Palladium-Catalyzed Direct Arylation of Pyrazole Derivatives: A Green Access to 4-Arylpyrazoles

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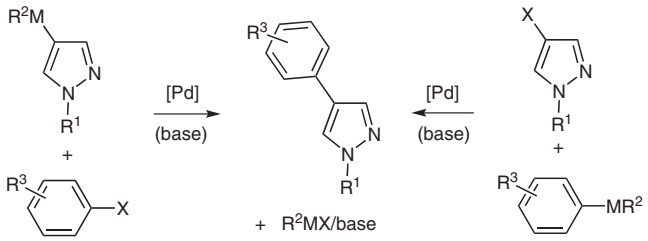
Abstract: 1,3,5-Trisubstituted pyrazoles were found to be suitable partners for palladium-catalyzed direct arylation via C–H activation/functionalization using aryl bromides. The reaction conditions and the catalyst have a determining influence on the yields. The system using palladium(II) acetate as the catalyst, potassium acetate as the base, and *N*,*N*-dimethylacetamide as the solvent promotes selective 4-arylations in moderate to high yields. Several aryl and heteroaryl bromide derivatives have been employed successfully; their electronic properties have a decisive influence on the yields of coupling products. Electron-poor aryl bromides gave satisfactory results, whereas the electron-rich ones gave lower yields.

Key words: pyrazoles, palladium catalysis, C–H arylation, aryl bromide

Heteroaryl derivatives, including arylpyrazoles, are important building blocks in organic synthesis due to their biological properties. The coupling reactions of pyrazoles with aryl halides provides an efficient method for the preparation of these compounds.[1] One of the classical methods to perform such coupling reactions is to employ an aryl halide with an organometallic pyrazole derivative or a halopyrazole with an organometallic aryl derivative using a palladium catalyst (Scheme 1). However, these reactions require the preliminary preparation of organometallic derivatives, such as $ArB(OR)_2$,[2] ArZnX,[3] ArMgX,[4] or $ArSnR_3$,[5] and provide either an organometallic or a salt (MX) as the byproduct.



R^2M = ZnX, MgX, $B(OR)_2$, $SnBu_3$

Scheme 1

Since the discovery by Ohta and co-workers of the palladium-catalyzed coupling of aryl halides with heteroaryl derivatives via C–H bond activation,[6] very exciting results for the coupling of a variety of heteroaryl derivatives with aryl iodides, bromides, and even chlorides have been reported by several groups.[7–15] On the other hand, to our knowledge, the direct coupling of pyrazoles with aryl halides via C–H bond activation/functionalization has attracted much less attention.[16–18] An intramolecular version of this reaction with the activation of the C–H bond in position C3 of a pyrazole has been reported.[16] Using a 4-substituted pyrazole, and palladium(II) acetate as the catalyst, the intramolecular cyclization produces a tetracyclic compound in 75% yield. Recently, Sames and co-workers have established the regioselectivity of the catalytic C–H arylation of pyrazoles.[17] [2-(Trimethylsilyl)ethoxymethyl]pyrazole (SEM-pyrazole) reacted with bromobenzene using palladium(II) acetate (5 mol%) and an electron-rich and congested phosphine di-1-adamantylbutylphosphine [$Bu(Ad)_2P$, 7.5 mol%] as the catalyst, gave a mixture of products, which indicated the higher reactivity of the 5-position relative to the 4-position, and very low reactivity of the 3-position. The arylation of 1-SEM-5-phenylpyrazole was quite selective, taking place at the 4-position to afford 1-SEM-4,5-diphenylpyrazole in 51% yield.

If an example of palladium-catalyzed intermolecular direct 4-arylation of a pyrazole has been described, to the best of our knowledge, the influence of the reaction conditions, palladium source, and loading and also the effect of the nature of the substituents on the aryl halides or on the pyrazole derivatives have not been reported. Here, we wish to report on the palladium-catalyzed 4-arylation of a set of 1,3,5-trisubstituted pyrazoles using of a wide variety of aryl bromides.

Our first goal was to determine the most suitable reaction conditions for the direct coupling of 4-bromoacetophenone with 1,3,5-trimethylpyrazole (**1**) (Table 1). We have already reported the direct 4-arylation of a range of pyrroles, furans, or thiophene derivatives using ligand-less palladium catalysts.[15] Based on these results, the first reactions were performed at 140–150 °C under argon in the presence 0.01–0.05 mol% palladium(II) acetate as the catalyst using several bases and solvents. The formation of product **2a** was observed in most cases, however, we ob-

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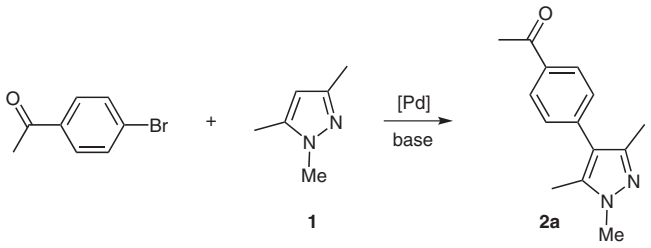
served that the reaction conditions and the nature of the base, solvent, and catalyst have a determining influence on the reaction yield. *N*,*N*-Dimethylacetamide (DMAc) as solvent and using potassium acetate as the base gave the coupling product **2a** in 92% yield, whereas *N*-methylpyrrolidin-2-one, *N*,*N*-dimethylformamide, or dimethyl sulfoxide led to partial conversions of 4-bromoacetophenone and to moderate yields of **2a** (Table 1, entries 1–4). Moreover, with *N*,*N*-dimethylacetamide, high selectivity in favor of the formation of **2a** was observed. Then, we examined the influence of the base for this reaction. Potassium carbonate and cesium carbonate led to the formation of **2a** in 7% and 17% yields, respectively (Table 1, entries 10 and 12). In the presence of palladium(II) acetate (0.5 mol%) as the catalyst, the most suitable base appears to be potassium acetate which gave **2a** in 75% yield, whereas sodium acetate gave **2a** in only 25% yield (Table 1, entries 9 and 13). Then, we examined the influence of the catalyst precursor on this reaction. We performed the coupling with $Pd(OAc)_2$, $PdCl_2(PhCN)_2$, $PdCl_2$, $Pd_2(dba)_3$, or $[PdCl(C_3H_5)]_2$ without added ligand (Table 1, entries 5–9). The best yield was obtained using palladium(II) acetate as the catalyst precursor. For this reaction, the presence of monodentate or bidentate phosphine ligands, such as triphenylphoshine, tricyclohexylphosphine, or 1,2-bis(diphenylphosphino)ethane, did not increase the yield of **2a** (Table 1, entries 14–16).

Then, we tried to evaluate the scope and limitations of this procedure using palladium(II) acetate as the catalyst, potassium acetate as the base, and *N*,*N*-dimethylacetamide as the solvent at 150 °C with several 1,3,5-trisubstituted pyrazole derivatives and aryl bromides (Scheme 2, Tables 2– 6). *para*-Substituted aryl bromides reacted with 1,3,5-trimethylpyrazole (**1**) to give satisfactory results in most cases (Scheme 2, Table 2). Electron-poor aryl bromides such as 4-bromobenzophenone, 4-bromobenzonitrile, or 1-bromo-4-(trifluoromethyl)benzene gave the 4-arylated pyrazoles **2b**–**f**,**h** in 71–84% yields (Table 2, en-

Table 1 Influence of the Reaction Conditions for Palladium-Catalyzed Coupling of 4-Bromoacetophenone with 1,3,5-Trimethylpyrazole

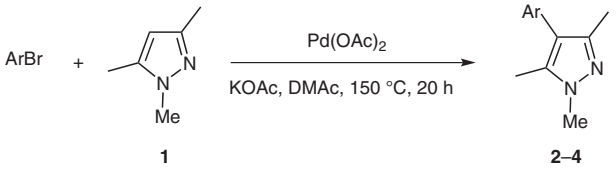


1 **2a**

Entry	Catalyst[a]	Ratio substrate/ catalyst	Solvent	Base	Temp. (°C)	Conv.[b]	Yield[c] (%)
1	$Pd(OAc)_2$	100	NMP	KOAc	140	85	40
2	$Pd(OAc)_2$	100	DMF	KOAc	140	90	51
3	$Pd(OAc)_2$	100	DMSO	KOAc	140	70	31
4	$Pd(OAc)_2$	100	DMAc	KOAc	140	100	92
5	$PdCl_2(PhCN)_2$	100	DMAc	KOAc	140	100	62
6	0.5 $[PdCl(C_3H_5)]_2$	200	DMAc	KOAc	140	100	51
7	$PdCl_2$	200	DMAc	KOAc	150	75	65
8	0.5 $Pd_2(dba)_3$	100	DMAc	KOAc	150	63	50
9	$Pd(OAc)_2$	200	DMAc	KOAc	150	90	75
10	$Pd(OAc)_2$	200	DMAc	K_2CO_3	150	10	7
11	$Pd(OAc)_2$	200	DMAc	$NaHCO_3$	150	0	–
12	$Pd(OAc)_2$	200	DMAc	Cs_2CO_3	150	22	17
13	$Pd(OAc)_2$	200	DMAc	NaOAc	150	35	25
14	$Pd(OAc)_2$, 2 Ph_3P	200	DMAc	KOAc	150	82	60
15	$Pd(OAc)_2$, 2 Cy_3P	200	DMAc	KOAc	150	84	64
16	$Pd(OAc)_2$, dppe	200	DMAc	KOAc	150	60	45

[a] Reagents and conditions: 4-bromoacetophenone (1 mmol), 1,3,5-trimethylpyrazole (**1**, 1.5 mmol), base (2 mmol), 20 h.
[b] Conversion of 4-bromoacetophenone determined by GC and NMR analysis.
[c] Isolated yield.

tries 1–5 and 7). A lower yield was obtained in the presence of 1-bromo-4-nitrobenzene due to the formation of side products (Table 2, entry 6). Slightly deactivated aryl bromides, 1-bromo-4-*tert*-butylbenzene or 4-bromotoluene were also found to give the desired coupling products **2i**,**j** in good yields (Table 2, entries 8 and 9). On the other hand, 4-bromoanisole and especially 1-bromo-4-(dimethylamino)benzene gave the expected compounds **2k**,**l** in low to moderate yields (Table 2, entries 10 and 11). The oxidative addition of the aryl bromides to palladium seems to be the rate-limiting step of the reaction in the presence of this ligand-less catalyst.



1 2–4

Scheme 2

Table 2 Palladium-Catalyzed Reaction of *para*-Substituted Aryl Bromides with 1,3,5-Trimethylpyrazole (**1**) (Scheme 2)[a]

Entry	Ar	Product	Yield[b] (%)
1	4-$OHCC_6H_4$	**2b**	82
2	4-BzC_6H_4	**2c**	80
3	4-$MeO_2CC_6H_4$	**2d**	71
4	4-NCC_6H_4	**2e**	84
5	4-$F_3CC_6H_4$	**2f**	80
6	4-$O_2NC_6H_4$	**2g**	41[c]
7	4-FC_6H_4	**2h**	78[c]
8	4-*t*-BuC_6H_4	**2i**	77[c]
9	4-MeC_6H_4	**2j**	74[c]
10	4-$MeOC_6H_4$	**2k**	55[c]
11	4-$Me_2NC_6H_4$	**2l**	11[c]

[a] Reagents and conditions: $Pd(OAc)_2$ (0.005 mmol), ArBr (1 mmol), 1,3,5-trimethylpyrazole (**1**, 1.5 mmol), KOAc (2 mmol), DMAc, 150 °C, 20 h.
[b] Isolated yields.
[c] $Pd(OAc)_2$ (0.01 mmol).

Next, we examined the reactivity of *meta*- or *ortho*-substituted aryl bromides (Scheme 2, Table 3). As expected, 1-bromo-3,5-bis(trifluoromethyl)benzene or 3-bromobenzaldehyde gave the coupling products **3a**,**b** in good yields (Table 3, entries 1 and 2). *ortho*-Substituents on aryl bromides generally have a more important effect on the rates and yields of palladium-catalyzed reactions due to their steric or coordination properties. However, we observed that 2-bromobenzaldehyde or 2-bromobenzonitrile, also gave high yields of products **3d**,**e** (Table 3, entries 4 and 5). 1,3,5-Trimethylpyrazole (**1**) was also successfully arylated on C4 using sterically congested aryl bromide, 1-bromonaphthalene, as the coupling partner (Table 3, entry 6).

Table 3 Palladium-Catalyzed Reaction of *meta*- or *ortho*-Substituted Aryl Bromides with 1,3,5-Trimethylpyrazole (**1**) (Scheme 2)[a]

Entry	Ar	Product	Yield[b] (%)
1	3,5-$(F_3C)_2C_6H_3$	**3a**	80
2	3-$OHCC_6H_4$	**3b**	74
3	6-methoxy-2-naphthyl	**3c**	78[c]
4	2-$OHCC_6H_4$	**3d**	79
5	2-NCC_6H_4	**3e**	80
6	1-naphthyl	**3f**	76

[a] Reagents and conditions: $Pd(OAc)_2$ (0.005 mmol), ArBr (1 mmol), 1,3,5-trimethylpyrazole (**1**, 1.5 mmol), KOAc (2 mmol), DMAc, 150 °C, 20 h
[b] Isolated yields.
[c] $Pd(OAc)_2$ (0.01 mmol).

Pyridines, quinolines, and pyrimidines are π-electron deficient heterocycles, therefore, their oxidative addition to palladium is generally easy. We observed that the reaction of 1,3,5-trimethylpyrazole (**1**) with 3- or 4-bromopyridines or 3-bromoquinoline gave **4a–c** in 73–80% yields (Scheme 2, Table 4, entries 1–3). Congested heteroaryl bromide, 4-bromoisoquinoline gave **4d** in 78% isolated yield (Table 4, entry 4). 5-Bromopyrimidine also led to the desired 4-arylated pyrazole **4e** in high yield (Table 4, entry 5).

Next, the reactivity of 3,5-dimethyl-1-phenylpyrazole (**5**) was examined (Table 5). To our knowledge, the direct 4-arylation of 1-arylpyrazole has not been reported so far. Such arylations should be useful as some of these compounds, such as Isofezolac or Pyrazolac, have biological properties (nonsteroidal anti-inflammatory drugs). 3,5-Dimethyl-1-phenylpyrazole (**5**) appears to be slightly less reactive than 1,3,5-trimethylpyrazole (**1**). This reactant gave the expected 4-arylated 1-phenylpyrazoles **6a–g** in

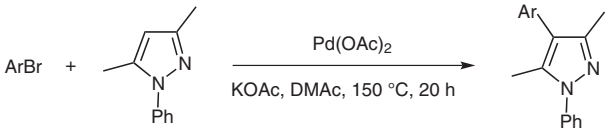
Table 4 Palladium-Catalyzed Reaction of Heteroaryl Bromides with 1,3,5-Trimethylpyrazole (**1**) (Scheme 2)[a]

Entry	Ar	Product	Yield[b] (%)
1	3-pyridyl	**4a**	80
2	4-pyridyl[c]	**4b**	73[d]
3	quinolin-3-yl	**4c**	75
4	isoquinolin-4-yl	**4d**	78
5	pyrimidin-5-yl	**4e**	80

[a] Reagents and conditions: $Pd(OAc)_2$ (0.005 mmol), ArBr (1 mmol), 1,3,5-trimethylpyrazole (**1**, 1.5 mmol), KOAc (2 mmol), DMAc, 150 °C, 20 h.
[b] Isolated yields.
[c] From 4-bromopyridine hydrochloride.
[d] $Pd(OAc)_2$ (0.01 mmol).

58–80% yields. However, the reaction is limited to electron-deficient aryl bromides such as 2- or 4-bromobenzonitrile or 4-bromobenzaldehyde and to bromopyridine derivatives. When we employed 4-bromoanisole as the coupling partner, no formation of 4-arylation product was detected.

Table 5 Palladium-Catalyzed Reaction of Aryl Bromides with 3,5-Dimethyl-1-phenylpyrazole (**5**)[a]



5 **6**

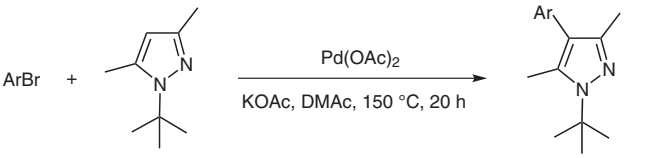
Entry	Ar	Product	Yield[b] (%)
1	4-$OHCC_6H_4$	**6a**	58
2	4-BzC_6H_4	**6b**	70
3	4-NCC_6H_4	**6c**	80
4	2-NCC_6H_4	**6d**	66
5	3-pyridyl	**6e**	69[c]
6	quinolin-3-yl	**6f**	64[c]
7	pyrimidin-5-yl	**6g**	80

[a] Reagents and conditions: $Pd(OAc)_2$ (0.01 mmol), ArBr (1 mmol), 3,5-dimethyl-1-phenylpyrazole (**5**, 1.5 mmol), KOAc (2 mmol), DMAc, 150 °C, 20 h.
[b] Isolated yields.
[c] $Pd(OAc)_2$ (0.02 mmol).

We also studied the reactivity of commercially available 1-*tert*-butyl-3,5-dimethylpyrazole (**7**) for such couplings (Table 6). The use of this reactant, which has not been employed so far for direct arylations, should be very useful in organic synthesis, as the *tert*-butyl substituent can be removed under acidic conditions to give the free N–H pyrazole.[19] The reactions performed in the presence of this pyrazole derivative were found to be very clean using our ligand-less palladium procedure. Both *para*- and *ortho*-substituted aryl bromides and also heteroaryl bromides gave the target compounds **8a–f** in good yields. For these couplings only 0.5 mol% palladium(II) acetate was employed as the catalyst.

Finally, we examined the reactivity of a pyrazole derivative substituted on position 5 by an ester (Schemes 3 and 4). When using the palladium ligand-less procedure, no formation of products **10** or **11** was detected. On the other hand, in the presence of palladium(II) acetate/di-1-adamantylbutylphosphine as the catalyst, the 4-arylated products **10** and **11** were obtained in low yields. In the course of these two reactions, an important amount of the aryl bromide homocoupling products was formed. The presence of such electron-withdrawing function on the pyrazole ring seems to slow down the arylation rate.

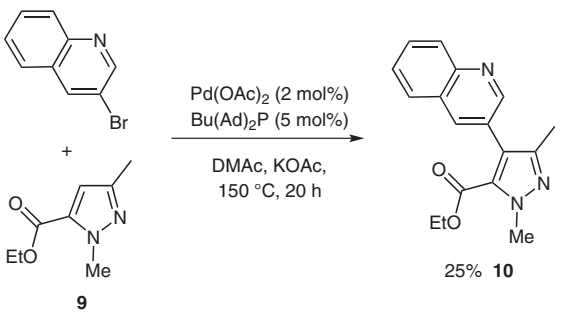
Table 6 Palladium-Catalyzed Reaction of Aryl Bromides with 1-*tert*-Butyl-3,5-dimethylpyrazole (**7**)[a]



7 **8**

Entry	Ar	Product	Yield[b] (%)
1	4-NCC_6H_4	**8a**	79
2	4-$OHCC_6H_4$	**8b**	74
3	4-BzC_6H_4	**8c**	77
4	2-NCC_6H_4	**8d**	73
5	quinolin-3-yl	**8e**	78
6	pyrimidin-5-yl	**8f**	79

[a] Reagents and conditions: $Pd(OAc)_2$ (0.005 mmol), ArBr (1 mmol), 1-*tert*-butyl-3,5-dimethylpyrazole (**7**, 1.5 mmol), KOAc (2 mmol), DMAc, 150 °C, 20 h.
[b] Isolated yields.



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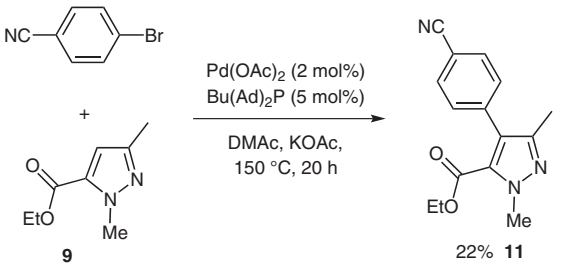
Scheme 3



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Scheme 4

In summary, 1,3,5-trisubstituted pyrazoles are useful reactants in palladium-catalyzed direct arylation using aryl bromides. The use of 0.5–1 mol% palladium(II) acetate with potassium acetate as the base and *N*,*N*-dimethylacetamide as the solvent generally led to high yields of the 4-arylated pyrazoles. The electronic properties of the aryl bromides have a determining influence on the reaction yields. If the electron-withdrawing substituents support the reactions, on the other hand, electron-donating substituents are unfavorable. A wide variety of substituents such

as acetyl, formyl, ester, nitrile, nitro, fluoro, or trifluoromethyl on the aryl bromide are tolerated. This procedure is economically attractive due to the easy access to several pyrazole derivatives and to aryl bromides, to the use of a relatively low loading of a commercially available catalyst, and also to the reduction of number of steps to prepare these compounds. Moreover, with this ligand-less procedure, there is no need to eliminate phosphine derivatives at the end of the reaction.

All reactions were run under argon using vacuum lines and oven-dried Schlenk tubes. Commercial pyrazoles, aryl bromides, analytical grade DMAc, $Pd(OAc)_2$, and KOAc (99%) were employed without purification. ^1H (300 MHz), ^{13}C (75 MHz) spectra were recorded for $CDCl_3$ solns relative to residual $CHCl_3$ (^1H, δ = 7.25 and ^{13}C, δ = 77.0 ppm). Flash chromatography was performed on silica gel (230–400 mesh).

4-Arylpyrazoles 2–4, 6, and 8; General Procedure

The aryl bromide (1 mmol), pyrazole derivative (1.5 or 1.25 mmol), KOAc (0.196 g, 2 mmol), and $Pd(OAc)_2$ (see Tables 2– 6) were dissolved in DMAc (3 mL) under an argon atmosphere. The mixture was stirred at 150 °C for 20 h. The solvent was removed in vacuo and then the crude product was purified by column chromatography (silica gel).

4-(1,3,5-Trimethylpyrazol-4-yl)acetophenone (2a)

Following the typical procedure using 4-bromoacetophenone (0.199 g, 1 mmol), **1** (0.165 g, 1.5 mmol), and $Pd(OAc)_2$ (1.1 mg, 0.005 mmol); yield: 171 mg (75%).

^1H NMR (300 MHz): δ = 7.97 (d, *J* = 8.5 Hz, 2 H), 7.32 (d, *J* = 8.5 Hz, 2 H), 3.76 (s, 3 H), 2.60 (s, 3 H), 2.24 (s, 6 H).

^{13}C NMR (75 MHz): δ = 197.7, 145.1, 139.6, 136.6, 134.9, 129.3, 128.6, 118.3, 36.1, 26.6, 12.6, 10.4.

Anal. Calcd for $C_{14}H_{16}N_2O$: C, 73.66; H, 7.06. Found: C, 73.81; H, 7.14.

4-(1,3,5-Trimethylpyrazol-4-yl)benzaldehyde (2b)

Following the typical procedure using 4-bromobenzaldehyde (0.185 g, 1 mmol), **1** (0.165 g, 1.5 mmol), and $Pd(OAc)_2$ (1.1 mg, 0.005 mmol); yield: 176 mg (82%).

^1H NMR (300 MHz): δ = 10.00 (s, 1 H), 7.90 (d, *J* = 8.5 Hz, 2 H), 7.38 (d, *J* = 8.5 Hz, 2 H), 3.77 (s, 3 H), 2.26 (s, 3 H), 2.25 (s, 3 H).

^{13}C NMR (75 MHz): δ = 191.7, 145.1, 141.0, 136.6, 134.1, 129.8, 129.6, 118.2, 36.0, 12.6, 10.3.

Anal. Calcd for $C_{13}H_{14}N_2O$: C, 72.87; H, 6.59. Found: C, 73.01; H, 6.47.

4-(1,3,5-Trimethylpyrazol-4-yl)benzophenone (2c)

Following the typical procedure using 4-bromobenzophenone (0.261 g, 1 mmol), **1** (0.165 g, 1.5 mmol), and $Pd(OAc)_2$ (1.1 mg, 0.005 mmol); yield: 232 mg (80%).

^1H NMR (300 MHz): δ = 7.82 (d, *J* = 8.5 Hz, 2 H), 7.79 (d, *J* = 8.5 Hz, 2 H), 7.50 (t, *J* = 7.8 Hz, 1 H), 7.43 (t, *J* = 7.8 Hz, 2 H), 7.31 (d, *J* = 8.5 Hz, 2 H), 3.74 (s, 3 H), 2.25 (s, 3 H), 2.24 (s, 3 H).

^{13}C NMR (75 MHz): δ = 196.0, 144.8, 138.8, 137.6, 136.4, 134.9, 132.0, 130.2, 129.7, 128.8, 128.1, 118.1, 35.8, 12.4, 10.2.

Anal. Calcd for $C_{19}H_{18}N_2O$: C, 78.59; H, 6.25. Found: C, 78.64; H, 6.40.

Methyl 4-(1,3,5-Trimethylpyrazol-4-yl)benzoate (2d)

Following the typical procedure using methyl 4-bromobenzoate (0.215 g, 1 mmol), **1** (0.165 g, 1.5 mmol), and $Pd(OAc)_2$ (1.1 mg, 0.005 mmol); yield: 173 mg (71%).

^1H NMR (300 MHz): δ = 8.05 (d, *J* = 8.5 Hz, 2 H), 7.30 (d, *J* = 8.5 Hz, 2 H), 3.92 (s, 3 H), 3.78 (s, 3 H), 2.25 (s, 6 H).

^{13}C NMR (75 MHz): δ = 167.1, 145.1, 139.2, 136.5, 129.7, 129.1, 127.7, 118.4, 52.1, 36.0, 12.6, 10.3.

Anal. Calcd for $C_{14}H_{16}N_2O_2$: C, 68.83; H, 6.60. Found: C, 68.69; H, 6.60.

4-(1,3,5-Trimethylpyrazol-4-yl)benzonitrile (2e)

Following the typical procedure using 4-bromobenzonitrile (0.182 g, 1 mmol), **1** (0.165 g, 1.5 mmol), and $Pd(OAc)_2$ (1.1 mg, 0.005 mmol); yield: 177 mg (84%).

^1H NMR (300 MHz): δ = 7.64 (d, *J* = 8.5 Hz, 2 H), 7.30 (d, *J* = 8.5 Hz, 2 H), 3.75 (s, 3 H), 2.23 (s, 3 H), 2.21 (s, 3 H).

^{13}C NMR (75 MHz): δ = 144.8, 139.3, 136.6, 132.1, 129.6, 118.9, 117.6, 109.4, 35.9, 12.4, 10.2.

Anal. Calcd for $C_{13}H_{13}N_3$: C, 73.91; H, 6.20. Found: C, 73.97; H, 6.30.

4-(4-Trifluoromethylphenyl)-1,3,5-trimethylpyrazole (2f)

Following the typical procedure using 1-bromo-4-(trifluoromethyl)benzene (0.225 g, 1 mmol), **1** (0.165 g, 1.5 mmol), and $Pd(OAc)_2$ (1.1 mg, 0.005 mmol); yield: 203 mg (80%).

^1H NMR (300 MHz): δ = 7.65 (d, *J* = 8.5 Hz, 2 H), 7.36 (d, *J* = 8.5 Hz, 2 H), 3.79 (s, 3 H), 2.26 (s, 6 H).

^{13}C NMR (75 MHz): δ = 144.9, 138.1, 136.5, 129.4, 128.0 (q, *J* = 32.7 Hz), 125.2 (q, *J* = 4.0 Hz), 124.1 (q, *J* = 271.4 Hz), 117.9, 35.9, 12.4, 10.2.

Anal. Calcd for $C_{13}H_{13}F_3N_2$: C, 61.41; H, 5.15. Found: C, 61.52; H, 5.31.

4-(4-Nitrophenyl)-1,3,5-trimethylpyrazole (2g)

Following the typical procedure using 1-bromo-4-nitrobenzene (0.202 g, 1 mmol), **1** (0.165 g, 1.5 mmol), and $Pd(OAc)_2$ (2.2 mg, 0.01 mmol); yield: 95 mg (41%).

^1H NMR (300 MHz): δ = 8.25 (d, *J* = 8.5 Hz, 2 H), 7.38 (d, *J* = 8.5 Hz, 2 H), 3.80 (s, 3 H), 2.29 (s, 3 H), 2.26 (s, 3 H).

^{13}C NMR (75 MHz): δ = 145.8, 145.0, 141.4, 136.8, 129.5, 123.7, 117.3, 36.0, 12.5, 10.3.

Anal. Calcd for $C_{12}H_{13}N_3O_2$: C, 62.33; H, 5.67. Found: C, 62.47; H, 5.48.

4-(4-Fluorophenyl)-1,3,5-trimethylpyrazole (2h)[2e]

Following the typical procedure using 1-bromo-4-fluorobenzene (0.175 g, 1 mmol), **1** (0.165 g, 1.5 mmol), and $Pd(OAc)_2$ (2.2 mg, 0.01 mmol); yield: 159 mg (78%).

^1H NMR (300 MHz): δ = 7.18 (dd, *J* = 8.2, 5.7 Hz, 2 H), 7.07 (t, *J* = 8.2 Hz, 2 H), 3.76 (s, 3 H), 2.20 (s, 6 H).

4-(4-*tert*-Butylphenyl)-1,3,5-trimethylpyrazole (2i)

Following the typical procedure using 1-bromo-4-*tert*-butylbenzene (0.213 g, 1 mmol), **1** (0.165 g, 1.5 mmol), and $Pd(OAc)_2$ (2.2 mg, 0.01 mmol); yield: 187 mg (77%).

^1H NMR (300 MHz): δ = 7.41 (d, *J* = 8.2 Hz, 2 H), 7.16 (d, *J* = 8.2 Hz, 2 H), 3.77 (s, 3 H), 2.25 (s, 3 H), 2.24 (s, 3 H), 1.35 (s, 9 H).

^{13}C NMR (75 MHz): δ = 148.8, 145.0, 136.1, 131.1, 128.9, 125.2, 118.9, 35.9, 34.4, 31.3, 12.5, 10.3.

Anal. Calcd for $C_{16}H_{22}N_2$: C, 79.29; H, 9.15. Found: C, 79.40; H, 9.21.

4-(4-Methylphenyl)-1,3,5-trimethylpyrazole (2j)
Following the typical procedure using 4-bromotoluene (0.171 g, 1 mmol), **1** (0.165 g, 1.5 mmol), and $Pd(OAc)_2$ (2.2 mg, 0.01 mmol); yield: 148 mg (74%).

^{1}H NMR (300 MHz): δ = 7.23 (d, *J* = 8.5 Hz, 2 H), 7.15 (d, *J* = 8.5 Hz, 2 H), 3.79 (s, 3 H), 2.40 (s, 3 H), 2.26 (s, 3 H), 2.25 (s, 3 H).

^{13}C NMR (75 MHz): δ = 144.9, 136.0, 135.7, 131.1, 129.2, 129.0, 119.0, 35.9, 21.1, 12.4, 10.2.

Anal. Calcd for $C_{13}H_{16}N_2$: C, 77.96; H, 8.05. Found: C, 77.99; H, 8.31.

4-(4-Methoxyphenyl)-1,3,5-trimethylpyrazole (2k)[2e]
Following the typical procedure using 4-bromoanisole (0.187 g, 1 mmol), **1** (0.165 g, 1.5 mmol), and $Pd(OAc)_2$ (2.2 mg, 0.01 mmol); yield: 119 mg (55%).

^{1}H NMR (300 MHz): δ = 7.15 (d, *J* = 8.5 Hz, 2 H), 6.94 (d, *J* = 8.5 Hz, 2 H), 3.83 (s, 3 H), 3.77 (s, 3 H), 2.22 (s, 3 H), 2.21 (s, 3 H).

4-[4-(Dimethylamino)phenyl]-1,3,5-trimethylpyrazole (2l)
Following the typical procedure using 1-bromo-4-(dimethylamino)benzene (0.200 g, 1 mmol), **1** (0.165 g, 1.5 mmol), and $Pd(OAc)_2$ (2.2 mg, 0.01 mmol); yield: 25 mg (11%).

^{1}H NMR (300 MHz): δ = 7.11 (d, *J* = 8.5 Hz, 2 H), 7.78 (d, *J* = 8.5 Hz, 2 H), 3.76 (s, 3 H), 2.97 (s, 6 H), 2.23 (s, 3 H), 2.21 (s, 3 H).

^{13}C NMR (75 MHz): δ = 148.9, 145.1, 135.9, 130.2, 122.2, 119.1, 112.5, 40.6, 35.9, 12.4, 10.2.

Anal. Calcd for $C_{14}H_{19}N_3$: C, 73.33; H, 8.35. Found: C, 73.41; H, 8.38.

4-[3,5-Bis(trifluoromethyl)phenyl]-1,3,5-trimethylpyrazole (3a)
Following the typical procedure using 3,5-bis(trifluoromethyl)bromobenzene (0.293 g, 1 mmol), **1** (0.165 g, 1.5 mmol), and $Pd(OAc)_2$ (1.1 mg, 0.005 mmol); yield: 258 mg (80%).

^{1}H NMR (300 MHz): δ = 7.80 (s, 1 H), 7.69 (s, 2 H), 3.82 (s, 3 H), 2.28 (s, 3 H), 2.27 (s, 3 H).

^{13}C NMR (75 MHz): δ = 144.9, 136.7 (d, *J* = 9.8 Hz), 131.7 (q, *J* = 32.6 Hz), 129.1, 129.0, 123.0 (q, *J* = 274.0 Hz), 119.8 (q, *J* = 4.5 Hz), 116.8, 36.1, 12.3, 10.1.

Anal. Calcd for $C_{14}H_{12}F_6N_2$: C, 52.18; H, 3.75. Found: C, 52.01; H, 3.80.

3-(1,3,5-Trimethylpyrazol-4-yl)benzaldehyde (3b)
Following the typical procedure using 3-bromobenzaldehyde (0.185 g, 1 mmol), **1** (0.165 g, 1.5 mmol), and $Pd(OAc)_2$ (1.1 mg, 0.005 mmol); yield: 159 mg (74%).

^{1}H NMR (300 MHz): δ = 10.01 (s, 1 H), 7.75 (d, *J* = 8.5 Hz, 1 H), 7.71 (s, 1 H), 7.53 (t, *J* = 7.7 Hz, 1 H), 7.47 (d, *J* = 8.5 Hz, 1 H), 3.75 (s, 3 H), 2.21 (s, 6 H).

^{13}C NMR (75 MHz): δ = 192.2, 144.8, 136.6, 136.3, 135.3, 135.2, 130.2, 129.0, 127.5, 117.9, 35.9, 12.3, 10.1.

Anal. Calcd for $C_{13}H_{14}N_2O$: C, 72.87; H, 6.59. Found: C, 72.80; H, 6.49.

4-(6-Methoxynaphthalen-2-yl)-1,3,5-trimethylpyrazole (3c)
Following the typical procedure using 2-bromo-6-methoxynaphthalene (0.237 g, 1 mmol), **1** (0.165 g, 1.5 mmol), and $Pd(OAc)_2$ (2.2 mg, 0.01 mmol); yield: 208 mg (78%).

^{1}H NMR (300 MHz): δ = 7.78 (d, *J* = 8.5 Hz, 1 H), 7.75 (d, *J* = 8.5 Hz, 1 H), 7.63 (s, 1 H), 7.40 (dd, *J* = 8.5, 1.7 Hz, 1 H), 7.25–7.15 (m, 2 H), 3.95 (s, 3 H), 3.82 (s, 3 H), 2.33 (s, 3 H), 2.29 (s, 3 H).

^{13}C NMR (75 MHz): δ = 157.5, 145.1, 136.2, 132.9, 129.4, 129.1, 129.0, 128.4, 127.6, 126.6, 119.1, 118.8, 105.6, 55.2, 35.9, 12.4, 10.2.

Anal. Calcd for $C_{17}H_{18}N_2O$: C, 76.66; H, 6.81. Found: C, 76.81; H, 6.59.

2-(1,3,5-Trimethylpyrazol-4-yl)benzaldehyde (3d)
Following the typical procedure using 2-bromobenzaldehyde (0.185 g, 1 mmol), **1** (0.165 g, 1.5 mmol), and $Pd(OAc)_2$ (1.1 mg, 0.005 mmol); yield: 169 mg (79%).

^{1}H NMR (300 MHz): δ = 9.87 (s, 1 H), 8.01 (d, *J* = 8.5 Hz, 1 H), 7.62 (t, *J* = 7.8 Hz, 1 H), 7.45 (t, *J* = 7.8 Hz, 1 H), 7.25 (d, *J* = 8.4 Hz, 1 H), 3.80 (s, 3 H), 2.11 (s, 6 H).

^{13}C NMR (75 MHz): δ = 192.6, 145.8, 137.7, 137.6, 134.4, 133.8, 132.1, 127.5, 127.4, 114.9, 36.1, 12.1, 10.0.

Anal. Calcd for $C_{13}H_{14}N_2O$: C, 72.87; H, 6.59. Found: C, 72.81; H, 6.46.

2-(1,3,5-Trimethylpyrazol-4-yl)benzonitrile (3e)
Following the typical procedure using 2-bromobenzonitrile (0.182 g, 1 mmol), **1** (0.165 g, 1.5 mmol), and $Pd(OAc)_2$ (1.1 mg, 0.005 mmol); yield: 169 mg (80%).

^{1}H NMR (300 MHz): δ = 7.72 (d, *J* = 8.5 Hz, 1 H), 7.60 (t, *J* = 7.8 Hz, 1 H), 7.38 (t, *J* = 7.8 Hz, 1 H), 7.31 (d, *J* = 8.5 Hz, 1 H), 3.78 (s, 3 H), 2.18 (s, 3 H), 2.17 (s, 3 H).

^{13}C NMR (75 MHz): δ = 145.3, 138.2, 137.4, 133.1, 132.5, 131.6, 127.1, 118.5, 116.1, 113.5, 36.0, 12.2, 10.5.

Anal. Calcd for $C_{13}H_{13}N_3$: C, 73.91; H, 6.20. Found: C, 73.99; H, 6.14.

1,3,5-Trimethyl-4-(naphthalen-1-yl)pyrazole (3f)
Following the typical procedure using 1-bromonaphthalene (0.207 g, 1 mmol), **1** (0.165 g, 1.5 mmol), and $Pd(OAc)_2$ (1.1 mg, 0.005 mmol); yield: 180 mg (76%).

^{1}H NMR (300 MHz): δ = 7.90 (d, *J* = 8.5 Hz, 1 H), 7.83 (d, *J* = 8.5 Hz, 1 H), 7.65 (d, *J* = 8.5 Hz, 1 H), 7.55–7.35 (m, 3 H), 7.30 (d, *J* = 8.5 Hz, 1 H), 3.84 (s, 3 H), 2.06 (s, 3 H), 2.05 (s, 3 H).

^{13}C NMR (75 MHz): δ = 146.2, 137.4, 133.8, 132.8, 131.7, 128.4, 128.3, 127.4, 126.1, 125.8, 125.6, 125.4, 117.3, 36.0, 12.3, 10.2.

Anal. Calcd for $C_{16}H_{16}N_2$: C, 81.32; H, 6.82. Found: C, 81.40; H, 6.78.

3-(1,3,5-Trimethylpyrazol-4-yl)pyridine (4a)
Following the typical procedure using 3-bromopyridine (0.158 g, 1 mmol), **1** (0.165 g, 1.5 mmol), and $Pd(OAc)_2$ (1.1 mg, 0.005 mmol); yield: 150 mg (80%).

^{1}H NMR (300 MHz): δ = 8.48 (m, 2 H), 7.52 (dt, *J* = 7.7, 2.1 Hz, 1 H), 7.32 (dd, *J* = 7.7, 4.9 Hz, 1 H), 3.76 (s, 3 H), 2.22 (s, 3 H), 2.21 (s, 3 H).

^{13}C NMR (75 MHz): δ = 150.1, 147.2, 145.2, 136.7, 136.5, 130.2, 123.3, 115.6, 36.0, 12.3, 10.2.

Anal. Calcd for $C_{11}H_{13}N_3$: C, 70.56; H, 7.00. Found: C, 70.47; H, 6.98.

4-(1,3,5-Trimethylpyrazol-4-yl)pyridine (4b)
Following the typical procedure using 4-bromopyridine hydrochloride (0.194 g, 1 mmol), **1** (0.165 g, 1.5 mmol), and $Pd(OAc)_2$ (2.2 mg, 0.01 mmol); yield: 137 mg (73%).

^{1}H NMR (300 MHz): δ = 8.59 (m, 2 H), 7.19 (d, *J* = 5.7 Hz, 2 H), 3.78 (s, 3 H), 2.28 (s, 3 H), 2.26 (s, 3 H).

^{13}C NMR (75 MHz): δ = 148.9, 145.2, 143.0, 137.1, 124.0, 116.5, 36.0, 12.5, 10.4.

Anal. Calcd for $C_{11}H_{13}N_3$: C, 70.56; H, 7.00. Found: C, 70.49; H, 6.92.

3-(1,3,5-Trimethylpyrazol-4-yl)quinoline (4c)
Following the typical procedure using 3-bromoquinoline (0.208 g, 1 mmol), **1** (0.165 g, 1.5 mmol), and $Pd(OAc)_2$ (1.1 mg, 0.005 mmol); yield: 178 mg (75%).

^{1}H NMR (300 MHz): δ = 8.79 (d, *J* = 1.5 Hz, 1 H), 8.06 (d, *J* = 8.5 Hz, 1 H), 7.90 (d, *J* = 1.5 Hz, 1 H), 7.75 (d, *J* = 8.5 Hz, 1 H), 7.62 (t, *J* = 7.8 Hz, 1 H), 7.47 (t, *J* = 7.8 Hz, 1 H), 3.74 (s, 3 H), 2.23 (s, 3 H), 2.22 (s, 3 H).

^{13}C NMR (75 MHz): δ = 151.6, 146.4, 145.2, 136.8, 134.9, 129.0, 128.9, 127.9, 127.4, 127.3, 126.6, 115.5, 35.9, 12.2, 10.1.

Anal. Calcd for $C_{15}H_{15}N_3$: C, 75.92; H, 6.37. Found: C, 76.01; H, 6.22.

4-(1,3,5-Trimethylpyrazol-4-yl)isoquinoline (4d)
Following the typical procedure using 4-bromoisoquinoline (0.208 g, 1 mmol), **1** (0.165 g, 1.5 mmol), and $Pd(OAc)_2$ (1.1 mg, 0.005 mmol); yield: 185 mg (78%).

^{1}H NMR (300 MHz): δ = 9.25 (s, 1 H), 8.32 (s, 1 H), 8.04 (d, *J* = 8.0 Hz, 1 H), 7.70-7.45 (m, 3 H), 3.83 (s, 3 H), 2.06 (s, 3 H), 2.04 (s, 3 H).

^{13}C NMR (75 MHz): δ = 151.0, 146.4, 143.1, 137.9, 135.6, 130.8, 128.1, 127.4, 124.9, 113.3, 35.9, 12.1, 10.1.

Anal. Calcd for $C_{15}H_{15}N_3$: C, 75.92; H, 6.37. Found: C, 75.81; H, 6.30.

5-(1,3,5-Trimethylpyrazol-4-yl)pyrimidine (4e)
Following the typical procedure using 5-bromopyrimidine (0.159 g, 1 mmol), **1** (0.165 g, 1.5 mmol), and $Pd(OAc)_2$ (1.1 mg, 0.005 mmol); yield: 151 mg (80%).

^{1}H NMR (300 MHz): δ = 9.03 (s, 1 H), 8.56 (s, 2 H), 3.72 (s, 3 H), 2.19 (s, 3 H), 2.17 (s, 3 H).

^{13}C NMR (75 MHz): δ = 156.4, 156.2, 145.1, 137.0, 128.3, 111.9, 36.0, 12.2, 10.1.

Anal. Calcd for $C_{10}H_{12}N_4$: C, 63.81; H, 6.43. Found: C, 63.89; H, 6.54.

4-(3,5-Dimethyl-1-phenylpyrazol-4-yl)benzaldehyde (6a)
Following the typical procedure using 4-bromobenzaldehyde (0.185 g, 1 mmol), **5** (0.258 g, 1.5 mmol), and $Pd(OAc)_2$ (2.2 mg, 0.01 mmol); yield: 160 mg (58%).

^{1}H NMR (300 MHz): δ = 10.06 (s, 1 H), 7.97 (d, *J* = 8.5 Hz, 2 H), 7.55–7.40 (m, 7 H), 2.39 (s, 3 H), 2.35 (s, 3 H).

^{13}C NMR (75 MHz): δ = 191.8, 147.0, 140.5, 139.5, 136.8, 134.3, 129.9, 129.7, 129.1, 127.8, 125.0, 119.8, 12.8, 11.9.

Anal. Calcd for $C_{18}H_{16}N_2O$: C, 78.24; H, 5.84. Found: C, 78.30; H, 5.75.

4-(3,5-Dimethyl-1-phenylpyrazol-4-yl)benzophenone (6b)
Following the typical procedure using 4-bromobenzophenone (0.261 g, 1 mmol), **5** (0.258 g, 1.5 mmol), and $Pd(OAc)_2$ (2.2 mg, 0.01 mmol); yield: 247 mg (70%).

^{1}H NMR (300 MHz): δ = 7.82 (d, *J* = 8.5 Hz, 2 H), 7.78 (d, *J* = 8.5 Hz, 2 H), 7.54 (t, *J* = 7.8 Hz, 1 H), 7.52–7.40 (m, 9 H), 2.41 (s, 3 H), 2.36 (s, 3 H).

^{13}C NMR (75 MHz): δ = 196.2, 147.0, 139.5, 138.4, 137.6, 136.7, 135.3, 132.2, 130.4, 129.9, 129.1, 129.0, 128.2, 127.6, 124.9, 119.9, 12.7, 11.9.

Anal. Calcd for $C_{24}H_{20}N_2O$: C, 81.79; H, 5.72. Found: C, 81.59; H, 5.99.

4-(3,5-Dimethyl-1-phenylpyrazol-4-yl)benzonitrile (6c)
Following the typical procedure using 4-bromobenzonitrile (0.182 g, 1 mmol), **5** (0.258 g, 1.5 mmol), and $Pd(OAc)_2$ (2.2 mg, 0.01 mmol); yield: 219 mg (80%).

^{1}H NMR (300 MHz): δ = 7.74 (d, *J* = 8.5 Hz, 2 H), 7.50–7.40 (m, 7 H), 2.36 (s, 3 H), 2.33 (s, 3 H).

^{13}C NMR (75 MHz): δ = 146.9, 139.4, 138.9, 136.8, 132.3, 129.8, 129.1, 127.8, 125.0, 119.3, 119.0, 109.8, 12.7, 11.8.

Anal. Calcd for $C_{18}H_{15}N_3$: C, 79.10; H, 5.53. Found: C, 79.22; H, 5.57.

2-(3,5-Dimethyl-1-phenylpyrazol-4-yl)benzonitrile (6d)
Following the typical procedure using 2-bromobenzonitrile (0.182 g, 1 mmol), **5** (0.258 g, 1.5 mmol), and $Pd(OAc)_2$ (2.2 mg, 0.01 mmol); yield: 180 mg (66%).

^{1}H NMR (300 MHz): δ = 7.79 (d, *J* = 8.5 Hz, 1 H), 7.67 (t, *J* = 7.7 Hz, 1 H), 7.60–7.30 (m, 7 H), 2.30 (s, 3 H), 2.28 (s, 3 H).

^{13}C NMR (75 MHz): δ = 147.2, 139.5, 137.8, 137.7, 133.2, 132.6, 131.7, 129.1, 127.7, 127.4, 125.0, 118.5, 117.8, 113.6, 12.4, 11.9.

Anal. Calcd for $C_{18}H_{15}N_3$: C, 79.10; H, 5.53. Found: C, 79.20; H, 5.64.

3-(3,5-Dimethyl-1-phenylpyrazol-4-yl)pyridine (6e)
Following the typical procedure using 3-bromopyridine (0.158 g, 1 mmol), **5** (0.258 g, 1.5 mmol), and $Pd(OAc)_2$ (4.4 mg, 0.02 mmol); yield: 172 mg (69%).

^{1}H NMR (300 MHz): δ = 8.59 (s, 1 H), 8.54 (d, *J* = 4.9 Hz, 1 H), 7.63 (d, *J* = 7.9 Hz, 1 H), 7.50–7.30 (m, 6 H), 2.32 (s, 3 H), 2.29 (s, 3 H).

^{13}C NMR (75 MHz): δ = 150.3, 147.6, 147.2, 139.6, 136.9, 136.6, 129.7, 129.1, 127.7, 125.0, 123.4, 117.3, 12.1, 11.3.

Anal. Calcd for $C_{16}H_{15}N_3$: C, 77.08; H, 6.06. Found: C, 77.01; H, 6.14.

3-(3,5-Dimethyl-1-phenylpyrazol-4-yl)quinoline (6f)
Following the typical procedure using 3-bromoquinoline (0.208 g, 1 mmol), **5** (0.258 g, 1.5 mmol), and $Pd(OAc)_2$ (4.4 mg, 0.02 mmol); yield: 192 mg (64%).

^{1}H NMR (300 MHz): δ = 8.93 (d, *J* = 2.0 Hz, 1 H), 8.13 (d, *J* = 8.5 Hz, 1 H), 8.05 (d, *J* = 1.9 Hz, 1 H), 7.84 (d, *J* = 8.5 Hz, 1 H), 7.75–7.30 (m, 7 H), 2.38 (s, 3 H), 2.34 (s, 3 H).

^{13}C NMR (75 MHz): δ = 151.7, 147.4, 146.7, 139.6, 137.1, 135.3, 129.3, 129.2, 129.1, 128.0, 127.7, 127.6, 127.0, 126.9, 124.9, 117.4, 12.6, 11.7.

Anal. Calcd for $C_{20}H_{17}N_3$: C, 80.24; H, 5.72. Found: C, 80.30; H, 5.94.

5-(3,5-Dimethyl-1-phenylpyrazol-4-yl)pyrimidine (6g)
Following the typical procedure using 5-bromopyrimidine (0.159 g, 1 mmol), **5** (0.258 g, 1.5 mmol), and $Pd(OAc)_2$ (2.2 mg, 0.01 mmol); yield: 200 mg (80%).

^{1}H NMR (300 MHz): δ = 9.18 (s, 1 H), 8.76 (s, 2 H), 7.50–7.30 (m, 5 H), 2.36 (s, 3 H), 2.33 (s, 3 H).

^{13}C NMR (75 MHz): δ = 156.7, 156.6, 147.1, 139.3, 137.3, 129.2, 128.2, 128.0, 125.0, 113.7, 12.5, 11.6.

Anal. Calcd for $C_{15}H_{14}N_4$: C, 71.98; H, 5.64. Found: C, 71.79; H, 5.80.

4-(1-*tert*-Butyl-3,5-dimethylpyrazol-4-yl)benzonitrile (8a)
Following the typical procedure using 4-bromobenzonitrile (0.182 g, 1 mmol), **7** (0.228 g, 1.5 mmol), and $Pd(OAc)_2$ (1.1 mg, 0.005 mmol); yield: 200 mg (79%).

^{1}H NMR (300 MHz): δ = 7.68 (d, *J* = 8.5 Hz, 2 H), 7.33 (d, *J* = 8.5 Hz, 2 H), 2.39 (s, 3 H), 2.21 (s, 3 H), 1.68 (s, 9 H).

^{13}C NMR (75 MHz): δ = 142.9, 139.6, 135.6, 132.0, 130.3, 119.8, 119.0, 109.4, 59.7, 30.1, 13.2, 12.5.

Anal. Calcd for $C_{16}H_{19}N_3$: C, 75.85; H, 7.56. Found: C, 75.80; H, 7.47.

4-(1-*tert*-Butyl-3,5-dimethylpyrazol-4-yl)benzaldehyde (8b)
Following the typical procedure using 4-bromobenzaldehyde (0.185 g, 1 mmol), **7** (0.228 g, 1.5 mmol), and $Pd(OAc)_2$ (1.1 mg, 0.005 mmol); yield: 190 mg (74%).

^{1}H NMR (300 MHz): δ = 10.01 (s, 1 H), 7.89 (d, *J* = 8.2 Hz, 2 H), 7.37 (d, *J* = 8.2 Hz, 2 H), 2.39 (s, 3 H), 2.22 (s, 3 H), 1.66 (s, 9 H).

^{13}C NMR (75 MHz): δ = 191.9, 143.1, 141.3, 135.7, 134.1, 130.3, 129.7, 120.3, 59.7, 30.2, 13.4, 12.6.

Anal. Calcd for $C_{16}H_{20}N_2O$: C, 74.97; H, 7.86. Found: C, 74.81; H, 7.80.

4-(1-*tert*-Butyl-3,5-dimethylpyrazol-4-yl)benzophenone (8c)
Following the typical procedure using 4-bromobenzophenone (0.261 g, 1 mmol), **7** (0.228 g, 1.5 mmol), and $Pd(OAc)_2$ (1.1 mg, 0.005 mmol); yield: 256 mg (77%).

^{1}H NMR (300 MHz): δ = 7.88 (d, *J* = 8.2 Hz, 2 H), 7.85 (d, *J* = 8.2 Hz, 2 H), 7.59 (t, *J* = 7.8 Hz, 1 H), 7.51 (d, *J* = 8.2 Hz, 2 H), 7.36 (d, *J* = 8.2 Hz, 2 H), 2.44 (s, 3 H), 2.27 (s, 3 H), 1.69 (s, 9 H).

^{13}C NMR (75 MHz): δ = 196.0, 144.8, 138.8, 137.6, 136.4, 134.9, 132.0, 130.2, 129.7, 128.8, 128.1, 118.1, 35.8, 12.4, 10.2.

Anal. Calcd for $C_{22}H_{24}N_2O$: C, 79.48; H, 7.28. Found: C, 79.58; H, 7.37.

2-(1-*tert*-Butyl-3,5-dimethylpyrazol-4-yl)benzonitrile (8d)
Following the typical procedure using 2-bromobenzonitrile (0.182 g, 1 mmol), **7** (0.228 g, 1.5 mmol), and $Pd(OAc)_2$ (1.1 mg, 0.005 mmol); yield: 185 mg (73%).

^{1}H NMR (300 MHz): δ = 7.73 (d, *J* = 8.5 Hz, 1 H), 7.58 (t, *J* = 7.8 Hz, 1 H), 7.37 (t, *J* = 7.8 Hz, 1 H), 7.31 (d, *J* = 8.5 Hz, 1 H), 2.31 (s, 3 H), 2.13 (s, 3 H), 1.66 (s, 9 H).

^{13}C NMR (75 MHz): δ = 143.4, 138.6, 136.6, 133.0, 132.4, 131.9, 127.0, 118.5, 118.3, 113.9, 59.8, 30.1, 13.6, 12.3.

Anal. Calcd for $C_{16}H_{19}N_3$: C, 75.85; H, 7.56. Found: C, 75.91; H, 7.49.

3-(1-*tert*-Butyl-3,5-dimethylpyrazol-4-yl)quinoline (8e)
Following the typical procedure using 3-bromoquinoline (0.208 g, 1 mmol), **7** (0.228 g, 1.5 mmol), and $Pd(OAc)_2$ (1.1 mg, 0.005 mmol); yield: 218 mg (78%).

^{1}H NMR (300 MHz): δ = 8.79 (d, *J* = 2.0 Hz, 1 H), 8.08 (d, *J* = 8.5 Hz, 1 H), 7.92 (d, *J* = 2.0 Hz, 1 H), 7.76 (d, *J* = 8.5 Hz, 1 H), 7.64 (t, *J* = 7.8 Hz, 1 H), 7.48 (t, *J* = 7.8 Hz, 1 H), 2.37 (s, 3 H), 2.22 (s, 3 H), 1.64 (s, 9 H).

^{13}C NMR (75 MHz): δ = 152.2, 146.4, 143.4, 135.9, 135.5, 129.0, 128.8, 127.9, 127.6, 127.4, 126.6, 117.7, 59.6, 30.0, 13.2, 12.4.

Anal. Calcd for $C_{18}H_{21}N_3$: C, 77.38; H, 7.58. Found: C, 77.32; H, 7.39.

5-(1-*tert*-Butyl-3,5-dimethylpyrazol-4-yl)pyrimidine (8f)
Following the typical procedure using 5-bromopyrimidine (0.159 g, 1 mmol), **7** (0.228 g, 1.5 mmol), and $Pd(OAc)_2$ (1.1 mg, 0.005 mmol); yield: 182 mg (79%).

^{1}H NMR (300 MHz): δ = 9.10 (s, 1 H), 8.59 (s, 2 H), 2.36 (s, 3 H), 2.18 (s, 3 H), 1.64 (s, 9 H).

^{13}C NMR (75 MHz): δ = 157.1, 156.3, 143.3, 136.2, 128.6, 114.1, 60.0, 30.1, 13.2, 12.3.

Anal. Calcd for $C_{13}H_{18}N_4$: C, 67.80; H, 7.88. Found: C, 67.64; H, 7.98.

Ethyl 1,3-Dimethyl-4-(quinolin-3-yl)pyrazole-5-carboxylate (10)
3-Bromoquinoline (0.208 g, 1 mmol), ethyl 1,3-dimethylpyrazole-5-carboxylate (**9**, 0.210 g, 1.25 mmol), KOAc (0.196 g, 2 mmol), $Bu(Ad)_2P$ (18 mg, 0.05 mmol), and $Pd(OAc)_2$ (4.4 mg, 0.02 mmol) were dissolved in DMAc (3 mL) under an argon atmosphere. The mixture was stirred at 150 °C for 20 h. The solvent was removed in vacuo, then the crude product was purified by column chromatography (silica gel) to give **10**; yield: 74 mg (25%).

^{1}H NMR (300 MHz): δ = 8.79 (d, *J* = 2.0 Hz, 1 H), 8.10 (d, *J* = 8.5 Hz, 1 H), 8.00 (d, *J* = 2.0 Hz, 1 H), 7.80 (d, *J* = 8.5 Hz, 1 H), 7.70 (t, *J* = 7.8 Hz, 1 H), 7.54 (t, *J* = 7.8 Hz, 1 H), 4.17 (s, 3 H), 4.10 (q, *J* = 7.5 Hz, 2 H), 2.20 (s, 3 H), 0.94 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (75 MHz): δ = 159.8, 152.3, 146.8, 146.3, 136.0, 130.4, 129.3, 129.2, 127.6, 127.4, 126.7, 126.5, 121.5, 60.9, 39.8, 13.6, 11.9.

Anal. Calcd for $C_{17}H_{17}N_3O_2$: C, 69.14; H, 5.80. Found: C, 69.30; H, 5.71.

Ethyl 4-(4-Cyanophenyl)-1,3-dimethylpyrazole-5-carboxylate (11)
4-Bromobenzonitrile (0.182 g, 1 mmol), ethyl 1,3-dimethylpyrazole-5-carboxylate (**9**, 0.210 g, 1.25 mmol), KOAc (0.196 g, 2 mmol), $Bu(Ad)_2P$ (18 mg, 0.05 mmol), and $Pd(OAc)_2$ (4.4 mg, 0.02 mmol) were dissolved in DMAc (3 mL) under an argon atmosphere. The mixture was stirred at 150 °C for 20 h. The solvent was removed in vacuo, then the crude product was purified by column chromatography (silica gel) to give **11**; yield: 59 mg (22%).

^{1}H NMR (300 MHz): δ = 7.68 (d, *J* = 8.0 Hz, 2 H), 7.37 (d, *J* = 8.0 Hz, 2 H), 4.18 (q, *J* = 7.5 Hz, 2 H), 4.16 (s, 3 H), 2.16 (s, 3 H), 1.07 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (75 MHz): δ = 159.7, 145.5, 138.4, 131.5, 130.9, 130.1, 123.5, 118.8, 110.8, 61.0, 39.7, 13.6, 11.8.

Anal. Calcd for $C_{15}H_{15}N_3O_2$: C, 66.90; H, 5.61. Found: C, 67.01; H, 5.57.

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