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Palladium-Catalyzed Chelation-Assisted Regioselective Oxidative Dehydrogenative Homocoupling/*Ortho*-Hydroxylation in *N*-Phenylpyrazoles

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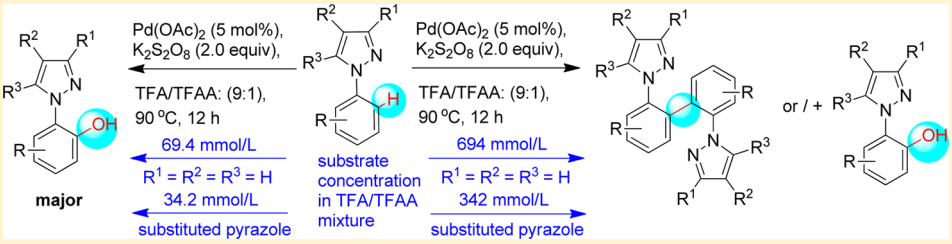
Supporting Information



ABSTRACT: A palladium-catalyzed pyrazole-directed regioselective oxidative C(sp2)−H functionalization of the *N*-phenyl ring in *N*-phenylpyrazoles to afford either a biaryl bis-pyrazole (via dehydrogenative homocoupling) or *N*-(*o*-hydroxyphenyl)pyrazole (via C−H oxygenation) or their mixture is described. The substitutions on the *N*-phenyl ring and the pyrazole ring and the dilution of the reaction medium with respect to the TFA/TFAA mixture (substrate concentration) have a remarkable influence on the outcome of the reaction. It was discovered that if the reactions were performed under highly dilute conditions (ca. 10 times) then *N*-(*o*-hydroxyphenyl)pyrazoles were the major or the sole products.

INTRODUCTION

The pyrazole nucleus, a privileged heteroarene, is encountered in several pharmaceutical agents including Viagra, Crizotinib, Lexiscan, and Celebrex.[1] In addition, many differently substituted pyrazole derivatives are endowed with diverse pharmacological properties.[2] Given such immense significance, there is continuing interest in development of new or alternative synthetic approaches toward efficient synthesis of substituted pyrazoles.[3] We have an ongoing program for formulating general routes to pyrazole derivatives of biological significance.[4] During the course of this work, we noticed that recently several compounds bearing a 1-(2-hydroxyphenyl)-pyrazole subunit were reported to be useful as antifungal agents **I**,[5] as antitrichophytic adhesive patch,[6] in the treatment of dermatophytosis and N-type Ca-channel blockers **II**,[7] as β-secretase inhibitors **III**,[8] and as Cu(II)-complexing ligandoside in DNA **IV**[9] (Figure 1). Established routes to their synthesis required starting reactants bearing the hydroxyl group which were either used directly or in the protected form. In principle, the *o*-hydroxyl group on the phenyl ring of 1-phenylpyrazole could be readily installed via transition-metal-catalyzed ligand-assisted *ortho*-directed oxidative C(sp2)−H functionalization.

During the past decade, transition-metal-catalyzed ligand-assisted *ortho*-directed oxidative C−H bond cleavage to accomplish regioselective functionalization of otherwise unreactive C−H bonds in aromatic molecules has been of considerable interest to synthetic organic chemists.[10,11] These transformations are considered to be green, sustainable, and efficient as they do not require preactivation of the substrate. Often, such transformations are catalyzed by rhodium, ruthenium, platinum, palladium, copper, nickel, and cobalt catalysts, but palladium catalysts are more widely investigated because of several advantages that they offer.[11] Among these reactions, metal-catalyzed oxidative functionalization of the C(sp2)−H bond proceeds regioselectively with the assistance of many directing groups including pyridine, triazole and several other aza-heterocycles, oxime, imine, amidine, ester, amide, ketone, phenol, and carboxylic acid. The approach has been effectively exploited to install aryl, alkyl, alkenyl, benzyl,

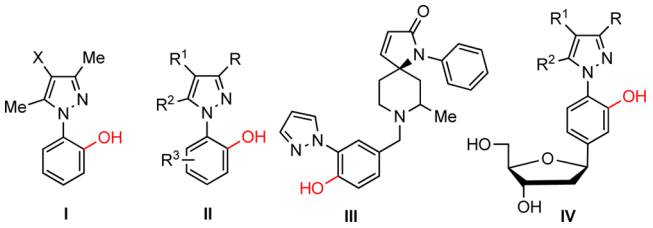


Figure 1. Recently reported 1-(2-hydroxyphenyl)pyrazole-based bioactive compounds.

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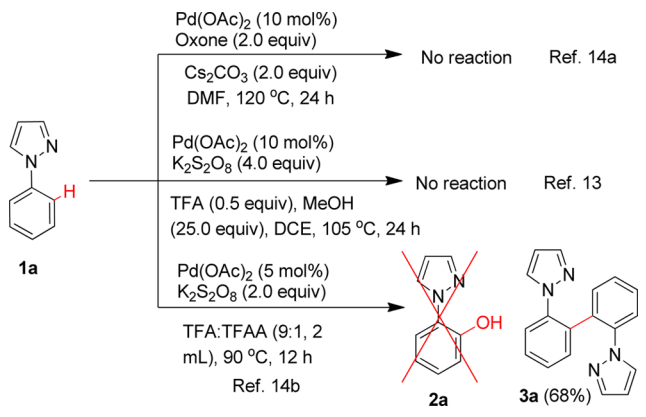
hydroxy, acetoxy, alkoxy, amide, trifluoromethyl, azide, nitro, nitrile, and halogen groups as proximal C−H bond to the directing group. Among the aza-heterocycles, 1-phenylpyrazole has been widely exemplified to undergo ligand-assisted oxidative C(sp2)−H functionalization for introducing some of the aforementioned groups.[12] Intriguingly, the transition-metal-catalyzed C−O bond formation in 1-phenylpyrazoles is limited to acetoxy and alkoxy groups, and the oxygenation reaction leading to 1-(2-hydroxyphenyl)pyrazole exclusively has yet not been demonstrated. Sanford et al.[12a,c] in their pioneering work on palladium-catalyzed ligand assisted acetoxylation disclosed *ortho*-acetoxylation of the phenyl ring in 1-phenylpyrazole. More recently, Kim et al. extended the palladium-catalyzed acetoxylation of the *ortho*-positions of different phenyl rings present in the pyrazole derivative.[12t] They summarized that the quantity of $PhI(OAc)_2$ influenced the degree of acetoxylation in the products formed. During investigations of the scope of palladium-catalyzed *ortho*-alkoxylation of 2-aryl-1,2,3-triazoles, Shi and Kuang reported that 1-phenylpyrazole resulted in the formation of 1-(2-hydroxy-6-methoxyphenyl)pyrazole in 42% yield.[13] Hence, we sought to probe the palladium-catalyzed *ortho*-hydroxylation of the phenyl ring in substituted 1-phenylpyrazoles and found that the success of the reaction in these substrates is remarkably influenced by the nature of substitutions present on the phenyl ring and the pyrazole ring and the substrate concentration in TFA/TFAA (9:1) mixture under which the reaction was performed. Herein we present the details of our study in this direction.

RESULTS AND DISCUSSION

The study commenced by probing a few reported methods for the palladium-mediated hydroxylation using 1-phenylpyrazole **1a** as the model substrate. Accordingly, **1a** (0.25 g, 1.74 mmol) was first treated with $Pd(OAc)_2$ (10 mol %), Oxone (2.0 equiv), and Cs_2CO_3 (2.0 equiv) in DMF (5 mL) at 120 °C for 24 h, but the starting material was recovered unreacted (Scheme 1).[14a] Next, **1a** was treated with $Pd(OAc)_2$ (10 mol %), $K_2S_2O_8$ (4.0 equiv), and TFA (0.5 equiv) in dichloroethane, but this reaction also failed.[13] However, it was gratifying to note that when **1a** was reacted with $Pd(OAc)_2$ (5 mol %), $K_2S_2O_8$ (2.0 equiv), and TFA/TFAA (9:1, v/v) (2.5 mL) at 90 °C for 12 h, a solid product in 68% yield was isolated after the workup.[15,14b] The structure of the product was delineated as 2,2′-di(1*H*-pyrazol-1-yl)biphenyl (**3a**) instead of 1-(2-hydroxyphenyl)pyrazole **2a**. The formation of **3a** was attributed to the oxidative dehydrogenative homocoupling by cleavage of the *ortho* C−H bond. Notably, such dehydrogenative homocoupling in 1-phenylpyrazole was previously reported in the presence of rhodium or ruthenium catalysts[16] but was unprecedented for the palladium catalyst. Therefore, we considered optimizing the reaction with palladium catalyst and examining its scope. As a result, several combinations of $Pd(OAc)_2$ and oxidants including $Na_2S_2O_8$, molecular oxygen, benzoyl peroxide, and TBHP were screened, and the results are summarized in Table 1. It is evident from Table 1 that $Pd(OAc)_2$ in combination with $K_2S_2O_8$ or Oxone offers superior yields of **3a** but the reaction in the presence of $K_2S_2O_8$ is relatively fast (entries 1 and 2). In contrast, $Na_2S_2O_8$, benzoyl peroxide, and TBHP afforded **3a** in low yield, while the reaction failed under molecular oxygen (entries 3−6). It is worth mentioning that during compilation of this work Sun et al.[17] reported palladium-catalyzed aryl C(sp2)−H bond hydroxylation of 2-arylpyridine in dichloroethane using TBHP as the sole oxidant, but this condition did not work in our hands for transformation of **1a** to **2a** or **3a** (entry 10). Thus, the conditions that offered the best yield of **3a** were heating **1a** (0.25 g at a concentration of 694 mmol/L), $Pd(OAc)_2$ (5 mol %), $K_2S_2O_8$ (2.0 equiv) in TFA/TFAA (9:1, v/v) at 90 °C for 12 h.

Scheme 1. Results of Initial Reactions Explored for Oxidative C(sp2)−H Hydroxylation in the Phenyl Ring in 1-Phenylpyrazole (1a)



With the optimized conditions in hand, we set out to test the scope of the methodology for a variety of 1-(substituted phenyl)pyrazoles **1b−q**, and the results are presented in Scheme 2. It was observed that in all cases except for **1l** and **1q** the corresponding biaryl bis-pyrazoles were isolated. Whereas the substrates carrying *ortho*- and *para*-substitution on the phenyl ring (**1b−e,h−k,m,n**) produced the corresponding products **3b−e,h−k,m,n** in good yields, the ones with *meta*-substitutions (**1f** and **1g**) furnished the respective products **3f** and **3g** in moderate yields only. Further, pyrazoles **1o** and **1p** bearing a dimethyl-substituted phenyl ring also furnished **3o** and **3p**, respectively, in good yields. The structure of the biaryl bis-pyrazole was unambiguously secured by the X-ray crystallographic analysis of the crystal of **3p** obtained from hexanes/EtOAc (see the Supporting Information). It is speculated that failure of the reaction in pyrazole **1l** could be due to the electron-donating character of the methoxy group, whereas failure of the reaction in pyrazole **1q** bearing an *N*-naphth-2-yl group may be because of steric constraints toward the formation of **3q**. In order to ascertain the limitation of scope for substrates bearing an electron-rich phenyl ring, we examined the reaction of 1-(3-methoxyphenyl)pyrazole (**1r**) and found that this substrate also failed to react under the optimized conditions. The formation of **3** can be readily explained on the basis of a mechanism involving Pd(IV) species as proposed by Sanford et al. (vide infra). The scope of the protocol was also tested with 1-benzylpyrazole (**4**), but this substrate failed to react under the standardized conditions (Scheme 3).

After studying the scope of the protocol with unsubstituted pyrazole derivatives, we turned our attention to a variety of substituted 1-phenylpyrazoles. Initially, in a pilot experiment, ethyl 1,5-diphenyl-1*H*-pyrazole-3-carboxylate (**5a**) (0.25 g) was subjected to reaction with $Pd(OAc)_2$ in TFA/TFAA (9:1, 2.5 mL) under the optimized conditions which upon workup and purification resulted in isolation of the major product in 76% yield and minor product in only 3% yield. We were

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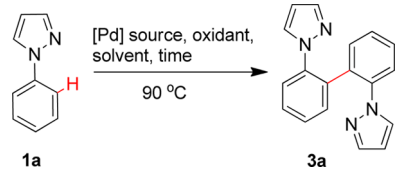
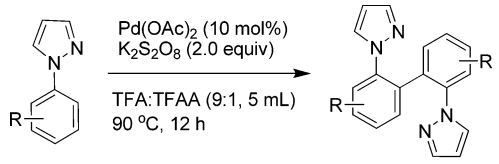
Table 1. Optimization[a] of the Palladium-Catalyzed Oxidative Dehydrogenative Homocoupling with 1-Phenylpyrazole 1a Leading to Biaryl Bis-pyrazole 3a



entry	catalyst (mol %)	solvent	oxidant (equiv)	time (h)	yield of 3a[b] (%)
1	$Pd(OAc)_2$ (5)	TFA/TFAA (9:1)	Oxone (2.0)	24	62
2	$Pd(OAc)_2$ (5)	TFA/TFAA (9:1)	$K_2S_2O_8$ (2.0)	12	68
3	$Pd(OAc)_2$ (5)	TFA/TFAA (9:1)	$Na_2S_2O_8$ (2.0)	24	27
4	$Pd(OAc)_2$ (5)	TFA/TFAA (9:1)	O_2 (balloon)	24	
5	$Pd(OAc)_2$ (5)	TFA/TFAA (9:1)	benzoyl peroxide (2.0)	24	20
6	$Pd(OAc)_2$ (5)	TFA/TFAA (9:1)	TBHP (2.0)	24	7
7[b]	$Pd(OAc)_2$ (5)	TFA/TFAA (9:1)	$K_2S_2O_8$ (1.5)	24	55
8[b]	$Pd(OAc)_2$ (5)	TFA	$K_2S_2O_8$ (2.0)	24	34
9	$Pd(OAc)_2$ (5)	TFAA	$K_2S_2O_8$ (2.0)	24	trace
10	$Pd(OAc)_2$ (5)	DCE	TBHP (6.0)	24	trace

[a]All reactions were performed using 0.25 g of pyrazole **1a** at a concentration of 694 mmol/L of solvent. [b]Yields of chromatographically pure product.

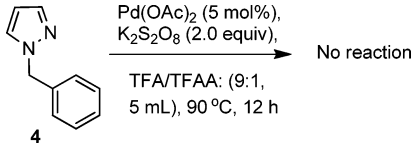
Scheme 2. Scope of Ligand-Assisted Palladium-Catalyzed Oxidative Dehydrogenative Homocoupling to Produce Biaryl Bis-pyrazoles in 1-(Substituted phenyl)pyrazoles[a,b]



1a	R = H	**3a**	R = H (68%)
1b	R = 2-Cl	**3b**	R = 2-Cl (83%)
1c	R = 2-Me	**3c**	R = 2-Me (80%)
1d	R = 2-CF_3	**3d**	R = 2-CF_3 (74%)
1e	R = 2-CO_2Et	**3e**	R = 2-CO_2Et (60%)
1f	R = 3-F	**3f**	R = 3-F (45%)
1g	R = 3-Cl	**3g**	R = 3-Cl (48%)
1h	R = 4-F	**3h**	R = 4-F (78%)
1i	R = 4-Cl	**3i**	R = 4-Cl (75%)
1j	R = 4-Br	**3j**	R = 4-Br (70%)
1k	R = 4-Me	**3k**	R = 4-Me (72%)
1l	R = 4-OMe	**3l**	R = 4-OMe (0%)
1m	R = 4-CF_3	**3m**	R = 4-CF_3 (74%)
1n	R = 4-CO_2Et	**3n**	R = 4-CO_2Et (72%)
1o	R = 2,4-Me_2	**3o**	R = 2,4-Me_2 (74%)
1p	R = 3,4-Me_2	**3p**	R = 3,4-Me_2 (70%)
1q	R = naphth-2-yl	**3q**	R = naphth-2-yl (0%)
1r	R = 3-OMe	**3r**	R = 3-OMe (0%)

[a]Reactions were performed with 0.5−0.77 g of pyrazoles (**1a**−**r**) at a substrate concentration of 694 mmol/L of solvent. [b]Yields after column chromatography.

Scheme 3. Result of the Reaction of 1-Benzylpyrazole under the Optimized Conditions[a]



[a]The reaction was performed with 0.55 g of pyrazole (**4**) at a substrate concentration of 694 mmol/L.

pleased to discover that the major product was spectroscopically characterized as ethyl 1-(2-hydroxyphenyl)-5-phenyl-1*H*-pyrazole-3-carboxylate (**6a**), whereas the minor product was identified to be the biaryl bis-pyrazole **7a**. However, it was realized that in this pilot reaction the substrate concentration of **5a** was 342 mmol/L instead of 694 mmol/L as optimized for the unsubstituted pyrazoles **1**. As a consequence, the reaction was repeated with **5a** (0.5 g) at a substrate concentration of 685 mmol/L. Although the presence of a lower amount of solvent made the reaction too cumbersome to perform, we could isolate the **6a** in 44% and **7a** in 10% yields in addition to unreacted **5a** and a mixture of unidentified products. Perhaps the presence of substitutions at the 3- and 5-positions in pyrazole **5a** may have induced certain steric constraints, thereby favoring the *ortho*-hydroxylation of the phenyl ring rather than dehydrogenative homocoupling. In view of our interest in synthesizing substituted 1-(2-hydroxyphenyl)pyrazoles exclusively coupled with ease of performing the reaction with optimal solvent amount, we decided to perform the reactions of substituted pyrazoles at a substrate concentration of 342 mmol/L. In order to examine the possibility of improving the yields of **6a**, we screened the reaction of **5a** with respect to different palladium sources, oxidants, and solvents, and the results are summarized in Table 2. Among several oxidants evaluated, $K_2S_2O_8$ gave the best result, whereas Oxone and $PhI(OAc)_2$ gave **6a** in slightly lower yields (compare entry 1 with entries 2 and 3). In contrast, the yield of **6a** in the presence of all other oxidants screened for the reaction was found to be inferior (entries 4−7). Reducing the amount of $K_2S_2O_8$ from 2.0 to 1.5 equiv reduced the yield of **6a** appreciably (entry 8). Performing the reaction in the presence of TFA or TFAA individually or any other organic solvent did not afford the required product **6a** in better yields (entries 9−12). Altering the palladium source revealed that $Pd(TFA)_2$ was as effective as $Pd(OAc)_2$ to afford **6a** in 75% yield, whereas $Pd(PPh_3)_2Cl_2$ failed to yield any product (entries 13 and 14). However, even in $Pd(TFA)_2$-mediated reactions, the presence of **7a** was detected. Therefore, it was decided to continue to investigate the scope further with the optimized conditions using a substrate concentration of 342 mmol/L.

In next stage of the study, we examined the scope of the reaction with several differently substituted pyrazoles. In the first set, reactions of various ethyl 1,5-diphenyl-1*H*-pyrazole-3-

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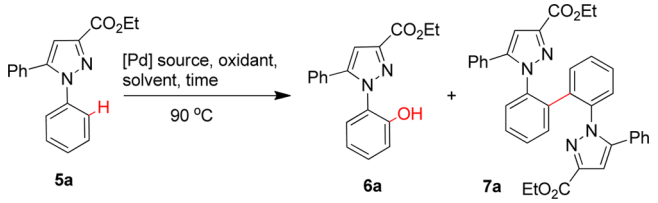
Table 2. Results of the Study To Examine the Effect of Different Palladium Source, Oxidants, and Solvents on the Formation of 6a from 5a[a]

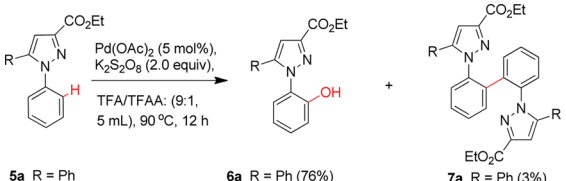


entry	catalyst (mol %)	solvent	oxidant (equiv)	time (h)	yield 6a[c] (%)
1	$Pd(OAc)_2$ (5)	TFA/TFAA (9:1)	$K_2S_2O_8$ (2.0)	12	76[d]
2[b]	$Pd(OAc)_2$ (5)	TFA/TFAA (9:1)	Oxone (2.0)	12	72[d]
3	$Pd(OAc)_2$ (5)	TFA/TFAA (9:1)	$PhI(OAc)_2$ (2.0)	12	70
4	$Pd(OAc)_2$ (5)	TFA/TFAA (9:1)	TBHP (2.0)	24	10
5	$Pd(OAc)_2$ (5)	TFA/TFAA (9:1)	benzoyl peroxide (2.0)	24	
6	$Pd(OAc)_2$ (5)	TFA/TFAA (9:1)	$Na_2S_2O_8$ (2.0)	24	30
7	$Pd(OAc)_2$ (5)	TFA/TFAA (9:1)	O_2 (ballon)	24	
8	$Pd(OAc)_2$ (5)	TFA/TFAA (9:1)	$K_2S_2O_8$ (1.5)	24	40[d]
9	$Pd(OAc)_2$ (5)	TFA	$K_2S_2O_8$ (2.0)	24	42[d]
10	$Pd(OAc)_2$ (5)	TFAA	$K_2S_2O_8$ (2.0)	24	
11	$Pd(OAc)_2$ (5)	IPA	$K_2S_2O_8$ (2.0)	24	
12	$Pd(OAc)_2$ (5)	DCE	$K_2S_2O_8$ (2.0)	72	20
13	$Pd(PPh_3)_2Cl_2$ (5)	TFA/TFAA (9:1)	$K_2S_2O_8$ (2.0)	12	
14	$Pd(TFA)_2$ (5)	TFA/TFAA (9:1)	$K_2S_2O_8$ (2.0)	12 h	75[d]

[a]Except for entry 2, all reactions were performed using 0.1 g of pyrazole (**5a**) at a concentration of 342 mmol/L of solvent. [b]Reaction in entry 2 was performed with 0.25 g of **5a** at identical substrate concentration. [c]Yields of chromatographically pure products. [d]2–3% of **7a** was isolated.

carboxylates (**5b–g**) carrying differently substituted 5-phenyl rings were probed as outlined in Scheme 4. It was observed

Scheme 4. Results of the Study of Scope of the Protocol for C-Hydroxylation with Substituted 5-(Substituted phenyl)-1-phenyl-1*H*-pyrazole-3-carboxylates 5a–i[a,b]

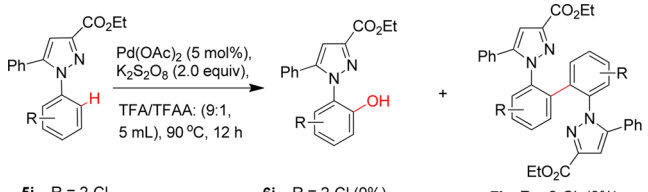


5a R = Ph	**6a** R = Ph (76%)	**7a** R = Ph (3%)
5b R = 2-Cl-C_6H_4	**6b** R = 2-Cl-C_6H_4 (45%)	**7b** R = 2-Cl-C_6H_4 (29%)
5c R = 4-F-C_6H_4	**6c** R = 4-F-C_6H_4 (70%)	**7c** R = 4-F-C_6H_4 (12%)
5d R = 4-Cl-C_6H_4	**6d** R = 4-Cl-C_6H_4 (44%)	**7d** R = 4-Cl-C_6H_4 (28%)
5e R = 4-Me-C_6H_4	**6e** R = 4-Me-C_6H_4 (74%)	**7e** R = 4-Me-C_6H_4 (8%)
5f R = 4-OMe-C_6H_4	**6f** R = 4-OMe-C_6H_4 (40%)	**7f** R = 4-OMe-C_6H_4 (32%)
5g R = 4-NO_2-C_6H_4	**6g** R = 4-NO_2-C_6H_4 (35%)	**7g** R = 4-NO_2-C_6H_4 (20%)
5h R = 2,4-Me_2-C_6H_3	**6h** R = 2,4-Me_2-C_6H_3 (44%)	**7h** R = 2,4-Me_2-C_6H_3 (30%)
5i R = 3,4,5-$(OMe)_3$-C_6H_2	**6i** R = 3,4,5-$(OMe)_3$-C_6H_2 (72%)	**7i** R = 3,4,5-$(OMe)_3$-C_6H_2 (0%)

[a]Reactions were performed with 0.5–0.65 g of pyrazoles **5a–i** at a substrate concentration of 342 mmol/L of solvent. [b]Yields after column chromatography.

that in each case substituted 1-(2-hydroxyphenyl)pyrazole **6b–d,f,g** and biaryl bis-pyrazole **7b–d,f,g** were isolated in variable ratios, but for compound **5e** bearing a 4-methyl substituent, the 1-(2-hydroxyphenyl)pyrazole derivative **6e** was isolated as the major product. Furthermore, substrate **5h** bearing a 3,4-dimethyl group also furnished the product as an isolable mixture of **6h** and **7h**, but the 3,4,5-trimethoxyphenyl ring bearing substrate **5i** afforded **6i** exclusively. In the next stage, we focused on the substrate set bearing different substitutions in the *N*-phenyl ring and unsubstituted 5-phenyl ring as presented in Scheme 5. Accordingly, pyrazoles **5j–p** were subjected to the palladium-catalyzed reaction, and it was found that all substrates (**5k–n,p**), except for **5j,o** with an

Scheme 5. Results of the Study of Scope of the Protocol for C-Hydroxylation with Substituted 5-Phenyl-1-(substituted phenyl)-1*H*-pyrazole-3-carboxylates 5j–p[a,b]



5j R = 2-Cl	**6j** R = 2-Cl (0%)	**7j** R = 2-Cl (0%)
5k R = 3-Cl	**6k** R = 3-Cl (78%)	**7k** R = 3-Cl (10%)
5l R = 4-F	**6l** R = 4-F (41%)	**7l** R = 4-F (24%)
5m R = 4-Cl	**6m** R = 4-Cl (48%)	**7m** R = 4-Cl (22%)
5n R = 4-Br	**6n** R = 4-Br (40%)	**7n** R = 4-Br (22%)
5o R = 2,5-Me_2	**6o** R = 2,5-Me_2 (0%)	**7o** R = 2,5-Me_2 (0%)
5p R = 3,4-Me_2	**6p** R = 3,4-Me_2 (38%)	**7p** R = 3,4-Me_2 (20%)

[a]Reactions were performed with 0.53–0.63 g of pyrazoles (**5j-p**) at a substrate concentration of 342 mmol/L. [b]Yields after column chromatography.

ortho-substituted *N*-phenyl ring, furnished a mixture of substituted 1-(2-hydroxyphenyl)pyrazoles **6k–n,p** and biaryl bis-pyrazoles **7k–n,p**. It seems that the presence of *ortho*-substituents in **5j** and **5o** offered resistance to chelation leading to the failure of the reaction. The structures for 1-(2-hydroxyphenyl)pyrazoles **6** and biaryl bis-pyrazoles **7** were secured by performing the X-ray crystallographic analysis of representative compounds **6l** (hexanes/EtOAc) and **7b** ($CHCl_3$/MeOH) (see the Supporting Information).

Following these results, we considered investigating the protocol using ethyl 1-substituted phenyl-5-alkyl-1*H*-pyrazole-3-carboxylates **8a–g** as the starting substrates (Scheme 6). In the first set, the reactions of 1-substituted phenyl-5-methyl-1*H*-pyrazole-3-carboxylates **8a–e** were examined which under the standardized conditions produced the corresponding 1-(2-hydroxyphenyl)pyrazoles **9a–e** only with no trace of biaryl

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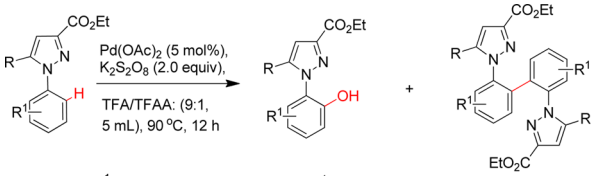
Scheme 6. Results of the Study of Scope of the Protocol for C-Hydroxylation with Ethyl 1-(Substituted phenyl)-5-alkyl-1*H*-pyrazole-3-carboxylates 8a−g[a,b]



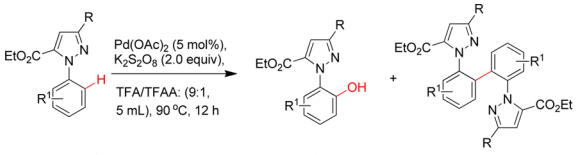
8a	R = Me, R^1 = H	**9a**	R = Me, R^1 = H (74%)	**10a**	R = Me, R^1 = H (0%)
8b	R = Me, R^1 = 3-Cl	**9b**	R = Me, R^1 = 3-Cl (74%)	**10b**	R = Me, R^1 = 3-Cl (0%)
8c	R = Me, R^1 = 4-F	**9c**	R = Me, R^1 = 4-F (72%)	**10c**	R = Me, R^1 = 4-F (0%)
8d	R = Me, R^1 = 4-Br	**9d**	R = Me, R^1 = 4-Br (75%)	**10d**	R = Me, R^1 = 4-Br (0%)
8e	R = Me, R^1 = 4-Me	**9e**	R = Me, R^1 = 4-Me (73%)	**10e**	R = Me, R^1 = 4-Me (0%)
8f	R = ^{n}Pr, R^1 = H	**9f**	R = ^{n}Pr, R^1 = H (35%)	**10f**	R = ^{n}Pr, R^1 = H (18%)
8g	R = ^{i}Pr, R^1 = H	**9g**	R = ^{i}Pr, R^1 = H (42%)	**10g**	R = ^{i}Pr, R^1 = H (20%)
8h	R = H, R^1 = H	**9h**	R = H, R^1 = H (0%)	**10h**	R = H, R^1 = H (80%)

[a]Reactions were performed with 0.37−0.53 g of pyrazoles **8a−h** at a substrate concentration of 342 mmol/L. [b]Yields after column chromatography.

bis-pyrazoles **10a−e**. Replacing the methyl group with propyl or isopropyl groups (**8f,g**), however, resulted in the formation of a mixture of 1-(2-hydroxyphenyl)pyrazoles **9f,g** and biaryl bis-pyrazoles **10f,g** in an approximately 2:1 ratio. Further, we discovered that if the 5-position in pyrazole ring was left unsubstituted as in **8h** then only the biaryl product **10h** was isolated with no trace of **9h**.

Subsequently, we examined the scope of the methodology with substituted pyrazoles **11a−c** and **14a−d** bearing a carboxylate group at the C-5 and C-4 position, respectively. In the first subset (**11a−c**), **11a,b** afforded the biaryl bis-pyrazoles **13a,b** exclusively in 70−72% yields, whereas **11c** was recovered unreacted under the optimized conditions (Scheme 7). In light of these results, it was speculated that

Scheme 7. Results of the Study of Scope of the Protocol for C-Hydroxylation with Ethyl 1-(Substituted phenyl)-1*H*-pyrazole-5-carboxylate 11a−c[a,b]



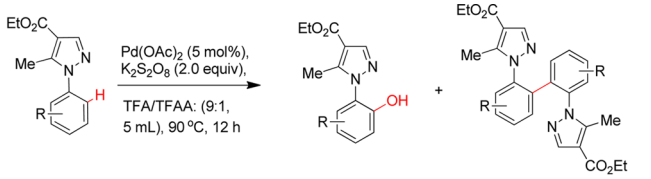
11a	R = H, R^1 = H	**12a**	R = H, R^1 = H (0%)	**13a**	R = H, R^1 = H (72%)
11b	R = H, R^1 = 4-Br-C_6H_4	**12b**	R = H, R^1 = 4-Br-C_6H_4 (0%)	**13b**	R = H, R^1 = 4-Br-C_6H_4 (70%)
11c	R = Ph, R^1 = H	**12c**	R = Ph, R^1 = H (0%)	**13c**	R = Ph, R^1 = H (0%)

[a]Reactions were performed with 0.37−0.5 g of pyrazoles **11a−c** at a substrate concentration of 342 mmol/L. [b]Yields after column chromatography.

the presence of a phenyl ring at the 3-position as in **11c** interfered with the stabilization of the palladium complex. Likewise, for ethyl 5-methyl-1-substituted phenyl-1*H*-pyrazole-4-carboxylates **14a−d**, it was found that whereas **14a** and **14b** furnished **16a** and **16b**, respectively, **14c,d** failed to react due to the presence of *ortho*-substituted *N*-phenyl ring (Scheme 8).

Finally, we investigated the protocol with 3-methyl-1,5-diphenyl-1*H*-pyrazole **17** and found that this substrate resulted in a complex mixture of products from which we could isolate the 1-(2-hydroxyphenyl)pyrazole (**18**) product in 7% yield only (Scheme 9). In addition, 3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one (**20**) was also investigated, but this

Scheme 8. Results of the Study of Scope of the Protocol for C-Hydroxylation with Ethyl 5-Methyl-1-(substituted phenyl)-1*H*-pyrazole-4-carboxylate 14a−d[a,b]

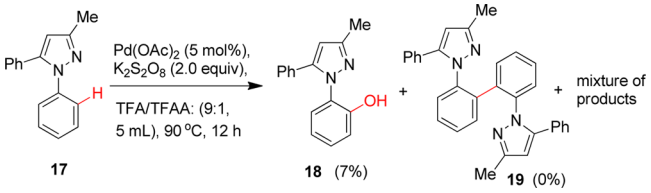


14a	R = H	**15a**	R = H (0%)	**16a**	R = H (78%)
14b	R = 4-Br	**15b**	R = 4-Br (0%)	**16b**	R = 4-Br (80%)
14c	R = 2-Me	**15c**	R = 2-Me (0%)	**16c**	R = 2-Me (0%)
14d	R = 2,4-Cl_2	**15d**	R = 2,4-Cl_2 (0%)	**16d**	R = 2,4-Cl_2 (0%)

[a]Reactions were performed with 0.39−0.52 g of pyrazoles **14a−d** at a substrate concentration of 342 mmol/L. [b]Yields after column chromatography.

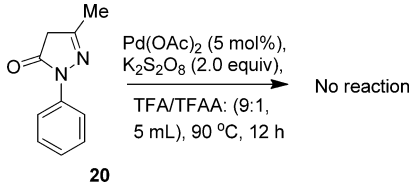
substrate failed to react under the optimized conditions (Scheme 10).

Scheme 9. Reaction of 3-Methyl-1,5-diphenyl-1*H*-pyrazole[a,b]



[a]Reaction was performed with 0.4 g of pyrazole **17**. [b]Yield after column chromatography.

Scheme 10. Reaction of 3-Methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one[a]



[a]Reaction was performed with 0.3 g of pyrazole **20** at a substrate concentration of 342 mmol/L.

The plausible mechanism for the reaction with **5a** as the model substrate is delineated in Scheme 11. As proposed by Sanford et al., the first C−H activation event in **5a** takes place at the Pd(II) stage leading to the formation of a five-membered cyclopalladium(II) dimeric intermediate **I** which, under the reaction conditions, gets oxidized to Pd(IV) intermediate **II**. A second C−H activation event at the Pd(IV) stage would result in the formation of intermediate **III**, which on reductive elimination gives biaryl bis-pyrazole **7a**. In contrast, if the second molecule of the **5a** is not activated to attack the intermediate **II**, then there is a likelihood that reductive elimination may occur to afford the intermediate **IV** that during aqueous workup furnish the substituted (*o*-hydroxyphenyl)pyrazole **6a**.

Based on the proposed mechanism and our initial optimization study with pyrazole **5a**, we were prompted to map product formation at different substrate concentrations in the TFA/TFAA mixture. It was presumed that under dilute

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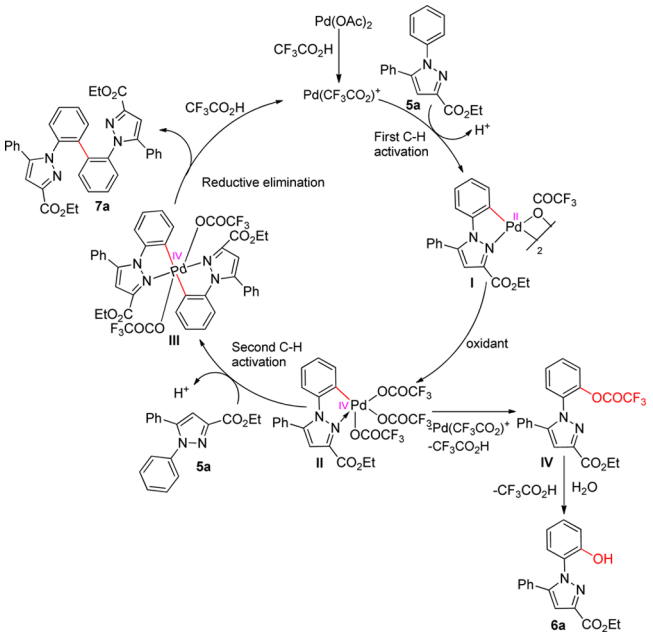
Scheme 11. Plausible Mechanism



conditions the transformation of **II** to **III** may get suppressed, driving the reaction to **IV** and therefore producing (*o*-hydroxylphenyl)pyrazole exclusively. In this context, pyrazole **5b**, which was known to afford both products **6b** and **7b** in a 5:3 ratio, was selected as the representative compound for the study. Accordingly, **5b** (0.11 g) was treated with $Pd(OAc)_2$ and $K_2S_2O_8$ under the optimized conditions with varying substrate to solvent (TFA/TFAA) concentration of 685−34.2 mmol/L, and the product distribution of the resulting crude mixture of products was monitored via HPLC (see the Supporting Information). We were delighted to discover that when the reaction was performed with **5b** at a substrate concentration of 34.2 mmol/L then **6b** was isolated in 68% yield, while **7b** was limited to 3% yield (Table 3, entry 1). Encouraged with the success, we tested **5d** and **5m** too under the identical reaction conditions (*ca* 10-folds dilution) and found that these substrates afforded **6d** and **6m**, respectively, as the major products (entries 2 and 3). Inspired by this success, we were prompted to examine the substrates from all other series including **8**, **11**, **14**, **17**, and **1**. Therefore, first **8h** was subjected to the reaction under dilute conditions, and we were pleased to discover that the ethyl 1-(2,6-dihydroxyphenyl)-1*H*-pyrazole-3-carboxylate **21** was isolated in 55% yield in addition to the biaryl bis-pyrazole **10h** in 20% yield (entry 4). However, when the carboxylate group was present at the 5-position in pyrazole as represented by series **11**, we found that whereas **11a**,**b** afforded the biaryl bis-pyrazole exclusively, compound **11c** gave the hydroxy derivative **12c** in trace amounts which could not be isolated but was evident upon detailed LC−MS investigations (entries 5−7). Likewise, for the set of pyrazole-bearing carboxylate groups at the 4-position as represented by **14**, we could not detect the presence of the corresponding (hydroxyphenyl)pyrazole product irrespective of dilution (entries 8−11). In contrast, for substituted pyrazole **17** we observed that under dilute reaction conditions the yield of 1-(2-hydroxyphenyl)pyrazole (**18**) improved to 60% (entry 12). Finally, **1a**,**b**,**e**,**j**, as representatives from series **1** which furnished the biaryl bis-pyrazoles **3** exclusively, were investigated under the altered conditions, and it was gratifying to discover that all substrates gave 1-(2-hydroxyphenyl)pyrazoles at a substrate concentration of 69.4 mmol/L. Whereas compound **1b** and **1e** afforded **2b** and **2e**, pyrazoles **1a** and **1j** furnished 2-(1*H*-pyrazol-1-yl)benzene-1,3-diol **22a** and **22j** as the major products in good yields, respectively (entries 13−16). These results clearly showed that *ortho*-hydroxylation in the phenyl ring in *N*-phenylpyrazoles is favored when the reaction is performed under excess of TFA/TFAA (9:1) mixture.

CONCLUSIONS

In summary, we have demonstrated the ligand-assisted palladium-catalyzed regioselective oxidative C(sp2)−H activation for dehydrogenative homocoupling and C−H oxygenation reactions in the phenyl ring of substituted 1-phenylpyrazoles. The scope has been explicitly investigated to demonstrate the effect of different substitutions on the outcome of the reaction. It was shown that the set of compounds wherein the pyrazole ring does not bear any substitution under low quantities of TFA/TFAA (9:1, v/v) mixture (higher substrate concentration) afforded the biaryl bis-pyrazoles via dehydrogenative homocoupling exclusively. However, the same substrates resulted in the (*o*-hydroxyphenyl)pyrazoles as the major products when the identical reaction was performed in the presence of an increased quantity of TFA/TFAA (9:1, v/v) mixture (low substrate concentration). Further, in this set of pyrazoles, if the phenyl ring carried an *ortho*-substituent then monohydroxylation took place but if both the *ortho*-positions were free then bis-hydroxylation prevailed under the conditions. Unlike in the set of compounds where the pyrazole ring carried the carboxylate group at the 3-position, in most of the cases a mixture of biaryl bis-pyrazoles and (*o*-hydroxyphenyl)-pyrazoles were formed under higher substrate concentration, but (*o*-hydroxyphenyl)pyrazoles were isolated in superior yields when the concentration of the starting material was low. In addition for these starting substrates, the protocol worked only when both *ortho*-positions of the phenyl ring were free since all compounds bearing an *ortho*-substituted phenyl ring failed to yield any product. Unlike for the pyrazole substrates bearing a carboxylate group at the C-5 or C-4 position, mostly biaryl bis-pyrazoles were isolated. Interestingly, for the pyrazoles bearing a phenyl group at the C-3 position in place of the carboxylate group at lower substrate concentration we could isolate only the (*o*-hydroxyphenyl)pyrazole with no trace of biaryl bis-pyrazoles. Further work to investigate the ligand-assisted C-oxygenation in the phenyl ring in other heterocyclic substrates is underway and will be reported in due course.

EXPERIMENTAL SECTION

General Methods. All experiments were monitored by analytical thin-layer chromatography (TLC) performed on precoated silica gel plates. After elution, plate was visualized under UV illumination at 254 nm for UV-active materials. Further visualization was achieved by staining with $KMnO_4$ and charring on a hot plate. Column chromatography was performed on silica gel (230−400 mesh) by standard techniques eluting with solvents as indicated. IR spectra were recorded using a FTIR spectrophotometer. ^1H NMR and ^{13}C NMR spectra were recorded on 400 MHz spectrometer using TMS as an internal standard (chemical shifts in δ). Peak multiplicities of NMR signals were designated as s (singlet), bs (broad singlet), d (doublet), dd (doublet of doublet), t (triplet), m (multiplet), etc. The ESI-MS were recorded on Ion Trap MS spectrometer and the

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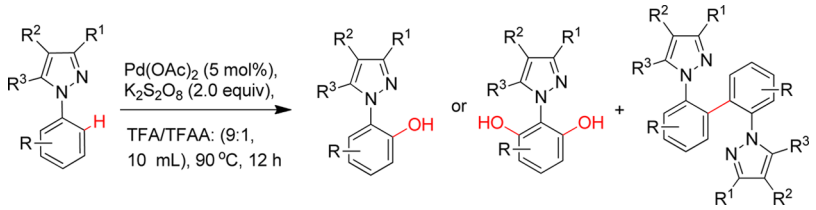
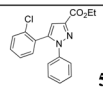
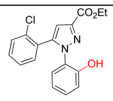
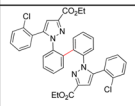
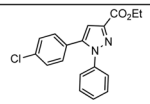
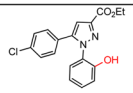
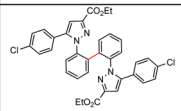
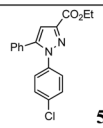
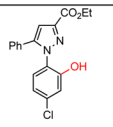
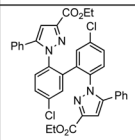
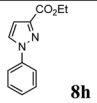
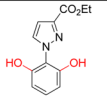
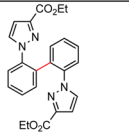
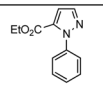
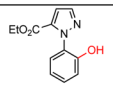
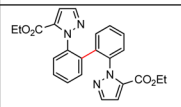
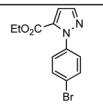
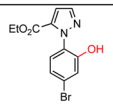
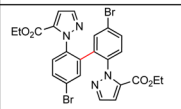
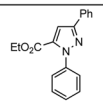
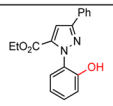
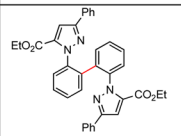
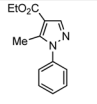
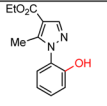
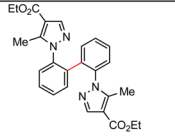
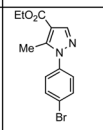
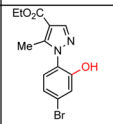
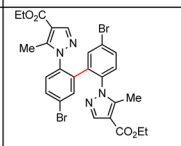
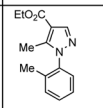
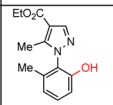
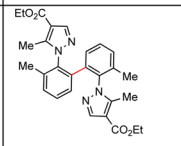
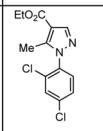
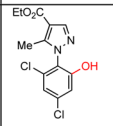
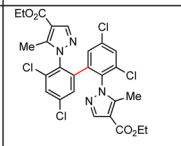
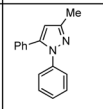
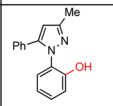
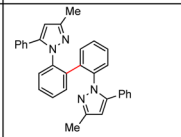
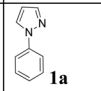
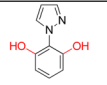
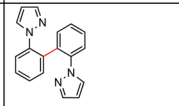
Table 3. Results of the Study toward Assessing Scope of the Protocol for C(sp2)-Hydroxylation under Dilute Conditions



entry	reactant	major product (yield %)[b]	minor product (yield %)[b]
1[a]	 **5b**	 **6b** (71)	 **7b** (3)
2[a]	 **5d**	 **6d** (66)	 **7d** (2)
3[a]	 **5m**	 **6m** (70)	 **7m** (2)
4[a]	 **8h**	 **21** (55)	 **10h** (20)
5[a]	 **11a**	 **12a** (0)	 **13a** (70)
6[a]	 **11b**	 **12b** (0)	 **13b** (65)
7[a]	 **11c**	 **12c** (trace)	 **13c** (0)
8[a]	 **14a**	 **15a** (0)	 **16a** (75)
9[a]	 **14b**	 **15b** (0)	 **16b** (76)
10[a]	 **14c**	 **15c** (0)	 **16c** (0)
11[a]	 **14d**	 **15d** (0)	 **16d** (0)
12[a]	 **17**	 **18** (60)	 **19** (0)
13[b]	 **1a**	 **22a** (60)	 **3a** (3)
14[b]	**1b**	**2b** (67)	**3b** (3)
15[b]	**1e**	**2e**(64)	**3e** (2)
16[b]	**1j**	**22b** (62)	**3j** (3)

[a]Reactions were performed with 0.079−0.112 g of pyrazoles **5**, **8**, **14**, **11**, or **17** at a substrate concentration of 34.3 mmol/L. [b]Reactions were performed with 0.1−0.15 g of pyrazoles **1** at a substrate concentration of 69.4 mmol/L. [c]Yields after column chromatography.

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HRMS spectra were recorded as ESI-HRMS on a Q-TOF LC−MS/MS mass spectrometer. Commercial grade reagents and solvents were used without further purification. As **12c** was formed in traces and mapped by LC−MS no physical or spectroscopic data (except ESMS) is provided.

The syntheses of different 1-(substituted phenyl)pyrazoles were carried out according to the literature procedures.

*1-Phenyl-1H-pyrazole (**1a**).* See ref 18.

*1-(2-Chlorophenyl)-1H-pyrazole (**1b**).* See ref 19.

*1-(2-Methylphenyl)-1H-pyrazole (**1c**).* See ref 19.

*1-(2-(Trifluoromethyl)phenyl)-1H-pyrazole (**1d**).* See ref 20.

*Ethyl 2-(1H-pyrazol-1-yl)benzoate (**1e**).* See ref 21.

*1-(3-Fluorophenyl)-1H-pyrazole (**1f**).* See ref 22.

*1-(3-Chlorophenyl)-1H-pyrazole (**1g**).* See ref 23.

*1-(4-Fluorophenyl)-1H-pyrazole (**1h**).* See ref 23.

*1-(4-Chlorophenyl)-1H-pyrazole (**1i**).* See ref 23.

*1-(4-Bromophenyl)-1H-pyrazole (**1j**).* See ref 23.

*1-(4-Methylphenyl)-1H-pyrazole (**1k**).* See ref 24.

*1-(4-Methoxyphenyl)-1H-pyrazole (**1l**).* See ref 24.

*1-(4-(Trifluoromethyl)phenyl)-1H-pyrazole (**1m**).* See ref 24.

*Ethyl 4-(1H-pyrazol-1-yl)benzoate (**1n**).* See ref 25.

*1-(2,4-Dimethylphenyl)-1H-pyrazole (**1o**).* See ref 25.

*1-(3,4-Dimethylphenyl)-1H-pyrazole (**1p**).* Yield: 85% (1.0 g from 1.5 g); brown oil. R_f = 0.68 (hexanes/EtOAc, 80:20, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.28 (s, 3H), 2.32 (s, 3H), 6.43 (t, J = 2.2 Hz, 1H), 7.19 (d, J = 8.1 Hz, 1H), 7.37 (dd, J_1 = 8.1 Hz, J_2 = 2.3 Hz, 1H), 7.50 (d, J = 1.9 Hz, 1H), 7.69 (d, J = 1.4 Hz, 1H), 7.87 (d, J = 2.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.4, 20.0, 107.3, 116.7, 120.8, 126.8, 130.5, 135.1, 138.4, 140.8. MS (ESI+): m/z = 173.2. ESI-HRMS: calcd for $C_{11}H_{13}N_2$ (M^+ + H) 173.1079, found 173.1074.

*1-(Naphthalen-2-yl)-1H-pyrazole (**1q**).* See ref 26.

*1-(3-Methoxyphenyl)-1H-pyrazole (**1r**).* See ref 27.

*1-Benzyl-1H-pyrazole (**4**).* See ref 28.

General Procedure for Oxidative Dehydrogenative Homocoupling of *N*-Arylpyrazoles (1a−r) As Exemplified for 3a. A 50 mL sealed tube charged with **1a** (0.5 g, 3.47 mmol), $K_2S_2O_8$ (1.87 g, 6.94 mmol), $Pd(OAc)_2$ (0.04 g, 0.017 mmol), TFA (4.5 mL), and TFAA (0.5 mL) was heated at 90 °C for 12 h. After completion as monitored by the TLC, the reaction mixture was evaporated to obtain a residue which was dissolved in EtOAc (25 mL) and washed with saturated aqueous $NaHCO_3$ solution (50 mL). The mixture was partitioned in a separating funnel, the organic layer separated, and the aqueous layer was further extracted with EtOAc (2 × 25 mL). The organic extracts were pooled, dried over anhyd Na_2SO_4, and evaporated in vacuum to afford the crude product which was purified by column chromatography (silica gel, 20% EtOAc in hexanes) to afford the pure **3a** (0.34 g, 68%) as a white solid.

*2,2′-Di(1H-pyrazol-1-yl)biphenyl (**3a**).* Mp: 107−109 °C. R_f = 0.26 (hexanes/EtOAc, 80:20, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.17 (s, 2H), 7.19−7.26 (m, 4H), 7.32 (t, J = 6.9 Hz, 2H), 7.40−7.44 (m, 2H), 7.48−7.52 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$):106.6, 125.7, 127.9, 128.9, 130.4, 131.2, 133.5, 139.0, 140.5. MS (ESI+): m/z = 287.0. ESI-HRMS: calcd for $C_{18}H_{15}N_4$ (M^+ + H) 287.1297, found 287.1293.

*1,1′-(3,3′-Dichlorobiphenyl-2,2′-diyl)bis(1H-pyrazole) (**3b**).* Yield: 83% (0.51 g from 0.62 g); white solid. Mp: 112−114 °C. R_f = 0.30 (hexanes/EtOAc, 80:20, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.26 (s, 2H), 6.92 (d, J = 7.1 Hz, 2H), 7.12 (t, J = 7.5 Hz, 2H), 7.42 (d, J = 7.7 Hz, 2H), 7.55 (brs, 2H), 7.71 (brs, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 106.5, 128.4, 129.3, 130.0, 132.7, 137.1, 138.2, 140.6. MS (ESI+): m/z = 354.8. ESI-HRMS: calcd for $C_{18}H_{13}Cl_2N_4$ (M^+ + H) 355.0517, found 355.0522.

*1,1′-(3,3′-Dimethylbiphenyl-2,2′-diyl)bis(1H-pyrazole) (**3c**).* Yield: 80% (0.44 g from 0.55 g); white solid. Mp: 144−146 °C. R_f = 0.38 (hexanes/EtOAc, 80:20, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.07 (s, 6H), 6.20 (t, J = 2.0 Hz, 2H), 6.84 (d, J = 7.6 Hz, 2H), 7.08 (t, J = 7.6 Hz, 2H), 7.16 (d, J = 7.5 Hz, 2H), 7.53−7.59 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): 17.8, 105.8, 127.7, 128.0, 130.1, 136.2, 136.8, 138.5, 139.8. MS (ESI+): m/z = 315.0. ESI-HRMS: calcd for $C_{20}H_{19}N_4$(M^+ + H) 315.1610, found 315.1612.

*1,1′-(3,3′-Bis(trifluoromethyl)biphenyl-2,2′-diyl)bis(1H-pyrazole) (**3d**).* Yield: 74% (0.54 g from 0.74 g); white solid. Mp: 147−149 °C. R_f = 0.20 (hexanes/EtOAc, 80:20, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.14 (s, 2H), 7.15−7.19 (m, 2H), 7.26 (t, J = 7.4 Hz, 2H), 7.42 (s, 2H), 7.62−7.63 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): 106.6, 121.6, 124.3, 127.0, 128.6, 133.4, 137.2, 138.1, 140.5. MS (ESI+): m/z = 423.0. ESI-HRMS: calcd for $C_{20}H_{13}F_6N_4$ (M^+ + H) 423.1044, found 423.1040.

*Diethyl 2,2′-Di(1H-pyrazol-1-yl)biphenyl-3,3′-dicarboxylate (**3e**).* Yield: 60% (0.45 g from 0.75 g); brown oil. R_f = 0.30 (hexanes/EtOAc, 80:20, v/v). IR (neat) ν_{max}: 1717 (CO_2Et) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.03 (t, J = 7.1 Hz, 6H), 4.01−4.06 (m, 4H), 6.14 (t, J = 2.1 Hz, 2H), 7.08 (dd, J_1 = 7.7 Hz, J_2 = 1.2 Hz, 2H), 7.22 (t, J = 7.7 Hz, 2H), 7.44 (d, J = 1.1 Hz, 2H), 7.51 (d, J = 2.0 Hz, 2H), 7.74 (dd, J_1 = 7.7 Hz, J_2 = 1.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.1, 61.7, 106.5, 128.2, 130.5, 130.6, 132.5, 133.4, 136.3, 138.2, 140.3, 166.1. MS (ESI+): m/z = 431.1. ESI-HRMS: calcd for $C_{24}H_{23}N_4O_4$ (M^+ + H) 431.1719, found 431.1716.

*1,1′-(4,4′-Difluorobiphenyl-2,2′-diyl)bis(1H-pyrazole) (**3f**).* Yield: 45% (0.25 g from 0.56 g); yellow solid. Mp: 120−122 °C. R_f = 0.32 (hexanes/EtOAc, 80:20, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.14 (t, J = 2.1 Hz, 2H), 6.97 (td, J_1 = 8.4 Hz, J_2 = 2.6 Hz, 2H), 7.06−7.09 (m, 2H), 7.15 (d, J = 2.3 Hz, 2H), 7.18−7.21 (m, 2H), 7.42 (d, J = 1.3 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 107.2, 113.1 (d, J = 25.2 Hz), 115.1 (d, J = 21.1 Hz), 128.5, 130.2, 132.6 (d, J = 8.6 Hz), 140.2 (d, J = 10.0 Hz), 141.0, 162.5 (d, J = 247.8 Hz,). MS (ESI+): m/z = 323.0. ESI-HRMS: calcd for $C_{18}H_{13}F_2N_4$ (M^+ + H) 323.1108, found 323.1105.

*1,1′-(4,4′-Dichlorobiphenyl-2,2′-diyl)bis(1H-pyrazole) (**3g**).* Yield: 48% (0.30 g from 0.62 g); yellow oil. R_f = 0.31 (hexanes/EtOAc, 80:20, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.16 (t, J = 2.1 Hz, 2H), 7.01 (d, J = 8.3 Hz, 2H), 7.18−7.19 (m, 2H), 7.23 (dd, J_1 = 8.3 Hz, J_2 = 2.1 Hz, 2H), 7.44 (d, J = 2.1 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): 107.3, 125.9, 130.3, 131.0, 132.1, 134.9, 139.6, 141.0. MS (ESI+): m/z = 354.9. ESI-HRMS: calcd for $C_{18}H_{13}Cl_2N_4$ (M^+ + H) 355.0517, found 355.0513.

*1,1′-(5,5′-Difluorobiphenyl-2,2′-diyl)bis(1H-pyrazole) (**3h**).* Yield: 78% (0.44 g from 0.56 g); off-white solid. Mp: 144−146 °C. R_f = 0.22 (hexanes/EtOAc, 80:20, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.16 (t, J = 2.2 Hz, 2H), 6.79 (dd, J_1 = 8.7 Hz, J_2 = 2.8 Hz, 2H), 7.02−7.07 (m, 2H), 7.23 (d, J = 2.4 Hz, 2H), 7.38 (dd, J_1 = 8.8 Hz, J_2 = 5.2 Hz, 2H), 7.42 (d, J = 1.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 106.9, 116.2 (d, J = 22.3 Hz), 117.4 (d, J = 23.4 Hz), 127.7 (d, J = 8.8 Hz), 130.6, 134.8 (d, J = 5.7 Hz), 135.3, 140.8, 161.6 (d, J = 247.7 Hz). MS (ESI+): m/z = 323.0. ESI-HRMS: calcd for $C_{18}H_{13}F_2N_4$ (M^+ + H) 323.1108, found 323.1104.

*1,1′-(5,5′-Dichlorobiphenyl-2,2′-diyl)bis(1H-pyrazole) (**3i**).* Yield: 75% (0.46 g from 0.62 g); white solid. Mp: 160−162 °C. R_f = 0.22 (hexanes/EtOAc, 80:20, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.21 (brs, 2H), 7.23−7.26 (m, 4H), 7.41 (brs, 4H), 7.48 (brs, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 107.3, 127.0, 129.6, 130.2, 130.9, 133.7, 133.9, 137.6, 141.1. MS (ESI+): m/z = 354.9. ESI-HRMS: calcd for $C_{18}H_{13}Cl_2N_4$ (M^+ + H) 355.0517, found 355.0520.

*1,1′-(5,5′-Dibromobiphenyl-2,2′-diyl)bis(1H-pyrazole) (**3j**).* Yield: 70% (0.54 g from 0.77 g); white solid. Mp: 112−114 °C. R_f = 0.30 (hexanes/EtOAc, 80:20, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.21 (s, 2H), 7.18−7.26 (m, 3H), 7.34−7.40 (m, 3H), 7.48 (s, 2H), 7.56 (d, J = 7.9 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 107.3, 121.4, 127.1, 130.1, 132.5, 133.8, 133.9, 138.0, 141.0. MS (ESI+): m/z = 442.9. ESI-HRMS: calcd for $C_{18}H_{13}Br_2N_4$ (M^+ + H) 442.9507, found 442.9510.

*1,1′-(5,5′-Dimethylbiphenyl-2,2′-diyl)bis(1H-pyrazole) (**3k**).* Yield: 72% (0.39 g from 0.55 g); off-white solid. Mp: 94−96 °C. R_f = 0.28 (hexanes/EtOAc, 80:20, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.27 (s, 6H), 6.08 (t, J = 2.1 Hz, 2H), 6.98 (d, J = 1.2 Hz, 2H), 7.06 (d, J = 2.3 Hz, 2H), 7.13 (dd, J_1 = 8.0 Hz, J_2 = 1.3 Hz, 2H), 7.29 (d, J = 8.1 Hz, 2H), 7.39 (d, J = 1.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 21.1, 106.3, 125.5, 129.5, 130.3, 131.6, 133.2, 136.7, 137.8,

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140.1. MS (ESI+): m/z = 315.0. ESI-HRMS: calcd for $C_{20}H_{19}N_4$ (M^+ + H) 315.1610, found 315.1610.

*1,1′-(5,5′-Bis(trifluoromethyl)biphenyl-2,2′-diyl)bis(1H-pyrazole) (**3m**).* Yield: 74% (0.55 g from 0.74 g); off-white solid. Mp: 83−85 °C. R_f = 0.40 (hexanes/EtOAc, 80:20, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.17−6.18 (m, 2H), 7.20 (d, J = 2.16 Hz, 2H), 7.38 (d, J = 0.8 Hz, 2H), 7.43 (d, J = 1.3 Hz, 2H), 7.58 (d, J = 8.4 Hz, 2H), 7.60 (dd, J_1 = 8.4 Hz, J_2 = 1.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 107.7, 123.6 (q, J = 272.6 Hz), 126.1, 126.5 (q, J = 3.6 Hz), 128.3 (q, J = 3.7 Hz), 130.1, 130.2 (q, J = 33.2 Hz), 132.9, 141.5, 141.6. MS (ESI+): m/z = 423.0. ESI-HRMS: calcd for $C_{20}H_{13}F_6N_4$ (M^+ + H) 423.1044, found 423.1044.

*Diethyl 6,6′-Di(1H-pyrazol-1-yl)biphenyl-3,3′-dicarboxylate (**3n**).* Yield: 72% (0.54 g from 0.75 g); off-white solid. Mp: 99−101 °C. R_f = 0.16 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max}: 1716 (CO_2Et) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.34 (t, J = 7.1 Hz, 6H), 4.33 (q, J = 7.1 Hz, 4H), 6.10 (t, J = 1.9 Hz, 2H), 7.02 (d, J = 2.4 Hz, 2H), 7.39 (d, J = 1.2 Hz, 2H), 7.50 (d, J = 1.7 Hz, 2H), 8.00 (d, J = 1.9 Hz, 2H), 8.07 (dd, J_1 = 8.5 Hz, J_2 = 1.9 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.5, 61.6, 107.5, 125.2, 129.9, 130.0, 130.7, 132.2, 133.0, 141.2, 142.1, 165.6. MS (ESI+): m/z = 431.1. ESI-HRMS: calcd for $C_{24}H_{23}N_4O_4$ (M^+ + H) 431.1719, found 431.1724.

*1,1′-(3,3′,5,5′-Tetramethylbiphenyl-2,2′-diyl)bis(1H-pyrazole) (**3o**).* Yield: 74% (0.44 g from 0.6 g); white solid. Mp: 127−128 °C. R_f = 0.55 (hexanes/EtOAc, 80:20, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.95 (s, 6H), 2.09 (s, 6H), 6.12 (t, J = 2.1 Hz, 2H), 6.57 (s, 2H), 6.88 (s, 2H), 7.44−7.46 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): 17.7, 21.0, 105.6, 128.3, 130.7, 132.2, 135.7, 135.9, 136.5, 137.8, 139.6. MS (ESI+): m/z = 343.1. ESI-HRMS: calcd for $C_{22}H_{23}N_4$ (M^+ + H) 343.1923, found 343.1925.

*1,1′-(4,4′,5,5′-Tetramethylbiphenyl-2,2′-diyl)bis(1H-pyrazole) (**3p**).* Yield: 70% (0.42 g from 0.6 g); white solid. Mp: 132−134 °C. R_f = 0.25 (hexanes/EtOAc, 80:20, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.17 (s, 6H), 2.21 (s, 6H), 6.06 (t, J = 2.2 Hz, 2H), 6.93 (s, 2H), 7.09 (d, J = 6.6 Hz, 2H), 7.18−7.20 (m, 2H), 7.38 (d, J = 1.3 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 19.6, 19.7, 106.4, 126.7, 130.3, 132.4, 136.5, 136.8, 137.6, 140.1. MS (ESI+): m/z = 343.1. ESI-HRMS: calcd for $C_{22}H_{23}N_4$ (M^+ + H) 343.1923, found 343.1928.

General Procedure for Oxidative *Ortho*-Hydroxylation in *N*-Arylpyrazoles 1a,b,e,j for the Synthesis of 2b,eand 22a,b As Exemplified for the Synthesis of 2b. A 50 mL sealed tube charged with **1b** (0.12 g, 0.69 mmol), $K_2S_2O_8$ (0.375 g, 1.38 mmol), $Pd(OAc)_2$ (0.008 g, 0.034 mmol), TFA (9.0 mL), and TFAA (1.0 mL) was heated at 90 °C for 12 h. Following a similar experimental procedure as reported for **3a**, a crude product was obtained which was purified by column chromatography (silica gel, 20% EtOAc in hexanes) to afford the pure **2b** (0.087 g, 67%) as a brown oil and **3b** (0.003 g, 3%) as a white solid.

*3-Chloro-2-(1H-pyrazol-1-yl)phenol (**2b**).* R_f = 0.22 (hexanes/EtOAc, 80:20, v/v). IR (neat) ν_{max} 3368 (OH) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.54 (s, 1H), 7.03 (t, J = 7.6 Hz, 2H), 7.17 (t, J = 6.9 Hz, 1H), 7.81 (d, J = 1.2 Hz, 1H), 8.11 (d, J = 2.4 Hz, 1H), 9.42 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 106.9, 117.1, 122.1, 124.8, 126.5, 129.1, 133.2, 141.1, 152.5. MS (ESI+): m/z = 194.8. ESI-HRMS: calcd for $C_9H_8ClN_2O$ (M^+ + H) 195.0325, found 195.0330.

*Ethyl 3-Hydroxy-2-(1H-pyrazol-1-yl)benzoate (**2e**).* Yield: 64% (0.103 g from 0.15 g); pale yellow solid. Mp: 125−127 °C. R_f = 0.18 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max}: 1718 (CO_2Et), 3390 (OH) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.11 (t, J = 7.1 Hz, 3H), 4.14 (q, J = 7.1 Hz, 2H), 6.42 (m, 1H), 7.15−7.18 (m, 1H), 7.21−7.29 (m, 2H), 7.50 (d, J = 2.2 Hz, 1H), 7.75 (d, J = 1.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.1, 61.7, 107.1, 121.4, 122.0, 125.1, 126.8, 132.6, 141.2, 151.6, 166.8. MS (ESI+): m/z = 232.9. ESI-HRMS: calcd for $C_{12}H_{13}N_2O_3$ (M^+ + H) 233.0926, found 233.0925. **2-(1*H*-Pyrazol-1-yl)benzene-1,3-diol (22a).** Yield: 60% (0.073 g from 0.1 g); brown oil. R_f = 0.22 (hexanes/EtOAc, 80:20, v/v). IR (neat) ν_{max} 3399 (OH) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.49 (t, J = 2.2 Hz, 1H), 6.57 (d, J = 8.2 Hz, 2H), 7.01 (t, J = 8.2 Hz, 1H), 7.73 (d, J = 1.8 Hz, 1H), 8.19 (brs, 2H), 8.36 (d, J = 2.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 106.1, 109.4, 127.7, 132.8, 138.6, 149.6. MS (ESI+): m/z = 176.8. ESI-HRMS: calcd for $C_9H_9N_2O_2$ (M^+ + H) 177.0664, found 177.0665.

*5-Bromo-2-(1H-pyrazol-1-yl)benzene-1,3-diol (**22b**).* Yield: 62% (0.109 g from 0.154 g); brown oil. R_f = 0.22 (hexanes/EtOAc, 80:20, v/v). IR (neat) ν_{max} 3399 (OH) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.50 (s, 1H), 6.77 (s, 2H), 7.75 (s, 1H), 8.38 (s, 1H), 8.97 (brs, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 106.3, 112.7, 114.5, 119.8, 132.8, 138.6, 150.2. MS (ESI+): m/z = 254.8. ESI-HRMS: calcd for $C_9H_8BrN_2O_2$ (M^+ + H) 254.9769, found 254.9765.

The syntheses of starting 5-(substituted phenyl)-1-phenyl-1*H*-pyrazole-3-carboxylates or 5-phenyl-1-(substituted phenyl)-1*H*-pyrazole-3-carboxylates were carried out via the reported methods.

*Ethyl 1,5-Diphenyl-1H-pyrazole-3-carboxylate (**5a**).* See ref 29.

*Ethyl 5-(2-Chlorophenyl)-1-phenyl-1H-pyrazole-3-carboxylate (**5b**).* Yield: 85% (1.1 g from 1.0 g); white solid. Mp: 65−67 °C. R_f = 0.47 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max} 1722 (CO_2Et) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.43 (t, J = 7.1 Hz, 3H), 4.46 (q, J = 7.1 Hz, 2H), 7.05 (s, 1H), 7.23−7.24 (m, 2H), 7.28 (brs, 4H), 7.30−7.34 (m, 2H), 7.38−7.40 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.6, 61.3, 111.9, 124.8, 127.0, 128.3, 129.0, 129.4, 130.2, 130.8, 132.2, 139.6, 142.5, 144.3, 162.5. MS (ESI+): m/z = 327.1. ESI-HRMS: calcd for $C_{18}H_{16}ClN_2O_2$ (M^+ + H) 327.0900, found 327.0897.

*Ethyl 5-(4-Fluorophenyl)-1-phenyl-1H-pyrazole-3-carboxylate (**5c**).* Yield: 90% (1.2 g from 1.0 g); white solid.Mp: 113−115 °C. R_f = 0.46 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max} 1721 (CO_2Et) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.42 (t, J = 7.1 Hz, 3H), 4.46 (q, J = 7.1 Hz, 2H), 6.98−7.03 (m, 3H), 7.17−7.21 (m, 2H), 7.29−7.33 (m, 2H), 7.35−7.37 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.6, 61.3, 110.0, 115.9 (d, J = 21.7 Hz), 125.9, 128.6, 129.2, 130.8 (d, J = 8.2 Hz), 139.5, 143.8, 144.5, 162.5, 162.9 (d, J = 248.1 Hz). MS (ESI+): m/z = 311.2. ESI-HRMS: calcd for $C_{18}H_{16}FN_2O_2$ (M^+ + H) 311.1196, found 311.1191.

*Ethyl 5-(4-Chlorophenyl)-1-phenyl-1H-pyrazole-3-carboxylate (**5d**).* See ref 30.

*Ethyl 1-Phenyl-5-p-tolyl-1H-pyrazole-3-carboxylate (**5e**).* Yield: 88% (1.1 g from 1.0 g); white solid. Mp: 84−86 °C. R_f = 0.5 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max} 1721 (CO_2Et) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.43 (t, J = 7.2 Hz, 3H), 2.34 (s, 3H), 4.45 (q, J = 7.0 Hz, 2H), 7.01 (s, 1H), 7.34 (m, 5H) . ^{13}C NMR (100 MHz, $CDCl_3$): 14.6, 21.4, 61.2, 109.8, 125.9, 126.8, 138.9, 139.8, 144.4, 144.9, 162.7. MS (ESI+): m/z = 307.2. ESI-HRMS: calcd for $C_{19}H_{19}N_2O_2$ (M^+ + H) 307.1447, found 307.1449.

*Ethyl 5-(4-Methoxyphenyl)-1-phenyl-1H-pyrazole-3-carboxylate (**5f**).* See ref 31.

*Ethyl 5-(4-Nitrophenyl)-1-phenyl-1H-pyrazole-3-carboxylate (**5g**).* Yield: 80% (1.0 g from 1.0 g); white solid. Mp: 128−130 °C. R_f = 0.2 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max} 1721 (CO_2Et) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.36 (t, J = 7.1 Hz, 3H), 4.39 (q, J = 7.1 Hz, 2H), 7.10 (s, 1H), 7.23−7.26 (m, 2H), 7.30−7.35 (m, 5H), 8.09 (d, J = 8.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.5, 61.5, 111.1, 124.0, 126.0, 129.2, 129.6, 135.8, 139.1, 142.4, 144.9, 147.8, 162.1. MS (ESI+): m/z = 338.2. ESI-HRMS: calcd for $C_{18}H_{16}N_3O_4$ (M^+ + H) 338.1141, found 338.1145.

*Ethyl 5-(2,4-Dimethylphenyl)-1-phenyl-1H-pyrazole-3-carboxylate (**5h**).* Yield: 72% (0.375 g from 0.5 g); brown oil. R_f = 0.56 (hexanes/EtOAc, 80:20, v/v). IR (neat) ν_{max} 1721 (CO_2Et) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.43 (t, J = 7.1 Hz, 3H), 1.96 (s, 3H), 2.32 (s, 3H), 4.46 (q, J = 7.1 Hz, 2H), 6.91 (s, 1H), 697−6.99 (m, 2H), 7.05−7.07 (m, 1H), 7.24−7.28 (m, 5H) . ^{13}C NMR (100 MHz, $CDCl_3$): 14.6, 19.9, 21.3, 61.2, 111.1, 124.5, 126.8, 127.9, 128.9, 130.6, 131.3, 137.0, 139.4, 139.8, 144.1, 144.2, 162.7. MS (ESI+): m/z = 321.2. ESI-HRMS: calcd for $C_{20}H_{21}N_2O_2$ (M^+ + H) 321.1603, found 321.1601.

*Ethyl 1-Phenyl-5-(3,4,5-trimethoxyphenyl)-1H-pyrazole-3-carboxylate (**5i**).* Yield: 88% (1.1 g from 1.0 g); white solid. Mp: 147−149 °C. R_f = 0.28 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max} 1717 (CO_2Et) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.43 (t, J = 7.1 Hz, 3H), 3.64 (s, 6H), 3.85 (s, 3H), 4.46 (q, J = 7.1 Hz, 2H), 6.39

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(s, 2H), 7.35−7.38 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.5, 56.1, 61.0, 61.3, 106.2, 109.4, 124.7, 126.1, 128.6, 129.1, 138.5, 139.8, 144.4, 144.7, 153.3, 162.5. MS (ESI+): m/z = 383.2. ESI-HRMS: calcd for $C_{21}H_{23}N_2O_5$ (M^+ + H) 383.1607, found 383.1602.

*Ethyl 1-(2-Chlorophenyl)-5-phenyl-1H-pyrazole-3-carboxylate (**5j**).* See ref 32.

*Ethyl 1-(3-Chlorophenyl)-5-phenyl-1H-pyrazole-3-carboxylate (**5k**).* See ref 33.

*Ethyl 1-(4-Fluorophenyl)-5-phenyl-1H-pyrazole-3-carboxylate (**5l**).* See ref 34.

*Ethyl 1-(4-Chlorophenyl)-5-phenyl-1H-pyrazole-3-carboxylate (**5m**).* See ref 34.

*Ethyl 1-(4-Bromophenyl)-5-phenyl-1H-pyrazole-3-carboxylate (**5n**).* See ref 34.

*Ethyl 1-(2,5-Dimethylphenyl)-5-phenyl-1H-pyrazole-3-carboxylate (**5o**).* Yield: 88% (1.3 g from 1.0 g); off-white solid. Mp: 98−100 °C. R_f = 0.53 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max} 1721 (CO_2Et) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.42 (t, J = 7.1 Hz, 3H), 1.82 (s, 3H), 2.32 (s, 3H), 4.45 (q, J = 7.1 Hz, 2H), 7.05−7.12 (m, 3H), 7.17−7.20 (m, 3H), 7.23−7.26 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.6, 17.1, 20.9, 61.2, 108.4, 127.9, 128.6, 128.7, 129.5, 130.4, 130.8, 132.1, 136.7, 138.9, 144.3, 145.7, 162.7. MS (ESI+): m/z = 321.2. ESI-HRMS: calcd for $C_{20}H_{21}N_2O_2$ (M^+ + H) 321.1603, found 321.1607.

*Ethyl 1-(3,4-Dimethylphenyl)-5-phenyl-1H-pyrazole-3-carboxylate (**5p**).*[35] The ethyl 5-(alkyl)-1-(substituted phenyl)-1*H*-pyrazole-3-carboxylates were prepared according to the literature procedure.[35]

*Ethyl 5-Methyl-1-phenyl-1H-pyrazole-3-carboxylate (**8a**).* See ref 36.

*Ethyl 1-(3-Chlorophenyl)-5-methyl-1H-pyrazole-3-carboxylate (**8b**).* See ref 37.

*Ethyl 1-(4-Fluorophenyl)-5-methyl-1H-pyrazole-3-carboxylate (**8c**).* See ref 38.

*Ethyl 1-(4-Bromophenyl)-5-methyl-1H-pyrazole-3-carboxylate (**8d**).* See ref 36.

*Ethyl 5-Methyl-1-p-tolyl-1H-pyrazole-3-carboxylate (**8e**).* See ref 36.

*Ethyl 1-Phenyl-5-propyl-1H-pyrazole-3-carboxylate (**8f**).*[39] See ref 39.

*Ethyl 5-Isopropyl-1-phenyl-1H-pyrazole-3-carboxylate (**8g**).* Yield: 85% (1.2 g from 1.5 g); brown oil. R_f = 0.56 (hexanes/EtOAc, 80:20, v/v). IR (neat): ν_{max} 1721 (CO_2Et) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.11 (d, J = 6.9 Hz, 6H), 1.32 (t, J = 7.1 Hz, 3H), 2.88−2.97 (m, 1H), 4.34 (q, J = 7.1 Hz, 6H), 6.69 (d, J = 0.4 Hz, 1H), 7.34−7.47 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.6, 22.9, 25.7, 61.1, 105.7, 126.5, 129.1, 129.3, 139.5, 144.0, 152.3, 162.9. MS (ESI+): m/z = 259.2. ESI-HRMS: calcd for $C_{15}H_{19}N_2O_2$ (M^+ + H) 259.1447, found 259.1450.

*Ethyl 1-Phenyl-1H-pyrazole-3-carboxylate (**8h**).* See ref 40.

*Ethyl 1-Phenyl-1H-pyrazole-5-carboxylate (**11a**).* See ref 41.

*Ethyl 1-(4-Bromophenyl)-1H-pyrazole-5-carboxylate (**11b**).* See ref 42.

*Ethyl 1,3-Diphenyl-1H-pyrazole-5-carboxylate (**11c**).*[29] The ethyl 5-methyl-1-(substituted phenyl)-1*H*-pyrazole-4-carboxylates were prepared according to the literature procedure.[36]

*Ethyl 5-Methyl-1-phenyl-1H-pyrazole-4-carboxylate (**14a**).* See ref 43.

*Ethyl 1-(4-Bromophenyl)-5-methyl-1H-pyrazole-4-carboxylate (**14b**).* See ref 36.

*Ethyl 5-Methyl-1-o-tolyl-1H-pyrazole-4-carboxylate (**14c**).* Yield: 86% (1.3 g from 1.0 g); brown oil; R_f = 0.5 (hexanes/EtOAc, 80:20, v/v). IR (neat): ν_{max} 1721 (CO_2Et) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.31 (t, J = 7.2 Hz, 3H), 1.96 (s, 3H), 2.27 (s, 3H), 4.26 (q, J = 7.2 Hz, 2H), 7.13 (dd, J_1 = 6.9 Hz, J_2 = 0.7 Hz, 1H), 7.22−7.28 (m, 2H), 7.32 (td, J_1 = 7.5 Hz, J_2 = 1.2 Hz, 1H), 7.97 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 11.3, 14.6, 17.3, 60.1, 112.1, 126.9, 127.7, 129.9, 131.3, 136.1, 137.8, 141.8, 144.5, 164.0. MS (ESI+): m/z = 245.3. ESI-HRMS: calcd for $C_{14}H_{17}N_2O_2$ (M^+ + H) 245.1290, found 245.1295.

*Ethyl 1-(2,4-Dichlorophenyl)-5-methyl-1H-pyrazole-4-carboxylate (**14d**).* See ref 36.

*3-Methyl-1,5-diphenyl-1H-pyrazole (**17**).* See ref 44.

*3-Methyl-1-phenyl-1H-pyrazol-5(4H)-one (**21**).* See ref 45.

General Procedure for Oxidative C(sp2)−H Functionalization in Substituted *N*-Arylpyrazoles 5a−p, 8a−h, 11a−c, 14a−d, and 17 Esters As Exemplified for 5a. To a 50 mL sealed tube were added **5a** (0.5 g, 1.7 mmol), $K_2S_2O_8$ (0.925 g, 3.42 mmol), $Pd(OAc)_2$ (0.019 g, 0.08 mmol), TFA (4.5 mL), and TFAA (0.5 mL), and the mixture was heated at 90 °C for 12 h. An experimental procedure similar to that described for **3a** afforded the crude product, which was purified by column chromatography (silica gel, 20% EtOAc in hexanes) to obtain pure **6a** (0.4 g, 76%) as a white solid and **7a** (0.015 g, 3%) also as a white solid.

*Ethyl 1-(2-Hydroxyphenyl)-5-phenyl-1H-pyrazole-3-carboxylate (**6a**).* Mp: 145−147 °C. R_f = 0.41 (hexanes/EtOAc, 80:20, v/v). IR (KBr): ν_{max} 1721 (CO_2Et), 3423 (OH) cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.32 (t, J = 7.0 Hz, 3H), 4.32 (q, J = 7.0 Hz, 2H), 6.89−6.95 (m, 2H), 7.10 (s, 1H), 7.30−7.35 (m, 7H), 9.99 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.2, 60.3, 107.8, 116.6, 119.1, 127.1, 127.4, 128.3, 128.4, 128.8, 129.3, 130.8, 143.1, 145.6, 152.7, 161.7. MS (ESI+): m/z = 309.0. ESI-HRMS: calcd for $C_{18}H_{17}N_2O_3$ (M^+ + H): 309.1239, found 309.1242.

*Diethyl 1,1′-(Biphenyl-2,2′-diyl)bis(5-phenyl-1H-pyrazole-3-carboxylate) (**7a**).* Mp: 137−139 °C. R_f = 0.27 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max} 1728 (CO_2Et) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.39 (t, J = 7.1 Hz, 6H), 4.38−4.39 (m, 4H), 6.09−6.10 (m, 2H), 6.55 (d, J = 7.4 Hz, 4H), 6.74 (s, 2H), 6.89 (s, 2H), 7.00 (t, J = 7.4 Hz, 4H), 7.14 (t, J = 7.4 Hz, 2H), 7.30 (t, J = 6.4 Hz, 2H), 7.43−7.45 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.5, 60.7, 109.8, 127.7, 127.8, 128.0, 128.3, 128.5, 128.8, 130.0, 131.8, 134.1, 137.0, 144.4, 144.8, 162.1. MS (ESI+): m/z = 583.2. ESI-HRMS: calcd for $C_{36}H_{31}N_4O_4$ (M^+ + H) 583.2345, found 583.2340.

*Ethyl 5-(2-Chlorophenyl)-1-(2-hydroxyphenyl)-1H-pyrazole-3-carboxylate (**6b**).* Yield: 45% (0.25 g from 0.55 g); white solid. Mp: 112−114 °C. R_f = 0.62 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max} 1719 (CO_2Et), 3428 (OH) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.43 (t, J = 6.7 Hz, 3H), 4.44−4.58 (m, 2H), 6.59−6.62 (m, 2H), 7.08−7.16 (m, 3H), 7.26−7.30 (m, 2H), 7.38−7.43 (m, 2H), 8.83 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.5, 61.6, 112.0, 118.8, 119.6, 123.7, 125.6, 127.2, 129.0, 129.6, 130.4, 131.1, 132.0, 134.2, 142.4, 144.0, 150.5, 161.7. MS (ESI+): m/z = 342.9. ESI-HRMS: calcd for $C_{18}H_{16}ClN_2O_3$ (M^+ + H) 343.0849, found 343.0854.

*Diethyl 1,1′-(Biphenyl-2,2′-diyl)bis(5-(2-chlorophenyl)-1H-pyrazole-3-carboxylate) (**7b**).* Yield: 29% (0.16 g from 0.55 g); white solid. Mp: 210−212 °C. R_f = 0.37 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max} 1724 (CO_2Et) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.39 (t, J = 6.3 Hz, 6H), 4.37−4.39 (m, 4H), 6.24 (brs, 2H), 6.41 (d, J = 6.8 Hz, 2H), 6.83−6.85 (m, 4H), 7.00 (s, 2H), 7.09−7.10 (m, 4H), 7.31−7.41 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.5, 60.8, 112.1, 126.6, 128.7, 128.9, 129.1, 129.3, 129.5, 129.7, 131.4, 131.8, 133.2, 133.8, 137.7, 141.7, 144.6, 162.1. MS (ESI+): m/z = 651.1. ESI-HRMS: calcd for $C_{36}H_{29}Cl_2N_4O_4$ (M^+ + H) 651.1566, found 651.1562.

*Ethyl 5-(4-Fluorophenyl)-1-(2-hydroxyphenyl)-1H-pyrazole-3-carboxylate (**6c**).* Yield: 70% (0.39 g from 0.53 g); white solid. Mp: 132−134 °C. R_f = 0.60 (hexanes/EtOAc, 80:20, v/v). IR (KBr): ν_{max} 1721 (CO_2Et), 3399 (OH) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.42 (t, J = 6.0 Hz, 3H), 4.44 (q, J = 6.6 Hz, 2H), 6.68−6.74 (m, 2H), 7.02−7.06 (m, 3H), 7.14 (d, J = 8.0 Hz, 1H), 7.20−7.26 (m, 3H), 8.41 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.4, 61.5, 110.1, 116.1 (d, J = 21.9 Hz), 118.9, 119.9, 125.5 (d, J = 3.3 Hz), 125.6, 125.9, 130.0, 130.8 (d, J = 8.3 Hz), 144.4, 144.7, 151.1, 161.9, 163.3 (d, J = 249.7 Hz). MS (ESI+): m/z = 327.0. ESI-HRMS: calcd for $C_{18}H_{16}FN_2O_3$ (M^+ + H) 327.1145, found 327.1142.

*Diethyl 1,1′-(Biphenyl-2,2′-diyl)bis(5-(4-fluorophenyl)-1H-pyrazole-3-carboxylate) (**7c**).* Yield: 12% (0.06 g from 0.53 g); white solid. Mp: 112−114 °C. R_f = 0.10 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max} 1727 (CO_2Et) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.39 (t, J = 6.7 Hz, 6H), 4.39 (brs, 4H), 6.15 (brs, 2H), 6.52 (brs, 4H), 6.71−6.77 (m, 6H), 6.99 (brs, 2H), 7.31 (t, J = 7.6 Hz, 2H), 7.46 (brs, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.5, 61.5, 110.3,

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116.1 (d, J = 21.8 Hz), 118.9, 119.9, 125.5 (d, J = 3.2 Hz), 125.5, 125.6, 130.0, 130.9 (d, J = 8.3 Hz), 144.5, 144.6, 150.9, 161.8, 163.4 (d, J = 250.4 Hz). MS (ESI+): m/z = 619.2. ESI-HRMS: calcd for $C_{36}H_{29}F_2N_4O_4$ (M^+ + H) 619.2157, found 619.2162.

*Ethyl 5-(4-Chlorophenyl)-1-(2-hydroxyphenyl)-1H-pyrazole-3-carboxylate (**6d**).* Yield: 44% (0.26 g from 0.55 g); white solid. Mp: 143−145 °C. R_f = 0.44 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max} 1722 (CO_2Et), 3403 (OH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.42 (t, J = 7.1 Hz, 3H), 4.44 (d, J = 7.1 Hz, 2H), 6.69−6.76 (m, 2H), 7.05 (s, 1H), 7.13−7.16 (m, 1H), 7.19−7.23 (m, 2H), 7.25−7.26 (m, 1H), 7.33 (d, J = 8.5 Hz, 2H), 7.34 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.5, 61.6, 110.4, 119.0, 120.0, 125.4, 125.7, 127.8, 129.3, 130.1, 135.6, 144.4, 144.6, 150.9, 161.7. MS (ESI+): m/z = 343.1. ESI-HRMS: calcd for $C_{18}H_{16}ClN_2O_3$ (M^+ + H) 343.0849, found 343.0846.

*Diethyl 1,1′-(Biphenyl-2,2′-diyl)bis(5-(4-chlorophenyl)-1H-pyrazole-3-carboxylate) (**7d**).* Yield: 28% (0.15 g from 0.55 g); white solid. Mp: 162−164 °C. R_f = 0.41 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max} 1722 (CO_2Et) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.40 (t, J = 7.1 Hz, 6H), 4.39 (brs, 4H), 6.1 (s, 1H), 6.48 (d, J = 7.8 Hz, 4H), 6.73 (s, 2H), 6.99 (d, J = 6.4 Hz, 6H), 7.26 (s, 1H), 7.32 (t, J = 7.4 Hz, 2H), 7.45 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.5, 60.9, 110.0, 128.2, 128.4, 128.6, 128.9, 129.1, 131.9, 133.7, 134.1, 136.7, 143.2, 145.0, 162.0. MS (ESI+): m/z = 650.9. ESI-HRMS: calcd for $C_{36}H_{29}Cl_2N_4O_4$ (M^+ + H) 651.1566, found 651.1562.

*Ethyl 1-(2-Hydroxyphenyl)-5-p-tolyl-1H-pyrazole-3-carboxylate (**6e**).* Yield: 74% (0.41 g from 0.52 g); white solid. Mp: 156−157 °C. R_f = 0.53 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max}: 1726 (CO_2Et), 3400 (OH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.42 (t, J = 6.7 Hz, 3H), 2.36 (s, 3H), 4.44 (q, J = 6.9 Hz, 2H,), 6.67 (t, J = 7.6 Hz, 1H), 6.77 (d, J = 7.7 Hz, 1H), 7.02 (s, 1H), 7.13−7.15 (m, 5H), 7.20 (t, J = 7.2 Hz, 1H), 8.53 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.5, 21.4, 61.4, 110.2, 118.8, 119.7, 125.4, 125.5, 126.4, 128.8, 129.6, 139.5, 144.3, 145.7, 150.8, 161.8. MS (ESI+): m/z = 323.0 ESI-HRMS: calcd for $C_{19}H_{19}N_2O_3$ (M^+ + H) 323.1396, found 323.1391.

*Diethyl 1,1′-(Biphenyl-2,2′-diyl)bis(5-p-tolyl-1H-pyrazole-3-carboxylate) (**7e**).* Yield: 8% (0.04 g from 0.52 g), yellow solid. Mp: 223−225 °C. R_f = 0.16 (hexanes/EtOAc, 60:40, v/v). IR (KBr) ν_{max}: 1727 (CO_2Et) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.37 (t, J = 6.7 Hz, 6H), 2.20 (s, 6H), 4.37 (brs, 4H), 6.44 (d, J = 5.0 Hz, 4H), 6.71 (s, 2H), 6.82 (d, J = 6.1 Hz, 4H), 6.91 (brs, 2H), 7.25−7.28 (m, 4H), 7.39 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.4, 21.3, 60.6, 109.4, 127.0, 127.6, 128.0, 128.4, 128.6, 128.9, 132.0, 134.2, 137.1, 137.7, 144.6, 144.7, 162.2. MS (ESI+): m/z = 611.4. ESI-HRMS: calcd for $C_{38}H_{35}N_4O_4$ (M^+ + H) 611.2658, found 611.2657.

*Ethyl 1-(2-Hydroxyphenyl)-5-(4-methoxyphenyl)-1H-pyrazole-3-carboxylate (**6f**).* Yield: 40% (0.23 g from 0.55 g); yellow solid. Mp: 115−117 °C. R_f = 0.20 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max}: 1724 (CO_2Et), 3409 (OH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.41 (t, J = 7.1 Hz, 3H), 3.82 (s, 3H), 4.43 (q, J = 7.1 Hz, 2H), 6.66−6.67 (m, 1H), 6.78 (dd, J_1 = 8.0 Hz, J_2 = 1.5 Hz, 1H), 6.86 (dd, J_1 = 8.8 Hz, J_2 = 1.9 Hz, 2H), 6.99 (s, 1H), 7.13 (dd, J_1 = 8.2 Hz, J_2 = 1.3 Hz, 1H), 7.17−7.22 (m, 3H), 8.53 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.5, 55.5, 61.4, 110.0, 114.4, 118.9, 119.7, 121.6, 125.4, 125.6, 129.6, 130.3, 144.4, 145.5, 150.9, 160.4, 161.9. MS (ESI+): m/z = 339.0 ESI-HRMS: calcd for $C_{19}H_{19}N_2O_4$ (M^+ + H) 339.1345, found 339.1340.

*Diethyl 1,1′-(Biphenyl-2,2′-diyl)bis(5-(4-methoxyphenyl)-1H-pyrazole-3-carboxylate) (**7f**).* Yield: 32% (0.18 g from 0.55 g); off-white solid. Mp: 165−168 °C. R_f = 0.08 (hexanes/EtOAc, 60:40, v/v). IR (KBr) ν_{max}: 1725 (CO_2Et) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.31 (t, J = 7.0 Hz, 6H), 3.68 (s, 6H), 4.30 (d, J = 5.0 Hz, 4H), 6.14−6.22 (m, 2H), 6.40−6.49 (m, 8H), 6.61 (s, 2H), 6.89 (s, 2H), 7.19−7.22 (m, 2H), 7.33 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$+DMSO-d_6): 14.2, 55.2, 60.4, 108.9, 113.5, 122.3, 127.8, 128.3, 128.5, 128.8, 131.6, 134.0, 136.8, 144.1, 144.4, 159.2, 162.0. MS (ESI+): m/z = 643.2. ESI-HRMS: calcd for $C_{38}H_{35}N_4O_6$ (M^+ + H) 643.2557, found 643.2559.

*Ethyl 1-(2-Hydroxyphenyl)-5-(4-nitrophenyl)-1H-pyrazole-3-carboxylate (**6g**).* Yield: 35% (0.21 g from 0.58 g); off-white solid. Mp: 192−194 °C. R_f = 0.40 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max}: 1726 (CO_2Et), 3400 (OH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.43 (t, J = 5.7 Hz, 3H), 4.45 (q, J = 5.7 Hz, 2H), 6.73−6.74 (m, 2H), 7.15−7.17 (m, 2H), 7.26−7.29 (m, 1H), 7.44−7.46 (m, 2H), 8.01 (s, 1H), 8.21 (dd, J_1 = 5.5 Hz, J_2 = 1.6 Hz, 2H), ^{13}C NMR (100 MHz, $CDCl_3$): 14.4, 61.7, 111.2, 119.2, 120.3, 124.1, 125.3, 125.9, 129.6, 130.6, 135.5, 143.2, 144.9, 148.0, 150.9, 161.5. MS (ESI+): m/z = 354.0 ESI-HRMS: calcd for $C_{18}H_{16}N_3O_5$ (M^+ + H) 354.1090, found 354.1093.

*Diethyl 1,1′-(Biphenyl-2,2′-diyl)bis(5-(4-nitrophenyl)-1H-pyrazole-3-carboxylate) (**7g**).* Yield: 20% (0.12 g from 0.58 g); white solid. Mp: 210−212 °C. R_f = 0.12 (hexanes/EtOAc, 60:40, v/v). IR (KBr) ν_{max}: 1733 (CO_2Et) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.42 (t, J = 7.1 Hz, 6H), 4.42−4.46 (m, 4H), 6.09 (brs, 2H), 6.72 (d, J = 7.5 Hz, 4H), 6.85 (s, 2H), 6.93 (brs, 2H), 7.39 (t, J = 7.7 Hz, 2H), 7.53 (s, 2H), 7.89 (d, J = 8.4 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.3, 60.9, 111.0, 123.4, 128.0, 128.3, 129.3, 129.4, 131.6, 133.0, 135.8, 136.4, 141.9, 145.2, 147.0, 161.5. MS (ESI+): m/z = 673.1. ESI-HRMS: calcd for $C_{36}H_{29}N_6O_8$ (M^+ + H) 673.2047, found 673.2046.

*Ethyl 5-(2,4-Dimethylphenyl)-1-(2-hydroxyphenyl)-1H-pyrazole-3-carboxylate (**6h**).* Yield: 44% (0.25 g from 0.55 g); white solid. Mp: 107−108 °C. R_f = 0.40 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max}: 1722 (CO_2Et), 3401 (OH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.42 (t, J = 7.1 Hz, 3H), 1.91 (s, 3H), 2.35 (s, 3H), 4.44 (q, J = 7.1 Hz, 2H), 6.59 (dt, J_1 = 6.8 Hz, J_2 = 1.7 Hz, 1H), 6.62 (dd, J_1 = 8.0 Hz, J_2 = 1.5 Hz, 1H), 6.93 (s, 1H), 7.01−7.04 (m, 2H), 7.09−7.12 (m, 2H), 7.13 (d, J = 1.8 Hz, 1H), 9.26 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.5, 19.6, 21.4, 61.5, 111.2, 118.8, 119.5, 123.4, 125.7, 126.4, 127.1, 129.2, 130.4, 131.6, 137.0, 139.9, 143.7, 145.2, 150.3, 161.8. MS (ESI+): m/z = 337.1. ESI-HRMS: calcd for $C_{20}H_{21}N_2O_3$ (M^+ + H) 337.1552, found 337.1552.

*Diethyl 1,1′-(Biphenyl-2,2′-diyl)bis(5-(2,4-dimethylphenyl)-1H-pyrazole-3-carboxylate) (**7h**).* Yield: 30% (0.165 g from 0.55 g); white solid. Mp: 70−72 °C. R_f = 0.24 (hexanes/EtOAc, 60:40, v/v). IR (KBr) ν_{max}: 1735 (CO_2Et) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.33 (t, J = 7.1 Hz, 6H), 1.63 (s, 6H), 2.14 (s, 6H), 4.30 (q, J = 7.1 Hz, 4H), 5.98 (d, J = 7.8 Hz, 2H,), 6.09 (d, J = 8.0 Hz, 2H), 6.46 (d, J = 8.0 Hz, 2H), 6.60 (s, 2H), 6.64 (s, 2H), 6.86 (t, J = 8.3 Hz, 2H), 7.20−7.24 (m, 2H), 7.32 (d, J = 7.9 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.4, 20.5, 21.3, 60.8, 111.0, 126.0, 126.1, 128.5, 128.7, 128.8, 129.7, 131.1, 131.6, 134.3, 137.0, 137.5, 137.9, 143.6, 144.4, 162.5. MS (ESI+): m/z = 639.4. ESI-HRMS: calcd for $C_{40}H_{39}N_4O_4$ (M^+ + H) 639.2971, found 639.2973.

*Ethyl 1-(2-Hydroxyphenyl)-5-(3,4,5-trimethoxyphenyl)-1H-pyrazole-3-carboxylate (**6i**).* Yield: 72% (0.49 g from 0.65 g); off-white solid. Mp: 150−152 °C. R_f = 0.12 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max} 1721 (CO_2Et), 3400 (OH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.43 (t, J = 7.1 Hz, 3H), 3.64 (s, 6H), 3.85 (s, 3H), 4.46 (d, J = 7.1 Hz, 2H), 6.39 (s, 2H), 7.04 (s, 1H), 7.37−7.39 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.5, 56.2, 61.1, 61.5, 106.2, 108.5, 109.9, 118.8, 119.9, 124.4, 125.9, 129.9, 138.9, 144.4, 145.5, 150.9, 153.4, 161.9. MS (ESI+): m/z = 399.5. ESI-HRMS: calcd for $C_{21}H_{23}N_2O_6$ (M^+ + H) 399.1556, found 399.1553.

*Ethyl 1-(5-Chloro-2-hydroxyphenyl)-5-phenyl-1H-pyrazole-3-carboxylate (**6k**).* Yield: 78% (0.46 g from 0.55 g); white solid. Mp: 118−120 °C. R_f = 0.36 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max} 1721 (CO_2Et), 3411 (OH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.42 (t, J = 6.9 Hz, 3H), 4.44 (d, J = 6.9 Hz, 2H), 6.73 (brs, 1H), 7.05−7.08 (m, 2H), 7.16−7.17 (m, 1H), 7.26−7.29 (m, 2H), 7.40−7.42 (m, 3H), 8.70 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.5, 61.6, 110.4, 110.3, 120.1, 124.3, 125.5, 126.2, 128.9, 129.1, 129.7, 129.8, 144.6, 146.0, 149.9, 161.7. MS (ESI+): m/z = 342.9. ESI-HRMS: calcd for $C_{18}H_{16}ClN_2O_3$ (M^+ + H) 343.0849, found 343.0853.

*Diethyl 1,1′-(4,4′-Dichlorobiphenyl-2,2′-diyl)bis(5-phenyl-1H-pyrazole-3-carboxylate) (**7k**).* Yield: 10% (0.06 g from 0.55 g); white solid. Mp: 230−232 °C. R_f = 0.30 (hexanes/EtOAc, 80:20, v/v). IR

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(KBr) ν_{max}: 1731 (CO_2Et) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.41 (t, J = 6.4 Hz, 6H), 4.40 (brs, 4H), 5.90 (brs, 2H), 6.60 (d, J = 7.2 Hz, 4H), 6.76 (s, 2H), 6.81 (d, J = 7.3 Hz, 2H), 7.70 (t, J = 6.7 Hz, 4H), 7.18 (t, J = 6.7 Hz, 2H), 7.55 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.9, 61.3, 110.6, 128.0, 128.5, 128.7, 128.9, 129.6, 130.1, 131.8, 132.7, 134.9, 138.1, 144.8, 145.8, 162.3. MS (ESI+): m/z = 651.0. ESI-HRMS: calcd for $C_{36}H_{29}Cl_2N_4O_4$ (M^+ + H) 651.1566, found 651.1563.

*Ethyl 1-(4-Fluoro-2-hydroxyphenyl)-5-phenyl-1H-pyrazole-3-carboxylate (**6l**).* Yield: 41% (0.23 g from 0.53 g); white solid. Mp: 224−226 °C. R_f = 0.51 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max}: 1730 (CO_2Et), 3400 (OH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.42 (t, J = 7.1 Hz, 3H), 4.44 (q, J = 7.1 Hz, 2H), 6.36−6.41 (m, 1H), 6.70 (dd, J_1 = 9.0 Hz, J_2 = 5.8 Hz, 1H), 6.85 (dd, J_1 = 9.8 Hz, J_2 = 2.8 Hz, 1H), 7.05 (s, 1H), 7.25−7.28 (m, 2H), 7.34−7.40 (m, 3H), 8.77 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.5, 61.6, 106.1 (d, J = 25.4 Hz), 106.9 (d, J = 23.4 Hz), 110.3, 122.0, 126.5, 126.6 (d, J = 10.4 Hz), 128.9 (d, J = 11.3 Hz), 129.5, 144.4, 145.7, 152.6 (d, J = 12.8 Hz), 161.7, 162.8 (d, J = 247.4 Hz). MS (ESI+): m/z = 327.3. ESI-HRMS: calcd for $C_{18}H_{16}FN_2O_3$ (M^+ + H) 327.1145, found 327.1141.

*Diethyl 1,1′-(5,5′-Difluorobiphenyl-2,2′-diyl)bis(5-phenyl-1H-pyrazole-3-carboxylate) (**7l**).* Yield: 24% (0.13 g from 0.53 g); yellow oil. R_f = 0.16 (hexanes/EtOAc, 60:40, v/v). IR (neat) ν_{max}: 1733 (CO_2Et) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.40 (t, J = 7.1 Hz, 6H), 4.38−4.40 (m, 4H), 5.65 (brs, 2H), 6.58 (d, J = 7.4 Hz, 4H), 6.75 (s, 2H), 7.00−7.05 (m, 2H), 7.08 (t, J = 7.8 Hz, 4H), 7.22 (t, J = 7.5 Hz, 2H), 7.46−7.48 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.5, 60.9, 109.8, 116.2 (d, J = 22.4 Hz), 118.0 (d, J = 23.7 Hz), 127.6, 128.4 (d, J = 12.1 Hz), 129.5, 130.0 (d, J = 8.8 Hz), 133.2, 134.8, 144.5, 145.1, 162.0, 162.2 (d, J = 250.7 Hz). MS (ESI+): m/z = 619.1. ESI-HRMS: calcd for $C_{36}H_{29}F_2N_4O_4$ (M^+ + H) 619.2157, found 619.2152.

*Ethyl 1-(4-Chloro-2-hydroxyphenyl)-5-phenyl-1H-pyrazole-3-carboxylate (**6m**).* Yield: 48% (0.28 g from 0.55 g); white solid. Mp: 170−172 °C; R_f = 0.21 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max}: 1722 (CO_2Et), 3400 (OH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.35 (t, J = 7.1 Hz, 3H), 4.37 (d, J = 7.1 Hz, 2H), 6.56−6.57 (m, 2H), 6.97 (s, 1H), 7.08−7.09 (m, 1H), 7.19−7.21 (m, 2H), 7.29−7.35 (m, 3H), 8.90 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.5, 61.6, 110.5, 119.2, 120.0, 124.3, 126.2, 128.9, 129.1, 129.6, 134.9, 144.5, 145.7, 151.8, 161.7. MS (ESI+): m/z = 343.3. ESI-HRMS: calcd for $C_{18}H_{16}ClN_2O_3$ (M^+ + H) 343.0849, found 343.0851.

*Diethyl 1,1′-(5,5′-Dichlorobiphenyl-2,2′-diyl)bis(5-phenyl-1H-pyrazole-3-carboxylate) (**7m**).* Yield: 22% (0.12 g from 0.55 g); white solid. Mp: 217−219 °C. R_f = 0.10 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max}: 1729 (CO_2Et) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.33 (t, J = 7.1 Hz, 6H), 4.33 (brs, 4H), 5.87 (s, 2H), 6.50 (d, J = 7.2 Hz, 4H), 6.68 (s, 2H), 7.03 (t, J = 7.6 Hz, 4H), 7.12−7.18 (m, 2H), 7.21−7.24 (m, 2H), 7.38 (d, J = 8.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.5, 60.9, 110.0, 127.5, 128.6, 128.7, 129.2, 129.4, 129.5, 131.2, 134.2, 134.8, 135.6, 144.5, 145.3, 162.0. MS (ESI+): m/z = 651.4. ESI-HRMS: calcd for $C_{36}H_{29}Cl_2N_4O_4$ (M^+ + H) 651.1566, found 651.1562.

*Ethyl 1-(4-Bromo-2-hydroxyphenyl)-5-phenyl-1H-pyrazole-3-carboxylate (**6n**).* Yield: 40% (0.26 g from 0.63 g); white solid. Mp: 122−124 °C. R_f = 0.30 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max} 1722 (CO_2Et), 3394 (OH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.42 (t, J = 7.1 Hz, 3H), 4.44 (d, J = 7.1 Hz, 2H), 6.60 (d, J = 8.6 Hz, 1H), 6.78 (dd, J_1 = 8.6 Hz, J_2 = 2.1 Hz, 1H), 7.04 (s, 1H), 7.26 (s, 1H), 7.27−7.28 (m, 1H), 7.31 (d, J = 2.1 Hz, 1H), 7.36−7.41 (m, 3H), 7.41 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.5, 61.6, 110.6, 122.3, 122.6, 122.9, 124.7, 126.3, 129.0, 129.1, 129.6, 144.5, 145.7, 151.8, 161.6. MS (ESI+): m/z = 387.0. ESI-HRMS: calcd for $C_{18}H_{16}BrN_2O_3$ (M^+ + H) 387.0344, found 387.0349.

*Diethyl 1,1′-(5,5′-Dibromobiphenyl-2,2′-diyl)bis(5-phenyl-1H-pyrazole-3-carboxylate) (**7n**).* Yield: 22% (0.14 g from 0.63 g); brown solid. Mp: 134−136 °C. R_f = 0.10 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max} 1732 (CO_2Et) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.40 (t, J = 7.1 Hz, 6H), 4.43 (q, J = 7.2 Hz, 4H), 6.09 (s, 1H), 6.56 (d, J = 7.2 Hz, 3H), 6.74 (s, 2H), 7.11 (t, J = 7.6 Hz, 4H), 7.26−7.32 (m, 4H), 7.36−7.46 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.3, 60.7, 109.9, 122.8, 127.2, 128.6, 128.9, 129.6, 132.3, 133.9, 134.1, 135.9, 144.4, 145.2, 161.8. MS (ESI+): m/z = 738.9. ESI-HRMS: calcd for $C_{36}H_{29}Br_2N_4O_4$ (M^+ + H) 739.0556, found 739.0557.

*Ethyl 1-(2-Hydroxy-4,5-dimethylphenyl)-5-phenyl-1H-pyrazole-3-carboxylate (**6p**).* Yield: 38% (0.22 g from 0.55 g); yellow solid. Mp: 122−123 °C. R_f = 0.28 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max}: 1720 (CO_2Et), 3400 (OH) cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ 1.35 (t, J = 7.1 Hz, 3H), 2.16 (s, 3H), 2.22 (s, 3H), 4.35 (q, J = 7.1 Hz, 2H), 6.73 (s, 1H), 7.01−7.11 (m, 2H), 7.34−7.36 (m, 5H), 9.63 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.5, 18.7, 19.8, 61.4, 110.0, 119.5, 123.1, 126.2, 127.9, 128.7, 128.9, 129.2, 129.6, 138.6, 144.1, 145.4, 148.4, 162 0. MS (ESI+): m/z = 337.4 ESI-HRMS: calcd for $C_{20}H_{21}N_2O_3$ (M^+ + H) 337.1552, found 337.1550.

*Diethyl 1,1′-(4,4′,5,5′-Tetramethylbiphenyl-2,2′-diyl)bis(5-phenyl-1H-pyrazole-3-carboxylate) (**7p**).* Yield: 20% (0.11 g from 0.55 g); yellow solid. Mp: 187−189 °C. R_f = 0.16 (hexanes/EtOAc, 60:40, v/v). IR (KBr) ν_{max}: 1733 (CO_2Et) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.32 (t, J = 7.2 Hz, 6H), 1.83 (s, 6H), 2.15 (s, 6H), 4.34 (q, J = 7.1 Hz, 4H), 5.62 (s, 2H), 6.50 (d, J = 7.4 Hz, 4H), 6.63 (s, 2H), 6.91 (t, J = 7.7 Hz, 4H), 7.05 (t, J = 7.4 Hz, 2H), 7.16 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.5, 19.4, 19.6, 60.7, 109.7, 127.5, 127.8, 127.9, 128.3, 130.0, 131.0, 132.7, 134.6, 137.1, 137.4, 144.2, 144.3, 162.2. MS (ESI+): m/z = 639.2. ESI-HRMS: calcd for $C_{40}H_{39}N_4O_4$ (M^+ + H) 639.2971, found 639.2968.

*Ethyl 1-(2-Hydroxyphenyl)-5-methyl-1H-pyrazole-3-carboxylate (**9a**).* Yield: 74% (0.31 g from 0.40 g); yellow solid. Mp: 141−142 °C; R_f = 0.16 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max}: 1721 (CO_2Et), 3400 (OH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.32 (t, J = 6.9 Hz, 3H), 2.35 (s, 3H), 4.33 (q, J = 7.1 Hz, 2H), 6.71 (s, 1H), 6.89 (t, J = 7.5 Hz, 1H), 7.05 (d, J = 8.1 Hz, 1H), 7.16−7.23 (m, 2H), 8.36 (s, 1H).^{13}C NMR (100 MHz, $CDCl_3$): 12.8, 14.5, 61.3, 109.7, 118.9, 120.0 124.7, 125.7, 130.0, 142.1, 144.0, 151.2, 162 0. MS (ESI+): m/z = 247.4 ESI-HRMS: calcd for $C_{13}H_{15}N_2O_3$ (M^+ + H) 247.1083, found 247.1089.

*Ethyl 1-(5-Chloro-2-hydroxyphenyl)-5-methyl-1H-pyrazole-3-carboxylate (**9b**).* Yield: 74% (0.4 g from 0.45 g); white solid. Mp: 131−132 °C. R_f = 0.20 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max}: 1723 (CO_2Et), 3393 (OH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.32 (t, J = 7.1 Hz, 3H), 2.36 (s, 3H), 4.32 (q, J = 7.1 Hz, 2H), 6.69 (s, 1H), 6.98 (d, J = 9.4 Hz, 1H), 7.16−7.19 (m, 2H), 8.63 (s, 1H);^{13}C NMR (100 MHz, $CDCl_3$): 12.7, 14.4, 61.4, 109.2, 120.4, 124.7, 125.3, 126.6, 130.2, 142.6, 144.0, 150.1, 161.7. MS (ESI+): m/z = 281.5 ESI-HRMS: calcd for $C_{13}H_{14}ClN_2O_3$ (M^+ + H) 281.0693, found 281.0697.

*Ethyl 1-(4-Fluoro-2-hydroxyphenyl)-5-methyl-1H-pyrazole-3-carboxylate (**9c**).* Yield: 72% (0.32 g from 0.42 g); white solid. Mp: 124−125 °C. R_f = 0.20 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max}: 1716 (CO_2Et), 3400 (OH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.32 (t, J = 7.1 Hz, 3H), 2.30 (s, 3H), 4.32 (q, J = 7.1 Hz, 2H), 6.60 (dt, J_1 = 8.2 Hz, J_2 = 2.6 Hz 1H), 6.68 (s, 1H), 6.73 (dd,, J_1 = 9.7 Hz,, J_2 = 2.6 Hz, 1H), 7.12 (m, 1H), 8.67 (s, 1H);^{13}C NMR (100 MHz, $CDCl_3$): 12.3, 14.4, 61.3, 106.3 (d, J = 25.2 Hz), 107.3 (d, J = 23.2 Hz), 109.1, 122.4, 126.7 (d, J = 10.6 Hz), 142.5, 143.8, 153.1 (d, J = 12.9 Hz), 161.8, 163.3 (d, J = 246.7 Hz). MS (ESI+): m/z = 264.9 ESI-HRMS: calcd for $C_{13}H_{14}FN_2O_3$ (M^+ + H) 265.0988, found 265.0983.

*Ethyl 1-(4-Bromo-2-hydroxyphenyl)-5-methyl-1H-pyrazole-3-carboxylate (**9d**).* Yield: 75% (0.42 g from 0.53 g); white solid. Mp: 165−167 °C. R_f = 0.20 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max} 1720 (CO_2Et), 3391 (OH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.33 (t, J = 7.1 Hz, 3H), 2.35 (s, 3H), 4.32 (q, J = 7.1 Hz, 2H), 6.68 (d, J = 0.5 Hz, 1H), 7.03 (d, J = 1.0 Hz, 2H), 7.19 (s, 1H), 8.88 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 12.5, 14.4, 61.4, 109.4, 122.4, 123.2, 123.3 125.1, 126.2, 142.5, 144.0, 152.2, 161.8. MS (ESI+): m/z = 324.9. ESI-HRMS: calcd for $C_{13}H_{14}BrN_2O_3$ (M^+ + H) 325.0188, found 325.0184.

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*Ethyl 1-(2-Hydroxy-4-methylphenyl)-5-methyl-1H-pyrazole-3-carboxylate (**9e**).* Yield: 73% (0.32 g from 0.42 g); white solid. Mp: 92−94 °C; R_f = 0.10 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max}: 1722 (CO_2Et), 3398 (OH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.33 (t, J = 7.0 Hz, 3H), 2.28 (s, 3H), 2.33 (s, 3H), 4.33 (q, J = 7.1 Hz, 2H), 6.68−6.70 (m, 2H), 6.87 (s, 1H), 7.04 (d, J = 8.0 Hz, 1H), 7.19 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 12.6, 14.5, 21.4, 61.2, 109.4, 119.2, 120.8, 123.4, 124.7, 140.5, 142.1, 143.7, 150.9, 162.1. MS (ESI+): m/z = 260.9. ESI-HRMS: calcd for $C_{14}H_{17}N_2O_3$ (M^+ + H) 261.1239, found 261.1235.

*Ethyl 1-(2-Hydroxyphenyl)-5-propyl-1H-pyrazole-3-carboxylate (**9f**).* Yield: 35% (0.16 g from 0.44 g); white solid. Mp: 68−70 °C. R_f = 0.20 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max}: 1716 (CO_2Et), 3400 (OH) cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ 0.85 (t, J = 7.4 Hz, 3H), 1.32 (t, J = 7.1 Hz, 3H), 1.50−159 (m, 2H), 2.44 (t, J = 7.6 Hz, 2H), 4.30 (q, J = 7.1 Hz, 2H), 6.71 (s, 1H), 6.97(td, J_1 = 7.7 Hz, J_2 = 1.0 Hz, 1H), 7.09 (dd, J_1 = 8.2 Hz, J_2 = 1.0 Hz, 1H), 7.27 (dd, J_1 = 7.8 Hz, J_2 = 1.5 Hz, 1H), 7.39 (td, J_1 = 7.8 Hz, J_2 = 1.7 Hz, 1H), 9.89 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 13.9, 14.5, 21.9, 28.4, 61.3, 108.4, 118.7, 120.1, 125.3, 125.9, 130.2, 144.2, 147.1, 151.3, 162.1; MS (ESI+): m/z = 275.0 ESI-HRMS: calcd for $C_{15}H_{19}N_2O_3$ (M^+ + H) 275.1396, found 275.1392.

*Diethyl 1,1′-(Biphenyl-2,2′-diyl)bis(5-propyl-1H-pyrazole-3-carboxylate) (**10f**).* Yield: 18% (0.08 g from 0.44 g); yellow oil. R_f = 0.32 (hexanes/EtOAc, 60:40, v/v). IR (neat) ν_{max}: 1733 (CO_2Et) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.81 (t, J = 7.4 Hz, 6H), 1.27 (t, J = 7.7 Hz, 6H), 1.45−1.49 (m, 4H), 2.45 (brs, 4H), 4.26 (q, J = 7.2 Hz, 4H), 6.54 (s, 2H), 6.83 (brs, 2H), 7.12−7.16 (m, 2H), 7.26 (d, J = 4.0 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): 13.6, 14.5, 21.9, 27.6, 60.8, 107.3, 128.4, 128.8, 129.2, 130.4, 135.1, 137.5, 143.7, 147.4, 162.8. MS (ESI+): m/z = 515.3. ESI-HRMS: calcd for $C_{30}H_{35}N_4O_4$ (M^+ + H) 515.2658, found 515.2657.

*Ethyl 1-(2-Hydroxyphenyl)-5-isopropyl-1H-pyrazole-3-carboxylate (**9g**).* Yield: 42% (0.20 g from 0.44 g); white solid. Mp: 142−144 °C. R_f = 0.22 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max}: 1720 (CO_2Et), 3399 (OH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.10 (d, J = 6.8 Hz, 6H), 1.31 (t, J = 7.1 Hz, 3H), 2.89−3.00 (m, 1H), 4.31 (q, J = 7.1 Hz, 2H), 6.69 (s, 1H), 6.85 (td, J_1 = 7.7 Hz, J_2 = 1.3 Hz, 1H), 6.96 (dd, J_1 = 7.0 Hz, J_2 = 1.2 Hz, 1H), 7.12−7.19 (m, 2H), 7.79 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.4, 22.7, 25.7, 29.8, 61.2, 105.9, 118.6, 120.2, 126.3, 130.5, 144.3, 151.7, 153.7, 162.3. MS (ESI+): m/z = 275.5. ESI-HRMS: calcd for $C_{15}H_{19}N_2O_3$ (M^+ + H) 275.1396, found 275.1391.

*Diethyl 1,1′-(Biphenyl-2,2′-diyl)bis(5-isopropyl-1H-pyrazole-3-carboxylate) (**10g**).* Yield: 20% (0.09 g from 0.44 g); white solid. Mp: 128−130 °C. R_f = 0.10 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max}: 1722 (CO_2Et) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.01 (s, 12H), 1.26 (t, J = 7.1 Hz, 6H), 3.08−3.19 (m, 2H), 4.25 (d, J = 7.1 Hz, 4H), 6.56 (s, 2H), 6.77 (d, J = 7.1 Hz, 2H), 7.12 (td, J_1 = 7.5 Hz, J_2 = 1.3 Hz, 2H), 7.26 (td, J_1 = 7.4 Hz, J_2 = 1.4 Hz, 2H), 7.32−7.33 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.4, 23.0, 25.1, 60.6, 105.1, 128.3, 128.6, 129.1, 129.9, 134.9, 137.5, 143.7, 154.0, 162.7. MS (ESI+): m/z = 515.5. ESI-HRMS: calcd for $C_{30}H_{35}N_4O_4$ (M^+ + H) 515.2658, found 515.2662.

*Diethyl 1,1′-(Biphenyl-2,2′-diyl)bis(1H-pyrazole-3-carboxylate) (**10h**).* Yield: 80% (0.296 g from 0.370 g); brown oil. R_f = 0.27 (hexanes/EtOAc, 80:20, v/v). IR (neat) ν_{max}: 1719 (CO_2Et) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.35 (t, J = 7.1 Hz, 6H), 4.34 (q, J = 7.1 Hz, 4H), 6.72 (d, J = 2.4 Hz, 2H), 7.21 (dd, J_1 = 7.7 Hz, J_2 = 1.3 Hz, 2H), 7.36 (td, J_1 = 7.0 Hz, J_2 = 1.4 Hz, 4H), 7.44 (td, J_1 = 7.5 Hz, J_2 = 1.5 Hz, 2H), 7.53 (dd, J_1 = 7.9 Hz, J_2 = 1.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.5, 61.0, 109.6, 126.5, 128.9, 129.3, 131.0, 132.1, 133.4, 138.6, 144.9, 162.3. MS (ESI+): m/z = 431.2. ESI-HRMS: calcd for $C_{24}H_{23}N_4O_4$ (M^+ + H) 431.1719, found 431.1714.

*Diethyl 1,1′-(Biphenyl-2,2′-diyl)bis(1H-pyrazole-5-carboxylate) (**13a**).* Yield: 72% (0.26 g from 0.37 g); off-white solid. Mp: 87−89 °C. R_f = 0.47 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max}: 1725 (CO_2Et) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.16 (t, J = 7.1 Hz, 6H), 4.14 (q, J = 7.1 Hz, 4H), 6.80 (d, J = 1.8 Hz, 2H), 7.23−7.26 (m, 4H), 7.33−7.36 (m, 4H), 7.46 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.1, 61.3, 112.0, 128.1, 128.3, 128.7, 131.9, 134.8, 135.2, 138.4, 139.4, 159.1. MS (ESI+): m/z = 431.2. ESI-HRMS: calcd for $C_{24}H_{23}N_4O_4$ (M^+ + H) 431.1719, found 431.1720.

*Diethyl 1,1′-(5,5′-Dibromo-[1,1′-biphenyl]-2,2′-diyl)bis(1H-pyrazole-5-carboxylate) (**13b**).* Yield: 70% (0.35 g from 0.50 g); brown oil. R_f = 0.16 (hexanes/EtOAc, 80:20, v/v). IR (neat) ν_{max}: 1724 (CO_2Et) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.15 (t, J = 7.1 Hz, 6H), 4.08 (q, J = 7.1 Hz, 4H), 6.70 (d, J = 1.9 Hz, 2H), 7.04 (d, J = 8.7 Hz, 2H), 7.36 (d, J = 1.8 Hz, 2H), 7.40−7.42 (m, 1H), 7.43 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 14.2, 61.4, 112.1, 122.1, 129.2, 131.7, 134.3, 135.0, 135.7, 137.6, 139.8, 159.0. MS (ESI+): m/z = 586.9. ESI-HRMS: calcd for $C_{24}H_{21}Br_2N_4O_4$ (M^+ + H) 586.9930, found 586.9931.

*Diethyl 1,1′-(Biphenyl-2,2′-diyl)bis(5-methyl-1H-pyrazole-4-carboxylate) (**16a**).* Yield: 78% (0.31 g from 0.39 g); white solid. Mp: 172−174 °C. R_f = 0.20 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max}: 1708 (CO_2Et) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.30 (t, J = 6.7 Hz, 6H), 2.38 (s, 6H), 4.27 (q, J = 6.7 Hz, 4H), 7.09 (brs, 2H), 7.22−7.26 (m, 2H), 7.32 (t, J = 7. Three Hz, 2H), 7.39 (t, J = 7.3 Hz, 2H), 7.81 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 11.9, 14.5, 60.0, 112.4, 128.2, 128.7, 129.2, 131.4, 135.6, 136.8, 141.6, 145.2, 163.9. MS (ESI+): m/z = 459.3. ESI-HRMS: calcd for $C_{26}H_{27}N_4O_4$ (M^+ + H) 459.2032, found 459.2035.

*Diethyl 1,1′-(5,5′-Dibromobiphenyl-2,2′-diyl)bis(5-methyl-1H-pyrazole-4-carboxylate) (**16b**).* Yield: 80% (0.42 g from 0.52 g); off-white solid. Mp: 196−198 °C. R_f = 0.45 (hexanes/EtOAc, 60:40, v/v). IR (KBr) ν_{max}: 1702 (CO_2Et) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.27 (t, J = 7.1 Hz, 6H), 2.22 (s, 6H), 4.21(q, J = 7.1 Hz, 4H), 7.00 (d, J = 8.4 Hz, 2H), 7.28 (s, 2H), 7.46 (dd, J_1 = 8.4 Hz, J_2 = 2.2 Hz, 2H), 7.74 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 11.8, 14.5, 60.1, 112.9, 123.0, 129.2, 132.2, 134.6, 135.7, 136.3, 141.9, 145.0, 163.6. MS (ESI+): m/z = 615.0. ESI-HRMS: calcd for $C_{26}H_{25}Br_2N_4O_4$ (M^+ + H) 615.0243, found 615.0245.

*2-(3-Methyl-5-phenyl-1H-pyrazol-1-yl)phenol (**18**).* Yield: 7% (0.03 g from 0.40 g); white solid. Mp: 145−147 °C. R_f = 0.50 (hexanes/EtOAc, 80:20, v/v). IR (KBr) ν_{max}: 1722 (CO_2Et), 3398 (OH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 2.32 (s, 3H), 6.23 (s, 1H), 6.49−6.53 (m, 1H), 6.56−6.58 (m, 1H), 7.04 (d, J = 3.6 Hz, 2H), 7.18−7.21 (m, 2H), 7.25−7.28 (m, 3H), 9.61 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 13.7, 108.3, 118.6, 119.2, 124.3, 125.6, 128.1, 128.7, 128.8, 129.0, 130.6, 144.5, 149.8, 150.7. MS (ESI+): m/z = 251.2. ESI-HRMS: calcd for $C_{16}H_{15}N_2O$ (M^+ + H) 251.1184, found 251.1187.

General Procedure for Oxidative *Ortho*-Hydroxylation in *N*-Arylpyrazoles 5b,d,m, 8h, 11a−c, 14a−d, and 17 for the Synthesis of 6b,d,m, 8h, and 18 As Exemplified for the Synthesis of 6b. A 50 mL sealed tube charged with **5b** (0.112 g, 0.34 mmol), $K_2S_2O_8$ (0.184 g, 0.68 mmol), $Pd(OAc)_2$ (0.004 g, 0.017 mmol), TFA (9.0 mL), and TFAA (1.0 mL) was heated at 90 °C for 12 h. Following an experimental procedure similar to that reported for **3a**, a crude product was obtained which was purified by column chromatography (silica gel, 20% EtOAc in hexanes) to afford the pure **6b** (0.085 g, 71%) as a brown oil and **7b** (0.003 g, 3%) as a white solid.

*Ethyl 1-(2,6-Dihydroxyphenyl)-1H-pyrazole-3-carboxylate (**21**).* Yield: 55% (0.047 g from 0.074 g); brown solid. Mp: 127−129 °C.R_f = 0.53 (hexanes/EtOAc, 60:40, v/v). IR (KBr) ν_{max}: 1728 (CO_2Et), 3413 (OH) cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ 1.30 (t, J = 7.1 Hz, 3H), 4.28 (q, J = 7.1 Hz, 2H), 6.46 (d, J = 8.2 Hz, 2H), 6.84 (d, J = 2.3 Hz, 1H), 7.09 (t, J = 8.2 Hz, 1H), 7.82 (d, J = 2.2 Hz, 1H), 9.86 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): 14.3, 60.1, 106.6, 108.0, 116.4, 130.1, 134.8, 143.0, 154.3, 161.9. MS (ESI+): m/z = 249.1. ESI-HRMS:calcd for $C_{12}H_{13}N_2O_4$ (M^+ + H) 249.0875, found 249.0876.

■ ASSOCIATED CONTENT

Supporting Information

X-ray crystallographic data (CIF files), ORTEP drawings for **3p**, **6l**, and **7b**, and copies of ^1H and ^{13}C NMR spectra for all

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Notes

The authors declare no competing financial interest.
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