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Palladium Catalyzed Arylation and Benzylation of Nitroarenes Using Aryl Sulfonates and Benzyl Acetates

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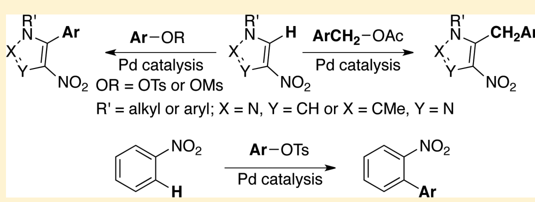
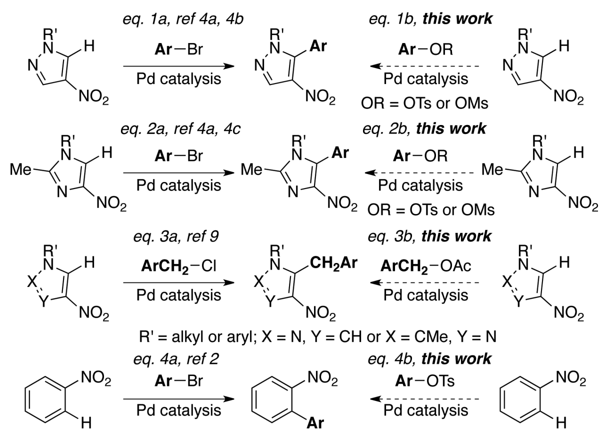
Supporting Information

ABSTRACT: Pd-catalyzed arylation or benzylation of nitroazoles using aryl sulfonates or benzyl acetates is described. Electronically varied aryl tosylates and mesylates, as well as benzyl acetates, afford the arylated and benzylated products. Arylation of nitrobenzene is also reported. The relative rate for the arylation of halides is greater than that of tosylates using the reported reaction parameters. These studies enhance the scope of electrophiles for nitroarene arylations and benzylations, which was hitherto limited to the use of halide electrophiles.



Nitroarenes are important building blocks for the synthesis of pharmaceuticals, agrochemicals, polymers, and fine chemicals.[1,2] Many nitroarenes are readily available at low cost via nitration of arenes.[2] Reduction of the nitro group serves as a versatile handle for structural elaboration through cross-coupling and functional group transformation of the resulting amino group.[3] In lieu of these applications of nitroarenes, a few reports have detailed the arylation of nitroazoles (Schemes 1a and 2a)[4] and nitrobenzene derivatives (Scheme 4a)[2,5] using halide electrophiles.[6−8] The allylation and benzylation of nitroazoles using allyl acetate and benzyl chloride, respectively, has also been realized (Scheme 3a).[9] Recently there have been increasing reports on the use of C−O electrophiles in place of halides for C−C bond formations.[8,10,11] The use of C−O electrophiles instead of halides presents several advantages including: (i) the availability of alcohols from natural sources, (ii) ready access of various *ortho*-substituted phenol derivatives using directed *ortho*-metalation, and (iii) requirement for different catalyst/ligand combinations than are used with halides, thereby presenting an opportunity to engage the C−X (X = halide) and C−O electrophiles at different stages in the context of multistep synthesis.[10,11] As part of our program on transition metal catalyzed functionalizations using C−O electrophiles,[12] we report herein the first general method for the direct arylation and benzylation of nitropyrazoles and nitroimidazoles using aryl sulfonates[11,13,14] and benzyl acetates (Schemes 1b−3b). A brief scope for the arylation of nitrobenzene is also described (Scheme 4b). Notably, functionalized pyrazoles, imidazoles, and nitrobenzene derivatives find applications in the synthesis of pharmaceuticals, agrochemicals, or ligands for transition metals.[1,9,4c]

Scheme 1. Literature Precedent and Present Study



Our studies commenced with the optimization of the arylation of nitropyrazole **1** using 2-naphthyl tosylate. As shown in Table 1, product **1a** can be obtained in the presence of $Pd(OAc)_2$ with XPhos or SPhos as ligands (entries 4 and 5). In contrast to the analogous reaction with halide electrophiles[4] the use of PPh_3 does not lead to **1a**. Additionally, the bidentate dcype ligand, which is effective for arylations of arenes using tosylates and mesylates,[12a,c] does not promote the arylation of nitropyrazole (entry 6). Substrate **1** has two distinct C−H bonds (H_a and H_b) that can undergo arylation. Consistent with previous reports on arylation using aryl halides[4] product **1a** is derived via the preferential arylation of the more acidic C−H_a bond.[15] Unlike arylations using aryl bromides,[4] transformations using aryl tosylates do not require copper(I) additives. Carbonate bases are effective at promoting the transformation (entries 4 and 7). Increasing the temperature leads to diminished yield of **1a**. Notably, 5−10% of diarylation product (**1aa**) is formed via functionalization of both C−H_a and C−H_b regardless of the temperature (entries 4, 5, 7, and 8).[16] No product is obtained in the absence of the $Pd(OAc)_2$ or the

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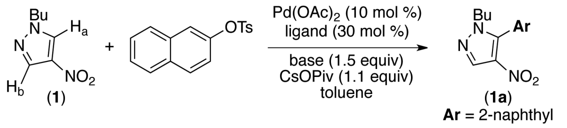
Table 1. Optimization of Nitropyrazole Arylation



entry	ligand	base	T (°C)	GC yield (%)[a]
1	PCy_3HBF_4	Cs_2CO_3	80	0
2	$P^tBu_3HBF_4$	Cs_2CO_3	80	0
3	PPh_3	Cs_2CO_3	80	0
4	X-Phos	Cs_2CO_3	80	89
5	S-Phos	Cs_2CO_3	80	88
6	dcype	Cs_2CO_3	80	0
7	X-Phos	K_2CO_3	80	87
8	X-Phos	Cs_2CO_3	120	56
9[b]	X-Phos	Cs_2CO_3	80	0
10	none	Cs_2CO_3	80	0

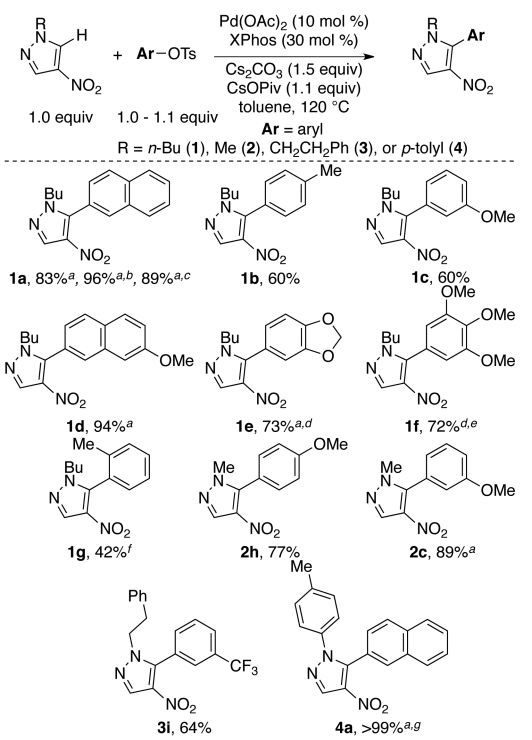
[a]Calibrated GC yields against hexadecane as the internal standard. [b]Reaction without $Pd(OAc)_2$ catalyst.

ligand (entries 9 and 10). However, comparable yields of **1a** are obtained with or without CsOPiv (Scheme 2). Importantly, use of *N*-methyl pyrazole in these arylations affords only trace product, suggesting the importance of the nitro group for efficiency of arylations using nitroazoles.

Scheme 2 depicts the scope of nitropyrazole arylation with respect to the substrate and the electrophile. The optimal temperature for these transformations (80 °C versus 120 °C) varied based on the nature of the aryl tosylate. Arylated products are obtained in good to excellent yields using electronically varied aromatic tosylates. Furthermore, pyrazole substrates bearing various *N*-alkyl (*N*-butyl (**1a**–**1g**), *N*-Me (**2c** and **2h**), and *N*-CH_2CH_2Ph (**3i**)) or *N*-aryl groups (**4a**) undergo arylation to afford the corresponding products in good yields.[17]

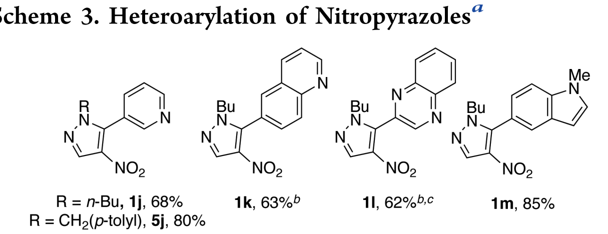
Heterocylic tosylates also couple with nitropyrazoles under the optimal conditions. For example, the use of tosylated pyridine, quinoline, and quinoxaline affords products **1j** (and **5j**), **1k**, and **1l**, respectively in good yields (Scheme 3). Furthermore, **1m** bearing a π-rich heterocycle is also obtained in good yield.[18]

Scheme 2. Scope of Nitropyrazole Arylations



[a]Conducted at 80 °C. [b]Without CsOPiv. [c]Reaction set up outside the glovebox under inert atmosphere. [d]*p*-Xylene used as solvent. [e]1.1 equiv of azole and 1.0 equiv of tosylate used. [f]General conditions with $Pd(OAc)_2$ (0.15 equiv) and XPhos (0.45 equiv). [g]NMR yield against 1,4-dinitrobenzene as the standard.

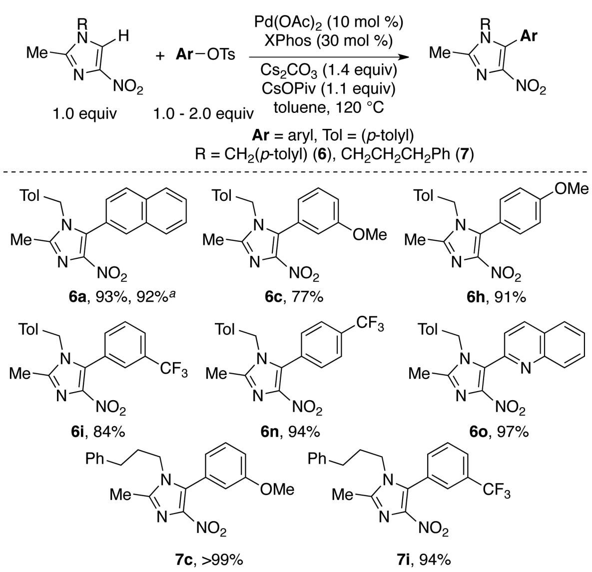
Scheme 3. Heteroarylation of Nitropyrazoles[a]



[a]Reaction conditions: Azole (1.0 equiv), tosylate (1.05–1.1 equiv), $Pd(OAc)_2$ (0.1 equiv), XPhos (0.3 equiv), Cs_2CO_3 (1.5 equiv), CsOPiv (1.1 equiv), *p*-xylene (or toluene), 120 °C. [b]Conducted at 80 °C. [c]General conditions but with $Pd(OAc)_2$ (0.15 equiv), XPhos (0.45 equiv).

The reaction conditions for pyrazole arylations are also effective for arylation of nitroimidazoles, with a similar substrate scope (Scheme 4). The higher yields for imidazole arylations are in part due to the absence of diarylation because these substrates contain only one acidic C–H bond.

Scheme 4. Scope of Nitroimidazole Arylations



[a]Reaction set up outside the glovebox under inert atmosphere.

A sequential tosylation/arylation protocol enhances the step economy of these arylations (Scheme 5).[12] Tosylation of the phenol derivative affords a solution of the corresponding tosylate, which is employed directly in the subsequent Pd-catalyzed arylations without purification of the intermediate tosylate. Pyrazole and imidazole substrates undergo sequential

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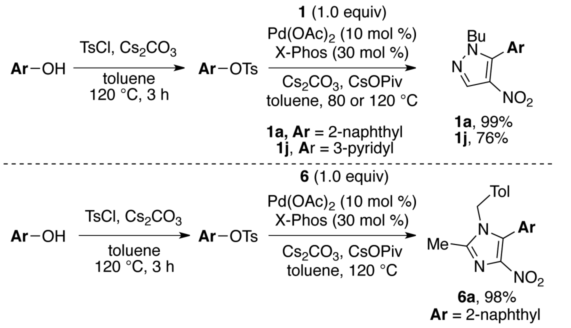
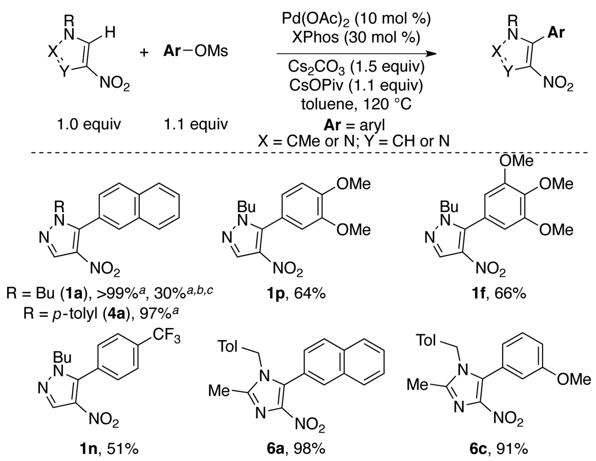
Scheme 5. Sequential Tosylation/Arylation



tosylation/arylation to afford products (**1a**, **1j**, and **6a**) in yields comparable to those obtained using preformed tosylates (Schemes 2−4).

We next investigated the use of the more atom economical mesylates in these reactions.[14] As shown in Scheme 6, both nitropyrazole (**1a**, **4a**, **1p**, **1f**, **1n**) and nitroimidazoles (**6a** and **6c**) are amenable to arylation with aromatic mesylates to afford the products in modest to good yields. Yields are generally higher with electron-neutral and electron-rich mesylates than with electron-deficient mesylates in part due to hydrolysis of the latter under the reaction conditions.

Scheme 6. Arylation of Nitroazoles Using Mesylates

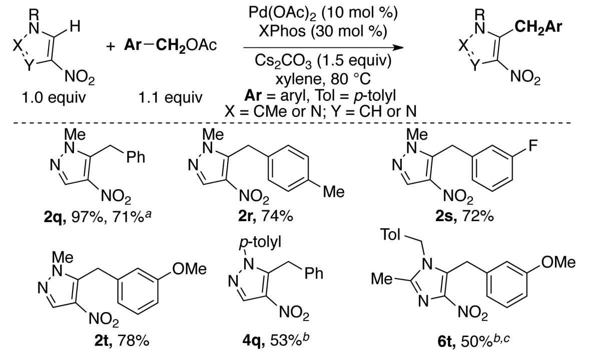


[a]Conducted at 80 °C. [b]Reaction set up outside the glovebox under inert atmosphere. [c]NMR yield against 1,4-dinitrobenzene as the standard.

By employing benzyl acetates instead of aryl sulfonates, pyrazoles and imidazoles can be benzylated in good yields under otherwise similar reaction conditions (Scheme 7).[19,20] Substituted benzyl acetates bearing electron-donating and electron-withdrawing groups are compatible with these transformations (**2s** and **2t**). As observed for arylations described above, good yields of benzylated products are obtained using X-Phos as the ligand. Notably, previous reports on benzylation of nitroazoles were limited to the use of benzyl chlorides; the use of benzyl acetate with the $Pd(OAc)_2/PPh_3$ catalyst combination was reported to give 0% yield of the desired product for the benzylation of *N*-benzylnitropyrazole.[9]

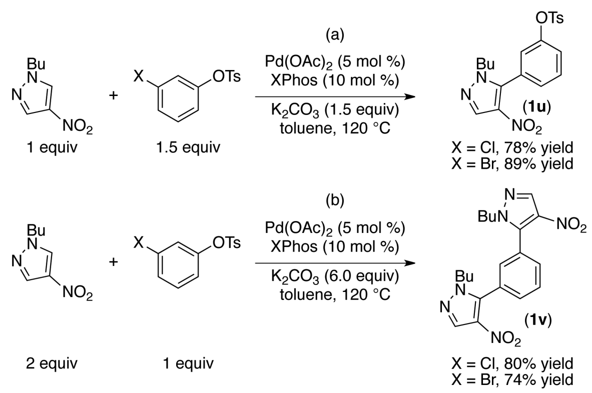
We next explored these nitroazole arylations using electrophiles containing two different leaving groups (Scheme 8). For example the reaction of (**1**) with *m*-haloaryl tosylate affords product **1u** via selective functionalization of the C−X (X = Cl, Br) bond (Scheme 8a).[21] When the same reactions were conducted in the presence of excess azole, diarylated product **1v** resulting from the sequential functionalization of the C−X and the C−OTs bonds is obtained in good yields (Scheme 8b). Similarly, and as expected, the arylation of azole **2** with *m*-chlorobenzyl acetate leads to **2w** via preferential cleavage of the more reactive C−Cl bond (Scheme 9a). However, use of excess azole results in product **2x** via sequential arylation and benzylation reactions (Scheme 9b). These results demonstrate the distinct reactivity of halides versus tosylates and benzyl acetates and support the potential for engaging these

Scheme 7. Scope for Benzylation of Nitroazoles

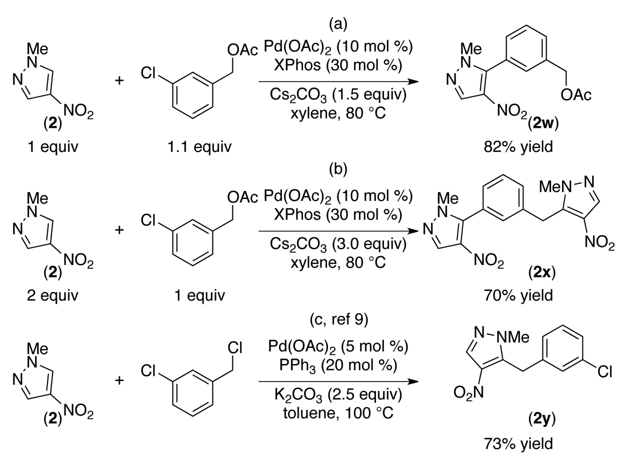


[a]Reaction set up outside the glovebox under inert atmosphere using toluene as solvent. [b]CsOPiv (1.1 equiv) added and toluene used as solvent. [c]Conducted at 120 °C.

Scheme 8. Mono- and Diarylation of Halotosylates



Scheme 9. Sequential Arylation and Benzylations



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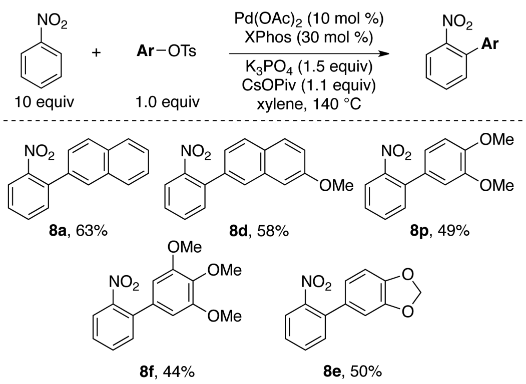
electrophiles selectively at different stages in a multistep synthetic sequence. Furthermore, the result of the reaction in Scheme 9a is orthogonal to that reported previously using *meta*-chloro benzyl choride.[9] As shown in Scheme 9c, the benzylated product (**2y**) is obtained preferentially for the arylation of azole **2** using *meta*-chloro benzyl chloride.

Having explored the arylations and benzylations of heteroaromatic nitroarenes with C−O electrophiles, we briefly examined the use of significantly less acidic nitrobenzene as a substrate for arylations using tosylates. K_3PO_4 is a more effective base (63% yield of **8a**) than Cs_2CO_3 (40% yield of **8a**) for arylation of nitrobenzene. Furthermore, CsOPiv is a necessary additive for these arylations to afford the products in significant yields. As shown in Scheme 10, electron-neutral (**8a**) and electron-rich aryl tosylates (**8d**, **8p**, **8f** and **8e**) can be used to afford the *ortho*-arylated products. The site-selectivity for the arylation of the *ortho* C−H bond clearly implicates the directing effect of the nitro group (either as a directing ligand and/or enhancing the acidity of the *ortho* C−H bond) and is consistent with previous reports using aryl halides.[2,5] Unlike the azole reactions, an excess of the substrate (10 equiv of nitrobenzene) and a higher temperature is required for these arylations.[2,5]

Scheme 10. Arylation of Nitrobenzene Using Tosylates



In summary, this manuscript describes the first report for the arylation and benzylation of nitroazoles using aryl sulfonates (tosylates and mesylates) and benzyl acetates, respectively. The products are obtained in good to excellent yields with electronically varied C−O electrophiles. The selective functionalization of halides in the presence of tosylates or benzyl acetates make these arylations amenable to sequential arylations and benzylations in the context of multistep synthesis. The arylations using the more challenging nitrobenzene substrate also afford the desired biaryls albeit in lower yields than the corresponding azoles.

■ EXPERIMENTAL METHODS

Materials and Methods. NMR spectra were obtained on a Bruker 400 (399.96 MHz for ^1H; 100.57 MHz for ^{13}C) spectrometer. ^1H NMR chemical shifts are reported in parts per million (ppm) relative to TMS, with the residual solvent peak used as an internal reference. Multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), triplet of doublets (td), triplet (t), doublet of triplets (dt), triplet of triplets (tt), multiplet (m), and broad resonance (br). IR spectra were obtained on a Thermo scientific Nicolet iS5 iD5 ATR spectrometer. Melting points were obtained on a Thomas-Hoover melting point apparatus. HRMS data were obtained from the University of Illinois Urbana−Champaign Mass Spectrometry Lab. Data were acquired on either a VG 70-VSE (EI+) or TOF (ES+) instrument.

Cesium pivalate, 2-naphthol, and 3-pyridyl phenol were obtained from Aldrich and used as received. $Pd(OAc)_2$ and XPhos were obtained from Strem chemical and used as received. Cesium carbonate was obtained from Acros and used as received. K_2CO_3 was obtained from JT Baker and used as received. The azoles,[4] tosylates,[12a] mesylates,[12c] and benzyl acetates were prepared using literature procedures. Anhydrous *p*-xylene was obtained from Aldrich and used as received. Toluene was purified using a Glass Contour solvent purification system column composed of neutral alumina and a copper catalyst. Other solvents were obtained from Fisher Chemical or VWR Chemical and used without further purification. Flash chromatography was performed on EM Science silica gel 60 (0.040−0.063 mm particle size, 230−400 mesh), and thin layer chromatography was performed on Analtech TLC plates precoated with silica gel 60 F_{254}.

General Procedures for Arylations. *General Procedure A for Azole Arylations Using Solid Electrophile.* Substrate, electrophile (tosylate or mesylate), and $Pd(OAc)_2$ were weighed into a 20 mL scintillation vial. The vial was taken into the glovebox, and XPhos, base (Cs_2CO_3 or K_2CO_3), CsOPiv, and solvent (toluene or xylene) were added. The vial was sealed with a Teflon lined cap and taken out of the glovebox, and the reaction mixture was allowed to stir at the indicated temperature for the indicated time. The reaction mixture was cooled to room temperature and filtered through a 1.5 in. plug of silica gel, eluting with EtOAc (100 mL). The filtrate was concentrated and chromatographed on a silica gel column to afford the product.

General Procedure B for Azole Arylations Using a Liquid Electrophile. Substrate and $Pd(OAc)_2$ were weighed into a 20 mL scintillation vial. The vial was taken into the glovebox, and XPhos, base (Cs_2CO_3 or K_2CO_3), CsOPiv, and a solution of the electrophile in the specified solvent (toluene or xylene) were added. The vial was sealed with a Teflon lined cap and taken out of the glovebox, and the reaction mixture was allowed to stir at the indicated temperature for the indicated time. The reaction mixture was cooled to room temperature and filtered through a 1.5 in. plug of silica gel, eluting with EtOAc (100 mL). The filtrate was concentrated and chromatographed on a silica gel column to afford the product.

General Procedure C for Sequential Tosylation/Arylation. A phenol derivative and tosyl chloride were weighed into a scintillation vial. The vial was taken into the glovebox, and Cs_2CO_3 and toluene were added to it. The vial was sealed with a Teflon lined cap, taken out of the glovebox, and stirred at 120 °C for 3 h. The reaction vial was cooled to rt and was taken into the glovebox. The tosylate solution was added to a vial containing azole, $Pd(OAc)_2$, XPhos, Cs_2CO_3, and CsOPiv. The vial was sealed with a Teflon lined cap and taken out of the glovebox, and the reaction mixture was allowed to stir at the indicated temperature for the indicated time. The reaction mixture was cooled to room temperature and filtered through a 1.5 in. plug of silica gel, eluting with EtOAc (100 mL). The filtrate was concentrated and chromatographed on a silica gel column to afford the product.

General Procedure D for Azole Benzylations. Substrate and $Pd(OAc)_2$ were weighed into a 20 mL scintillation vial. The vial was taken into the glovebox, and XPhos, Cs_2CO_3, CsOPiv (if added), and a solution of the acetate in the specified solvent (toluene or xylene) were added. The vial was sealed with a Teflon lined cap and taken out of the glovebox, and the reaction mixture was allowed to stir at the indicated temperature for the indicated time. The reaction mixture was cooled to room temperature and filtered through a 1.5 in. plug of silica gel, eluting with EtOAc (100 mL). The filtrate was concentrated and chromatographed on a silica gel column to afford the product.

General Procedure E for Nitrobenzene Arylations. $Pd(OAc)_2$ and tosylate was weighed into a 20 mL scintillation vial. The vial was taken into the glovebox and XPhos, K_3PO_4, and CsOPiv were added. Xylene and nitrobenzene were added sequentially, the vial was sealed with a Teflon lined cap and taken out of the glovebox, and the reaction mixture was allowed to stir at the indicated temperature for the indicated time. The reaction mixture was cooled to room temperature and filtered through a 1.5 in. plug of silica gel, eluting with EtOAc (100

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mL). The filtrate was concentrated and chromatographed on a silica gel column to afford the product.

General Procedure F for Azole Arylations Using Solid Electrophile. Substrate, electrophile (tosylate or mesylate), $Pd(OAc)_2$, XPhos, base (Cs_2CO_3 or K_2CO_3), and CsOPiv were weighed into a 20 mL scintillation vial. The vial was sealed with a Teflon lined cap having a septum. The headspace of the vial was purged with nitrogen. Anhydrous toluene was added, and the reaction mixture was allowed to stir at the indicated temperature for the indicated time. The reaction mixture was cooled to room temperature and filtered through a 1.5 in. plug of silica gel, eluting with EtOAc (100 mL). The filtrate was concentrated and chromatographed on a silica gel column to afford the product.

General Procedure G for Azole Benzylations. Substrate, $Pd(OAc)_2$, XPhos, and Cs_2CO_3 were weighed into a 20 mL scintillation vial. The vial was sealed with a Teflon lined cap having a septum. The headspace of the vial was purged with nitrogen. A toluene solution of the acetate was added, and the reaction mixture was allowed to stir at the indicated temperature for the indicated time. The reaction mixture was cooled to room temperature and filtered through a 1.5 in. plug of silica gel, eluting with EtOAc (100 mL). The filtrate was concentrated and chromatographed on a silica gel column to afford the product.

Synthesis and Characterization of Substrates. *1-Methyl-1H-indol-5-yl 4-methylbenzene-1-sulfonate*[22] *^{1}H NMR ($CDCl_3$).* δ 7.70 (d, *J* = 8.3 Hz, 2H), 7.28 (d, *J* = 8.5 Hz, 2H), 7.21 (d, *J* = 2.3 Hz, 1H), 7.17 (d, *J* = 8.5 Hz, 1H), 7.07 (d, *J* = 3.1 Hz, 1H), 6.83 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.41 (dd, *J* = 3.1, 0.9 Hz, 1H), 3.77 (s, 3H), 2.44 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 144.9, 143.2, 135.0, 132.6, 130.4, 129.5, 128.5, 128.3, 116.1, 114.0, 109.5, 101.3, 32.9, 29.6. IR (neat): 2924, 1486, 1337, 1237, 1215, 1189, 1086, 839, 816, 771, 756, 741, 734, 708, 698, 657 cm^{-1}. Mp = 135−137 °C. HRMS: [EI+, M+] calcd for $C_{16}H_{15}NO_3S$, 301.0773; found, 301.0766.

Product Synthesis and Characterization (Scheme 2). *1-Butyl-5-(naphthalen-2-yl)-4-nitro-1H-pyrazole (**1a**).* Following general procedure **A**, **1** (84.6 mg, 0.500 mmol, 1.0 equiv), 2-naphthyl tosylate (149 mg, 0.500 mmol, 1.0 equiv), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (244 mg, 0.750 mmol, 1.5 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous toluene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 80 °C for 16 h. Chromatography on a silica gel column using 95/5 hexanes/EtOAc (R_f = 0.18 in 95% hexanes/5% ethyl acetate) yielded product **1a** as a yellow oil (122.8 mg, 83% yield). ^{1}H NMR ($CDCl_3$): δ 8.26 (s, 1H), 8.00 (d, *J* = 8.5 Hz, 1H), 7.95−7.90 (m, 2H), 7.87 (s, 1H), 7.64−7.57 (m, 2H), 7.43 (dd, *J* = 8.5, 1.7 Hz, 1H), 4.00 (t, *J* = 7.3 Hz, 2H), 1.80−1.73 (m, 2H), 1.25−1.15 (m, 2H), 0.81 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 141.4, 136.4, 133.7, 133.1, 132.8, 129.7, 128.7, 128.4, 128.0, 127.6, 127.0, 126.3, 124.1, 50.1, 31.8, 19.5, 13.4. IR (neat): 2959, 2932, 1555, 1505, 1471, 1400, 1320, 828 cm^{-1}. HRMS: [TOF, ES+, M+H] calcd for $C_{17}H_{17}N_3O_2$, 296.1399; found, 296.1402.

Procedure without the Glovebox. Following general procedure **F**, **1** (84.6 mg, 0.500 mmol, 1.0 equiv), 2-naphthyl tosylate (149 mg, 0.500 mmol, 1.0 equiv), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (244 mg, 0.750 mmol, 1.5 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous toluene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 80 °C for 16 h. Chromatography on a silica gel column using 95/5 hexanes/EtOAc (R_f = 0.18 in 95% hexanes/5% ethyl acetate) yielded product **1a** as a yellow oil (131 mg, 89% yield). The spectroscopic data of the product were identical to those described above.

*1-Butyl-5-(4-methylphenyl)-4-nitro-1H-pyrazole (**1b**).* Following general procedure **A**, **1** (84.6 mg, 0.500 mmol, 1.0 equiv), *para*-methylphenyl tosylate (138 mg, 0.525 mmol, 1.05 equiv), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (244 mg, 0.750 mmol, 1.5 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous toluene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 120 °C for 16 h. Chromatography on a silica gel column using 93/7 hexanes/EtOAc (R_f = 0.23 in 93% hexanes/7% ethyl acetate) yielded product **1b** as a yellow oil (77.4 mg, 60% yield). ^{1}H NMR ($CDCl_3$): δ 8.20 (s, 1H), 7.34 (d, *J* = 7.9 Hz, 2H), 7.25 (d, *J* = 8.3 Hz, 2H), 3.95 (t, *J* = 7.2 Hz, 2H), 2.45 (s, 3H), 1.78−1.71 (m, 2H), 1.25−1.16 (m, 2H), 0.83 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (DMSO-d_6): δ 141.3, 139.8, 136.1, 132.3, 129.7, 129.3, 123.6, 49.4, 30.9, 21.0, 18.9, 13.2. The spectroscopic data are consistent with those previously reported in the literature.[4b]

*1-Butyl-5-(3-methoxyphenyl)-4-nitro-1H-pyrazole (**1c**).* Following general procedure **A**, **1** (84.6 mg, 0.500 mmol, 1.0 equiv), *meta*-methoxyphenyl tosylate (153 mg, 0.550 mmol, 1.1 equiv), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (244 mg, 0.750 mmol, 1.5 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous toluene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 120 °C for 16 h. Chromatography on a silica gel column using 93/7 hexanes/EtOAc (R_f = 0.19 in 93% hexanes/7% EtOAc) yielded product **1c** as a yellow oil (83.0 mg, 60% yield). ^{1}H NMR ($CDCl_3$): δ 8.18 (s, 1H), 7.43 (t, *J* = 8.0 Hz, 1H), 7.08−7.05 (m, 1H), 6.92 (dt, *J* = 7.6, 1.4 Hz, 1H), 6.88−6.87 (m, 1H), 3.94 (t, *J* = 7.2 Hz, 2H), 3.83 (s, 3H), 1.78−1.71 (m, 2H), 1.25−1.16 (m, 2H), 0.82 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 159.6, 141.1, 136.3, 132.8, 129.9, 127.8, 121.7, 115.7, 115.2, 55.4, 50.0, 31.7, 19.5, 13.4. IR (neat): 1582, 1556, 1497, 1465, 1434, 1358, 1318, 1286, 1252, 1216, 1177, 1156, 1047, 1031, 855, 815, 786, 770, 743, 692 cm^{-1}. HRMS: [TOF, ES+, M+H] calcd for $C_{14}H_{17}N_3O_3$, 276.1348 found, 276.1347.

*1-Butyl-5-(7-methoxynaphthalen-2-yl)-4-nitro-1H-pyrazole (**1d**).* Following general procedure **A**, **1** (84.6 mg, 0.500 mmol, 1.0 equiv), 7-methoxynaphthyl tosylate (164 mg, 0.500 mmol, 1.0 equiv), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (244 mg, 0.750 mmol, 1.5 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous toluene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 80 °C for 16 h. Chromatography on a silica gel column using 85/15 hexanes/EtOAc (R_f = 0.21 in 85% hexanes/15% EtOAc) yielded product **1d** as a yellow solid (153 mg, 94% yield), mp = 84.7 °C. ^{1}H NMR ($CDCl_3$): δ 8.25 (s, 1H), 7.91 (d, *J* = 8.4 Hz, 1H), 7.83 (d, *J* = 9.0 Hz, 1H), 7.76 (s, 1H), 7.28−7.25 (m, 2H), 7.17 (d, *J* = 2.4 Hz, 1H), 4.00 (t, *J* = 7.2 Hz, 2H), 3.94 (s, 3H), 1.80−1.73 (m, 2H), 1.25−1.15 (m, 2H), 0.81 (t, *J* = 7.3 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 158.4, 141.6, 136.4, 134.1, 133.0, 129.4, 129.2, 128.43, 128.39, 124.5, 123.9, 120.6, 106.1, 55.4, 50.1, 31.8, 19.5, 13.4. IR (neat): 3138, 2976, 2958, 2926, 1607, 1509, 1496, 1466, 1437, 1397, 1367, 1335, 1244, 1229, 1216, 1176, 1028, 901, 850, 836, 828 cm^{-1}. HRMS: [TOF, ES+, M+H] calcd for $C_{18}H_{19}N_3O_3$, 326.1505; found, 326.1505.

*5-(2H-1,3-Benzodioxol-5-yl)-1-butyl-4-nitro-1H-pyrazole (**1e**).* Following general procedure **A**, **1** (84.6 mg, 0.500 mmol, 1.0 equiv), sesamol tosylate (161 mg, 0.550 mmol, 1.1 equiv), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (244 mg, 0.750 mmol, 1.5 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous xylene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 80 °C for 16 h. Chromatography on a silica gel column using 90/10 hexanes/EtOAc (R_f = 0.16 in 90% hexanes/10% ethyl acetate) yielded product **1e** as an off white solid (105 mg, 73% yield), mp = 63.4 °C. ^{1}H NMR ($CDCl_3$): δ 8.18 (s, 1H), 6.95 (d, *J* = 8.5 Hz, 1H), 6.82 (dd, *J* = 6.4, 1.8 Hz, 2H), 6.08 (s, 2H), 3.96 (t, *J* = 7.3 Hz, 2H), 1.79−1.71 (m, 2H), 1.27−1.17 (m, 2H), 0.85 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 149.2, 148.0, 140.9, 136.2, 132.8, 123.7, 119.6, 109.9, 108.6, 101.7, 49.9, 31.7, 19.5, 13.4. IR (thin film, CH_2Cl_2): 2963, 2932, 1508, 1497, 1484, 1465, 1397, 1343, 1318, 1243, 1221, 1034, 976, 864, 826, 810, 763 cm^{-1}. HRMS: [TOF, ES+, M+H] calcd for $C_{14}H_{15}N_3O_4$, 290.1141; found, 290.1142.

*1-Butyl-4-nitro-5-(3,4,5-trimethoxyphenyl)-1H-pyrazole (**1f**).* Following general procedure **A**, **1** (93.1 mg, 0.550 mmol, 1.1 equiv), 3,4,5-trimethoxyphenyl tosylate (169 mg, 0.500 mmol, 1.0 equiv), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (244 mg, 0.750 mmol, 1.5 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous xylene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture

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was allowed to stir at 120 °C for 16 h. Chromatography on a silica gel column using 80/15/5 hexanes/CH_2Cl_2/acetone (R_f = 0.13 in 80% hexanes/15% CH_2Cl_2/5% acetone) yielded product **1f** as a yellow oil (121 mg, 72% yield). ^{1}H NMR ($CDCl_3$): δ 8.20 (s, 1H), 6.55 (s, 2H), 3.97 (t, *J* = 7.2 Hz, 2H), 3.94 (s, 3H), 3.87 (s, 6H), 1.82−1.74 (m, 2H), 1.29−1.20 (m, 2H), 0.86 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 153.5, 141.2, 139.44, 139.42, 136.3, 132.7, 121.7, 106.89, 106.86, 60.9, 56.3, 50.1, 31.9, 19.6, 13.5. IR (thin film, CH_2Cl_2): 2959, 2936, 1584, 1557, 1505, 1463, 1400, 1341, 1302, 1239, 1124, 1002, 840 cm^{-1}. HRMS: [TOF, ES+, M+H] calcd for $C_{16}H_{21}N_3O_5$, 336.1559; found, 336.1558.

*1-Butyl-5-(2-methylphenyl)-4-nitro-1H-pyrazole (**1g**).* Following general procedure **A**, **1** (84.6 mg, 0.500 mmol, 1.0 equiv), *ortho*-tolyl tosylate (144 mg, 0.550 mmol, 1.1 equiv), $Pd(OAc)_2$ (16.8 mg, 0.075 mmol, 0.15 equiv), XPhos (107 mg, 0.225 mmol, 0.45 equiv), Cs_2CO_3 (244 mg, 0.750 mmol, 1.5 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous toluene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 120 °C for 16 h. Chromatography on a silica gel column using 95/5 hexanes/EtOAc (R_f = 0.18 in 95% hexanes/5% EtOAc) yielded product **1g** as a yellow oil (54.7 mg, 42% yield). ^{1}H NMR ($CDCl_3$): δ 8.23 (s, 1H), 7.45 (td, *J* = 7.6, 1.5 Hz, 1H), 7.37 (d, *J* = 7.5 Hz, 1H), 7.33 (t, *J* = 7.5 Hz, 1H), 7.17 (dd, *J* = 7.7, 1.4 Hz, 1H), 3.93−3.75 (m, 2H), 2.12 (s, 3H), 1.76−1.68 (m, 2H), 1.25−1.16 (m, 2H), 0.83 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 140.9, 137.7, 136.2, 133.3, 130.5, 130.4, 129.3, 126.5, 126.1, 49.8, 31.5, 19.5, 19.4, 13.4. IR (neat): 2958, 2873, 1557, 1504, 1486, 1458, 1400, 1322, 828, 762, 730 cm^{-1}. HRMS: [EI+, M+] calcd for $C_{14}H_{17}N_3O_2$, 259.1321; found, 259.1316.

*5-(4-Methoxyphenyl)-1-methyl-4-nitro-1H-pyrazole (**2h**).* Following general procedure **A**, 1-methyl-4-nitro-1*H*-pyrazole (**2**) (63.6 mg, 0.500 mmol, 1.0 equiv), *para*-methoxyphenyl tosylate (146 mg, 0.525 mmol, 1.05 equiv), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (244 mg, 0.750 mmol, 1.5 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous toluene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 120 °C for 16 h. Chromatography on a silica gel column using 85/10/5 hexanes/CH_2Cl_2/acetone (R_f = 0.28 in 85% hexanes/10% methylene chloride/5% acetone) yielded product **2h** as a light yellow solid (89.4 mg, 77% yield). ^{1}H NMR ($CDCl_3$): δ 8.19 (s, 1H), 7.33 (d, *J* = 8.8 Hz, 2H), 7.05 (d, *J* = 8.7 Hz, 2H), 3.89 (s, 3H), 3.75 (s, 3H). The spectroscopic data are consistent with those previously reported in the literature.[4b]

*5-(3-Methoxyphenyl)-1-methyl-4-nitro-1H-pyrazole (**2c**).* Following general procedure **A**, **2** (63.6 mg, 0.500 mmol, 1.0 equiv), *meta*-methoxyphenyl tosylate (153.1 mg, 0.55 mmol, 1.1 equiv), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (244 mg, 0.750 mmol, 1.5 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous toluene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 80 °C for 16 h. Chromatography on a silica gel column using 80% hexanes/20% EtOAc (R_f = 0.20 in 80% hexanes/20% EtOAc) yielded product **2c** as a yellow solid (104 mg, 89% yield). ^{1}H NMR ($CDCl_3$): δ 8.19 (s, 1H), 7.45 (t, *J* = 7.9 Hz, 1H), 7.08 (dd, *J* = 8.4, 2.6 Hz, 1H), 6.95 (dt, *J* = 7.6, 1.2 Hz, 1H), 6.90 (t, *J* = 2.1 Hz, 1H), 3.85 (s, 3H), 3.74 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 159.6, 141.2, 136.2, 132.9, 129.9, 127.6, 121.7, 115.8, 115.2, 55.4, 37.9. The spectroscopic data are consistent with those previously reported in the literature.[4b]

*4-Nitro-1-(2-phenylethyl)-5-[3-(trifluoromethyl)phenyl]-1H-pyrazole (**3i**).* Following general procedure **A**, 4-nitro-1-(2-phenylethyl)-1*H*-pyrazole (**3**) (109 mg, 0.500 mmol, 1.0 equiv), *meta*-trifluoromethylphenyl tosylate (174 mg, 0.550 mmol, 1.1 equiv), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (244 mg, 0.750 mmol, 1.5 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous toluene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 120 °C for 16 h. Chromatography on a silica gel column using 85/15 hexanes/EtOAc (R_f = 0.21 in 85% hexanes/15% EtOAc) yielded product **3i** as a light yellow solid (115 mg, 64% yield). ^{1}H NMR ($CDCl_3$): δ 8.30 (s, 1H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.26−7.19 (m, 3H), 7.02 (s, 1H), 6.94 (d, *J* = 7.8 Hz, 1H), 6.79 (d, *J* = 6.6 Hz, 2H), 4.13 (t, *J* = 6.4 Hz, 2H), 3.14 (t, *J* = 6.5 Hz, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 140.5, 136.8, 136.7, 133.0, 132.9, 131.1 (*J* = 33 Hz), 129.1, 128.9, 128.6, 127.2, 127.1, 126.9 (*J* = 3.6 Hz), 126.4 (*J* = 3.8 Hz), 123.4 (*J* = 271 Hz), 51.6, 35.8. The spectroscopic data are consistent with those previously reported in the literature.[4b]

*1-(4-Methylphenyl)-5-(naphthalen-2-yl)-4-nitro-1H-pyrazole (**4a**).* Following general procedure **A**, 1-(4-methylphenyl)-4-nitro-1*H*-pyrazole (**4**) (50.8 mg, 0.250 mmol, 1.0 equiv), 2-naphthyl tosylate (74.6 mg, 0.250 mmol, 1.0 equiv), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol, 0.10 equiv), XPhos (35.8 mg, 0.075 mmol, 0.30 equiv), Cs_2CO_3 (122 mg, 0.375 mmol, 1.5 equiv), CsOPiv (64.4 mg, 0.275 mmol, 1.1 equiv), and anhydrous toluene (0.5 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 80 °C for 16 h. The reaction was filtered through a 1-in. pad of silica gel eluting with EtOAc (100 mL). The filtrate was concentrated. ^{1}H NMR spectroscopic analysis of the crude product against 1,4-dinitrobenzene as the standard showed >99% yield of **4a**.

*1-Butyl-3,5-bis(naphthalen-2-yl)-4-nitro-1H-pyrazole (**1aa**).* Following general procedure **A**, **1** (84.6 mg, 0.500 mmol, 1.0 equiv), 2-naphthyl tosylate (298 mg, 1.00 mmol, 2.0 equiv), $Pd(OAc)_2$ (22.5 mg, 0.10 mmol, 0.20 equiv), XPhos (143 mg, 0.30 mmol, 0.60 equiv), Cs_2CO_3 (489 mg, 1.50 mmol, 3.0 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous toluene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 120 °C for 16 h. Chromatography on a silica gel column using 95/5 hexanes/EtOAc (R_f = 0.15 in 95% hexanes/5% ethyl acetate) yielded product **1aa** as a light yellow solid (159 mg, 76% yield). Mp = 137−140 °C. ^{1}H NMR ($CDCl_3$): δ 8.24 (s, 1H), 8.03 (d, *J* = 8.4 Hz, 1H), 7.97−7.88 (m, 6H), 7.81 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.66−7.59 (m, 2H), 7.56−7.50 (m, 3H), 4.06 (t, *J* = 7.4 Hz, 2H), 1.89−1.81 (m, 2H), 1.29−1.24 (m, 2H), 0.84 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 147.3, 142.9, 133.6, 133.5, 133.0, 132.8, 130.7, 129.6, 128.7, 128.6, 128.5, 128.3, 128.1, 127.9, 127.8, 127.7, 127.6, 126.9, 126.6, 126.5, 126.3, 126.2, 124.6, 50.2, 31.9, 19.6, 13.5. IR (neat): 2927, 1553, 1498, 1456, 1418, 1356, 926, 776, 766 cm^{-1}. HRMS: [EI+, M+] calcd for $C_{27}H_{23}N_3O_2$, 421.1790; found, 421.1789.

Product Synthesis and Characterization (Scheme 3). *3-(1-Butyl-4-nitro-1H-pyrazol-5-yl)pyridine (**1j**).* Following general procedure **A**, **1** (120 mg, 0.710 mmol, 1.0 equiv), 3-pyridyl tosylate (187 mg, 0.750 mmol, 1.05 equiv), $Pd(OAc)_2$ (15.9 mg, 0.071 mmol, 0.10 equiv), XPhos (101 mg, 0.213 mmol, 0.30 equiv), Cs_2CO_3 (347 mg, 1.065 mmol, 1.5 equiv), CsOPiv (183 mg, 0.781 mmol, 1.1 equiv), and anhydrous xylene (1.42 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 120 °C for 24 h. Chromatography on a silica gel column using 60/40 hexanes/EtOAc (R_f = 0.27 in 60% hexanes/40% EtOAc) yielded product **1j** as a yellow oil (119 mg, 68% yield). ^{1}H NMR ($CDCl_3$): δ 8.80 (d, *J* = 4.9 Hz, 1H), 8.64 (s, 1H), 8.24 (s, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.52−7.49 (m, 1H), 3.97 (t, *J* = 7.3 Hz, 2H), 1.81−1.73 (m, 2H), 1.26−1.17 (m, 2H), 0.84 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 151.3, 149.8, 137.9, 137.6, 136.5, 133.5, 123.5, 123.3, 50.3, 31.8, 19.5, 13.4. IR (neat): 1502, 1477, 1460, 1398, 1322, 830, 761, 711 cm^{-1}. HRMS: [TOF, ES+, M+H] calcd for $C_{12}H_{14}N_4O_2$, 247.1195; found, 247.1195.

*6-(1-Butyl-4-nitro-1H-pyrazol-5-yl)quinoline (**1k**).* Following general procedure **A**, **1** (84.6 mg, 0.500 mmol, 1.0 equiv), 6-quinolyl tosylate (157 mg, 0.525 mmol, 1.05 equiv), $Pd(OAc)_2$ (11.2 mg, 0.05 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (244 mg, 0.750 mmol, 1.5 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous xylene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 80 °C for 24 h. Chromatography on a silica gel column using 50/50 hexanes/EtOAc (R_f = 0.27 in 50% hexanes/50% EtOAc) yielded product **1k** as a yellow solid (93 mg, 63% yield). Mp = 80−83 °C. ^{1}H NMR ($CDCl_3$): δ 9.06 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.29−8.23 (m, 3H), 7.89 (d, *J* = 2.0 Hz, 1H), 7.68 (dd, *J* = 8.7, 2.0 Hz, 1H), 7.53 (dd, *J* = 8.3, 4.2 Hz, 1H), 4.00 (t, *J* = 7.2 Hz, 2H), 1.81−1.73 (m, 2H), 1.25−1.16 (m, 2H), 0.81 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 152.0, 148.3, 140.5, 136.4, 133.2, 130.4, 129.9, 129.8, 127.8, 124.9, 122.1, 50.2, 31.7,

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19.5, 13.4 two carbon peaks are overlapping. IR (neat): 1556, 1502, 1470, 1401, 1374, 1329, 1310, 915, 861, 843, 825, 813, 776, 769, 759, 598 cm^{-1}. HRMS: [TOF, ES+, M+H] calcd for $C_{16}H_{16}N_4O_2$, 297.1352; found, 297.1357.

*2-(1-Butyl-4-nitro-1H-pyrazol-5-yl)quinoxaline (**1l**).* Following general procedure **A**, **1** (84.6 mg, 0.500 mmol, 1.0 equiv), quinoxalin-2-yl 4-methylbenzene-1-sulfonate (157 mg, 0.525 mmol, 1.05 equiv), $Pd(OAc)_2$ (16.8 mg, 0.075 mmol, 0.15 equiv), XPhos (107 mg, 0.225 mmol, 0.45 equiv), Cs_2CO_3 (244 mg, 0.750 mmol, 1.5 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous xylene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 80 °C for 24 h. Chromatography on a silica gel column using 85/15 hexanes/EtOAc (R_f = 0.20 in 85% hexanes/15% EtOAc) yielded product **1l** as a yellow solid (92 mg, 62% yield). Mp = 43−46 °C. ^1H NMR ($CDCl_3$): δ 9.09 (s, 1H), 8.28 (s, 1H), 8.24 (dd, *J* = 8.0, 1.8 Hz, 1H), 8.17 (dd, *J* = 7.9, 1.9 Hz, 1H), 7.95−7.87 (m, 2H), 4.24 (t, *J* = 7.4 Hz, 2H), 1.88−1.80 (m, 2H), 1.30−1.21 (m, 2H), 0.84 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 146.2, 142.1, 141.9, 141.6, 136.5, 136.1, 133.8, 131.7, 130.9, 129.55, 129.54, 51.1, 31.9, 19.5, 13.4. IR (neat): 1537, 1508, 1492, 1478, 1461, 1452, 1402, 1388, 1368, 1335, 1315, 1271, 1225, 1197, 1131, 1049, 980, 964, 954, 923, 850, 825, 799, 757, 747, 731, 623, 589 cm^{-1}. HRMS: [TOF, ES+, M+H] calcd for $C_{15}H_{15}N_5O_2$, 298.1304; found, 298.1295.

*5-(1-Butyl-4-nitro-1H-pyrazol-5-yl)-1-methyl-1H-indole (**1m**).* Following general procedure **A**, **1** (42.3 mg, 0.25 mmol, 1.0 equiv), 1-methyl-1*H*-indol-5-yl 4-methylbenzene-1-sulfonate (83.3 mg, 0.275 mmol, 1.1 equiv), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol, 0.10 equiv), XPhos (35.6 mg, 0.075 mmol, 0.30 equiv), Cs_2CO_3 (122 mg, 0.375 mmol, 1.5 equiv), CsOPiv (64.4 mg, 0.275 mmol, 1.1 equiv), and anhydrous toluene (0.5 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 120 °C for 16 h. Chromatography on a silica gel column using 80/20 hexanes/EtOAc (R_f = 0.23 in 80% hexanes/20% EtOAc) yielded product **1m** as a viscous yellow oil (63.7 mg, 85% yield). ^1H NMR ($CDCl_3$): δ 8.23 (s, 1H), 7.62 (s, 1H), 7.46 (d, *J* = 8.4 Hz, 1H), 7.18 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.16 (d, *J* = 3.3 Hz, 1H), 6.57 (d, *J* = 3.2 Hz, 1H), 3.98 (t, *J* = 7.3 Hz, 2H), 3.86 (s, 3H), 1.79−1.72 (m, 2H), 1.24−1.15 (m, 2H), 0.81 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 142.9, 137.1, 136.4, 132.8, 130.2, 128.3, 122.7, 122.5, 117.2, 109.7, 101.7, 49.9, 33.0, 31.8, 19.6, 13.5. IR (neat): 2958, 1734, 1555, 1502, 1459, 1398, 1372, 1337, 1318, 1285, 1242, 1177, 1045, 828, 803, 761, 724 cm^{-1}. HRMS: [EI+, M+] calcd for $C_{16}H_{18}N_4O_2$, 298.1429; found, 298.1424.

*3-{1-[(4-Methylphenyl)methyl]-4-nitro-1H-pyrazol-5-yl}pyridine (**5j**).* Following general procedure **A**, 1-[(4-methylphenyl)methyl]-4-nitro-1*H*-pyrazole (**5**) (109 mg, 0.500 mmol, 1.0 equiv), 3-pyridyl tosylate (131 mg, 0.525 mmol, 1.05 equiv), $Pd(OAc)_2$ (11.2 mg, 0.05 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (244 mg, 0.750 mmol, 1.5 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous xylene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 120 °C for 24 h. Chromatography on a silica gel column using 60/40 hexanes/EtOAc (R_f = 0.18 in 60% hexanes/40% EtOAc) yielded product **5j** as a yellow solid (117 mg, 80% yield). ^1H NMR ($CDCl_3$): δ 8.77 (d, *J* = 5.0 Hz, 1H), 8.54 (s, 1H), 8.28 (s, 1H), 7.61 (dt, *J* = 7.9, 2.0 Hz, 1H), 7.43 (dd, *J* = 7.8, 4.9 Hz, 1H), 7.09 (d, *J* = 7.8 Hz, 2H), 6.89 (d, *J* = 8.0 Hz, 2H), 5.15 (s, 2H), 2.31 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 151.3, 149.9, 138.5, 138.2, 137.6, 136.6, 133.9, 131.7, 129.6, 127.3, 123.3, 123.2, 54.4, 21.1. The spectroscopic data are consistent with those previously reported in the literature.[4b]

Product Synthesis and Characterization (Scheme 4). *2-Methyl-1-[(4-methylphenyl)methyl]-5-(naphthalen-2-yl)-4-nitro-1H-imidazole (**6a**).* Following general procedure **A**, 2-methyl-1-[(4-methylphenyl)methyl]-4-nitro-1*H*-imidazole (**6**) (116 mg, 0.500 mmol, 1.0 equiv), 2-naphthyl tosylate (167 mg, 0.550 mmol, 1.1 equiv), $Pd(OAc)_2$ (11.2 mg, 0.05 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (224 mg, 0.690 mmol, 1.4 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous toluene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 120 °C for 14 h. Chromatography on a silica gel column using 42/55/3 hexanes/EtOAc/acetone (R_f = 0.30 in 42% hexanes/55% EtOAc/3% acetone) yielded product **6a** as a yellow solid (165 mg, 93% yield). Mp = 128−131 °C. ^1H NMR ($CDCl_3$): δ 7.89 (t, *J* = 8.2 Hz, 2H), 7.77 (s, 1H), 7.76 (d, *J* = 7.0 Hz, 1H), 7.58−7.50 (m, 2H), 7.37 (dd, *J* = 8.9, 1.8 Hz, 1H), 7.12 (d, *J* = 7.9 Hz, 2H), 6.78 (d, *J* = 7.9 Hz, 2H), 4.97 (s, 2H), 2.41 (s, 3H), 2.33 (s, 3H). ^{13}C NMR ($CDCl_3$): 144.3, 143.3, 137.9, 133.4, 133.0, 132.5, 131.6, 129.9, 129.6, 128.4, 128.2, 127.7, 127.3, 126.8, 126.6, 125.7, 124.4, 47.8, 20.9, 13.7. δ. IR (neat): 1569, 1534, 1506, 1433, 1400, 1384, 1356, 1329, 1310, 1287, 1274, 1236, 1227, 1197, 1184, 1144, 1123, 1110, 1036, 1019, 938, 923, 870, 840, 830, 813, 801, 772, 765, 750, 716, 694, 663, 630, 613, 577, 567, 555 cm^{-1}. HRMS: [TOF, ES+, M+H] calcd for $C_{22}H_{19}N_3O_2$, 358.1556; found, 358.1553.

Procedure without the Glovebox. Following general procedure **F**, **6** (116 mg, 0.500 mmol, 1.0 equiv), 2-naphthyl tosylate (167 mg, 0.550 mmol, 1.1 equiv), $Pd(OAc)_2$ (11.2 mg, 0.05 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (224 mg, 0.690 mmol, 1.4 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous toluene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 120 °C for 14 h. Chromatography on a silica gel column using 42/55/3 hexanes/EtOAc/acetone (R_f = 0.30 in 42% hexanes/55% EtOAc/3% acetone) yielded product **6a** as a yellow solid (164 mg, 92% yield).

*5-(3-Methoxyphenyl)-2-methyl-1-[(4-methylphenyl)methyl]-4-nitro-1H-imidazole (**6c**).* Following general procedure **A**, **6** (116 mg, 0.500 mmol, 1.0 equiv), *meta*-methoxyphenyl tosylate (150 mg, 0.540 mmol, 1.1 equiv), $Pd(OAc)_2$ (11.2 mg, 0.05 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (224 mg, 0.690 mmol, 1.4 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous toluene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 120 °C for 14 h. Chromatography on a silica gel column using 42/55/3 hexanes/EtOAc/acetone (R_f = 0.13 in 42% hexanes/55% EtOAc/3% acetone) yielded product **6c** as a light yellow solid (130 mg, 77% yield). ^1H NMR ($CDCl_3$): δ 7.34 (t, *J* = 7.9 Hz, 1H), 7.13 (d, *J* = 7.9 Hz, 2H), 7.01−6.98 (m, 1H), 6.87 (d, *J* = 7.3 Hz, 1H), 6.79−6.77 (m, 3H), 4.92 (s, 2H), 3.69 (s, 3H), 2.37 (s, 3H), 2.33 (s, 3H). ^{13}C NMR ($CDCl_3$): 159.4, 144.1, 143.0, 137.9, 132.8, 131.7, 129.7, 129.6, 128.2, 125.6, 122.1, 115.8, 115.2, 55.0, 47.8, 20.9, 13.6.[4c]

*5-(4-Methoxyphenyl)-2-methyl-1-[(4-methylphenyl)methyl]-4-nitro-1H-imidazole (**6h**).* Following general procedure **A**, **6** (116 mg, 0.500 mmol, 1.0 equiv), *para*-methoxyphenyl tosylate (209 mg, 0.750 mmol, 1.5 equiv), $Pd(OAc)_2$ (11.2 mg, 0.05 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (224 mg, 0.690 mmol, 1.4 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous toluene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 120 °C for 14 h. Chromatography on a silica gel column using 42/55/3 hexanes/EtOAc/acetone (R_f = 0.28 in 42% hexanes/55% EtOAc/3% acetone) yielded product **6h** as a yellow solid (153 mg, 91% yield). ^1H NMR ($CDCl_3$): δ 7.22 (d, *J* = 8.8 Hz, 2H), 7.13 (d, *J* = 7.9 Hz, 2H), 6.94 (d, *J* = 8.8 Hz, 2H), 6.78 (d, *J* = 7.9 Hz, 2H), 4.92 (s, 2H), 3.83 (s, 3H), 2.35 (s, 3H), 2.33 (s, 3H). ^{13}C NMR ($CDCl_3$): 160.7, 144.0, 143.1, 137.9, 133.1, 131.7, 131.5, 129.7, 125.6, 118.8, 114.1, 55.2, 47.7, 21.0, 13.7.[4c]

*2-Methyl-1-[(4-methylphenyl)methyl]-4-nitro-5-[3-(trifluoromethyl)phenyl]-1H-imidazole (**6i**).* Following general procedure **A**, **6** (116 mg, 0.500 mmol, 1.0 equiv), *meta*-trifluoromethylphenyl tosylate (174 mg, 0.550 mmol, 1.1 equiv), $Pd(OAc)_2$ (11.2 mg, 0.005 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (224 mg, 0.690 mmol, 1.4 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous toluene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 120 °C for 14 h. Chromatography on a silica gel column using 42/55/3 hexanes/EtOAc/acetone (R_f = 0.30 in 42% hexanes/55% EtOAc/3% acetone) yielded product **6i** as a light yellow solid (160 mg, 84% yield). ^1H NMR ($CDCl_3$): δ 7.72 (d, *J* = 7.8 Hz, 1H), 7.55 (t, *J* = 7.9 Hz, 1H), 7.46 (d, *J* = 6.2 Hz, 1H), 7.46 (s, 1H), 7.12 (d, *J* = 7.8 Hz, 2H), 6.72 (d, *J* = 7.8 Hz, 2H), 4.91 (s, 2H), 2.45 (s, 3H), 2.33 (s, 3H). ^{13}C NMR ($CDCl_3$): 144.7, 143.4, 138.3, 133.4, 131.2, 130.97, 130.96 (*J* = 33

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Hz), 129.7, 129.2, 128.1, 127.1 (J = 3.7 Hz), 126.6 (J = 3.6 Hz), 125.6, 123.4 (J = 271 Hz), 48.1, 20.9, 13.6.[4c]

*2-Methyl-1-[(4-methylphenyl)methyl]-4-nitro-5-[4-(trifluoromethyl)phenyl]-1H-imidazole (**6n**).* Following general procedure **A**, **6** (116 mg, 0.500 mmol, 1.0 equiv), *para*-trifluoromethylphenyl tosylate (174 mg, 0.550 mmol, 1.1 equiv), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (224 mg, 0.689 mmol, 1.4 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous toluene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 120 °C for 14 h. Chromatography on a silica gel column using 42/55/3 hexanes/EtOAc/acetone (R_f = 0.28 in 42% hexanes/55% EtOAc/3% acetone) yielded product **6n** as a yellow solid (176 mg, 94% yield). Mp = 131−134 °C. ^{1}H NMR ($CDCl_3$): δ 7.68 (d, J = 7.7 Hz, 2H), 7.40 (d, J = 8.3 Hz, 2H), 7.13 (d, J = 7.9 Hz, 2H), 6.74 (d, J = 7.8 Hz, 2H), 4.91 (s, 2H), 2.41 (s, 3H), 2.33 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 144.8, 143.3, 138.2, 131.7 (q, J = 33 Hz), 131.17, 131.16, 130.89, 130.88, 130.6, 129.8, 125.5 (m), 123.5 (q, J = 271 Hz), 47.9, 20.9, 13.6. IR (neat): 1513, 1493, 1402, 1385, 1320, 1294, 1258, 1166, 1108, 1066, 1027, 1007, 859, 809, 781, 752, 723, 698, 673, 619 cm^{-1}. HRMS: [TOF, ES+, M+H] calcd for $C_{19}H_{16}F_3N_3O_2$, 376.1273; found, 376.1262.

*2-{2-Methyl-1-[(4-methylphenyl)methyl]-4-nitro-1H-imidazol-5-yl}quinoline (**6o**).* Following general procedure **A**, **6** (116 mg, 0.500 mmol, 1.0 equiv), 2-quinolyl tosylate (299 mg, 1.00 mmol, 2.0 equiv), $Pd(OAc)_2$ (11.2 mg, 0.05 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (224 mg, 0.690 mmol, 1.4 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous toluene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 120 °C for 14 h. Chromatography on a silica gel column using 42/55/3 hexanes/EtOAc/acetone (R_f = 0.28 in 42% hexanes/55% EtOAc/3% acetone) yielded product **6o** as a light yellow solid (174 mg, 97% yield). Mp = 137−139 °C. ^{1}H NMR ($CDCl_3$): δ 8.21 (d, J = 8.5 Hz, 1H), 8.07 (d, J = 8.4 Hz, 1H), 7.88 (d, J = 8.3 Hz, 1H), 7.77 (t, J = 7.3 Hz, 1H), 7.65−7.61 (m, 2H), 7.00 (d, J = 7.8 Hz, 2H), 6.78 (d, J = 7.7 Hz, 2H), 5.30 (s, 2H), 2.46 (s, 3H), 2.27 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 147.4, 147.3, 145.1, 143.6, 137.7, 136.3, 131.5, 130.8, 130.0, 129.29, 129.26, 127.7, 127.6, 127.3, 126.3, 123.9, 48.2, 20.8, 13.7. IR (neat): 2921, 1495, 1402, 1389, 1334, 1304, 1292, 868, 842, 831, 815, 808, 792, 773, 768, 757 cm^{-1}. HRMS: [EI+, M+] calcd for $C_{21}H_{18}N_4O_2$, 358.1429; found, 358.1422.

*5-(3-Methoxyphenyl)-2-methyl-4-nitro-1-(3-phenylpropyl)-1H-imidazole (**7c**).* Following general procedure **A**, 2-methyl-4-nitro-1-(3-phenylpropyl)-1*H*-imidazole (**7**) (124 mg, 0.506 mmol, 1.0 equiv), *meta*-methoxyphenyl tosylate (150 mg, 0.540 mmol, 1.1 equiv), $Pd(OAc)_2$ (11.2 mg, 0.05 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (224 mg, 0.690 mmol, 1.4 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous toluene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 120 °C for 14 h. Chromatography on a silica gel column using 40/55/5 hexanes/EtOAc/acetone (R_f = 0.29 in 40% hexanes/55% EtOAc/5% acetone) yielded product **7c** as a light yellow solid (178 mg, >99% yield). Mp = 113−114 °C. ^{1}H NMR ($CDCl_3$): δ 7.39 (t, J = 8.0 Hz, 1H), 7.26−7.17 (m, 3H), 7.04 (dd, J = 8.2, 2.6 Hz, 1H), 6.99−6.97 (m, 2H), 6.89 (d, J = 7.4 Hz, 1H), 6.83 (t, J = 2.2 Hz, 1H), 3.82 (s, 3H), 3.74−3.70 (m, 2H), 2.50 (t, J = 7.4 Hz, 2H), 2.39 (s, 3H), 1.89−1.82 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 159.5, 143.3, 143.0, 139.4, 132.0, 129.9, 128.51, 128.46, 127.9, 126.3, 121.9, 115.37, 115.34, 55.2, 44.0, 32.3, 31.0, 13.3. IR (neat): 1604, 1588, 1566, 1535, 1496, 1447, 1403, 1381, 1329, 1300, 1280, 1261, 1249, 1222, 1044, 1023, 904, 849, 837, 822, 800, 747, 695 cm^{-1}. HRMS: [TOF, ES+, M+H] calcd for $C_{20}H_{21}N_3O_3$, 352.1661; found, 352.1665.

*2-Methyl-4-nitro-1-(3-phenylpropyl)-5-[3-(trifluoromethyl)phenyl]-1H-imidazole (**7i**).* Following general procedure **A**, **7** (124 mg, 0.506 mmol, 1.0 equiv), *meta*-trifluoromethylphenyl tosylate (174 mg, 0.550 mmol, 1.1 equiv), $Pd(OAc)_2$ (11.2 mg, 0.05 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (224 mg, 0.690 mmol, 1.4 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous toluene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 120 °C for 14 h. Chromatography on a silica gel column using 40/55/5 hexanes/EtOAc/acetone (R_f = 0.29 in 40% hexanes/55% EtOAc/5% acetone) yielded product **7i** as a cream solid (186 mg, 94% yield). ^{1}H NMR ($CDCl_3$): δ 7.77 (d, J = 7.9 Hz, 1H), 7.60 (t, J = 7.8 Hz, 1H), 7.58 (s, 1H), 7.51 (d, J = 7.6 Hz, 1H), 7.26−7.18 (m, 3H), 6.95 (d, J = 7.3 Hz, 2H), 3.71−3.67 (m, 2H), 2.51 (t, J = 7.2 Hz, 2H), 2.42 (s, 3H), 1.88−1.81 (m, 2H). ^{13}C NMR ($CDCl_3$): 143.9, 143.2, 139.1, 133.4, 131.1 (J = 33 Hz), 130.2, 129.4, 128.5, 128.3, 127.7, 126.6 (J = 4.2 Hz), 126.5 (J = 3.6 Hz), 126.3, 123.4 (J = 271 Hz), 44.0, 32.2, 31.1, 13.2. The spectroscopic data are consistent with those previously reported in the literature.[4c]

Product Synthesis and Characterization (Scheme 5). *1-Butyl-5-(naphthalen-2-yl)-4-nitro-1H-pyrazole (**1a**).* Following general procedure **C**, 2-naphthol (79.3 mg, 0.550 mmol, 1.1 equiv), *para*-toluenesulfonyl chloride (107 mg, 0.560 mmol, 1.12 equiv), Cs_2CO_3 (269 mg, 0.825 mmol, 1.6 equiv), and anhydrous toluene (2.0 mL) were combined in a 20 mL scintillation vial for step 1. For step 2, the reaction mixture from step 1 was combined with **1** (84.6 mg, 0.500 mmol, 1.0 equiv), $Pd(OAc)_2$ (11.2 mg, 0.05 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (244 mg, 0.550 mmol, 1.5 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous toluene (1.0 mL) in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 80 °C for 24 h. Chromatography on a silica gel column using 85/15 hexanes/EtOAc (R_f = 0.34 in 85% hexanes/15% EtOAc) yielded product **1a** as a yellow oil (146 mg, 99% yield). The spectroscopic data are consistent with those of the product isolated using 2-naphthyl tosylate.

*3-(1-Butyl-4-nitro-1H-pyrazol-5-yl)pyridine (**1j**).* Following general procedure **C**, 3-hydroxy pyridine (52.3 mg, 0.550 mmol, 1.1 equiv), *para*-toluenesulfonyl chloride (107 mg, 0.560 mmol, 1.12 equiv), Cs_2CO_3 (269 mg, 0.8250 mmol, 1.6 equiv), and anhydrous toluene (2.0 mL) were combined in a 20 mL scintillation vial for step 1. For step 2, the reaction mixture from step 1 was combined with **1** (84.6 mg, 0.500 mmol, 1.0 equiv), $Pd(OAc)_2$ (11.2 mg, 0.05 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (244 mg, 0.550 mmol, 1.5 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous toluene (1.0 mL) in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 120 °C for 24 h. Chromatography on a silica gel column using 40/60 hexanes/EtOAc (R_f = 0.15 in 40% hexanes/60% EtOAc) yielded product **1j** as a yellow oil (94.1 mg, 76% yield). The spectroscopic data are consistent with those of the product isolated using 3-pyridyl tosylate.

*2-Methyl-1-[(4-methylphenyl)methyl]-5-(naphthalen-2-yl)-4-nitro-1H-imidazole (**6a**).* Following general procedure **C**, 2-naphthol (79.3 mg, 0.550 mmol, 1.1 equiv), *para*-toluenesulfonyl chloride (107 mg, 0.560 mmol, 1.12 equiv), Cs_2CO_3 (269 mg, 0.8250 mmol, 1.6 equiv), and anhydrous toluene (2.0 mL) were combined in a 20 mL scintillation vial for step 1. For step 2, the reaction mixture from step 1 was combined with **6** (116 mg, 0.500 mmol, 1.0 equiv), $Pd(OAc)_2$ (11.2 mg, 0.05 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (244 mg, 0.550 mmol, 1.5 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous toluene (1.0 mL) in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 120 °C for 14 h. Chromatography on a Biotage purification system silica gel column using 45/55 hexanes/EtOAc (R_f = 0.36 in 45% hexanes/55% EtOAc) yielded product **6a** as a yellow solid (176 mg, 98% yield). The spectroscopic data are consistent with those of the product isolated using 2-naphthyl tosylate.

Product Synthesis and Characterization (Scheme 6). *1-Butyl-5-(naphthalen-2-yl)-4-nitro-1H-pyrazole (**1a**).* Following general procedure **A**, **1** (84.6 mg, 0.500 mmol, 1.0 equiv), 2-naphthyl mesylate (124 mg, 0.556 mmol, 1.1 equiv), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (244 mg, 0.750 mmol, 1.5 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous toluene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 80 °C for 16 h. Chromatography on a silica gel column using 95/5 hexanes/EtOAc (R_f = 0.24 in 95% hexanes/5% ethyl acetate) yielded product **1a** as a yellow oil (148 mg, > 99% yield). The spectroscopic data are consistent with those of the product isolated using 2-naphthyl tosylate.

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Procedure outside the Glovebox. Following general procedure **F**, **1** (42.3 mg, 0.250 mmol, 1.0 equiv), 2-naphthyl mesylate (61.1 mg, 0.275 mmol, 1.1 equiv), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol, 0.10 equiv), XPhos (35.8 mg, 0.075 mmol, 0.30 equiv), Cs_2CO_3 (122 mg, 0.375 mmol, 1.5 equiv), CsOPiv (64.4 mg, 0.275 mmol, 1.1 equiv), and anhydrous toluene (0.5 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 80 °C for 16 h. The reaction was filtered through a 1-in. pad of silica gel eluting with EtOAc (100 mL). The filtrate was concentrated. ^1H NMR spectroscopic analysis of the crude product against 1,4-dinitrobenzene as the standard showed 30% yield of the desired product and 70% of azole **1**.

*1-(4-Methylphenyl)-5-(naphthalen-2-yl)-4-nitro-1H-pyrazole (**4a**)*. Following general procedure **A**, **4** (50.8 mg, 0.25 mmol, 1.0 equiv), 2-naphthyl mesylate (61.1 mg, 0.275 mmol, 1.1 equiv), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol, 0.10 equiv), XPhos (35.8 mg, 0.075 mmol, 0.30 equiv), Cs_2CO_3 (122 mg, 0.375 mmol, 1.5 equiv), CsOPiv (64.4 mg, 0.275 mmol, 1.1 equiv), and anhydrous toluene (0.5 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 80 °C for 16 h. Chromatography on a silica gel column using 95/5 hexanes/EtOAc (R_f = 0.15 in 95% hexanes/5% ethyl acetate) yielded product **4a** as a light yellow solid (79.5 mg, 97% yield). Mp = 129−134 °C ^1H NMR ($CDCl_3$): δ 8.43 (s, 1H), 7.87−7.83 (m, 3H), 7.79 (d, J = 7.8 Hz, 1H), 7.59−7.50 (m, 2H), 7.33 (dd, J = 8.6, 1.7 Hz, 1H), 7.12−7.05 (m, 4H), 2.29 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 140.8, 138.9, 137.4, 136.1, 134.0, 133.5, 132.6, 130.8, 129.7, 128.5, 128.3, 127.8, 127.6, 126.71, 126.65, 125.0, 123.8, 21.0. IR (thin film, CH_2Cl_2): 2923, 1549, 1512, 1499, 1393, 1318, 821 cm^{-1}. HRMS: [EI+, M+] calcd for $C_{20}H_{15}N_3O_2$, 329.1164; found, 329.1161.

*1-Butyl-5-(3,4-dimethoxyphenyl)-4-nitro-1H-pyrazole (**1p**)*. Following general procedure **A**, **1** (84.6 mg, 0.500 mmol, 1.0 equiv), 3,4-dimethoxyphenyl mesylate (128 mg, 0.550 mmol, 1.1 equiv), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (244 mg, 0.750 mmol, 1.5 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous toluene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 120 °C for 16 h. Chromatography on a silica gel column using 85/15 hexanes/EtOAc (R_f = 0.18 in 85% hexanes/15% ethyl acetate) yielded product **1p** as a viscous yellow oil (97.0 mg, 64% yield). ^1H NMR ($CDCl_3$): δ 8.20 (s, 1H), 7.00 (d, J = 8.2 Hz, 1H), 6.93 (dd, J = 8.2, 2.0 Hz, 1H), 6.85 (d, J = 1.9 Hz, 1H), 3.97 (t, J = 7.2 Hz, 2H), 3.96 (s, 3H), 3.90 (s, 3H), 1.80−1.72 (m, 2H), 1.27−1.18 (m, 2H), 0.84 (t, J = 7.3 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 150.5, 149.1, 141.2, 136.4, 132.7, 122.5, 118.6, 112.6, 111.1, 56.1, 55.9, 50.0, 31.8, 19.6, 13.5. IR (thin film, CH_2Cl_2): 2958, 2934, 1508, 1463, 1398, 1320, 1262, 1249, 1218, 1174, 1140, 1023, 857, 826, 759 cm^{-1}. HRMS: [TOF, ES+, M+H] calcd for $C_{15}H_{19}N_3O_4$, 306.1454; found, 306.1454.

*1-Butyl-4-nitro-5-(3,4,5-trimethoxyphenyl)-1H-pyrazole (**1f**)*. Following general procedure **A**, **1** (84.6 mg, 0.500 mmol, 1.0 equiv), 3,4,5-trimethoxyphenyl mesylate (144 mg, 0.550 mmol, 1.1 equiv), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (244 mg, 0.750 mmol, 1.5 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous toluene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 120 °C for 16 h. Chromatography on a silica gel column using 80/20 hexanes/EtOAc (R_f = 0.20 in 80% hexanes/20% EtOAc) yielded product **1f** as a yellow oil (111 mg, 66% yield). The spectroscopic data are consistent with those of the product isolated using 3,4,5-trimethoxyphenyl tosylate.

*1-Butyl-4-nitro-5-[4-(trifluoromethyl)phenyl]-1H-pyrazole (**1n**)*. Following general procedure **B**, **1** (84.6 mg, 0.500 mmol, 1.0 equiv), *para*-trifluoromethylphenyl mesylate (132 mg, 0.550 mmol, 1.1 equiv), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (244 mg, 0.750 mmol, 1.5 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous toluene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 120 °C for 16 h. Chromatography on a silica gel column using 90/10 hexanes/EtOAc (R_f = 0.18 in 90% hexanes/10% EtOAc) yielded product **1n** as a yellow oil (80 mg, 51% yield). ^1H NMR ($CDCl_3$): δ 8.23 (s, 1H), 7.81 (d, J = 8.1 Hz, 2H), 7.52 (d, J = 8.1 Hz, 2H), 3.94 (t, J = 7.2 Hz, 2H), 1.79−1.72 (m, 2H), 1.27−1.16 (m, 2H), 0.84 (t, J = 7.3 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 139.7, 136.4, 133.1, 132.3 (q, J = 33 Hz), 130.5, 130.3, 125.8 (q, J = 3.7 Hz), 123.6 (q, J = 271 Hz), 50.3, 31.8, 19.5, 13.4. IR (neat): 2962, 1567, 1514, 1498, 1461, 1400, 1320, 1166, 1125, 1109, 1066, 1025, 847, 826, 762 cm^{-1}. HRMS: [TOF, ES+, M+H] calcd for $C_{14}H_{14}F_3N_3O_2$, 314.1116; found, 314.1115.

*2-Methyl-1-[(4-methylphenyl)methyl]-5-(naphthalen-2-yl)-4-nitro-1H-imidazole (**6a**)*. Following general procedure **A**, **6** (116 mg, 0.500 mmol, 1.0 equiv), 2-naphthyl mesylate (122 mg, 0.550 mmol, 1.1 equiv), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (224 mg, 0.690 mmol, 1.4 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous toluene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 120 °C for 14 h. Chromatography on a silica gel column using 42/55/3 hexanes/EtOAc/acetone (R_f = 0.28 in 42% hexanes/55% EtOAc/3% acetone) yielded product **6a** as a light yellow solid (176 mg, 98% yield). The spectroscopic data are consistent with those of the product isolated using 2-naphthyl tosylate.

*5-(3-Methoxyphenyl)-2-methyl-1-[(4-methylphenyl)methyl]-4-nitro-1H-imidazole (**6c**)*. Following general procedure **B**, **6** (116 mg, 0.500 mmol, 1.0 equiv), *meta*-methoxyphenyl mesylate (111 mg, 0.550 mmol, 1.1 equiv), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (224 mg, 0.690 mmol, 1.4 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous toluene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 120 °C for 14 h. Chromatography on a silica gel column using 42/55/3 hexanes/EtOAc/acetone (R_f = 0.28 in 42% hexanes/55% EtOAc/3% acetone) yielded product **6c** as a light yellow solid (153 mg, 91% yield). The spectroscopic data are consistent with those of the product isolated using 3-methoxy phenyl tosylate.

Product Synthesis and Characterization (Scheme 7). *5-Benzyl-1-methyl-4-nitro-1H-pyrazole (**2q**)*. Following general procedure **D**, **2** (63.6 mg, 0.500 mmol, 1.0 equiv), benzyl acetate (82.6 mg, 0.550 mmol, 1.1 equiv), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (244 mg, 0.750 mmol, 1.5 equiv), and anhydrous xylene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 80 °C for 16 h. Chromatography on a silica gel column using 55/45 hexanes/EtOAc (R_f = 0.45 in 55% hexanes/45% EtOAc) yielded product **2q** as a light yellow solid (106 mg, 97% yield). ^1H NMR ($CDCl_3$): δ 8.13 (s, 1H), 7.34−7.24 (m, 3H), 7.13 (d, J = 7.5 Hz, 2H), 4.49 (s, 2H), 3.77 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 140.7, 136.1, 134.8, 133.1, 129.0, 128.0, 127.3, 37.6, 29.9. The spectroscopic data are consistent with those previously reported in the literature.[9]

Procedure outside the Glovebox. Following general procedure **G**, **2** (63.6 mg, 0.500 mmol, 1.0 equiv), benzyl acetate (82.6 mg, 0.550 mmol, 1.1 equiv), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (244 mg, 0.750 mmol, 1.5 equiv), and anhydrous toluene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 80 °C for 16 h. Chromatography on a silica gel column using 55/45 hexanes/EtOAc (R_f = 0.45 in 55% hexanes/45% EtOAc) yielded product **2q** as a light yellow solid (77.1 mg, 71% yield).

*1-Methyl-5-[(4-methylphenyl)methyl]-4-nitro-1H-pyrazole (**2r**)*. Following general procedure **D**, **2** (63.6 mg, 0.500 mmol, 1.0 equiv), *para*-methylbenzyl acetate (90.3 mg, 0.550 mmol, 1.1 equiv), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (244 mg, 0.750 mmol, 1.5 equiv), and anhydrous xylene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 80 °C for 16 h. Chromatography on a silica gel column using 80/20 hexanes/EtOAc (R_f = 0.22 in 80% hexanes/20% EtOAc) yielded product **2r** as a yellow solid (86.1 mg, 74% yield). ^1H NMR ($CDCl_3$): δ 8.12 (s, 1H), 7.11 (d, J = 7.9 Hz, 2H), 7.02 (d, J = 7.9 Hz, 2H), 4.44 (s, 2 H), 3.77 (s, 3H), 2.32 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 140.9, 136.9, 136.1, 133.0, 131.6,

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129.6, 127.9, 37.5, 29.5, 20.9. The spectroscopic data are consistent with those previously reported in the literature.[9]

5-[(3-Fluorophenyl)methyl]-1-methyl-4-nitro-1H-pyrazole (**2s**). Following general procedure **D**, **2** (63.6 mg, 0.500 mmol, 1.0 equiv), *meta*-fluorobenzyl acetate (92.5 mg, 0.550 mmol, 1.1 equiv), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (244 mg, 0.750 mmol, 1.5 equiv), and anhydrous xylene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 80 °C for 16 h. Chromatography on a silica gel column using 75/25 hexanes/EtOAc (R_f = 0.20 in 75% hexanes/25% EtOAc) yielded product **2s** as a light yellow solid (84.8 mg, 72% yield). ^1H NMR ($CDCl_3$): δ 8.14 (s, 1H), 7.32−7.26 (m, 1H), 6.97 (t, *J* = 8.5 Hz, 1H), 6.91 (d, *J* = 7.8 Hz, 1H), 6.84 (d, *J* = 9.3 Hz, 1H), 4.49 (s, 2H), 3.79 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 163.0 (*J* = 246 Hz), 139.9, 137.1 (*J* = 7.4 Hz), 136.2, 133.2, 130.5 (*J* = 8.1 Hz), 123.7 (*J* = 2.9 Hz), 115.1 (*J* = 22 Hz), 114.3 (*J* = 21 Hz), 37.6, 29.6 (*J* = 2.1 Hz). The spectroscopic data are consistent with those previously reported in the literature.[9]

5-[(3-Methoxyphenyl)methyl]-1-methyl-4-nitro-1H-pyrazole (**2t**). Following general procedure **D**, **2** (63.6 mg, 0.500 mmol, 1.0 equiv), *meta*-methoxybenzyl acetate (99.1 mg, 0.550 mmol, 1.1 equiv), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (244 mg, 0.750 mmol, 1.5 equiv), and anhydrous xylene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 80 °C for 16 h. Chromatography on a silica gel column using 60/40 hexanes/EtOAc (R_f = 0.35 in 60% hexanes/40% EtOAc) yielded product **2t** as a yellow viscous oil (95.7 mg, 78% yield). ^1H NMR ($CDCl_3$): δ 8.12 (s, 1H), 7.23 (t, *J* = 7.9 Hz, 1H), 6.79 (dd, *J* = 8.0, 2.5 Hz, 1H), 6.70 (d, *J* = 7.7 Hz, 1H), 6.67 (t, *J* = 2.2 Hz, 1H), 4.46 (s, 2H), 3.77 (s, 6H). The spectroscopic data are consistent with those previously reported in the literature.[9]

5-Benzyl-1-(4-methylphenyl)-4-nitro-1H-pyrazole (**4q**). Following general procedure **D**, **4** (50.8 mg, 0.25 mmol, 1.0 equiv), benzyl acetate (41.3 mg, 0.275 mmol, 1.1 equiv), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol, 0.10 equiv), XPhos (35.8 mg, 0.075 mmol, 0.30 equiv), Cs_2CO_3 (122 mg, 0.375 mmol, 1.5 equiv), CsOPiv (64.4 mg, 0.275 mmol, 1.1 equiv), and anhydrous toluene (0.5 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 80 °C for 16 h. Chromatography on a silica gel column using 90/10 hexanes/EtOAc (R_f = 0.26 in 90% hexanes/10% EtOAc) yielded product **4q** as a clear viscous oil (39.1 mg, 53% yield). ^1H NMR ($CDCl_3$): δ 8.31 (s, 1H), 7.27−7.15 (m, 7H), 6.96 (dd, *J* = 7.6, 2.1 Hz, 2H), 4.42 (s, 2H), 2.42 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 141.5, 140.1, 137.1, 135.8, 135.5, 133.8, 130.0, 128.7, 128.0, 127.0, 125.7, 30.6, 21.2. IR (neat): 2922, 1544, 1504, 1494, 1463, 1401, 1318, 1178, 829, 821, 804, 778, 757, 723, 712, 694 cm^{-1}. HRMS: [EI+, M+] calcd for $C_{17}H_{15}N_3O_2$, 293.1164; found, 293.1162.

5-[(3-methoxyphenyl)methyl]-2-methyl-1-[(4-methylphenyl)-methyl]-4-nitro-1H-imidazole (**6t**). Following general procedure **D**, **6** (115.6 mg, 0.500 mmol, 1.0 equiv), *meta*-methoxybenzyl acetate (99.1 mg, 0.550 mmol, 1.1 equiv), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (244 mg, 0.750 mmol, 1.5 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous toluene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 120 °C for 14 h. Chromatography on a silica gel column using 12/30/58 acetone/CH_2Cl_2/hexanes (R_f = 0.36 in 12% acetone/30% CH_2Cl_2/58% hexanes) yielded product **6t** as a viscous oil (88.0 mg, 50% yield). ^1H NMR ($CDCl_3$): δ 7.19 (t, *J* = 7.9 Hz, 1H), 7.14 (d, *J* = 7.9 Hz, 2H), 6.77 (d, *J* = 8.4 Hz, 1H), 6.76 (d, *J* = 8.0 Hz, 2H), 6.68 (d, *J* = 7.8 Hz, 1H), 6.64 (t, *J* = 2.1 Hz, 1H), 4.93 (s, 2H), 4.34 (s, 2H), 3.75 (s, 3H), 2.35 (s, 3H), 2.34 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 160.0, 144.2, 144.0, 138.2, 137.2, 132.1, 130.8, 129.92, 129.89, 125.5, 120.3, 114.0, 112.2, 55.2, 47.6, 30.0, 21.0, 13.5. IR (neat): 1599, 1584, 1567, 1540, 1488, 1455, 1435, 1406, 1386, 1338, 1281, 1257, 1161, 1145, 1043, 858, 792, 764, 740, 690 cm^{-1}. HRMS: [TOF, ES+, M+H] calcd for $C_{20}H_{21}N_3O_3$, 352.1661; found, 352.1657.

Product Synthesis and Characterization (Scheme 8). *3-(1-Butyl-4-nitro-1H-pyrazol-5-yl)phenyl 4-methylbenzene-1-sulfonate* (**1u**). Following general procedure **A**, **1** (42.3 mg, 0.25 mmol, 1.0 equiv), 3-chloro phenyl tosylate (106 mg, 0.375 mmol, 1.5 equiv), $Pd(OAc)_2$ (2.80 mg, 0.012 mmol, 0.05 equiv), XPhos (11.8 mg, 0.025 mmol, 0.10 equiv), K_2CO_3 (51.8 mg, 0.375 mmol, 1.5 equiv), and anhydrous toluene (0.25 mL) were combined in a 4 mL scintillation vial. The reaction mixture was allowed to stir at 120 °C for 24 h. Chromatography on a silica gel column using 80/20 hexanes/EtOAc (R_f = 0.28 in 80% hexanes/20% EtOAc) yielded product **1u** as a yellow oil (81.3 mg, 78% yield). ^1H NMR ($CDCl_3$): 8.18 (s, 1H), 7.72 (d, *J* = 8.3 Hz, 2H), 7.48 (t, *J* = 8.0 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.27−7.25 (m, 1H), 7.21 (ddd, *J* = 8.3, 2.4, 1.1 Hz, 1H), 7.03 (t, *J* = 1.7 Hz, 1H), 3.88 (t, *J* = 7.2 Hz, 2H), 2.44 (s, 3H), 1.74−1.67 (m, 2H), 1.23−1.15 (m, 2H), 0.83 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 149.6, 145.8, 139.4, 136.1, 132.9, 131.7, 130.2, 129.9, 128.43, 128.38, 128.2, 124.3, 123.8, 50.1, 31.6, 21.6, 19.4, 13.3. IR (neat): 1557, 1505, 1481, 1463, 1400, 1374, 1324, 1257, 1192, 1180, 1147, 1120, 1091, 890, 828, 814, 804, 763, 748, 732, 689, 661 cm^{-1}. HRMS: [EI+, M+] calcd for $C_{20}H_{21}N_3O_5S$, 415.1202; found, 415.1206.

3-(1-Butyl-4-nitro-1H-pyrazol-5-yl)phenyl 4-methylbenzene-1-sulfonate (**1u**). Following general procedure **A**, **1** (42.3 mg, 0.25 mmol, 1.0 equiv), 3-bromo phenyl tosylate (123 mg, 0.375 mmol, 1.5 equiv), $Pd(OAc)_2$ (2.80 mg, 0.012 mmol, 0.05 equiv), XPhos (11.8 mg, 0.025 mmol, 0.10 equiv), K_2CO_3 (51.8 mg, 0.375 mmol, 1.5 equiv), and anhydrous toluene (0.25 mL) were combined in a 4 mL scintillation vial. The reaction mixture was allowed to stir at 120 °C for 24 h. Chromatography on a silica gel column using 80/20 hexanes/EtOAc (R_f = 0.28 in 80% hexanes/20% EtOAc) yielded product **1u** as a yellow oil (92.3 mg, 89% yield). The spectroscopic data are identical to those of the product obtained using 3-chlorophenyl tosylate.

1-Butyl-5-[3-(1-butyl-4-nitro-1H-pyrazol-5-yl)phenyl]-4-nitro-1H-pyrazole (**1v**). Following general procedure **A**, **1** (169 mg, 1.00 mmol, 2.0 equiv), 3-chloro phenyl tosylate (141 mg, 0.500 mmol, 1.0 equiv), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol, 0.05 equiv), XPhos (23.5 mg, 0.05 mmol, 0.10 equiv), K_2CO_3 (415 mg, 3.00 mmol, 6.0 equiv), and anhydrous toluene (0.5 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 120 °C for 24 h. Chromatography on a silica gel column using 80/20 hexanes/EtOAc (R_f = 0.25 in 80% hexanes/20% EtOAc) yielded product **1v** as a yellow oil (165 mg, 80% yield). ^1H NMR ($CDCl_3$): 8.23 (s, 2H), 7.73 (t, *J* = 7.8 Hz, 1H), 7.56 (dd, *J* = 7.7, 1.7 Hz, 2H), 7.45 (t, *J* = 1.8 Hz, 1H), 4.05 (t, *J* = 7.3 Hz, 4H), 1.78−1.72 (m, 4H), 1.28−1.18 (m, 4H), 0.83 (t, *J* = 7.3 Hz, 6H). ^{13}C NMR ($CDCl_3$): δ 139.8, 136.3, 133.0, 131.6, 131.3, 129.4, 127.6, 50.4, 31.7, 19.5, 13.4. IR (neat): 1551, 1502, 1480, 1464, 1398, 1321, 1267, 1190, 910, 831, 807, 761, 730, 704 cm^{-1}. HRMS: [EI+, M+] calcd for $C_{20}H_{24}N_6O_4$, 412.1859; found, 412.1860.

1-Butyl-5-[3-(1-butyl-4-nitro-1H-pyrazol-5-yl)phenyl]-4-nitro-1H-pyrazole (**1v**). Following general procedure **A**, **1** (169 mg, 1.00 mmol, 2.0 equiv), 3-bromo phenyl tosylate (164 mg, 0.500 mmol, 1.0 equiv), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol, 0.05 equiv), XPhos (23.5 mg, 0.05 mmol, 0.10 equiv), K_2CO_3 (415 mg, 3.00 mmol, 6.0 equiv), and anhydrous toluene (0.5 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 120 °C for 24 h. Chromatography on a silica gel column using 80/20 hexanes/EtOAc (R_f = 0.25 in 80% hexanes/20% EtOAc) yielded product **1v** as a yellow oil (152 mg, 74% yield). The spectroscopic data are identical to those of the product obtained using 3-chlorophenyl tosylate.

Product Synthesis and Characterization (Scheme 9). *[3-(1-Methyl-4-nitro-1H-pyrazol-5-yl)phenyl]methyl Acetate* (**2w**). Following general procedure **D**, **2** (63.6 mg, 0.50 mmol, 1.0 equiv), 3-chloro benzyl acetate (101 mg, 0.550 mmol, 1.1 equiv), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), Cs_2CO_3 (244 mg, 0.750 mmol, 1.5 equiv), and anhydrous xylene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 80 °C for 24 h. Chromatography on a silica gel column using 65/35 hexanes/EtOAc (R_f = 0.25 in 65% hexanes/35% EtOAc) yielded product **2w** as a white solid (114 mg, 82% yield). Mp = 102−105 °C. ^1H NMR ($CDCl_3$): 8.20 (s, 1H), 7.55−7.54 (m, 2H), 7.40 (s, 1H), 7.37−7.35 (m, 1H), 5.18 (s, 2H), 3.75 (s, 3H), 2.13 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 170.6, 140.9, 136.9, 136.3, 132.9, 130.0, 129.4, 129.3, 129.0, 126.8, 65.4, 38.0,

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20.9. IR (neat): 1732, 1499, 1469, 1406, 1381, 1360, 1328, 1288, 1195, 1178, 1029, 893, 825, 800, 762, 682, 644, 621, 605, 582 cm^{-1}. HRMS: [TOF, ES+, M+H] calcd for $C_{13}H_{14}N_3O_4$, 276.0984; found, 276.0989.

*1-Methyl-5-{3-[(1-methyl-4-nitro-1H-pyrazol-5-yl)methyl]-phenyl}-4-nitro-1H-pyrazole (**2x**).* Following general procedure **D**, **2** (63.6 mg, 0.50 mmol, 2.0 equiv), 3-chloro benzyl acetate (46.2 mg, 0.25 mmol, 1.0 equiv), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol, 0.10 equiv), XPhos (35.3 mg, 0.075 mmol, 0.30 equiv), Cs_2CO_3 (244 mg, 0.750 mmol, 3.0 equiv), and anhydrous xylene (0.5 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 80 °C for 24 h. Chromatography on a silica gel column using 100% diethyl ether (R_f = 0.30 in 100% diethyl ether) yielded product **2x** as an off white solid (60.0 mg, 70% yield). Mp = 70−72 °C. ^{1}H NMR ($CDCl_3$): 8.19 (s, 1H), 8.14 (s, 1H), 7.51 (t, *J* = 7.8 Hz, 1H), 7.34−7.29 (m, 2H), 7.21−7.20 (m, 1H), 4.57 (s, 2H), 3.84 (s, 3H), 3.73 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 140.6, 139.8, 136.3, 136.2, 135.7, 133.2, 132.9, 130.0, 129.7, 129.5, 128.5, 127.2, 38.1, 37.7, 29.8. IR (neat): 1552, 1497, 1432, 1404, 1317, 1193, 870, 832, 786, 772, 764, 752 cm^{-1}. HRMS: [EI+, M+] calcd for $C_{15}H_{14}N_6O_4$, 342.1077; found, 342.1075.

Product Synthesis and Characterization (Scheme 10). *2-(2-Nitrophenyl)naphthalene (**8a**).* Following general procedure **E**, nitrobenzene (616 mg, 5.00 mmol, 10 equiv), 2-naphthyl tosylate (149 mg, 0.500 mmol, 1.0 equiv), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), K_3PO_4 (159 mg, 0.750 mmol, 1.5 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous xylene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 140 °C for 24 h. Chromatography on a silica gel column using 97/3 hexanes/EtOAc (R_f = 0.12 in 97% hexanes/3% EtOAc) yielded product **8a** as a yellow solid (78 mg, 63% yield). ^{1}H NMR ($CDCl_3$): 7.94−7.85 (m, 4H), 7.82 (s, 1H), 7.66 (td, *J* = 7.6, 1.4 Hz, 1H), 7.56−7.50 (m, 4H), 7.41 (dd, *J* = 8.5, 1.9 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 149.3, 136.4, 134.9, 133.2, 132.8, 132.4, 132.3, 128.3, 128.2, 128.1, 127.7, 126.9, 126.5, 125.7, 124.2. The spectroscopic data are consistent with those previously reported in the literature.[23]

*2-Methoxy-7-(2-nitrophenyl)naphthalene (**8d**).* Following general procedure **E**, nitrobenzene (616 mg, 5.00 mmol, 10 equiv), 7-methoxynaphthyl tosylate (164 mg, 0.500 mmol, 1.0 equiv), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), K_3PO_4 (159 mg, 0.750 mmol, 1.5 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous xylene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 140 °C for 24 h. Chromatography on a silica gel column using 93/7 hexanes/EtOAc (R_f = 0.31 in 93% hexanes/7% EtOAc) yielded product **8d** as a yellow oil (80 mg, 58% yield). ^{1}H NMR ($CDCl_3$): 7.90 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.81 (d, *J* = 8.4 Hz, 1H), 7.77 (d, *J* = 9.0 Hz, 1H), 7.70 (d, *J* = 1.7 Hz, 1H), 7.65 (td, *J* = 7.6, 1.4 Hz, 1H), 7.55−7.49 (m, 2H), 7.27 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.19 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.15 (d, *J* = 2.6 Hz, 1H), 3.93 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 158.1, 149.3, 136.4, 135.4, 134.4, 132.3, 132.1, 129.2, 128.3, 128.09, 128.06, 125.8, 124.1, 123.4, 119.4, 106.0, 55.3. HRMS: [TOF, ES+, M+H] calcd for $C_{17}H_{13}NO_3$, 280.0974; found, 280.0971. IR (thin film, CH_2Cl_2): 3002, 1630, 1610, 1519, 1460, 1391, 1350, 1237, 1212, 1174, 1125, 1024, 838, 742 cm^{-1}.

*1,2-Dimethoxy-4-(2-nitrophenyl)benzene (**8p**).* Following general procedure **E**, nitrobenzene (616 mg, 5.00 mmol, 10 equiv), 3,4-dimethoxyphenyl tosylate (154 mg, 0.500 mmol, 1.0 equiv), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), K_3PO_4 (159 mg, 0.750 mmol, 1.5 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous xylene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 140 °C for 24 h. Chromatography on a silica gel column using 88/12 hexanes/EtOAc (R_f = 0.24 in 88% hexanes/12% EtOAc) yielded product **8p** as a yellow solid (64 mg, 49% yield). ^{1}H NMR ($CDCl_3$): δ 7.80 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.60 (td, *J* = 7.6, 1.3 Hz, 1H), 7.48−7.43 (m, 2H), 6.93−6.87 (m, 2H), 6.83 (d, *J* = 1.9 Hz, 1H), 3.92 (s, 3H), 3.88 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 149.5, 149.1, 149.0, 135.8, 132.0, 131.8, 129.7, 127.8, 123.8, 120.3, 111.2, 111.1, 55.90, 55.86. The spectroscopic data are consistent with those previously reported in the literature.[24]

*1,2,3-Trimethoxy-5-(2-nitrophenyl)benzene (**8f**).* Following general procedure **E**, nitrobenzene (616 mg, 5.00 mmol, 10 equiv), 3,4,5-trimethoxyphenyl tosylate (169 mg, 0.500 mmol, 1.0 equiv), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), K_3PO_4 (159 mg, 0.750 mmol, 1.5 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous toluene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 140 °C for 24 h. Chromatography on a silica gel column using 80/20 hexanes/EtOAc (R_f = 0.30 in 80% hexanes/20% EtOAc) yielded product **8f** as a yellow solid (63 mg, 44% yield). ^{1}H NMR ($CDCl_3$): δ 7.80 (d, *J* = 8.0 Hz, 1H), 7.61 (t, *J* = 7.6 Hz, 1H), 7.50−7.45 (m, 2H), 6.52 (s, 2H), 3.89 (s, 3H), 3.86 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 153.3, 149.4, 137.9, 135.9, 132.6, 132.0, 131.6, 128.1, 123.7, 105.0, 60.8, 56.1. HRMS: [TOF, ES+, M+H] calcd for $C_{15}H_{15}NO_5$, 290.1028; found, 290.1030.

*5-(2-Nitrophenyl)-2H-1,3-benzodioxole (**8e**).* Following general procedure **E**, nitrobenzene (616 mg, 5.00 mmol, 10 equiv), sesimol tosylate (146 mg, 0.500 mmol, 1.0 equiv), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol, 0.10 equiv), XPhos (71.5 mg, 0.150 mmol, 0.30 equiv), K_3PO_4 (159 mg, 0.750 mmol, 1.5 equiv), CsOPiv (129 mg, 0.550 mmol, 1.1 equiv), and anhydrous xylene (1.0 mL) were combined in a 20 mL scintillation vial. The reaction mixture was allowed to stir at 140 °C for 24 h. Chromatography on a silica gel column using 97/3 hexanes/EtOAc (R_f = 0.26 in 97% hexanes/3% EtOAc) yielded product **8e** as a dark orange solid (60.4 mg, 50% yield). ^{1}H NMR ($CDCl_3$): δ 7.80 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.59 (td, *J* = 7.6, 1.3 Hz, 1H), 7.45 (td, *J* = 7.8, 1.4 Hz, 1H), 7.42 (dd, *J* = 7.8, 1.4 Hz, 1H), 6.86 (d, *J* = 7.8 Hz, 1H), 6.80−6.76 (m, 2H), 6.02 (s, 2H). The spectroscopic data are consistent with those previously reported in the literature.[25]

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b00550.

NMR spectra of all isolated products and new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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(15) The site-selectivity of pyrazole arylations is assigned based on analogy to arylations affording products **1b**, **2h**, **2c**, **3i**, and **5j** (vide infra, Schemes 2 and 3). The ^{1}H NMR spectra of products **1b**, **2h**, **2c**, **3i**, and **5j** isolated under reaction conditions depicted in Schemes 2 and 3 are consistent with previously reported spectral data for these products (ref 4b).
(16) The mass balance of the reaction is poor at 120 °C.
(17) The majority of arylations in Schemes 2−4 and 6 were conducted at 120 °C since conversion of azole to products is near-complete at this temperature. The azole and the products have very similar retention factors on TLC thereby facilitating purification with higher conversions of the azole to the product. Only trace amounts of diarylation products were observed by GC/MS analysis of the crude reaction mixtures for reactions in Schemes 2 and 3 (*vide infra*). The mass balance was higher with azoles **2**, **3**, **5**, **6**, and **7** with a less than quantitative yield being accounted for by the remaining azole. For reactions using azole **1**, near-complete conversion of **1** is observed in most cases but the mass balance is poor at 120 °C.
(18) CsOPiv is necessary for higher conversions using very electron-rich (e.g., *p*-methoxyphenyl tosylate) or electron-deficient (*m*-trifluoromethylphenyl and heteroaryl) electrophiles.
(19) The site-selectivity for pyrazole benzylations was established by comparison of the spectral data of the isolated products with those previously reported in the literature (ref 9).
(20) Use of CsOPiv leads to higher yields of **4q** and **6t**. The benzylation of **2** using benzyl tosylate affords **2q** in lower yield (40%) than obtained using benzyl acetate.
(21) For an example of C−H arylation for which aryl tosylates react faster than aryl chlorides, see ref 13e. This selectivity is opposite to that observed for arylations depicted in Scheme 8.
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