghai, 200433, P. R. China

Supporting Information

ABSTRACT: Considering that the strong σ-donor property of ylidenes derived from π-extended imidazolium salts is conducive to increasing the catalytic activity of the resulting palladium N-heterocyclic carbene complexes, robust acenaphthoimidazol-ylidene palladium complexes **3a−c** with varying bulky substituted groups were prepared from the corresponding acenaphthoimidazolium chlorides by heating with $PdCl_2$ and K_2CO_3 in neat 3-chloropyridine in satisfactory yields. Even at a catalyst loading as low as 0.25 mol %, complex **3a** exhibited extremely high catalytic activity toward Negishi cross-coupling of alkylzinc reagents with a wide range of (hetero)aryl halides under mild reaction conditions within 30 min. Besides a great number of bromoarenes, various less expensive and inactive (hetero)aryl chlorides were coupled successfully with the alkyl- and arylzinc reagents, in which active functional groups (such as $-NH_2$) were well tolerated even in one-pot dicoupling transformations without protection. In addition, in the case of coupling with secondary alkylzinc reagents, undesired β-hydride elimination leading to isomerized linear products was efficaciously suppressed. The catalyst system also displayed superiority in the construction of heterobiaryls through the coupling of heteroarylzinc reagents and heterocylic chloroarenes which were hardly accessible from the corresponding organoboron reagents by Suzuki-coupling reactions. Therefore, the protocol described in this paper represents a mild, general, and scalable approach to access various structurally intriguing and functionalized (hetero)aryls.

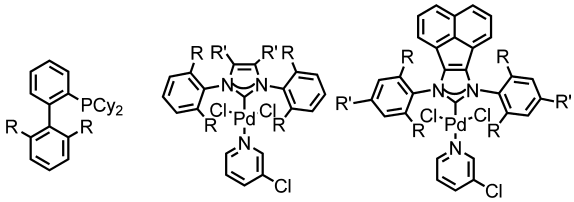


INTRODUCTION

Palladium-catalyzed cross-coupling reactions constitute practical and powerful methods for construction of C−C and C−N bonds with wide applications in organic synthesis, functional materials, and pharmaceuticals.[1] Although the reactivity of organozinc reagents is lower than that of Grignard and organolithium analogues, from a synthetic perspective, Negishi coupling is still regarded as a preferred option and has been utilized extensively in the synthesis of natural products due to its high functional-group tolerance.[2,3] Ever since the first general protocol of aryl and vinyl chlorides for Pd-catalyzed Negishi coupling reactions was reported by Fu and co-workers,[4] a great number of catalytic procedures have been successfully developed.[3] In recent years, research efforts have mainly focused on coupling reactions of aryl halides with sp^2- and sp^3-hybridized organic zinc compounds; among them, the coupling between secondary alkylzinc halides and sterically congested or heterocyclic substrates remains one of the most challenging tasks, especially at low catalyst loadings.[5]

In general, increasing the steric hindrance of the ligands is considered to be not only a useful practical strategy to suppress the undesired β-hydride elimination to form isomerized linear products in the couplings with secondary alkylzinc halides but also an efficient tactic in the ligand design to access sterically hindered ortho-substituted biaryls.[6] For example, Buchwald and Knochel groups recently reported efficient Pd-catalyzed coupling of secondary alkylzinc halides with bromo- and chloroarenes by using the bulky ligand **1a** (CPhos) (Scheme 1) under quite mild conditions, although the isomerized products formed by β-hydride elimination could not be completely eliminated (the ratio of branched and linear products is up to 58:1).[7] When **1b** (SPhos) and **1c** (RuPhos) were applied instead, a variety of sterically bulky biaryls were also accessible. Inspired by the "flexible steric bulky" concept proposed by Glorius and co-workers,[6c] Organ and co-workers successfully accomplished these couplings with palladium N-heterocyclic

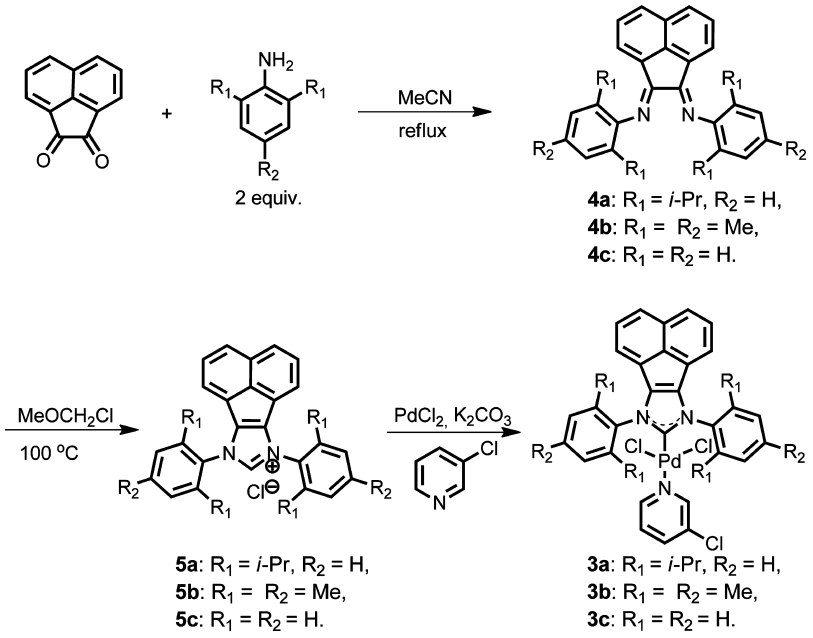
Scheme 1. A Selection of Representative Ligands and Complexes in Pd-Catalyzed Negishi Cross-Coupling Reactions



Received: April 26, 2013

   dx.doi.org/10.1021/jo400803s | J. Org. Chem. XXXX, XXX, XXX−XXX

Scheme 2. Synthesis of Pd−NHC Complexes 3a−c



carbene (NHC) complexes **2a**, **2b**, and **2c** (Scheme 1).[8] By slightly modifying complex **2a** to its isopentyl analogues **2b** and **2c**, they finally revealed a better performance with **2c** in the Negishi cross-coupling reactions with either secondary alkyzinc halides or ortho-substituted substrates. Despite these advances, in most reports of the Negishi cross-coupling reactions, prolonged reaction time, elevated temperature, and high catalyst loadings (usually 1−5 mol %) are still required, especially for challenging sterically congested or heterocyclic substrates,[7] which highlights the urgency for developing both more general and more mild catalyst systems.

Recently, we found that less-studied ylidenes derived from π-extended arylimidazolium salts exhibited stronger σ-donor and weaker π-acceptor properties, which can further increase the electron density of the metal center and result in better catalytic activity than their imidazolium analogues.[9] It provides another opportunity to tune the catalyst activity by alternating the electronic properties of ligands along with increasing their bulkiness. For instance, robust Pd−NHC complexes **3a−c** turned out to be highly efficient and practical catalysts in the sterically hindered Suzuki-Miyaura coupling and amination reactions.[9b,c] Following our recent research on the synthesis of metal complexes and their potential application in soft materials and catalysis,[9,10] we would like to further explore how to influence catalytical activities of the palladium N-heterocyclic carbene (Pd−NHC) complexes in Negishi coupling reactions by using ylidenes with strong σ-donor and weak π-acceptor properties.

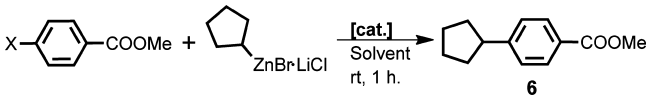
RESULTS AND DISCUSSION

Palladium complexes **3a−c** were readily accessible in good yields from the corresponding acenaphthoimidazolium salts by heating with $PdCl_2$ and K_2CO_3 in neat 3-chloropyridine with vigorous stirring at 90 °C for 24 h (Scheme 2). The π-extended imidazolium salts **5a−c** were synthesized as follows:[11] acenaphthenequinone was suspended in acetonitrile and was heated under reflux conditions for 1 h. After acetic acid was added, the resulting reaction mixture was heated until the acenaphthenequinone had been completely dissolved. Then the corresponding aniline was added dropwise over 30 min, and the resulting mixture was heated under reflux conditions for another 5 h to produce imines **4a−c** in good yields. These were readily converted to the corresponding imidazolium chlorides **5a−c** by mixing with methoxy (methyl)chloride in the sealed reaction vessel at 100 °C for 16 h.

In consideration of the possible product isomerization resulting from secondary alkylzinc reagents, initially, cyclopentylzinc bromide was selected to optimize the coupling reaction conditions with methyl 4-chlorobenzoate. In contrast with **3b** and **3c**, Pd−NHC complex **3a** with bulkier isopropyl groups revealed a higher catalytic activity, and almost identical isolated yields were observed in dioxane within 0.5 h at room temperature even in the presence of catalyst loadings as low as 0.25 mol % (entries 1−5, Table 1), which further proved that the bulkiness of the ligand is essential during the catalytic transformation.[6c] Further decreasing the catalyst loading to 0.1 and 0.025 mol %, the reactions still afforded 70% and 32% yields, respectively, whereas no reaction was observed in the blank test (entries 6−8, Table 1). When other solvents such as tetrahydrofuran (THF) and toluene were involved, slightly lower results were observed with 0.25 mol % **3a** (71% and 52%, entries 9 and 10, respectively, Table 1). In the case of dimethylformamide (DMF), only trace products could be detected by GC−MS analysis (entry 11, Table 1), which indicated strong solvent effects in the coupling process. The protocol also applies to coupling with aryl iodide and bromide analogues (entries 12−15, Table 1). In the bromide case, even with a 50 ppm catalyst loading, a 12% yield was still obtained (entry 15, Table 1). In comparison with the results obtained by other well-known catalysts derived from commerically available bulky monophosphinobiaryl ligands (**1b** and **1c**, entries 16 and 17, respectively, Table 1) and NHC ligands (**2a** and **2b**, entries 18 and 19, respectively, Table 1) under the optimized condition, complex **3a** still exhibited a comparatively higher catalytic activity. Even under the optimal reaction conditions for the Negishi cross-coupling reactions with these four ligands reported in the literature,[7a,8b] up to 96% GC yields were

dx.doi.org/10.1021/jo400803s | J. Org. Chem. XXXX, XXX, XXX−XXX

Table 1. Condition Screening and Optimization[a]



entry	[cat.] (mol %)	X	solvent	yield (%)[b]
1	**3a** (1)	Cl	dioxane	>99
2	**3b** (1)	Cl	dioxane	2[c]
3	**3c** (1)	Cl	dioxane	trace[c]
4	**3a** (0.5)	Cl	dioxane	>99
5	**3a** (0.25)	Cl	dioxane	98
6	**3a** (0.1)	Cl	dioxane	70[c]
7	**3a** (0.025)	Cl	dioxane	32[c]
8	blank	Cl	dioxane	NR[c]
9	**3a** (0.25)	Cl	THF	71[c]
10	**3a** (0.25)	Cl	toluene	52[c]
11	**3a** (0.25)	Cl	DMF	trace[c]
12	**3a** (0.25)	I	dioxane	35[c]
13	**3a** (0.25)	Br	dioxane	99
14	**3a** (0.02)	Br	dioxane	64
15	**3a** (0.005)	Br	dioxane	12[c]
16	**1b** (0.5) + $Pd(OAc)_2$ (0.25)	Cl	toluene	64[c]/trace[d]
17	**1c** (0.5) + $Pd(OAc)_2$ (0.25)	Cl	toluene	88[c]/81[c,d]
18	**2a** (0.25)	Cl	toluene	57[c]/50[c,d]
19	**2b** (0.25)	Cl	toluene	97[e]/96[d,e]
20	**3a** (0.25)	Cl	dioxane	99[f]
21	**3a** (0.25)	Cl	dioxane	94[g]

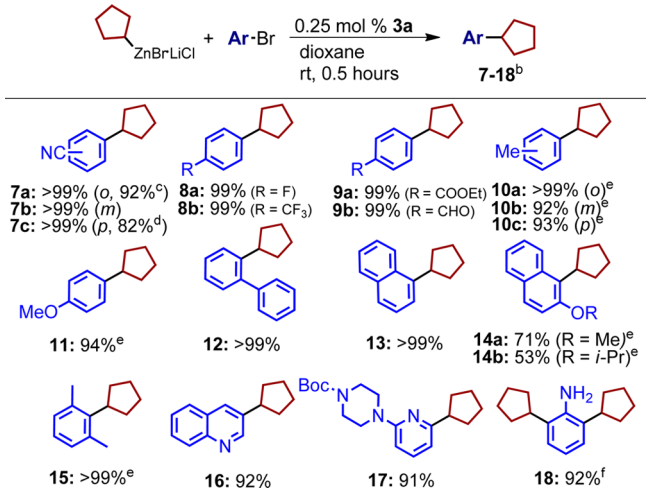
[a]0.5 mmol scale at rt for 1 h. [b]Isolated yield. [c]GC yield after 6 h. [d]With dioxane as solvent. [e]GC yield after 12 h. [f]After 30 min. [g]After 15 min.

observed after 12 h with a 0.25 mol % catalyst loading (entries 16−19, Table 1). To our delight, with 0.25 mol % of complex **3a**, full conversion of the coupling process could be achieved within 30 min, which was further confirmed by GC−MS analysis (entries 20−21, Table 1).

Delightedly, the optimized conditions were suitable for the couplings of cyclopentylzinc bromide with a broad range of (hetero)aryl bromides (Scheme 3). The relative position of substituents hardly hampered the process, and all resulted in similarly excellent isolated yields (**7a−c** and **10a−c**). Electron-poor substituents were much more favorable than electron-rich ones (**7−9** vs **10−12**). In the latter case, the reactions were performed at 80 °C for 24 h with 1 mol % **3a** with additional N-methylimidazole (NMI) as an additive to achieve excellent isolated yields (up to 99%, **10** and **11**).[12] Even with 0.25 mol % **3a**, mono-ortho-substituted and N-heterocyclic bulky bromoarenes were well tolerated and resulted in up to quantitative yields (**12**, **13**, **16**, and **17**). For highly steric disubstituted substrates, the reaction conditions aforementioned for electron-rich bromoarenes had to be applied to obtain gratifying results (**14a**, **14b**, and **15**). In addition, free amino groups did not impede the transformation even for a one-pot dicoupling process (**18**), which nowadays is still regarded as an intriguing and challenging task.[13] In addition, this protocol could be readily scaled up, and a 92% isolated yield was present in a 10 g (60 mmol) reaction with 0.25 mol % of complex **3a** for 24 h (**7a**, Scheme 3), indicating the practical applicability of the protocol.

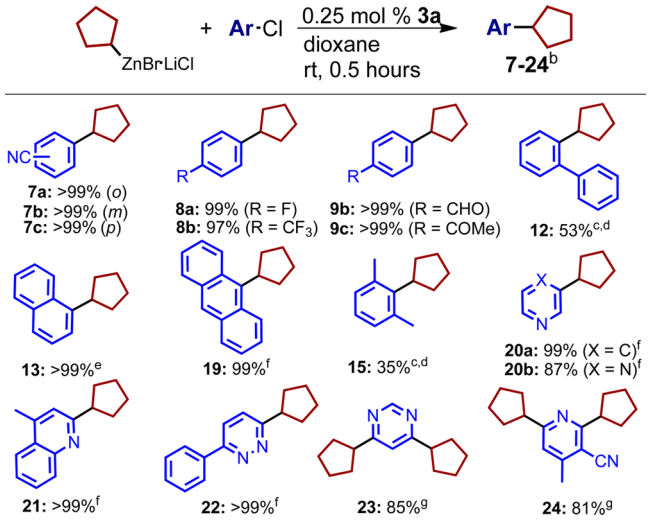
With these results in hand, a variety of less expensive (hetero)aryl chlorides[14] were then examined. As shown in Scheme 4, the protocol was applicable to each of the selected chloroarenes. Again, electron-withdrawing groups were more

Scheme 3. Negishi Cross-Coupling Reactions of Cyclopentylzinc Bromide with Various Bromoarenes[a]



[a]0.5 mmol scale at rt for 0.5 h. [b]Isolated yield. [c]60 mmol scale at rt for 24 h. [d]GC yield, with 0.05 mol % **3a** at 80 °C for 24 h. [e]With 1 mol % **3a** at 80 °C for 24 h in the presence of 0.6 mmol of NMI. [f]With 2 mol % **3a**, 3 equiv of alkylzinc reagent, and 0.6 mmol of NMI at 80 °C for 24 h.

Scheme 4. Negishi Cross-Coupling Reactions of Cyclopentylzinc Bromide with Various Chloroarenes[a]



[a]0.5 mmol scale at rt for 0.5 h. [b] Isolated yield. [c]GC yield. [d]With 1 mol % complex **3a** and 0.6 mmol of NMI at 80 °C for 12 h. [e]Containing 10% 2-isomer. [f]After 6 h. [g]With 2 mol % **3a**, 3 equiv of alkylzinc reagent and 0.6 mmol of NMI at 80 °C for 6 h.

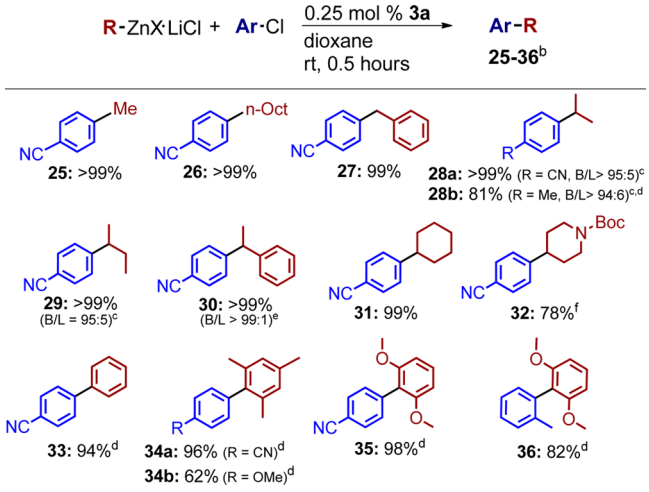
efficient than their electron-donating analogues and resulted in almost quantitative yields (**7−9** vs **12**, Scheme 4). To our surprise, unlike aryl bromides, sterically more hindered aryl chlorides such as 1-chloronaphthalene and 9-chloroanthracene were easily coupled even at ambient conditions, whereas the other bulky substrates resulted in worse yields even with 1 mol % catalyst loading at 80 °C after longer reaction times (**13** and **19** vs **12** and **15**). In addition, a number of N-heterocyclic halides were well tolerated substrates and afforded up to quantitative yields (**20−22**). Delightedly, dicoupling reactions in the one-pot manner were accomplished within 6 h at 80 °C,

dx.doi.org/10.1021/jo400803s | J. Org. Chem. XXXX, XXX, XXX−XXX

which further emphasized the broad scope of the protocol (**23** and **24**).

Encouraged by the excellent outcomes with a broad range of (hetero)aryl halides, we turned our attention to probe the scope of other alkyl and arylzinc reagents. The results are compiled in Scheme 5. For primary alkylzinc halides, the length

Scheme 5. Negishi Cross-Coupling Reactions of Chloroarenes with Various Alkyl and Arylzinc Reagents[a]



[a]0.5 mmol scale at rt for 0.5 h. [b]Isolated yield. [c]With NMI as additive; B/L ratio was determined by GC–MS. [d]At 80 °C for 24 h. [e]For 12 h. [f]NMI was added.

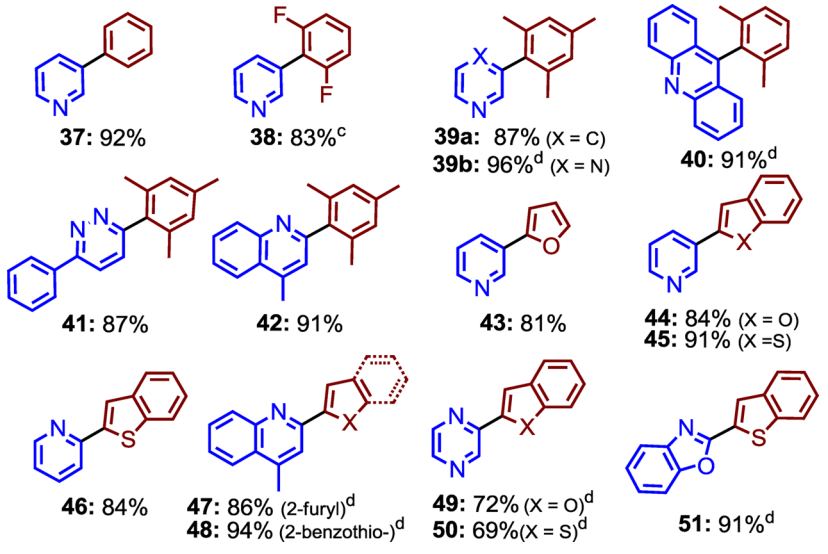
of the alkyl chain and phenyl substitution scarcely disturbed the coupling process resulting in up to quantitative yields (**25**–**27**). For secondary organic zinc reagents with isopropyl and isobutyl substituents, quantitative yields and a high selectivity for branched products were observed (**28**–**30**). The ring size of the cycloalkylzinc bromides barely affected the coupling process (**31** vs **7c**). However, N-heterocyclic alkylzinc bromide led to a slightly lower yield (78%, **32**). In the case of arylzinc reagents, sterically bulky ortho-substitution was well tolerated (up to 98% yields, **34**–**36**). Unlike the chloroarenes containing electron-withdrawing groups, only moderate yields were observed for the substrates with electron-donating substituents with 0.25 mol % **3a** at 80 °C for 24 h (**34b** and **36**).

In light of the significant role played by heterocyclic compounds in material sciences and medicinal chemistry,[15] we paid further attention to the heteroaryl substrates (Scheme 6). At first, 3-chloropyridine was selected to react with phenyl zinc reagent with 0.25 mol % **3a** at 80 °C for 24 h, and a satisfactory isolated yield was observed (92%, **37**). Because the preparation of polyfluorinated heterocyclic biaryls constitutes one of the challenging tasks in synthesis,[16] 2,6-difluorophenyl zinc bromide was used, and a moderate yield was obtained at 60 °C within 6 h (83%, **38**). Following our recent interest in the sterically hindered cross-coupling reactions,[9] several (bulky) N-heterocyclic chlorides were tested in the coupling of bulky phenyl zinc reagents, and up to 96% yields were obtained (**39**–**42**). Because of their rapid proto-deboronation, five-membered heteroaromatic organo-boron reagents are considered poor substrates in the Suzuki cross-coupling to furnish hetero-biaryls.[17,18] To our delight, with our catalyst system, 2-(benzo)furanylzinc and benzothiophenylzinc chlorides were able to couple with various N-heterocyclic substrates, and up to 94% yields of heterobiaryls were obtained (**43**–**51**). In addition, except for pyridylzinc chlorides (81–91%, **43**–**46**), 1 mol % catalyst loading was required to achieve the satisfactory conversion (69–94%, **47**-**51**).

CONCLUSION

In summary, Pd–NHC complex **3a** exhibits an extremely high activity toward the Negishi cross-coupling reactions of alkyl or (hetero)arylzinc reagents with various (hetero)aryl halides under mild reaction conditions with catalyst loading at 0.25 mol %. Not only was the undesired β-hydride elimination to form isomerized linear products successfully suppressed in the coupling with secondary alkylzinc halides, but also the challenging sterically congested coupling with sterically bulky arylzinc chlorides as well as the syntheses of functionalized heterobiaryls were realized, which may give the credit to the

Scheme 6. Negishi Cross-Coupling Reactions of Heterocyclic Chloroarenes with Various (Hetero)arylzinc Reagents[a]



[a]0.5 mmol scale at 80 °C for 24 h. [b]Isolated yield. [c]With 1 mol % **3a** at 60 °C for 6 h. [d]With 1 mol % **3a**.

dx.doi.org/10.1021/jo400803s | J. Org. Chem. XXXX, XXX, XXX–XXX

strong σ-donor of the acenaphtho-ring and the bulkiness of the isopropyl groups of complex **3a**. Although, in the cases of substrates containing electron-donating groups or challenging bulky and heterocylic substrates, 1 mol % catalyst loading and higher reaction temperature are required, the results still imply that it is a useful strategy to tune the catalyst activity, increase the bulkiness of the catalysts, and modify the electronic properties of the ligands.

EXPERIMENTAL SECTION

All commercial reagents and solvents were used directly as purchased without further purification. Anhydrous THF, 1,4-dioxane, and toluene were distilled from sodium/benzophenone prior to use. Zinc dust was activated by washing with 1 M HCl followed by EtOH and Et_2O. All ^{13}C NMR spectra were referenced to the carbon signal of $CDCl_3$ (77.0 ppm) and DMSO (39.4 ppm), and they were obtained with complete ^1H decoupling. The chemical shifts (δ) for ^1H NMR spectra were given in parts per million (ppm) referenced to the residual proton signal of the deuterated solvents ($CHCl_3$ at δ = 7.26 ppm and DMSO at δ = 2.50 ppm); coupling constants were expressed in hertz (Hz).

Pd−NHC Complexes 3a−c. To a Schlenk tube containing $PdCl_2$ (0.088 g, 0.5 mmol), acenaphthoimidazolium chlorides (0.55 mmol), K_2CO_3 (0.345 g, 5.0 mmol), 3-chloropyridine (2.0 mL), and a stir bar were added. The reaction mixture was heated with vigorous stirring at 90 °C for 24 h. After cooling to room temperature, the reaction mixture was diluted with CH_2Cl_2 and passed through a short pad of silica gel covered with a pad of Celite eluting with CH_2Cl_2 until the product was completely recovered. Most of the CH_2Cl_2 was removed (rotary evaporator) at room temperature, and 3-chloropyridine was then vacuum-distilled (water aspirator vacuum) and saved for reuse. The pure Pd−NHC complexes **3a−c** were isolated after triturating with pentane, decanting the supernatant, and drying in high vacuum.

Pd−NHC ***3a***. Yield: 0.305 g, 76%. ^1H NMR (400 MHz, $CDCl_3$, 298 K): δ = 8.68 (d, J = 2.0 Hz, 1H), 8.61 (d, J = 5.2 Hz, 1H), 7.70 (d, J = 8.4 Hz, 2H), 7.64 (t, J = 8.0 Hz, 2H), 7.57 (d, J = 8.0 Hz 1H), 7.48 (d, J = 8.0 Hz, 4H), 7.34 (t, J = 7.6 Hz, 2H), 7.10 (dd, J = 8.0 Hz, 5.6 Hz, 1H), 6.80 (d, J = 7.32 Hz, 2H), 3.45−3.35 (m, 4H), 1.46 (d, J = 6.4 Hz, 12H), 0.92 (d, J = 6.4 Hz, 12H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 159.1, 150.5, 149.5, 147.2, 140.3, 137.3, 133.8, 131.8, 130.6, 129.5, 129.0, 128.1, 127.2, 126.0, 124.7, 124.2, 122.1, 28.9, 25.8, 24.2; HRMS (ESI-TOF) m/z: $[M - PyCl - 2Cl]^+$ calcd for $C_{37}H_{40}N_2Pd$ 617.2242; found, 617.2163.

Pd−NHC ***3b***. Yield: 0.611 g, 81%. ^1H NMR (400 MHz, $CDCl_3$, 298 K): δ = 8.65 (s, 1H), 8.56 (d, J = 5.2 Hz, 1H), 7.74 (d, J = 8 Hz, 2H), 7.56 (d, J = 8 Hz, 1H), 7.38 (t, J = 7.6 Hz, 2H), 7.14 (s, 4H), 7.11−7.06 (m, 1H), 6.95 (d, J = 6.8 Hz, 2H), 2.44 (s, 24H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 156.1, 150.6, 149.7, 139.4, 138.8, 137.6, 136.2, 133.7, 132.0, 129.7, 129.3, 128.2, 127.7, 125.7, 124.4, 120.9, 21.5, 19.3; HRMS (ESI-TOF) m/z: $[M - Cl]^+$ calcd for $C_{36}H_{32}Cl_2N_3Pd$ 684.1012; found, 684.1036.

Pd−NHC ***3c***. Yield: 0.319 g, 51%. ^1H NMR (400 MHz, $CDCl_3$, 298 K): δ = 8.74 (d, J = 2.4 Hz,1H), 8.65 (d, J = 5.2 Hz,1H), 8.31 (d, J = 8 Hz,4H), 7.78−7.61 (m, 9H), 7.43 (t, J = 7.6 Hz,2H), 7.37 (d, J = 6.8 Hz, 2H), 7.18 (dd, J = 8.0 and 5.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 150.2, 149.2, 138.5, 138.2, 137.8, 137.8, 132.4, 129.7, 129.5, 129.1, 128.5, 127.4, 126.4, 125.3, 124.7, 124.6, 121.7; HRMS (ESI-TOF) m/z: $[M - Cl]^+$ calcd for $C_{30}H_{20}Cl_2N_3Pd$ 600.0073; found, 600.0054.

General Procedure for Preparation of Secondary Alkylzinc Halides.[19] A 100 mL Schlenk tube was charged with zinc dust (3.9 g, 60 mmol) and LiCl (2.53 g, 60 mmol). It was heated for about 10 min under vacuum with a heat gun and backfilled with N_2 after cooling to room temperature. Dry THF (30 mL) and 1,2-dibromoethane (1.5 mmol) were added to the vessel under N_2. The reaction mixture was heated at 60 °C for 20 min. Then trimethylsilyl chloride (0.3 mmol) and a solution of iodine in THF (0.3 mL, 0.5 M) were added via syringe. The resulting mixture was heated at 60 °C for another 20 min and then cooled to room temperature. Alkyl halide (30 mmol) was added slowly, and the reaction mixture was stirred at 50 °C for about 20 h. The new prepared organozinc halides were rested for 1 h at room temperature, and then the supernatant solution was transferred to a dry vessel via cannula carefully. The solution of organozinc halide was titrated with a 0.5 M solution of iodine in THF.[20]

General Procedure for Negishi Couplings of Aryl Halides and Alkyl Zinc Halides. A 50 mL Schlenk tube containing a magnetic stir bar was vacuumed and backfilled with N_2 (three times). The vessel was charged with catalyst **3a**, *N*-methylimidazole (0.6 mmol, if needed) and dioxane (1 mL). The aryl halide (0.5 mmol, 1 equiv) was added under N_2. Alkyl zinc halide (ca. 0.5 M in THF, 0.75 mmol, 1.5 equiv) was then added dropwise at 0 °C. The resulting mixture was stirred at room temperature for 0.5−6 h or at 80 °C for 12 h, and the reaction was monitored by TLC. The reaction mixture was cooled to room temperature (if heated), quenched with saturated NH_4Cl solution, and extracted with EtOAc (3 × 10 mL). The organic phases were combined, dried over Na_2SO_4, and concentrated in vacuo followed by silica gel flash chromatography.

General Procedure for the Preparation of (Hetero)aryl Zinc Halides and Negishi Cross-Couplings of Aryl Halides and Aryl Zinc Halides. A 50 mL Schlenk tube containing a magnetic stir bar was evacuated and backfilled with N_2 (3 times). The vessel was charged with aryl bromides (0.75 mmol, 1.5 equiv) and dry THF (1 mL). The solution was cooled to −78 °C, and the *n*-butyllithium (0.825 mmol, 1.65 equiv) was added dropwise. It was stirred at −78 °C for 1 h, and then $ZnCl_2$ (0.9 mmol, 1.8 equiv) was added in one portion under N_2. After another 30 min at −78 °C, the Schlenk tube was allowed to warm to room temperature slowly and stirred for 1 h. The solution was added to a 50 mL Schlenk tube containing precatalyst **3a**, aryl halides (0.5 mmol, 1 equiv), and 1 mL dioxane at 0 °C. The mixture was stirred in a preheated oil bath at 100 or 80 °C for about 24 or 12 h, and the reaction was monitored by TLC. The reaction mixture was cooled to room temperature, quenched with water (3 mL), and extracted with EtOAc (3 × 10 mL). The organic phases were combined, dried over Na_2SO_4, and concentrated in vacuo followed by silica gel flash chromatography.

Analytical Data of the Compounds 6−51. *Methyl 4-Cyclopentylbenzoate,* ***6***. Colorless oil. Yield: 103 mg, >99%. ^1H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.95 (d, J = 7.6 Hz, 2H), 7.29 (d, J = 7.6 Hz, 2H), 3.89 (s, 3H), 3.10−2.95 (m, 1H), 2.07 (m, 2H), 1.81 (m, 2H), 1.69 (m, 2H), 1.60−1.59 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 167.1, 152.1, 129.5, 127.6, 127.0, 51.8, 45.9, 34.4, 25.5. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{13}H_{17}O_2$ 205.1229; found, 205.1237.

2-Cyclopentylbenzonitrile, ***7a***.[8b] Colorless oil. Yield: 86 mg, >99%. ^1H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.58 (d, J = 7.2 Hz, 1H), 7.51 (t, J = 7.4 Hz, 1H), 7.38 (d, J = 7.6 Hz, 1H), 7.26−7.22 (m, 1H), 3.41 (quintet, J = 8.2 Hz, 1H), 2.25−2.05 (m, 2H), 1.95−1.55 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 150.5, 132.8, 126.5, 126.2, 118.4, 112.3, 44.0, 34.3, 25.7; MS: m/z = 171 $[M]^+$, 143, 129, 115, 102.

3-Cyclopentylbenzonitrile, ***7b***.[21] Colorless oil. Yield: 87 mg, >99%. ^1H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.51 (s, 1H), 7.46 (m, 2H), 7.36 (m, 1H), 2.91−3.09 (m, 1H), 2.08 (m, 2H), 1.81 (m, 2H), 1.70 (m, 2H), 1.56 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 147.9, 131.7, 130.6, 129.3, 128.9, 119.1, 112.1, 45.4, 34.3, 25.3.

4-Cyclopentylbenzonitrile, ***7c***.[22] Colorless oil. Yield: 86 mg, >99%. ^1H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.54 (d, J = 7.2 Hz, 2H), 7.31 (d, J = 7.6 Hz, 2H), 3.10−2.95 (m, 1H), 2.08 (m, 2H), 1.81 (m, 2H), 1.70 (m, 2H), 1.56 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 152.2, 131.9, 127.8, 119.1, 109.2, 45.9, 34.3, 25.4.

1-Cyclopentyl-4-fluorobenzene, ***8a***.[23] Colorless oil. Yield: 82 mg, 99%. ^1H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.25−7.18 (m, 2H), 7.01 (t, J = 8.0 Hz, 2H), 3.08−2.80 (m, 1H), 2.05−2.15 (m, 2H), 1.70−1.85 (m, 2H), 1.60−1.70 (m, 2H), 1.50−1.60 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 162.3, 159.9, 142.0, 128.3, 128.2, 114.9, 114.7, 45.2, 34.7, 25.4.

1-Cyclopentyl-4-(trifluoromethyl)benzene, ***8b***.[22] Colorless oil. Yield: 107 mg, 99%. ^1H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.54 (d, J = 7.6 Hz, 2H), 7.35 (d, J = 7.6 Hz, 2H), 3.09−3.01 (m, 1H), 2.09

dx.doi.org/10.1021/jo400803s | J. Org. Chem. XXXX, XXX, XXX−XXX

(m, 2H), 1.83 (m, 2H), 1.72 (m, 2H), 1.61 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 150.8, 127.4, 125.2, 125.1, 45.6, 34.9, 25.5.

Ethyl 4-Cyclopentylbenzoate, ***9a***. Colorless oil. Yield: 109 mg, 99%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.93 (d, J = 8.0 Hz, 2H), 7.25 (d, J = 8.0 Hz, 2H), 4.32 (q, J = 7.2 Hz, 2H), 3.05−2.94 (m, 1H), 2.08−1.98 (m, 2H), 1.84−1.71 (m, 2H), 1.69−1.61 (m, 2H), 1.58−1.49 (m, 2H), 1.34 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 166.5, 151.9, 129.4, 127.9, 126.9, 60.6, 45.8, 34.4, 25.4, 14.2. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{14}H_{18}O_2Na$ 241.1204; found, 241.1168.

4-Cyclopentylbenzaldehyde, ***9b***.[24] Colorless oil. Yield: 87 mg, 99%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 9.95 (s, 1H), 7.79 (d, J = 8.0 Hz, 2H), 7.38 (d, J = 7.6 Hz, 2H), 3.08−3.02 (m, 1H), 2.09 (m, 2H), 1.83 (m, 2H), 1.71 (m, 2H), 1.62 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 191.9, 154.1, 134.4, 129.8, 127.8, 46.1, 34.4, 25.5.

1-Cyclopentyl-2-methylbenzene, ***10a***.[25] Colorless oil. Yield: 82 mg, >99%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.28−7.20 (m, 1H), 7.19−7.03 (m, 3H), 3.18 (quintet, J = 8.4 Hz, 1H), 2.34 (s, 3H), 2.10−1.95 (m, 2H), 1.87−1.75 (m, 2H), 1.75−1.63 (m, 2H), 1.63−1.51 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 144.5, 135.9, 130.0, 126.0, 125.4, 125.2, 41.6, 33.6, 25.6, 19.8; MS: m/z = 160 $[M]^+$, 131, 117, 91, 77.

1-Cyclopentyl-3-methylbenzene, ***10b***.[25] Colorless oil. Yield: 74 mg, 92%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.30−6.96 (m, 4H), 3.10−2.90 (m, 1H), 2.36 (s, 3H), 2.15−2.00 (bs, 2H), 1.95−1.50 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 146.5, 137.7, 128.1, 127.8, 126.4, 124.1, 45.9, 34.6, 25.5, 21.5; MS: m/z = 160 $[M]^+$, 131, 117, 91, 77.

1-Cyclopentyl-4-methylbenzene, ***10c***.[23] Colorless oil. Yield: 75 mg, 93%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.20−7.05 (m, 4H), 3.02−2.88 (m, 1H), 2.33 (s, 3H), 2.10−2.05 (m, 2H), 1.90−1.74 (m, 2H), 1.74−1.62 (m, 2H), 1.62−1.50 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 143.4, 135.1, 128.9, 127.0, 45.6, 34.7, 25.5, 21.0; MS: m/z = 160 $[M]^+$, 131, 117, 91, 77.

1-Cyclopentyl-4-methoxybenzene, ***11***.[26] Colorless oil. Yield: 83 mg, 94%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.17 (d, J = 8.0 Hz, 2H), 6.84 (d, J = 8.0 Hz, 2H), 3.79 (s, 3H), 2.95 (quintet, J = 8.4 Hz, 1H), 2.15−1.95 (m, 2H), 1.85−1.74 (m, 2H), 1.74−1.62 (m, 2H), 1.61−1.46 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 157.7, 138.6, 128.0, 113.7, 45.2, 34.8, 29.8, 25.5.

2-Cyclopentylbiphenyl, ***12***. Colorless oil. Yield: 112 mg, >99%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.60−7.35 (m, 7H), 7.35−7.27 (m, 2H), 3.24−3.08 (m, 1H), 2.10−1.95 (m, 2H), 1.95−1.80 (m, 2H), 1.80−1.55 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 144.3, 142.3, 141.9, 129.8, 129.3, 127.9, 127.6, 126.6, 126.2, 125.1, 41.6, 35.8, 26.0.

1-Cyclopentylnaphthalene, ***13***. Colorless oil. Yield: 89 mg, >99%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 8.26 (d, J = 8.0 Hz, 1H), 7.94 (d, J = 7.2 Hz, 1H), 7.83−7.74 (m, 1H), 7.65−7.40 (m, 4H), 3.95−3.78 (m, 1H), 2.38−2.18 (m, 2H), 2.05−1.70 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 142.1, 133.9, 132.2, 128.7, 126.2, 125.5, 125.4, 125.2, 123.9, 121.9, 41.2, 33.6, 25.3.

1-Cyclopentyl-2-methoxynaphthalene, ***14a***. Light yellow oil. Yield: 81 mg, 71%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 8.19 (d, J = 8.8 Hz, 1H), 7.84 (d, J = 8.0 Hz, 1H), 7.76 (d, J = 8.8 Hz, 1H), 7.51 (t, J = 7.6 Hz, 1H), 7.38 (t, J = 7.2 Hz, 1H), 7.32 (d, J = 8.8 Hz, 1H), 4.18−4.04 (m, 1H), 3.97 (s, 3H), 2.25−2.12 (m, 2H), 2.12−1.96 (m, 4H), 1.92−1.78 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 155.0, 133.0, 129.6, 128.9, 127.5, 127.2, 125.7, 123.6, 123.0, 114.3, 56.5, 36.7, 31.8, 27.4. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{16}H_{19}O$ 227.1436; found, 227.1436.

1-Cyclopentyl-2-isopropoxynaphthalene, ***14b***. Yellow oil. Yield: 68 mg, 53%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 8.09 (d, J = 8.4 Hz, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.65 (d, J = 8.8 Hz, 1H), 7.42 (t, J = 7.6 Hz, 1H), 7.30 (t, J = 7.2 Hz, 1H,), 7.23 (d, J = 8.0 Hz, 1H), 4.75−4.57 (m, 1H), 4.14−3.97 (m, 1H), 2.25−2.08 (m, 2H), 2.08−1.85 (m, 4H), 1.85−1.70 (m, 2H), 1.37(d, J = 5.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 153.0, 133.1, 129.7, 128.8, 127.9, 127.3, 125.5, 123.8, 122.9, 116.5, 71.1, 36.7, 31.6, 27.5, 22.4.

2-Cyclopentyl-1,3-dimethylbenzene, ***15***.[27] Colorless oil. Yield: 87 mg, >99%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.03 (s, 3H), 3.62−3.48 (m, 1H), 2.43 (m, 8H), 1.94 (bs, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 141.6, 136.5, 129.2, 125.4, 40.5, 30.9, 27.0, 21.4.

3-Cyclopentylquinoline, ***16***.[22] Yellow oil. Yield: 91 mg, 92%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 8.82 (d, J = 2.4 Hz, 1H), 8.06 (d, J = 8.4 Hz, 1H), 7.90 (s, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.65−7.57 (m, 1H), 7.52−7.44 (m, 1H), 3.21−3.09 (m, 1H), 2.20−2.09 (m, 2H), 1.90−1.80 (m, 2H), 1.80−1.60 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 151.4, 146.7, 138.8, 132.3, 128.9, 128.3, 128.1, 127.3, 126.4, 43.3, 34.2, 25.4.

tert-Butyl 4-(6-cyclopentylpyridin-2-yl)piperazine-1-carboxylate, ***17***.[8b] Light yellow solid. Yield: 151 mg, 91%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.38 (t, J = 7.8 Hz, 1H), 6.52 (d, J = 7.2 Hz, 1H), 6.42 (d, J = 8.4 Hz, 1H), 3.52 (s, 8H), 3.10−2.90 (m, 1H), 2.10−1.90 (m, 2H), 1.90−1.70 (m, 4H), 1.70−1.55 (m, 2H), 1.48 (s,9H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 164.1, 158.8, 154.8, 137.6, 111.5, 104.0, 79.9, 47.6, 45.1, 33.2, 28.4, 25.8.

2,6-Dicyclopentylaniline, ***18***.[8b] Orange oil. Yield: 105 mg, 92%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 6.95 (d, J = 7.2 Hz, 2H), 6.67 (t, J = 6.8 Hz, 1H), 3.65 (bs, 2H), 3.05−2.85 (m, 2H), 2.04−1.88 (m, 4H), 1.80−1.66 (m, 4H), 1.66−1.48 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 141.9, 130.0, 123.5, 118.0, 40.1, 32.2, 25.1.

1-(4-Cyclopentylphenyl)ethanone, ***9c***.[28] Yellow oil. Yield: 95 mg, 92%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.88 (d, J = 8.0 Hz, 2H), 7.31 (d, J = 8.4 Hz, 2H), 3.10−2.97 (m, 1H), 2.57 (s, 3H), 2.15−2.00 (m, 2H), 1.86−1.77 (m, 2H), 1.74−1.66 (m, 2H), 1.64−1.52 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 197.8, 152.5, 134.9, 128.4, 127.2, 45.9, 34.5, 26.5, 25.5.

9-Cyclopentylanthracene, ***19***. Orange oil. Yield: 123 mg, 99%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 8.40 (d, J = 7.6 Hz, 2H), 8.35 (s, 1H), 8.03 (d, J = 6.4 Hz, 2H), 7.47 (m, 4H), 4.75−4.55 (m, 1H), 2.43 (m, 2H), 2.26 (m, 4H), 2.01(m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 138.1, 131.9, 129.6, 129.5, 126.2, 124.9, 124.7, 124.5, 39.5, 33.6, 27.8.

3-Cyclopentylpyridine, ***20a***.[28] Yellow oil. Yield: 73 mg, 99%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 8.51 (s, 1H), 8.43 (s, 1H), 7.57 (d, J = 6.8 Hz, 1H), 7.23 (m, 1H), 2.90−3.05 (m, 1H), 2.06 (m, 2H), 1.80 (m, 2H), 1.69 (m, 2H), 1.54 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 148.6, 146.8, 142.1, 135.1, 123.6, 43.2, 34.3, 25.3.

2-Cyclopentylpyrazine, ***20b***. Yellow oil. Yield: 65 mg, 87%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 8.44 (s, 2H), 8.33 (s, 1H), 3.30−3.00 (m, 1H), 2.15−1.95 (m, 2H), 1.90−1.55 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 161.1, 143.9, 143.8, 141.9, 45.1, 33.2, 25.8. HR-MS (ESI) m/z: $[M+H]^+$ calcd for $C_9H_{13}N_2$ 149.1078; found, 149.1056.

2-Cyclopentyl-4-methylquinoline, ***21***.[29] Yellow oil. Yield: 106 mg, >99%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 8.05 (d, J = 8.4 Hz, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.64 (t, J = 7.2 Hz, 1H), 7.46 (t, J = 7.2 Hz, 1H), 7.16 (s, 1H), 3.40−3.20 (m, 1H), 2.64 (s, 3H), 2.16 (m, 2H), 1.88 (m, 4H), 1.74 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 165.7, 147.4, 144.0, 129.3, 128.8, 126.8, 125.3, 123.4, 120.6, 48.6, 33.4, 25.9, 18.7.

3-Cyclopentyl-6-phenylpyridazine, ***22***. White solid, mp 90.0−91.3 °C. Yield: 112 mg, >99%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 8.06 (d, J = 7.2 Hz, 2H), 7.75 (d, J = 8.8 Hz, 1H), 7.50−7.38 (m, 3H), 7.38 (d, J = 8.4 Hz, 1H), 3.50−3.30 (m, 1H), 2.25−2.05 (m, 2H), 1.95−1.80 (m, 4H), 1.80−1.70 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 165.2, 156.9, 136.2, 129.4, 128.6, 126.5, 125.6, 123.7, 45.5, 33.1, 25.6. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{15}H_{17}N_2$ 225.1391; found, 225.1363.

4,6-Dicyclopentylpyrimidine, ***23***. Yellow oil. Yield: 92 mg, 85%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 8.99 (d, J = 1.2 Hz, 1H), 7.02 (d, J = 0.8 Hz, 1H), 3.12−2.90 (m, 2H), 2.10−1.90 (m, 4H), 1.85−1.55 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 173.8, 158.3, 117.1, 47.2, 33.0, 25.9. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{14}H_{21}N_2$ 217.1704; found, 217.1689.

2,6-Dicyclopentyl-4-methylnicotinonitrile, ***24***. Colorless oil. Yield: 103 mg, 81%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 6.89 (s, 1H),

dx.doi.org/10.1021/jo400803s | J. Org. Chem. XXXX, XXX, XXX−XXX

3.68−3.52 (m, 1H), 3.18−3.05 (m, 1H), 2.46 (s, 3H), 2.10−1.92 (m, 4H), 1.90−1.55 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 168.7, 168.2, 150.6, 120.0, 117.0, 106.1, 47.8, 45.7, 33.3, 33.0, 26.1, 25.9, 20.4. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{17}H_{23}N_2$ 255.1861; found, 255.1877.

4-Methylbenzonitrile, ***25****.*[30] Colorless oil. Yield: 59 mg, >99%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.48 (d, J = 8.0 Hz, 2H), 7.22 (d, J = 7.6 Hz, 2H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 143.5, 131.8, 129.7, 119.0, 109.0, 21.6.

4-Octylbenzonitrile, ***26****.*[31] Colorless oil. Yield: 115 mg, >99%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.52 (d, J = 7.6 Hz, 2H), 7.24 (d, J = 7.6 Hz, 2H), 2.63 (t, J = 7.6 Hz, 2H), 1.59 (m, 2H), 1.35−1.15 (m, 10H), 0.85 (t, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 148.5, 131.9, 129.1, 119.0, 109.3, 36.0, 31.7, 30.8, 29.2, 29.1, 22.5, 13.9.

4-Benzylbenzonitrile, ***27****.*[32] Colorless oil. Yield: 96 mg, 99%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.57 (d, J = 8.4 Hz, 2H), 7.38−7.22 (m, 5H), 7.18 (d, J = 7.2 Hz, 2H), 4.05 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 146.6, 139.2, 132.2, 129.5, 128.8, 128.6, 126.5, 118.9, 109.9, 41.8; MS: m/z = 193 $[M]^+$, 165, 91.

4-iso-Propylbenzonitrile, ***28a****.*[8b] Colorless oil. Yield: 73 mg, >99%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.57 (d, J = 6.8 Hz, 2H), 7.31 (d, J = 6.8 Hz, 2H), 3.04−2.86 (m, 1H), 1.25 (d, J = 6.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 154.3, 132.2, 127.2, 119.1, 109.5, 34.3, 23.5.

p-Cymene, ***28b****.*[33] Colorless oil. Yield: 59 mg, 91%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ =7.30−7.25 (m, 4H), 3.10−2.90 (m, 1H), 2.49 (s, 3H), 1.41 (d, J = 7.6 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 145.8, 135.1, 129.0, 126.3, 33.7, 24.1, 20.9.

4-sec-Butylbenzonitrile, ***29****.*[34] Colorless oil. Yield: 80 mg, >99%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.56 (d, J = 7.6 Hz, 2H), 7.26 (d, J = 7.6 Hz, 2H), 2.72−2.55 (m, 1H), 1.66−1.49 (m, 2H), 1.22 (d, J = 6.8 Hz, 3H), 0.79 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 153.4, 132.1, 127.8, 119.1, 109.6, 41.8, 30.7, 21.3, 12.0.

4-(1-Phenylethyl)benzonitrile, ***30****.*[8b] Orange oil. Yield: 104 mg, >99%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.57 (dt, J = 8.4, 1.8 Hz, 2H), 7.36−7.27 (m, 4H), 7.27−7.16 (m, 3H), 4.22 (q, J = 7.2 Hz, 1H), 1.66 (d, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 151.8, 144.6, 132.2, 128.6, 128.4, 127.5, 126.5, 119.0, 109.8, 44.8, 21.3; MS: m/z = 207 $[M]^+$, 192, 165, 77.

4-Cyclohexylbenzonitrile, ***31****.*[35] White solid. Yield: 92 mg, 99%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.56 (d, J = 7.6 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 2.60−2.45 (m, 1H), 1.92−1.70 (m, 5H), 1.50−1.15 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 153.4, 132.1, 127.6, 119.1, 109.5, 44.7, 33.9, 26.5, 25.8.

tert-Butyl 4-(4-cyanophenyl)piperidine-1-carboxylate, ***32****.*[36] Colorless oil. Yield: 112 mg, 78%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.56 (d, J = 8.4 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 4.38−4.13 (m, 2H), 2.78 (t, J = 10.8 Hz, 2H), 2.69 (tt, J = 12, 3.4 Hz, 1H), 1.78 (d, J = 12.8 Hz, 2H), 1.57 (qd, J = 12.4, 4 Hz, 2H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 154.6, 151.0, 132.2, 127.5, 118.8, 110.1, 79.5, 42.7, 32.6, 28.3.

4-Phenylbenzonitrile, ***33****.*[37] White solid. Yield: 84 mg, 94%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.73 (d, J = 8.0 Hz, 2H), 7.68 (d, J = 8.4 Hz, 2H), 7.59 (d, J = 7.6 Hz, 2H), 7.49 (t, J = 7.4 Hz, 2H), 7.43 (t, J = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 145.7, 139.2, 132.6, 129.1, 128.6, 127.7, 127.2, 118.9, 110.9.

4-Mesitylbenzonitrile, ***34a****.*[38] White solid. Yield: 106 mg, 96%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.71 (d, J = 8.0 Hz, 2H), 7.27 (d, J = 8.0 Hz, 2H), 6.97 (s, 2H), 2.35 (s, 3H), 1.99 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 146.3, 137.4, 137.0, 135.1, 132.2, 130.2, 128.3, 118.8, 110.5, 20.9, 20.5.

4-Mesitylanisole, ***34b****.*[39] White solid. Yield: 70 mg, 62%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.08−7.03 (m, 2H), 6.98−6.92 (m, 4H), 3.86 (s, 3H), 2.33 (s, 3H), 2.01 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 158.1, 143.2, 138.6, 136.4, 133.2, 130.3, 128.0, 113.7, 55.2, 21.0, 20.8.

4-(2,6-Dimethoxyphenyl)benzonitrile, ***35****.* White solid, mp 138.4−139.7 °C. Yield: 117 mg, 98%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.67 (dt, J = 8.4, 2.0 Hz, 2H), 7.46 (dt, J = 8.4, 2.0 Hz, 2H), 7.33 (t, J = 8.4 Hz, 1H), 6.66 (d, J = 8.4 Hz, 2H), 3.74 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 157.3, 139.5, 131.9, 131.3, 129.8, 117.5, 110.2, 104.1, 55.8. HRMS (ESI) m/z: $[M]^+$ calcd for $C_{15}H_{13}NO_2$ 239.0946; found, 239.0963.

2,6-Dimethoxy-2′-methyl-1,1′-biphenyl, ***36****.*[40] White solid. Yield: 94 mg, 82%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.27−7.22 (m, 4H), 7.22−7.16 (m, 1H), 6.68 (d, J = 8.4 Hz, 2H), 3.73 (s, 6H), 2.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 157.7, 137.3, 134.2, 130.7, 129.5, 128.6, 127.2, 125.2, 118.9, 103.9, 55.8, 55.7, 19.7.

3-Phenylpyridine, ***37****.*[41] Colorless oil. Yield: 71 mg, 92%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 8.84 (d, J = 2.0 Hz, 1H), 8.58 (dd, J = 4.8, 1.2 Hz, 1H), 7.85 (dt, J = 8.0, 1.8 Hz, 1H), 7.58−7.54 (m, 2H), 7.46 (t, J = 7.8 Hz, 2H), 7.42−7.30 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 148.3, 137.7, 136.5, 134.2, 129.0, 128.7, 128.0, 127.0, 123.4.

3-(2,6-Difluorophenyl)pyridine, ***38****.*[42] Light yellow oil. Yield: 79 mg, 83%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 8.73 (s, 1H), 8.64 (d, J = 4.0 Hz, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.41 (dd, J = 4.8, 7.6 Hz, 1H), 7.31−7.38 (m, 1H), 7.02 (t, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 161.3, 150.8, 149.2, 137.6, 129.9, 125.5, 123.2, 111.9.

3-Mesitylpyridine, ***39a****.*[43] Yellow oil. Yield: 86 mg, 87%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 8.60 (d, J = 3.6 Hz, 1H), 8.43 (s, 1H), 7.50 (dt, J = 8.0, 1.6 Hz, 1H), 7.40−7.34 (m, 1H), 6.97 (s, 2H), 2.34 (s, 3H), 2.00 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 150.3, 148.0, 137.5, 137.0, 136.7, 136.2, 134.9, 128.3, 123.4, 21.0, 20.8.

2-Mesitylpyrazine, ***39b****.*[44] Yellow oil. Yield: 95 mg, 96%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 8.68 (t, J = 2.0 Hz, 1H), 8.52 (d, J = 2.0 Hz, 2H), 6.96 (s, 2H), 2.33 (s, 3H), 2.02 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 155.8, 145.9, 144.3, 142.4, 138.4, 136.0, 133.9, 128.5, 21.0, 20.1.

9-(2,6-Dimethylphenyl)acridine, ***40****.*[9b] Light yellow solid. Yield: 129 mg, 91%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ= 8.29 (d, J = 7.2 Hz, 2H), 7.76 (t, J = 7.2 Hz, 2H), 7.48−7.46 (m, 2H), 7.37−7.25 (m, 5H), 1.73 (s, 6H), ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 149.2, 146.6, 136.9, 135.1, 130.2, 130.0, 128.5, 127.7, 126.0, 124.9, 20.1.

3-Mesityl-6-phenylpyridazine, ***41****.*[44] White solid. Yield: 119 mg, 87%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 8.20−8.16 (m, 2H), 7.93 (d, J = 8.4, 1H), 7.58−7.48 (m, 3H), 7.42 (d, J = 8.8 Hz, 1H), 6.99 (s, 2H), 2.36 (s, 3H), 2.09 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 160.6, 157.2, 138.2, 136.2, 136.0, 134.4, 129.9, 128.9, 128.5, 128.4, 126.9, 123.5, 21.0, 20.2.

2-Mesityl-4-methylquinoline, ***42****.* Yellow oil. Yield: 119 mg, 91%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 8.18 (d, J = 8.4 Hz, 1H), 8.05 (dd, J = 8.4, 0.8 Hz, 1H), 7.76−7.71 (m, 1H), 7.62−7.57 (m, 1H), 7.22 (s, 1H), 6.97 (s, 2H), 2.75 (s, 3H), 2.36 (s, 3H), 2.07 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 160.3, 147.9, 144.2, 137.9, 137.4, 135.5, 130.0, 129.0, 128.3, 126.7, 126.0, 123.6, 123.4, 21.0, 20.1, 18.7. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{19}H_{20}N$ 262.1596; found, 262.1579.

3-(Furan-2-yl)pyridine, ***43****.*[45] Light yellow solid. Yield: 59 mg, 81%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 8.92 (s, 1H), 8.50−8.40 (m, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.52−7.50 (m, 1H), 7.74−7.72 (m, 1H), 6.74 (m, J = 3.2 Hz, 1H), 6.52−6.48 (m, 1H). MS: m/z = 145 $[M]^+$, 116, 90.

3-(Benzofuran-2-yl)pyridine, ***44****.*[46] Light yellow solid. Yield: 82 mg, 84%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 9.10 (s, 1H), 8.57 (d, J = 8.0 Hz, 1H), 8.09 (d, J = 8.0 Hz, 1H), 7.60 (d, J = 7.2 Hz, 1H), 7.53 (d, J = 8.0 Hz, 1H), 7.40−7.20 (m, 3H), 7.09 (s, 1H). MS: m/z = 195 $[M]^+$, 166, 139, 87, 69.

3-(Benzo[b]thiophen-2-yl)pyridine, ***45****.*[47] Light yellow solid. Yield: 96 mg, 91%. ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 9.02 (s, 1H), 8.58 (d, J = 8.4 Hz, 1H), 8.17 (d, J = 8.0 Hz, 1H), 8.06−7.98 (m, 2H), 7.89 (d, J = 7.2 Hz, 1H), 7.56−7.48 (m, 1H), 7.46−7.36 (m, 2H). MS: m/z = 211 $[M]^+$, 167, 139, 79.

2-(Benzo[b]thiophen-2-yl)pyridine, ***46****.*[48] Light yellow solid. Yield: 89 mg, 84%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ 8.64 (d, J = 5.2 Hz, 1H), 7.90−7.78 (m, 4H), 7.74 (td, J_1 = 7.6 Hz, J_2 = 1.2 Hz, 1H),

dx.doi.org/10.1021/jo400803s | J. Org. Chem. XXXX, XXX, XXX−XXX

7.40−7.32 (m, 2H), 7.24−7.18 (m, 1H). MS: m/z = 211 $[M]^+$, 167, 139, 79.

2-(Furan-2-yl)-4-methylquinoline, ***47****.*[49] White solid. Yield: 89 mg, 86%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 8.12 (d, J = 8.4 Hz, 1H), 7.93 (d, J = 8.0 Hz, 1H), 7.74−7.55 (m, 3H), 7.50 (t, J = 7.5 Hz, 1H), 7.19 (t, J = 4.4 Hz, 1H), 6.57 (t, J = 1.6 Hz, 1H), 2.72 (s, 3H). MS: m/z = 209 $[M]^+$, 180, 152.

2-(Benzo[b]thiophen-2-yl)-4-methylquinoline, ***48****.* Light yellow solid, mp 132.5 −134.1 °C. Yield: 129 mg, 94%. ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 8.34 (s, 1H), 8.17 (s, 1H), 8.09 (d, J = 8.0 Hz, 1H), 8.01 (d, J = 8.0 Hz, 2H), 7.96−7.88 (m, 1H), 7.78 (t, J = 7.6 Hz, 1H), 7.62 (t, J = 7.6 Hz, 1H), 7.46−7.38 (m, 2H), 2.76 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6, 298 K): δ = 151.4, 147.1, 145.1, 140.2, 129.9, 129.1, 127.2, 126.5, 125.5, 124.7, 124.4, 124.2, 123.3, 122.6, 118.3, 18.3. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{18}H_{13}NS$ 276.0847; found, 276.0838.

2-(Benzofuran-2-yl)pyrazine, ***49****.* Light yellow solid, mp 81.2−82.7 °C. Yield: 71 mg, 72%. ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 9.21 (s, 1H), 8.74 (s, 1H), 8.65 (s, 1H), 7.80−7.65 (m, 3H), 7.43 (t, J = 7.6 Hz, 1H), 7.33 (t, J = 7.6 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6, 298 K): δ = 154.8, 152.2, 144.7, 144.1, 143.9, 141.0, 127.9, 126.0, 123.6, 122.0, 111.5, 106.8. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{12}H_9N_2O$ 197.0715; found, 197.0743.

2-(Benzo[b]thiophen-2-yl)pyrazine, ***50****.*[50] Light yellow solid. Yield: 73 mg, 69%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): 9.11 (s, 1H), 8.59 (s, 1H), 8.48 (d, J = 2 Hz, 1H), 7.96 (s, 1H), 7.92−7.82 (m, 2H), 7.46−7.38 (m, 2H). MS: m/z = 212 $[M]^+$, 159.

2-(Benzo[b]thiophen-2-yl)benzo[d]oxazole, ***51****.*[51] Yellow solid. Yield: 114 mg, 91%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 8.34 (s, 1H), 8.10 (d, J = 8.0 Hz, 1H), 8.04 (s, J = 7.2 Hz, 1H), 7.84−7.77 (m, 2H), 7.58−7.32 (m, 4H). MS: m/z = 251 $[M]^+$, 222, 159, 125.

■ ASSOCIATED CONTENT

Supporting Information

NMR spectra for the important compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: taotu@fudan.edu.cn.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Financial support from the National Natural Science Foundation of China (No. 91127041 and 21172045), the Changjiang Scholars and Innovative Research Team in University (IRT1117), the Shanghai Shuguang Program (No. 11SG04) and Pujiang Program, the Shanghai Leading Academic Discipline Project (B108), and the Department of Chemistry at Fudan University is gratefully acknowledged.

■ REFERENCES

(1) (a) Suzuki, A. *Angew. Chem., Int. Ed.* **2011**, *50*, 6722. (b) *Modern Arylation Methods*; Ackermann, L., Ed.; Wiley-VCH: Weinheim, Germany, 2009; (c) *Metal-Catalyzed Cross-Coupling Reactions*; de Meijere, A., Diederich, F., Eds.; Wiley-VCH: New York, 2004; (d) *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E.-I., Ed.; Wiley-Interscience: New York, 2002.

(2) (a) *The Chemistry of Organozinc Compounds*; Rappoport, Z., Marek, I., Eds.; Wiley: New York, 2006. (b) Boudier, A.; Bromm, L. O.; Lotz, M.; Knochel, P. *Angew. Chem., Int. Ed.* **2000**, *39*, 4414. (c) *Organozinc Reagents, A Practical Approach*; Knochel, P., Jones, P., Eds.; Oxford: New York, 1999. (d) Erdik, E. *Organozinc Reagents in Organic Synthesis*; CRC Press: Boston, 1996.

(3) (a) Jana, R.; Pathak, T. P.; Sigman, M. S. *Chem. Rev.* **2011**, *111*, 1417. (b) Valente, C.; Çalimsiz, S.; Hoi, K. H.; Mallik, D.; Sayah, M.; Organ, M. G. *Angew. Chem., Int. Ed.* **2012**, *51*, 3314. (c) Fortman, G. C.; Nolan, S. P. *Chem. Soc. Rev.* **2011**, *40*, 5151. (d) Manolikakes, G.; Dong, Z.; Mayr, H.; Li, J.; Knochel, P. *Chem.—Eur. J.* **2009**, *15*, 1324. (e) Liu, J.; Deng, Y.; Wang, H.; Zhang, H.; Yu, G.; Wu, B.; Zhang, H.; Li, Q.; Marder, T. B.; Yang, Z.; Lei, A. *Org. Lett.* **2008**, *10*, 2661.

(4) Dai, C.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 2719.

(5) (a) Rudolph, A.; Lautens, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 2656. (b) McGlacken, G. P.; Bateman, L. M. *Chem. Soc. Rev.* **2009**, *38*, 2447.

(6) (a) Melzig, L.; Metzger, A.; Knochel, P. *Chem.—Eur. J.* **2011**, *17*, 2948. (b) Martin, R.; Buchwald, S. L. *Acc. Chem. Res.* **2008**, *41*, 1461. (c) Surry, D. S.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2008**, *47*, 6338. (d) Altenhoff, G.; Goddard, R.; Lehmann, C. W.; Glorius, F. *J. Am. Chem. Soc.* **2004**, *126*, 15195.

(7) (a) Han, C.; Buchwald, S. L. *J. Am. Chem. Soc.* **2009**, *131*, 7532. (b) Manolikakes, G.; Schade, M. A.; Hernandez, C. M.; Mayr, H.; Knochel, P. *Org. Lett.* **2008**, *10*, 2765. (c) Sase, S.; Jaric, M.; Metzger, A.; Malakhov, V.; Knochel, P. *J. Org. Chem.* **2008**, *73*, 7380. (d) Shen, Q.; Shekhar, S.; Stambuli, J. P.; Hartwig, J. F. *Angew. Chem., Int. Ed.* **2005**, *44*, 1371.

(8) (a) Pompeo, M.; Froese, R. D. J.; Hadei, N.; Organ, M. G. *Angew. Chem., Int. Ed.* **2012**, *51*, 11354. (b) Çalimsiz, S.; Organ, M. G. *Chem. Commun.* **2011**, 5181. (c) Çalimsiz, S.; Sayah, M.; Mallik, D.; Organ, M. G. *Angew. Chem., Int. Ed.* **2010**, *49*, 2014. (d) Organ, M. G.; Avola, S.; Dubovyk, I.; Hadei, N.; Kantchev, E. A. B.; O'Brien, C. J.; Valente, C. *Chem.—Eur. J.* **2006**, *12*, 4749.

(9) (a) Fang, W.; Jiang, J.; Xu, Y.; Zhou, J.; Tu, T. *Tetrahedron* **2013**, *69*, 673. (b) Tu, T.; Sun, Z.; Fang, W.; Xu, M.; Zhou, Y. *Org. Lett.* **2012**, *14*, 4250. (c) Tu, T.; Fang, W.; Jiang, J. *Chem. Commun.* **2011**, 12358. (d) Wang, Z.; Feng, X.; Fang, W.; Tu, T. *Synlett* **2011**, 951. (e) Tu, T.; Feng, X.; Wang, Z.; Liu, X. *Dalton Trans.* **2010**, 10598. (f) Tu, T.; Mao, H.; Herbert, C.; Xu, M.; Dötz, K. H. *Chem. Commun.* **2010**, 7796. (g) Tu, T.; Malineni, J.; Bao, X.; Dötz, K. H. *Adv. Synth. Catal.* **2009**, *351*, 1029. (h) Tu, T.; Malineni, J.; Dötz, K. H. *Adv. Synth. Catal.* **2008**, *350*, 1791.

(10) (a) Tu, T.; Fang, W.; Bao, X.; Li, X.; Dötz, K. H. *Angew. Chem., Int. Ed.* **2011**, *50*, 6601. (b) Tu, T.; Bao, X.; Assenmacher, W.; Peterlik, H.; Daniels, J.; Dötz, K. H. *Chem.—Eur. J.* **2009**, *15*, 1853. (c) Tu, T.; Assenmacher, W.; Peterlik, H.; Schnakenburg, G.; Dötz, K. H. *Angew. Chem., Int. Ed.* **2008**, *47*, 7127. (d) Tu, T.; Assenmacher, W.; Peterlik, H.; Weisbarth, R.; Nieger, M.; Dötz, K. H. *Angew. Chem., Int. Ed.* **2007**, *46*, 6368.

(11) (a) Dastgir, S.; Coleman, K. S.; Cowley, A. R.; Green, L. H. M. *Organometallics* **2010**, *29*, 4858. (b) Vasudevan, K. V.; Butorac, R. R.; Abernethy, C. D.; Cowley, A. H. *Dalton Trans.* **2010**, 7401.

(12) (a) Zhu, L.; Gao, T.-T.; Shao, L.-X. *Tetrahedron* **2011**, *67*, 5150. (b) Krasovskiy, A.; Lipshutz, B. H. *Org. Lett.* **2011**, *13*, 3822. (c) Zhou, J.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 12527. (d) Inoue, S.; Yokoo, Y. *J. Organomet. Chem.* **1972**, *39*, 11. (e) Inoue, S.; Furukawa, K. *J. Organomet. Chem.* **1972**, *37*, 25. (f) Inoue, S.; Imanaka, Y. *J. Organomet. Chem.* **1972**, *35*, 1.

(13) Lee, D.-H.; Jin, M.-J. *Org. Lett.* **2011**, *13*, 252.

(14) Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 4176.

(15) (a) Joule, J. A.; Mills, K. *Heterocyclic Chemistry*, 5th ed.; Wiley: Chichester, U.K., 2010. (b) Leurs, R.; Bakker, R. A.; Timmerman, H.; de Esch, I. J. P. *Nat. Rev. Drug Discovery* **2005**, *4*, 107.

(16) (a) Purser, S.; Moore, P. R.; Swallow, S.; Gouverneur, V. *Chem. Soc. Rev.* **2008**, *37*, 320. (b) Amii, H.; Uneyama, K. *Chem. Rev.* **2009**, *109*, 2119 and references therein.

(17) (a) Kinzel, T.; Zhang, Y.; Buchwald, S. L. *J. Am. Chem. Soc.* **2010**, *132*, 14073. (b) Molander, G. A.; Biolatto, B. *J. Org. Chem.* **2003**, *68*, 4302. (c) Ishiyama, T.; Ishida, K.; Miyaura, N. *Tetrahedron* **2001**, *57*, 9813.

(18) Schnürch, M.; Flasik, R.; Khan, A. F.; Spina, M.; Mihovilovic, M. D.; Stanetty, P. *Eur. J. Org. Chem.* **2006**, 3283.

(19) Krasovskiy, A.; Malakhov, V.; Gavryushin, A.; Knochel, P. *Angew. Chem., Int. Ed.* **2006**, *45*, 6040.

(20) Krasovskiy, A.; Knochel, P. *Synthesis* **2006**, *5*, 890.

(21) Zhou, J.; Fu, G. C. *J. Am. Chem. Soc.* **2004**, *126*, 1340.

(22) van den Hoogenband, A.; Lange, J. H. M.; Terpstra, J. W.; Koch, M.; Visser, G. M.; Visser, M.; Korstanje, T. J.; Jastrzebski, J. T. B. H. *Tetrahedron Lett.* **2008**, *49*, 4122.
(23) Xue, F.; Zhao, J.; Hor, T. S. A. *Dalton Trans.* **2011**, *40*, 8935.
(24) Booth, B. L.; El-Fekky, T. A.; Noori, G. F. M. *J. Am. Chem. Soc., Perkin Trans. 1* **1980**, 181.
(25) Batke, B.; Lauterbach, G.; Pritzkow, W.; Sebald, F.; Voerckel, V. *J. Prakt. Chem.* **1988**, *330*, 671.
(26) González-Bobes, F.; Fu, G. C. *J. Am. Chem. Soc.* **2006**, *128*, 5360.
(27) Paschaew.; et al. *Azerb. Khim. Zh.* **1969**, *3*, 73.
(28) Dreher, S. D.; Dormer, P. G.; Sandrock, D. L.; Molander, G. A. *J. Am. Chem. Soc.* **2008**, *130*, 9257.
(29) Molander, G. A.; Colombel, V.; Braz, V. A. *Org. Lett.* **2011**, *13*, 1852.
(30) Yeung, P. Y.; So, C. M.; Lau, C. P.; Kwong, F. Y. *Org. Lett.* **2011**, *13*, 648.
(31) Ito, S.; Fujiwara, Y.; Nakamura, E.; Nakamura, M. *Org. Lett.* **2009**, *11*, 4306.
(32) Amatore, M.; Gosmini, C. *Chem. Commun.* **2008**, 5019.
(33) Martin-Luengo, M. A.; Yates, M.; Rojo, E. S.; Arribas, D. H.; Aguilar, D.; Hitzky, E. R. *Appl. Catal. A-Gen.* **2010**, *387*, 141.
(34) Kondolff, I.; Doucet, H.; Santelli, M. *Organometallics* **2006**, *25*, 5219.
(35) Wang, S.; Qian, Q.; Gong, H. *Org. Lett.* **2012**, *14*, 3352.
(36) Oslob, J. D.; Johnson, R. J.; Cai, H.; Feng, S. Q.; Hu, L.; Kosaka, Y.; Lai, J.; Sivaraja, M.; Tep, S.; Yang, H.; Zaharia, C. A.; Evanchik, M. J.; McDowell, R. S. *ACS Med. Chem. Lett.* **2013**, *4*, 113.
(37) Yamada, Y. M. A.; Sarkar, S. M.; Uozumi, Y. *J. Am. Chem. Soc.* **2012**, *134*, 3190.
(38) Gerber, R.; Blacque, O.; Frech, C. M. *Dalton Trans.* **2011**, *40*, 8996.
(39) Hatakeyama, T.; Hashimoto, S.; Ishizuka, K.; Nakamura, M. *J. Am. Chem. Soc.* **2009**, *131*, 11949.
(40) Diebolt, O.; Braunstein, P.; Nolan, S. P.; Cazin, C. S. J. *Chem. Commun.* **2008**, 3190.
(41) Hanhan, M. E.; Martínez-Máñez, R. M.; Ros-Lis, J. V. *Tetrahedron Lett.* **2012**, *53*, 2388.
(42) Shang, R.; Fu, Y.; Wang, Y.; Xu, Q.; Yu, H.-Z.; Liu, L. *Angew. Chem., Int. Ed.* **2009**, *48*, 9350.
(43) Kondolff, I.; Doucet, H.; Santelli, M. *Synlett* **2005**, *13*, 2057.
(44) Organ, M. G.; Abdel-Hadi, M.; Avola, S.; Hadei, N.; Nasielski, J.; O'Brien, C. J.; Valente, C. *Chem.—Eur. J.* **2007**, *13*, 150.
(45) Verbeeck, S.; Meyers, C.; Franck, P.; Jutand, A.; Maes, B. U. W. *Chem.—Eur. J.* **2010**, *16*, 12831.
(46) Denmark, S. E.; Smith, R. C.; Chang, W.-T.; Muhuhi, J. M. *J. Am. Chem. Soc.* **2009**, *131*, 3104.
(47) Sun, L.-L.; Deng, C.-L.; Tang, R.-Y.; Zhang, X.-G. *J. Org. Chem.* **2011**, *76*, 7546.
(48) Thomas, S. W., III; Venkatesan, K.; Müller, P.; Swager, T. M. *J. Am. Chem. Soc.* **2006**, *128*, 16641.
(49) Qiang, L. G.; Baine, N. H. *Tetrahedron Lett.* **1988**, *29*, 3517.
(50) O'Brien, C. J.; Kantchev, E. A. B.; Valente, C.; Hadei, N.; Chass, G. A.; Lough, A.; Hopkinson, A. C.; Organ, M. G. *Chem.—Eur. J.* **2006**, *12*, 4743.
(51) Pottorf, R. S.; Chadha, N. K.; Katkevics, M.; Ozola, V.; Suna, E.; Ghane, H.; Regberg, T.; Player, M. R. *Tetrahedron Lett.* **2003**, *44*, 175.

dx.doi.org/10.1021/jo400803s | *J. Org. Chem.* XXXX, XXX, XXX−XXX