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Palladium-Catalyzed Denitrogenative Synthesis of Aryl Ketones from Arylhydrazines and Nitriles Using O_2 as Sole Oxidant

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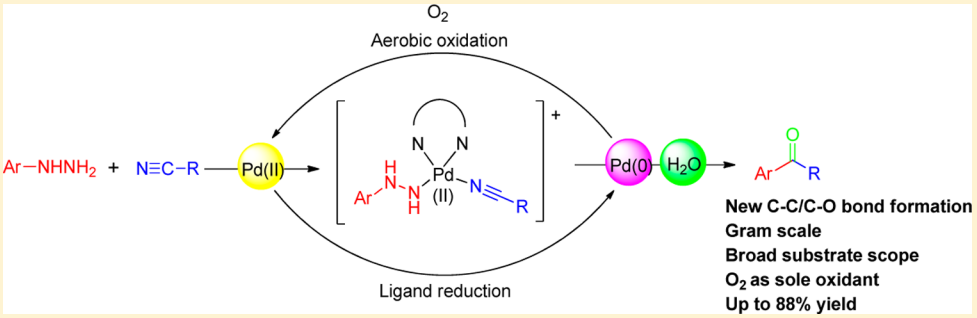
Supporting Information



ABSTRACT: An efficient and simple palladium-catalyzed approach for the synthesis of aryl ketones from low-cost nitriles and arylhydrazines using molecular oxygen (O_2) as sole oxidant via C−N bond cleavage is reported. Various aryl ketones were synthesized in moderate to good yields under mild conditions. A possible mechanism involving the Pd^{II}/Pd^{0} catalytic cycle process is depicted, and a cationic palladium intermediate was detected by ESI-MS.

Aryl ketones represent an important class of organic building blocks since there are numerous compounds of fragrances, natural products, and pharmaceuticals containing this structural motif.[1] Classically, aryl ketones were synthesized by Friedel−Crafts acylation, and stoichiometric amounts of Lewis acids were required.[2] In recent years, many novel strategies were developed to afford aryl ketone derivatives;[3−8,15−24] among them, the insertion of nitrile groups is a useful route to synthesize aryl ketones from arylpalladium species, since they provide unique organic transformations which are not readily available by classic methods (Scheme 1). For example, Lu[3] and Larock[4] et al., respectively, reported the synthesis of aryl ketones via palladium-catalyzed insertion of nitriles by using arylboronic acids as aryl sources. In 2010, benzoic acids have been proven to be useful as precursors of arylpalladium species for ketone synthesis by Larhed and coworkers.[5] Similarly, Larhed,[6] Deng,[7] and Wang[8] independently developed the addition of aryl sulfinic acids or their salts to nitriles via arylpalladium complexes. Despite these contributions, they often suffered from some drawbacks (e.g., substrate availability, functional group compatibility, unstable nature of the substrates and toxic byproducts, etc.) as a result of limited application. Thus, there is still room for broadening the scope of more environmentally friendly and more economic "green" arylation reagents to achieve aryl ketone derivatives.

In addition, arylhydrazines are used as organic synthesis blocks[9] and important identification reagents[10] due to their high reactivity, low cost, and easy availability. However, to date, relatively little attention has been paid to utilize arylhydrazines as aryl sources by denitrogenation,[11] which is due to a high dissociation energy required in direct activation of the C−N bond.[12] Generally, the methods for activating the arylhydrazine C−N bond include the conversions to *N*′-tosylarylhydrazines[13] or diazonium salts.[14] Nevertheless, most of these approaches often face significant limitations, such as instability, substrate availability, involvement of multistage synthesis, and harsh reaction conditions. Therefore, the development of the "green" and atom economy of the arylhydrazine C−N bond cleavage process is always needed. Herein, we describe a palladium-

Scheme 1. Palladium-Catalyzed Synthesis of Ketones from Nitriles

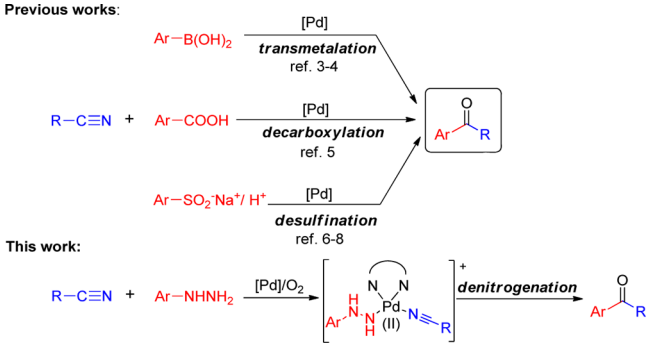


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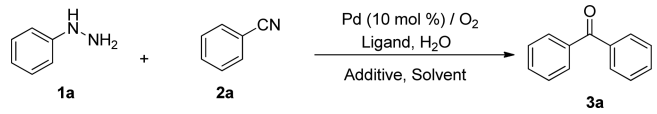
Table 1. Optimization of Reaction Conditions[a]



entry	catalyst	ligand	additive[c]	solvent	yield (%)[b]
1	$Pd(OAc)_2$	phen		1,4-dioxane	22
2	$Pd(OAc)_2$	phen	AgOAc	1,4-dioxane	<5
3	$Pd(OAc)_2$	phen	$Cu(OAc)_2$	1,4-dioxane	<5
4	$Pd(OAc)_2$	phen	$K_2S_2O_8$	1,4-dioxane	17
5	$Pd(OAc)_2$	phen	TFA	1,4-dioxane	49
6	$Pd(OAc)_2$	bipyridine	TFA	1,4-dioxane	76
7	$Pd(OAc)_2$	neocuproine	TFA	1,4-dioxane	42
8	$Pd(OAc)_2$	PPh_3	TFA	1,4-dioxane	n.d.
9	$Pd(OAc)_2$	DPPP	TFA	1,4-dioxane	n.d.
10	$PdCl_2$	bipyridine	TFA	1,4-dioxane	7
11	$Pd(dba)_2$	bipyridine	TFA	1,4-dioxane	n.d.
12	$PdBr_2$	bipyridine	TFA	1,4-dioxane	n.d.
13	$PdCl_2(PPh_3)_2$	bipyridine	TFA	1,4-dioxane	<5
14	$Pd(OAc)_2$	bipyridine	TFA	DMSO	42
15	$Pd(OAc)_2$	bipyridine	TFA	PhCl	n.d.
16	$Pd(OAc)_2$	bipyridine	TFA	DMF	30
17[d]	$Pd(OAc)_2$	bipyridine	TFA	1,4-dioxane	93
18[e]	**$Pd(OAc)_2$**	**bipyridine**	**TFA**	**1,4-dioxane**	**92 (88)**[f]

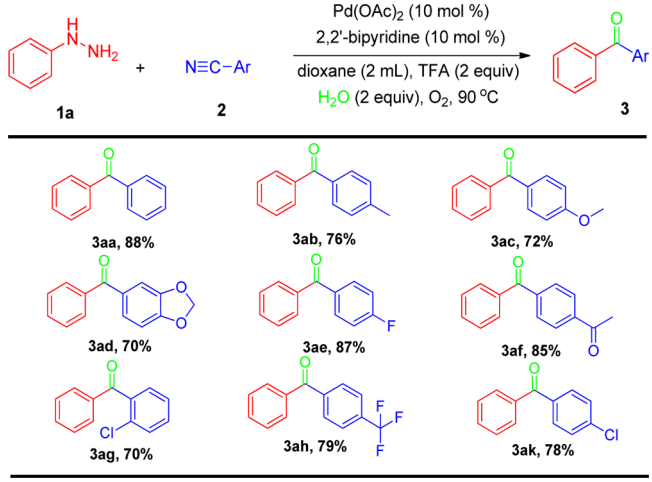
[a]All reactions were carried out under the following conditions: **1a** (0.3 mmol), **2a** (0.2 mmol), Pd catalyst (10 mol %), ligand (10 mol %), solvents (2 mL), and H_2O (2 equiv), 100 °C, 24 h, under O_2. Bipyridine = 2,2′-bipyridine. n.d. = not detected. [b]GC yield based on **2a** using dodecane as internal standard. [c]2.0 equiv. [d]**1a** (0.2 mmol), **2a** (0.3 mmol), 24 h. GC yield based on **1a** using dodecane as internal standard. [e]90 °C. [f]Isolated yield.

catalyzed denitrogenative synthesis of aryl ketones from arylhydrazines and nitriles via C−N bond cleavage using molecular oxygen as oxidant, which generates nitrogen and water as the only byproducts.

To identify suitable conditions for the reaction, a series of catalysts, ligands, additives, and solvents were screened, and the results are shown in Table 1. Initially, hydrazine (**1a**, 0.3 mmol) was treated with benzonitrile (**2a**, 0.2 mmol) in the presence of $Pd(OAc)_2$ (10 mol %), 1,10-phenanthroline (phen; 10 mol %), and H_2O (2 equiv) in dioxane at 100 °C under an oxygen atmosphere for 24 h, and the desired benzophenone product **3aa** was observed in 22% yield (entry 1). Subsequently, various additives were tested and TFA provided the best result (entries 2−5). Several different ligands were also evaluated, and 2,2′-bipyridine was found to improve the efficiency of the reaction, affording **3aa** in 76% yield (entries 6−9). The examination of different palladium salts revealed that $Pd(OAc)_2$ was the most suitable catalyst for this reaction system (entries 10−13). However, the use of toluene, DMSO, or DMF as solvent was proven to be disadvantageous to the reaction, as the yields were significantly decreased (entries 14−16). Notably, when the initial substrate ratio was changed, the yield of **3aa** enhanced from 76% to 93% (entries 6 vs 17). Moreover, lowering the reaction temperature to 90 °C did not affect the reaction efficiency (entries 17 vs 18). Hence, **1a** (0.2 mmol), **2a** (0.3 mmol), $Pd(OAc)_2$ (10 mol %), 2,2′-bipyridine (10 mol %), H_2O (2 equiv), and TFA (2 equiv) in dioxane (2 mL) at 90 °C under an oxygen atmosphere was chosen as the optimized conditions.

With the optimal reaction conditions in hand, we started to investigate the scope and limitation of this reaction. Typical results are shown in Tables 2 and 3. We first investigated the substrate scope of benzonitriles with hydrazine (**1a**, Table 2).

Table 2. Synthesis of Aryl Ketones from Phenylhydrazine and Arylnitriles[a,b]



[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), $Pd(OAc)_2$ (10 mol %), 2,2′-bipyridine (10 mol %), dioxane (2 mL), TFA (2 equiv), and H_2O (2 equiv), 90 °C, 24 h, under O_2. [b]Isolated yields.

To our delight, a series of functional groups participated well under the optimized reaction conditions and gave the corresponding aryl ketones in excellent yields (**3ab**−**3ah**). The benzonitriles **2b**−**2d** possessing an electron-donating group, such as 4-methyl, 4-methoxy, and 1,3-methylenedioxy, at the aryl ring could transfer to the desired products **3ab**−**3ad** in 70%−76% yields, and some substrates bearing an electron-withdrawing group, including 4-fluoro, 4-acetyl, 2-chloro, and 4-trifluoromethyl, at the benzene ring also reacted smoothly and afforded the desired products **3ae**−**3ah** in 70−87% yields.

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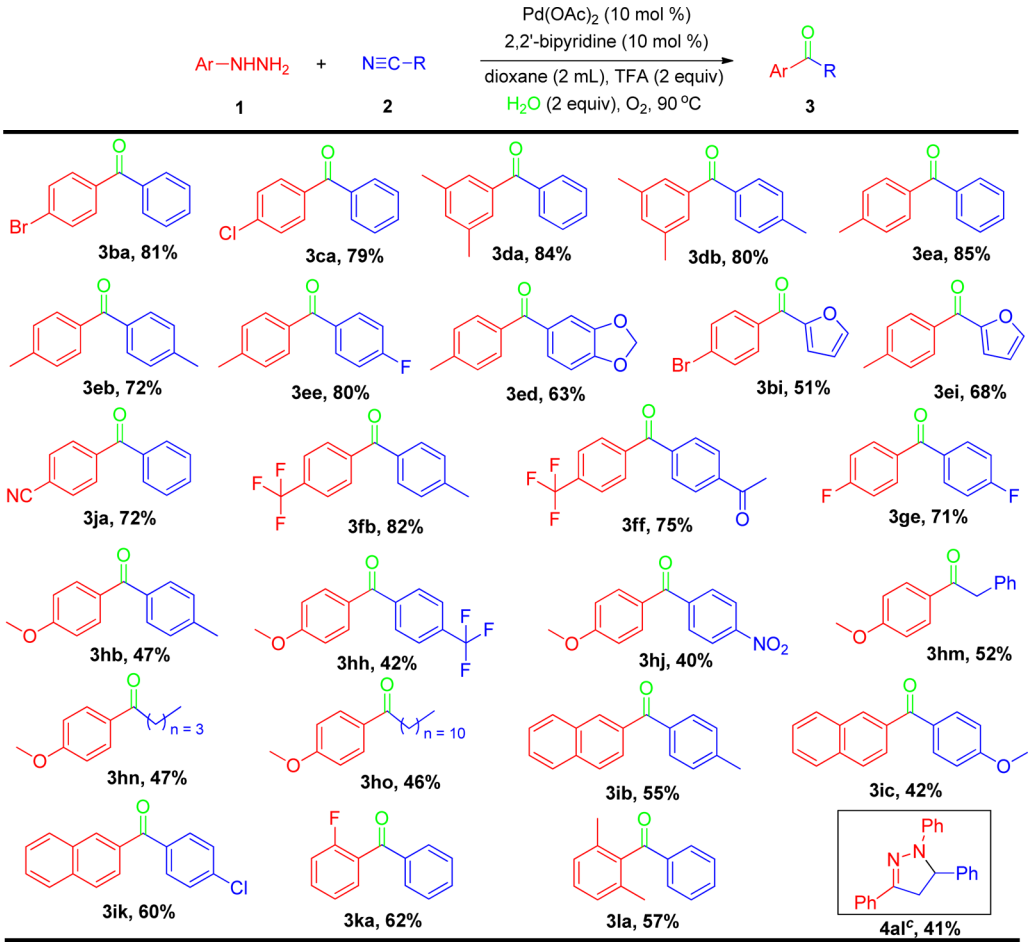
Table 3. Synthesis of Aryl Ketones from Arylhydrazines and Nitriles[a,b]

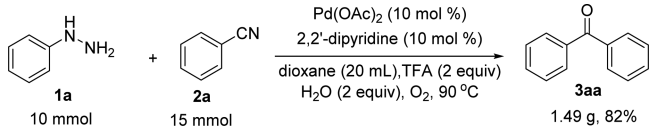


[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), $Pd(OAc)_2$ (10 mol %), 2,2′-bipyridine (10 mol %), dioxane (2 mL), TFA (2 equiv), and H_2O (2 equiv), 90 °C, 24 h, under O_2. [b]Isolated yields. [c]Under air.

Subsequently, to expand the scope of this method, a wide range of aromatic hydrazines and substituted nitriles were examined (Table 3). It was found that most aromatic hydrazines with various functional groups including methyl, dimethyl methoxy, fluoro, chloro, bromo, cyano, and trifluoromethyl were successfully transformed to the desired aryl ketones in moderate to good yields (**3ba**−**3la**). The reactions of aromatic hydrazines with electron-withdrawing substituents at the benzene ring gave the corresponding products in higher yields, and the yields were markedly lower with methoxy groups (**3hb**, **3hh**, and **3hj**). Nitriles bearing a heterocyclic substituent such as 2-furonitrile also gave the desired products in 51% and 68% yields (**3bi**, **3ei**). To our delight, the aliphatic nitrile substrates could be converted to the desired aryl ketone products (**3hm**−**3ho**) in moderate yields. Unfortunately, the aliphatic hydrazines were not applicable for this reaction under the current conditions, since the aliphatic hydrazines presumably are not conducive to the formation of intermediate **C** (Scheme 4). In addition, 2-naphthylhydrazine was well tolerated in this reaction system, with **3ib**, **3ic**, and **3ik** obtained in 55, 42, and 60% yields, respectively. When the *ortho*-position of arylhydrazine was substituted with a fluoro or dimethyl group, the yield of products **3ka** and **3la** decreased dramatically to 62% and 57%, which was probably due to the *ortho* steric hindrance. It is worth noting that the ability to incorporate the halogen substituents (R = F, Cl, Br) into the product makes this process have potential applications in further functionalization. To our surprise, the reaction of hydrazine (0.6 mmol) with cinnamonitrile (0.2 mmol) produced the dihydropyrazole derivative **4al** in 41% yield under the standard conditions.

Fortunately, the reaction could be scaled up to 10 mmol under the standard conditions and produced the desired product **3aa** in 82% yield (Scheme 2).

Scheme 2. Gram Scale Experiment



In order to investigate the mechanism of this reaction, a series of control experiments were conducted (Scheme 3). When the reaction was carried out under a nitrogen atmosphere, the corresponding aryl ketone **3aa** was not obtained (Scheme 3a), which indicated that the reaction required the presence of oxygen. Next, some control reactions with other oxidants under a nitrogen atmosphere were performed to test the role of oxygen. We found that, although some oxidants did produce the desired product **3aa**, the yields were inferior to that obtained with oxygen as oxidant (Scheme 3b). The ^{18}O-labeling experiment was also performed to get

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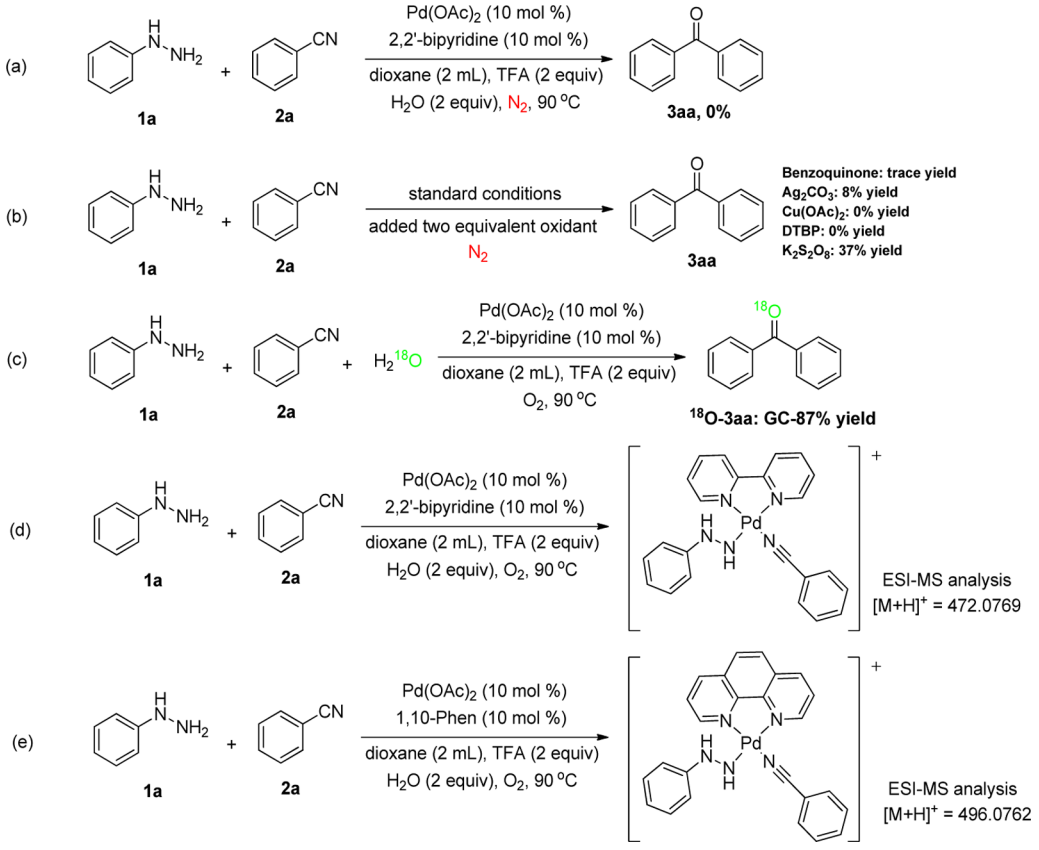
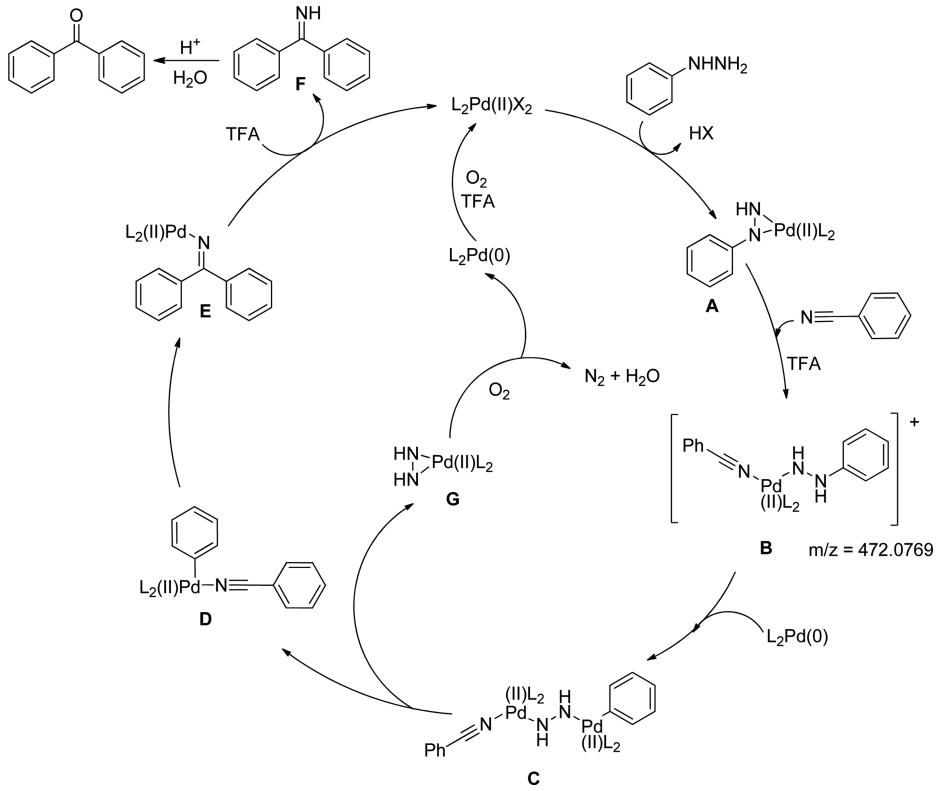
Scheme 3. Control Experiments



Scheme 4. Possible Reaction Mechanism



more insights into this reaction process (Scheme 3c), indicating that the oxygen atom in the ketone molecule was derived from H_2O. Furthermore, the technology ESI-MS was used to monitor the reaction between hydrazine and benzonitrile, and

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the result shows that cationic palladium complex **B** (m/z = 472.0769) was detected in the reaction mixture (Scheme 3d). When 1,10-phen was used as the ligand, the ESI-MS(+) could also detect a similar cationic palladium complex (m/z = 496.0762) in the reaction mixture (Scheme 3e). This result demonstrated that the reaction might go through a cationic palladium intermediate process.

On the basis of the above results and previous reports,[11] we proposed a plausible reaction mechanism for this transformation detailed in Scheme 4. The first step is the formation of the palladiaziridine intermediate **A** via the metathesis of phenyl hydrazide with $L_2Pd(II)X_2$ (X = OAc). Subsequently, the coordination of the nitrile group with **A** forms complex **B**, and **B** undergoes the oxidative addition of $L_2Pd(0)$ to afford the two palladium(II) centered intermediate **C** through C−N bond cleavage. Next, cracking of the intermediate **C** gives the complex **D** and the palladiaziridine complex **G**, which would be decomposed into $L_2Pd(0)$, nitrogen gas, and water by oxygen. Then, 1,2-addition of the coordinated aryl group to the nitrile group generates the ketimine intermediate **E**. Protonation of ketimine intermediate **E** by the acid affords the ketimine **F** and Pd(II) species. Finally, the hydrolysis of the ketimine **F** under acidic conditions would release the desired aryl ketone products and regenerate Pd(II) species to resume the catalytic cycle.

In conclusion, we have successfully developed a novel method to synthesize a series of aryl ketone derivatives from arylhydrazines and inexpensive nitriles via a palladium-catalyzed C−N bond cleavage reaction. Taking into account the combination of some desirable features, such as readily accessible starting materials, operational simplicity, molecular oxygen as the sole oxidant, good tolerance to scale-up synthesis, as well as nontoxic gaseous N_2 as the byproducts, this cost-effective method will provide a new arena of aryl ketone synthesis for both academia and industry.

EXPERIMENTAL SECTION

General Information. NMR spectra were obtained using a 400 spectrometer (^{1}H at 400 MHz, and ^{13}C at 101 MHz). Chemical shifts for ^{1}H NMR spectra are reported in parts per million (ppm) from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 7.26 ppm). Chemical shifts for ^{13}C NMR spectra are reported in parts per million (ppm) from tetramethylsilane with the solvent as the internal standard ($CDCl_3$: δ 77.0 ppm). IR spectra were obtained either as potassium bromide pellets or as liquid films between two potassium bromide pellets with a spectrometer. GC−MS was obtained using electron ionization. HRMS was obtained with an LCMS-IT-TOF mass spectrometer. Unless stated otherwise, commercial reagents were used without further purification. All reagents were weighed and handled in air at room temperature.

Typical Procedure for Palladium(II)-Catalyzed Denitrogenative Reactions. The reaction mixture of arylhydrazines **1** (0.2 mmol), nitriles **2** (0.3 mmol), $Pd(OAc)_2$ (10 mol %), 2,2′-bipyridine (10 mol %), TFA (2 equiv), and H_2O (2 equiv) was added to 1,4-dioxane (2 mL). The mixture was stirred at 90 °C for 24 h under O_2, and monitored periodically by TLC. Upon completion, the reaction mixture was diluted with water (30 mL) and extracted with ethyl acetate (3 × 30 mL). The combined organic layers were washed with water and brine, dried over Na_2SO_4, and filtered. The solvent was removed under vacuum. The residue was purified by flash column chromatography to afford aryl ketones **3**.

Procedure for Large Scale Reaction. The reaction mixture of arylhydrazine **1a** (10 mmol), nitrile **2a** (15 mmol), $Pd(OAc)_2$ (10 mol %), 2,2′-bipyridine (10 mol %), TFA (2 equiv), and H_2O (2 equiv) was added to 1,4-dioxane (20 mL). The mixture was stirred at 90 °C for 24 h under O_2, and monitored periodically by TLC. Upon completion, the reaction mixture was diluted with water (30 mL) and extracted with ethyl acetate (3 × 30 mL). The combined organic layers were washed with water and brine, dried over Na_2SO_4, and filtered. The solvent was removed under vacuum. The residue was purified by flash column chromatography to afford aryl ketones **3aa**.

Benzophenone (**3aa**).[15] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 88% (32.0 mg) as a white solid: 47−49 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 7.81 (d, J = 7.6 Hz, 4H), 7.59 (t, J = 7.1 Hz, 2H), 7.48 (t, J = 7.3 Hz, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 196.8, 137.6, 132.4, 130.1, 128.1. **IR** (KBr, cm^{-1}): 3060, 1659, 1599, 1313, 1150, 700. **HRMS** (ESI) m/z: calcd for $C_{13}H_{10}NaO$ $[M + Na]^+$ 205.0624; found 205.0625.

Phenyl(p-tolyl)methanone (**3ab**).[6] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 76% (29.8 mg) as a white solid: 55−57 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 7.77 (d, J = 7.5 Hz, 2H), 7.71 (d, J = 8.1 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 7.27 (d, J = 7.9 Hz, 2H), 2.43 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 196.4, 143.1, 137.9, 134.9, 132.1, 130.2, 129.8 128.9, 128.1, 21.6. **IR** (KBr, cm^{-1}): 3050, 1653, 1603, 1312, 1176, 694. **HRMS** (ESI) m/z: calcd for $C_{14}H_{12}NaO$ $[M + Na]^+$ 219.0780; found 219.0783.

(4-Methoxyphenyl)(phenyl)methanone (**3ac**).[6] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 72% (30.5 mg) as a yellow solid: 61−63 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 7.83 (d, J = 8.2 Hz, 2H), 7.75 (d, J = 7.6 Hz, 2H), 7.55 (d, J = 7.2 Hz, 1H), 7.47 (t, J = 7.5 Hz, 2H), 6.96 (d, J = 8.2 Hz, 2H), 3.89 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 195.5, 163.2, 138.3, 132.5, 131.9, 130.2, 129.7, 128.2, 113.6, 55.5. **IR** (KBr, cm^{-1}): 2922, 1650, 1598, 1259, 1027, 746. **HRMS** (ESI) m/z: calcd for $C_{14}H_{12}NaO_2$ $[M + Na]^+$ 235.0730; found 235.0728.

Benzo[d][1,3]dioxol-5-yl(phenyl)methanone (**3ad**).[20] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 70% (31.6 mg) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 7.74 (d, J = 7.8 Hz, 2H), 7.56 (t, J = 7.3 Hz, 1H), 7.46 (t, J = 7.5 Hz, 2H), 7.37 (d, J = 8.4 Hz, 2H), 6.85 (d, J = 8.0 Hz, 1H), 6.05 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 195.1, 151.5, 147.9, 138.1, 131.9, 131.8, 129.6, 128.2, 126.8, 109.9, 107.7, 101.8. **IR** (KBr, cm^{-1}): 2918, 1648, 1602, 1266, 1035, 748. **HRMS** (ESI) m/z: calcd for $C_{14}H_{10}NaO_3$ $[M + Na]^+$ 249.0522; found 249.0526.

(4-Fluorophenyl)(phenyl)methanone (**3ae**).[15] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 87% (34.9 mg) as a white solid: 47−48 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 7.87−7.81 (m, 2H), 7.80−7.73 (m, 2H), 7.59 (t, J = 7.4 Hz, 1H), 7.48 (t, J = 7.6 Hz, 2H), 7.15 (t, J = 8.6 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 195.2, 166.5 (d, J = 252.6 Hz), 137.5, 133.80 (d, J = 3.1 Hz), 132.6 (d, J = 9.1 Hz), 132.4, 129.8, 128.3, 115.4 (d, J = 2.1 Hz). **IR** (KBr, cm^{-1}): 3060, 1649, 1585, 1283, 1091, 731. **HRMS** (ESI) m/z: calcd for $C_{13}H_9FNaO$ $[M + Na]^+$ 223.0530; found 223.0527.

1-(4-Benzoylphenyl)ethanone (**3af**).[18] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 85% (38.0 mg) as a yellow solid: 82−84 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 8.04 (d, J = 8.3 Hz, 2H), 7.84 (d, J = 8.3 Hz, 2H), 7.78 (d, J = 7.3 Hz, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.48 (t, J = 7.6 Hz, 2H), 2.65 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 197.5, 195.9, 141.3, 139.6, 136.9, 133.1, 130.1, 130.0, 128.5, 128.2, 26.9. **IR** (KBr, cm^{-1}): 3055, 1656, 1601, 1269, 1016, 736. **HRMS** (ESI) m/z: calcd for $C_{15}H_{12}NaO_2$ $[M + Na]^+$ 247.0730; found 247.0727.

(2-Chlorophenyl)(phenyl)methanone (**3ag**).[20] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 70% (30.2 mg) as a white solid: 46−47 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 7.82 (d, J = 7.8 Hz, 2H), 7.59 (t, J = 7.3 Hz, 1H), 7.50−7.33 (m, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 195.3, 138.7, 136.5, 133.7, 1313, 131,2, 130.1, 129.1, 128.6, 126.7. **IR** (KBr, cm^{-1}): 3063, 1671, 1592, 1286, 1058, 744. **HRMS** (ESI) m/z: calcd for $C_{13}H_9ClNaO$ $[M + Na]^+$ 239.0234; found 239.0237.

Phenyl(4-(trifluoromethyl)phenyl)methanone (**3ah**).[16] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 79% (39.5 mg) as a white solid: 108−110 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 7.82 (d, J = 7.8 Hz, 2H), 7.59 (t, J = 7.3 Hz, 1H), 7.50−7.33 (m, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 195.5,

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140.8, 136.8, 133.7 (q, J = 32 Hz), 133.0, 130.1, 130.0, 128.5, 125.3 (q, J = 3.7 Hz), 122.3 (q, J = 273 Hz). **IR** (KBr, cm^{-1}): 2972, 1653, 1605, 1272, 1067, 696. **HRMS** (ESI) m/z: calcd for $C_{14}H_9F_3NaO$ $[M + Na]^+$ 273.0498; found 273.0496.

*(4-Chlorophenyl)(phenyl)methanone (**3ak**).*[6] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 78% (37.2 mg) as a yellow solid: 75−77 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 7.83−7.71 (m, 4H), 7.63−7.57 (m, 1H), 7.54−7.42 (m, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 195.5, 138.9, 137.3, 135.9, 132.6, 131.5, 129.9, 128.7, 128.4. **IR** (KBr, cm^{-1}): 2958, 1726, 1655, 1272, 1082, 695. **HRMS** (ESI) m/z: calcd for $C_{13}H_9ClNaO$ $[M + Na]^+$ 239.0234; found 239.0233.

*(4-Bromophenyl)(phenyl)methanone (**3ba**).*[6] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 81% (41.9 mg) as a yellow solid: 79−80 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 7.78−7.76 (m, 2H), 7.68−7.58 (m, 5H), 7.50−7.46(m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 195.5, 137.2, 136.3, 132.6, 131.6, 131.5, 129.9, 128.4, 127.5. **IR** (KBr, cm^{-1}): 2923, 1651, 1586, 1268, 1067, 746. **HRMS** (ESI) m/z: calcd for $C_{13}H_9BrNaO$ $[M + Na]^+$ 282.9729; found 282.9727.

*(4-Chlorophenyl)(phenyl)methanone (**3ca**).*[6] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 79% (34.1 mg) as a yellow solid: 75−77 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 7.79−7.66 (m, 4H), 7.56 (t, J = 7.4 Hz, 1H), 7.48−7.36 (m, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 195.1, 138.6, 137.0, 135.7, 132.4, 131.24, 129.7, 128.4, 128.2. **IR** (KBr, cm^{-1}): 2364, 1650, 1585, 1273, 1093, 743. **HRMS** (ESI) m/z: calcd for $C_{13}H_9ClNaO$ $[M + Na]^+$ 239.0234; found 239.0236.

*(3,5-Dimethylphenyl)(phenyl)methanone (**3da**).*[19] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 84% (35.2 mg) as a yellow solid: 58−60 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 7.80 (d, J = 7.5 Hz, 2H), 7.58 (t, J = 7.4 Hz, 1H), 7.48 (t, J = 7.6 Hz, 2H), 7.41 (s, 2H), 7.22 (s, 1H), 2.38 (s, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 197.1, 137.9, 137.8, 137.7, 134.1, 132.2, 130.0, 128.2, 127.8, 21.2. **IR** (KBr, cm^{-1}): 2920, 1658, 1598, 1315, 1022, 725. **HRMS** (ESI) m/z: calcd for $C_{15}H_{15}O$ $[M + H]^+$ 211.1117; found 211.1113.

*(3,5-Dimethylphenyl)(p-tolyl)methanone (**3db**).* Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 80% (35.8 mg) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 7.71 (d, J = 7.3 Hz, 2H), 7.37 (s, 2H), 7.27 (d, J = 7.7 Hz, 2H), 7.20 (s, 1H), 2.43 (s, 3H), 2.36 (s, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 196.9, 143.0, 138.1, 137.8, 135.2, 133.8, 130.2, 128.9, 127.7, 21.6, 21.2. **IR** (KBr, cm^{-1}): 1663, 1614, 1384, 1135, 756. **HRMS** (ESI) m/z: calcd for $C_{16}H_{16}NaO$ $[M + Na]^+$ 247.1093; found 247.1095.

*Phenyl(p-tolyl)methanone (**3ea**).*[6] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 85% (37.2 mg) as a white solid: 55−57 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 7.80−7−77 (m, 2H), 7.75−7.69 (m, 2H), 7.60−7.55 (m, 1H), 7.51−7.44 (m, 2H), 7.28 (d, J = 7.9 Hz, 2H), 2.44 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 196.5, 143.2, 138.0, 134.9, 132.2, 130.3, 129.9, 129.0, 128.2, 21.7. **IR** (KBr, cm^{-1}): 2959, 1655, 1587, 1272, 1082, 749. **HRMS** (ESI) m/z: calcd for $C_{14}H_{12}NaO$ $[M + Na]^+$ 219.0780; found 219.0776.

*Di-p-tolylmethanone (**3eb**).*[7] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 72% (30.2 mg) as a white solid: 89−91 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 7.69 (d, J = 8.0 Hz, 4H), 7.26 (d, J = 7.9 Hz, 4H), 2.42 (s, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 196.2, 142.9, 135.3, 130.2, 128.9, 21.6. **IR** (KBr, cm^{-1}): 1644, 1605, 1272, 1116, 746. **HRMS** (ESI) m/z: calcd for $C_{15}H_{15}O$ $[M + H]^+$ 211.1117; found 211.1118.

*(4-Fluorophenyl)(p-tolyl)methanone (**3ee**).*[7] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 80% (34.2 mg) as a yellow solid: 92−94 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 7.82 (dd, J = 8.7, 5.5 Hz, 2H), 7.68 (d, J = 8.1 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 7.14 (t, J = 8.6 Hz, 2H), 2.44 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 194.9, 165.2 (d, J = 252.0 Hz), 143.3, 134.8, 134.1 (d, J = 2.6 Hz), 132.5 (d, J = 9.1 Hz), 130.1, 129.0, 115.3 (d, J = 21.9 Hz). **IR** (KBr, cm^{-1}): 1647, 1268, 753. **HRMS** (ESI) m/z: calcd for $C_{14}H_{11}FNaO$ $[M + Na]^+$ 237.0686; found 237.0687.

*Benzo[d][1,3]dioxol-5-yl(p-tolyl)methanone (**3ed**).* Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 80% (30.2 mg) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 7.66 (d, J = 7.6 Hz, 2H), 7.40−7.31 (m, 2H), 7.27 (d, J = 6.7 Hz, 2H), 6.85 (d, J = 8.0 Hz, 1H), 6.05 (s, 2H), 2.43 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 194.9, 151.3, 147.8, 142.7, 135.3, 132.2, 129.9, 128.9, 126.5, 109.9, 107.6, 101.8, 21.6. **IR** (KBr, cm^{-1}): 2920, 1652, 1606, 1270, 1038, 752. **HRMS** (ESI) m/z: calcd for $C_{15}H_{12}NaO_3$ $[M + Na]^+$ 263.0679; found 263.0683.

*(4-Bromophenyl)(furan-2-yl)methanone (**3bi**).*[21] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 51% (25.4 mg) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 7.88 (d, J = 8.1 Hz, 2H), 7.71 (s, 1H), 7.65 (d, J = 8.1 Hz, 2H), 7.27 (s, 1H), 6.66−6.55 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 181.2, 152.2, 147.2, 135.9, 131.7, 130.9, 127.7, 120.5, 112.4. **IR** (KBr, cm^{-1}): 2921, 1641, 1582, 1294, 1069, 753. **HRMS** (ESI) m/z: calcd for $C_{11}H_7BrNaO_2$ $[M + Na]^+$ 272.9522; found 272.9518.

*Furan-2-yl(p-tolyl)methanone (**3ei**).*[15] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 68% (25.3 mg) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 7.89 (d, J = 7.7 Hz, 2H), 7.69 (s, 1H), 7.29 (d, J = 7.8 Hz, 2H), 7.22 (d, J = 3.4 Hz, 1H), 6.62−6.52 (m, 1H), 2.43 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 182.2, 152.5, 146.8, 143.4, 134.6, 129.5, 129.1, 120.1, 112.1, 21.6. **IR** (KBr, cm^{-1}): 2922, 1641, 1562, 1298, 1020, 752. **HRMS** (ESI) m/z: calcd for $C_{12}H_{10}NaO_2$ $[M + Na]^+$ 209.0573; found 209.0578.

*4-Benzoylbenzonitrile (**3ja**).*[18] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 72% (29.8 mg) as a white solid: 110−112 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 7.90−7.85 (m, 2H), 7.82−7.73 (m, 4H), 7.67−7.61 (m, 1H), 7.55- 7.48 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 195.0, 141.3, 136.4, 133.3, 132.2, 130.2, 130.0, 128.6, 118.0, 115.7. **IR** (KBr, cm^{-1}): 2920, 1764, 1652, 1248, 1056, 750. **HRMS** (ESI) m/z: calcd for $C_{14}H_{10}NO$ $[M + H]^+$ 208.0757; found 208.0754.

*p-Tolyl(4-(trifluoromethyl)phenyl)methanone (**3fb**).*[7] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 82% (43.3 mg) as a yellow solid: 135−137 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 7.87 (d, J = 8.0 Hz, 2H), 7.79−7.64 (m, 4H), 7.30 (d, J = 7.7 Hz, 2H), 2.45 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 195.2, 144.1, 141.1, 134.1, 133.5 (q, J = 33 Hz), 130.3, 130.0, 129.2, 125.3 (q, J = 3.9 Hz), 123.3(q, J = 272 Hz), 21.7. **IR** (KBr, cm^{-1}): 1645, 1267, 1128, 750. **HRMS** (ESI) m/z: calcd for $C_{15}H_{11}F_3NaO$ $[M + Na]^+$ 287.0654; found 287.0656.

*1-(4-(4-(Trifluoromethyl)benzoyl)phenyl)ethanone (**3ff**).*[16] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 75% (43.8 mg) as a yellow solid: 124−126 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 8.07 (d, J = 7.9 Hz, 2H), 7.89 (t, J = 9.7 Hz, 4H), 7.78 (d, J = 7.8 Hz, 2H), 2.67 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 197.3, 194.8, 140.3, 140.1, 140.0, 139.9, 139.8, 130.1 (q, J = 33 Hz), 128.3, 125.5 (q, J = 3.7 Hz), 122.2 (q, J = 274 Hz), 26.9. **IR** (KBr, cm^{-1}): 2922, 1645, 1523, 1264, 1064, 748. **HRMS** (ESI) m/z: calcd for $C_{16}H_{11}F_3NaO_2$ $[M + Na]^+$ 315.0603; found 315.0607.

*Bis(4-fluorophenyl)methanone (**3ge**).*[19] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 71% (30.9 mg) as a white solid: 106−108 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 7.89−7.71 (m, 4H), 7.15 (t, J = 8.1 Hz, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 193.7, 166.4 (d, J = 252.7 Hz), 133.71 (d, J = 3.1 Hz), 132.47 (d, J = 9.2 Hz), 115.5 (d, J = 2.2 Hz). **IR** (KBr, cm^{-1}): 1647, 1595, 1267, 1149, 755. **HRMS** (ESI) m/z: calcd for $C_{13}H_8F_2NaO$ $[M + Na]^+$ 241.0435; found 241.0437.

*(4-Methoxyphenyl)(p-tolyl)methanone (**3hb**).*[7] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 47% (21.2 mg) as a yellow solid: 85−87 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 7.85−7.77 (m, 2H), 7.68 (d, J = 8.1 Hz, 2H), 7.27 (d, J = 8.5 Hz, 2H), 6.96 (d, J = 8.8 Hz, 2H), 3.89 (s, 3H), 2.44 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 195.4, 163.0, 142.6, 135.5, 132.4, 130.5, 130.0, 128.9, 113.5, 55.5, 21.6. **IR** (KBr, cm^{-1}):

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2920, 1642, 1285, 1119, 746. **HRMS** (ESI) *m*/*z*: calcd for $C_{15}H_{14}NaO_2$ $[M + Na]^+$ 249.0886; found 249.0887.

(4-Methoxyphenyl)(4-(trifluoromethyl)phenyl)methanone (**3hh**).[17] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 42% (23.5 mg) as a yellow solid: 118−120 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 7.83 (t, *J* = 8.3 Hz, 4H), 7.74 (d, *J* = 7.9 Hz, 2H), 6.98 (d, *J* = 8.5 Hz, 2H), 3.90 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 194.3, 163.7, 141.5, 133.1, 132.6, 129.6 (q, *J* = 32 Hz), 128.7, 125.26 (q, *J* = 3.8 Hz), 122.3 (q, *J* = 273 Hz), 113.8, 55.6. **IR** (KBr, cm^{-1}): 2921, 1645, 1602, 1264, 1032, 755. **HRMS** (ESI) *m*/*z*: calcd for $C_{15}H_{11}F_3NaO_2$ $[M + Na]^+$ 303.0603; found 303.0606.

(4-Methoxyphenyl)(4-nitrophenyl)methanone (**3hj**).[17] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 40% (20.5 mg) as a white solid: 122−124 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 8.33 (d, *J* = 8.7 Hz, 2H), 7.88 (d, *J* = 8.7 Hz, 2H), 7.81 (d, *J* = 8.9 Hz, 2H), 6.99 (d, *J* = 8.9 Hz, 2H), 3.91 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 193.5, 164.0, 149.6, 143.8, 132.7, 130.3, 129.0, 123.5, 114.0, 55.6. **IR** (KBr, cm^{-1}): 2922, 1641, 1594, 1263, 1111, 741. **HRMS** (ESI) *m*/*z*: calcd for $C_{14}H_{11}NNaO_4$ $[M + Na]^+$ 280.0580; found 280.0587.

1-(4-Methoxyphenyl)-2-phenylethanone (**3hm**).[6] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 52% (23.5 mg) as a white solid: 76−77 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 8.06−7.96 (m, 2H), 7.37−7.22 (m, 5H), 7.02−6.84 (m, 2H), 4.24 (s, 2H), 3.84 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 196.2, 163.6, 135.1, 131.0, 129.7, 129.4, 128.7, 126.8, 113.8, 55.5, 45.3. **IR** (KBr, cm^{-1}): 3022, 1671, 1594, 1318, 1166, 707. **HRMS** (ESI) *m*/*z*: calcd for $C_{15}H_{14}NaO_2$ $[M + Na]^+$ 249.0886; found 249.0883.

1-(4-Methoxyphenyl)pentan-1-one (**3hn**).[7] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 47% (18.1 mg) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 7.92 (d, *J* = 8.9 Hz, 2H), 6.91 (d, *J* = 8.9 Hz, 2H), 3.84 (s, 3H), 2.88 (t, *J* = 7.4 Hz, 2H), 1.75−1.63 (m, 2H), 1.44−1.32 (m, 2H), 0.93 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 199.2, 163.3, 130.2, 130.1, 113.7, 55.4, 38.0, 26.8, 22.5, 13.9. **IR** (KBr, cm^{-1}): 2952, 1674, 1597, 1457, 1170, 754. **HRMS** (ESI) *m*/*z*: calcd for $C_{12}H_{16}NaO_2$ $[M + Na]^+$ 215.1043; found 215.1039.

1-(4-Methoxyphenyl)dodecan-1-one (**3ho**).[22] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 46% (26.7 mg) as a white solid: 55−57 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 7.94 (d, *J* = 8.9 Hz, 2H), 6.92 (d, *J* = 8.9 Hz, 2H), 3.86 (s, 3H), 2.90 (t, *J* = 7.5 Hz, 2H), 1.79−1.66 (m, 2H), 1.39−1.23 (m, 16H), 0.88 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 199.3, 163.3, 130.3, 130.2, 113.7, 55.4, 38.3, 31.9, 29.6, 29.5, 29.4, 29.3, 29.2, 24.7, 22.7, 14.1. **IR** (KBr, cm^{-1}): 2971, 1676, 1599, 1317, 1172, 724. **HRMS** (ESI) *m*/*z*: calcd for $C_{19}H_{30}NaO_2$ $[M + Na]^+$ 313.2138; found 313.2141.

Naphthalen-2-yl(p-tolyl)methanone (**3ib**).[15] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 55% (27.0 mg) as a yellow solid: 85−87 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 8.26 (s, 1H), 7.92 (d, *J* = 11.2 Hz, 4H), 7.79 (d, *J* = 7.7 Hz, 2H), 7.58 (dd, *J* = 15.4, 8.0 Hz, 2H), 7.32 (d, *J* = 7.8 Hz, 2H), 2.47 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 196.5, 143.2, 139.0, 135.2, 135.1, 132.3, 131.5, 130.3, 129.3, 129.0, 128.2, 128.1, 127.8, 126.7, 125.8, 21.7. **IR** (KBr, cm^{-1}): 3190, 1663, 1615, 1385, 1137, 751. **HRMS** (ESI) *m*/*z*: calcd for $C_{18}H_{14}NaO$ $[M + Na]^+$ 269.0937; found 269.0940.

(4-Methoxyphenyl)(naphthalen-2-yl)methanone (**3ic**).[15] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 42% (22.0 mg) as a yellow solid: 88−90 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 8.24 (s, 1H), 8.00−7.80 (m, 6H), 7.62−7.53 (m, 2H), 7.00 (d, *J* = 8.0 Hz, 2H), 3.91 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 195.6, 163.3, 135.5, 135.0, 132.6, 132.3, 131.1, 130.5, 129.3, 128.1, 128.0, 127.8, 126.7, 125.9, 113.6, 55.5. **IR** (KBr, cm^{-1}): 1663 1613, 1384, 1138, 773. **HRMS** (ESI) *m*/*z*: calcd for $C_{18}H_{14}NaO_2$ $[M + Na]^+$ 285.0886; found 285.0889.

(4-Chlorophenyl)(naphthalen-2-yl)methanone (**3ik**).[8] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 60% (27.1 mg) as a yellow solid: 122−124 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 8.23 (s, 1H), 8.00−7.88 (m, 4H), 7.82 (d, *J* = 8.1 Hz, 2H), 7.64−7.55(m, 2H), 7.50 (d, *J* = 8.0 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 138.9, 136.2, 135.4, 134.5, 133.6, 132.3, 131.7, 131.5, 129.4, 128.7, 128.5, 128.4, 127.9, 126.9, 125.6. **IR** (KBr, cm^{-1}): 1660, 1616, 1384, 1136, 753. **HRMS** (ESI) *m*/*z*: calcd for $C_{17}H_{11}ClNaO$ $[M + Na]^+$ 289.0391; found 289.0389.

(2-Fluorophenyl)(phenyl)methanone (**3ka**).[23] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 62% (24.8 mg) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) δ 7.82 (d, *J* = 8.2 Hz, 2H), 7.59−7.42 (m, 5H), 7.26−7.22 (m, 1H), 7.13 (t, *J* = 9.0 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 193.6, 160.1(d, *J* = 2501.0 Hz),, 137.4, 133.4, 133.1 (d, *J* = 8.3 Hz), 130.8 (d, *J* = 2.9 Hz), 129.8, 128.5, 127.1 (d, *J* = 14.9 Hz), 124.3 (d, *J* = 3.6 Hz), 116.4, 116.3(d, *J* = 21.6 Hz). **IR** (KBr, cm^{-1}): 2926, 1668, 1594, 1451, 1165, 771. **HRMS** (ESI) *m*/*z*: calcd for $C_{13}H_9FNaO$ $[M + Na]^+$ 223.0530; found 223.0534.

(2,6-Dimethylphenyl)(phenyl)methanone (**3la**).[24] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 57% (23.9 mg) as a yellow solid: 62−64 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 7.80 (d, *J* = 7.3 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.25−7.20 (m, 1H), 7.07 (d, *J* = 7.6 Hz, 2H), 2.12 (s, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 200.5, 139.7, 137.1, 134.2, 133.7, 129.4, 128.9, 128.7, 127.6, 19.4. **IR** (KBr, cm^{-1}): 2927, 1665, 1599, 1449, 1162, 755. **HRMS** (ESI) *m*/*z*: calcd for $C_{15}H_{14}NaO$ $[M + Na]^+$ 233.0937; found 233.0943.

Procedure for Product 4al. The reaction mixture of arylhydrazines **1a** (0.6 mmol), cinnamonitrile **2l** (0.2 mmol), $Pd(OAc)_2$ (10 mol %), 2,2′-bipyridine (10 mol %), TFA (2 equiv), and H_2O (2 equiv) was added to 1,4-dioxane (2 mL). The mixture was stirred at 90 °C for 24 h under air, and monitored periodically by TLC. Upon completion, the reaction mixture was diluted with water (30 mL) and extracted with ethyl acetate (3 × 30 mL). The combined organic layers were washed with water and brine, dried over Na_2SO_4, and filtered. The solvent was removed under vacuum. The residue was purified by flash column chromatography to afford dihydropyrazole derivative **4al**.

1,3,5-Triphenyl-4,5-dihydro-1H-pyrazole (**4al**).[9e] Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 41% (24.4 mg) as a yellow solid: 137−139 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm) 7.72−7.54 (m, 2H), 7.29 (dd, *J* = 12.3, 4.7 Hz, 3H), 7.24 (d, *J* = 5.0 Hz, 5H), 7.09 (dd, *J* = 8.3, 7.5 Hz, 2H), 7.02−6.97 (m, 2H), 6.70 (t, *J* = 7.2 Hz, 1H), 5.18 (dd, *J* = 12.4, 7.3 Hz, 1H), 3.75 (dd, *J* = 17.1, 12.4 Hz, 1H), 3.05 (dd, *J* = 17.1, 7.3 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$, δ ppm) 146.7, 144.9, 142.6, 132.8, 129.1, 128.9, 128.6, 128.5, 127.6, 125.8, 125.7, 119.1, 113.4, 64.6, 43.6. **IR** (KBr, cm^{-1}): 3041, 2920, 1594, 1494, 1451, 1385, 1260, 1109, 872, 806, 753, 690. **HRMS** (ESI) *m*/*z*: calcd for $C_{21}H_{18}N_2Na$ $[M + Na]^+$ 321.1362; found 321.1359.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02697.

The NMR and HRMS spectral data for all new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Boger, D. L.; Hong, J.; Hikota, M.; Ishida, M. *J. Am. Chem. Soc.* **1999**, *121*, 2471. (b) Reux, B.; Nevalainen, T.; Raitio, K. H.; Koskinen, A. M. *Bioorg. Med. Chem.* **2009**, *17*, 4441. (c) Wang, W.; Zeng, Y. H.; Osman, K.; Shinde, K.; Rahman, M.; Gibbons, S.; Mu, Q. *J. Nat. Prod.* **2010**, *73*, 1815. (d) Chong, Y. M.; Yin, W. F.; Ho, C. Y.; Mustafa, M. R.; Hadi, A. H. A.; Awang, K.; Narrima, P.; Koh, C.-L.; Appleton, D. R.; Chan, K.-G. *J. Nat. Prod.* **2011**, *74*, 2261.

(2) (a) Calloway, N. O. *Chem. Rev.* **1935**, *17*, 327. (b) Gore, P. H. *Chem. Rev.* **1955**, *55*, 229.

(3) (a) Zhao, B.; Lu, X. *Tetrahedron Lett.* **2006**, *47*, 6765. (b) Zhao, B.; Lu, X. *Org. Lett.* **2006**, *8*, 5987.

(4) (a) Zhou, C.; Larock, R. C. *J. Am. Chem. Soc.* **2004**, *126*, 2302. (b) Zhou, C.; Larock, R. C. *J. Org. Chem.* **2006**, *71*, 3551.

(5) Lindh, J.; Sjöberg, P. J. R.; Larhed, M. *Angew. Chem., Int. Ed.* **2010**, *49*, 7733.

(6) Behrends, M.; Sävmarker, J.; Sjöberg, P. J. R.; Larhed, M. *ACS Catal.* **2011**, *1*, 1455.

(7) Liu, J.; Zhou, X.; Rao, H.; Xiao, F.; Li, C.-J.; Deng, G.-J. *Chem. - Eur. J.* **2011**, *17*, 7996.

(8) Miao, T.; Wang, G.-W. *Chem. Commun.* **2011**, *47*, 9501.

(9) (a) Tomakinian, T.; Guillot, R.; Kouklovsky, C.; Vincent, G. *Chem. Commun.* **2016**, *52*, 5443. (b) Wei, W.; Wen, J.; Yang, D.; Guo, M.; Wang, Y.; You, J.; Wang, H. *Chem. Commun.* **2015**, *51*, 768. (c) Senadi, G. C.; Hu, W. P.; Lu, T. Y.; Garkhedkar, A. M.; Vandavasi, J. K.; Wang, J. J. *Org. Lett.* **2015**, *17*, 1521. (d) Wu, Q.; Liu, P.; Pan, Y.-M.; Xu, Y.- L.; Wang, H.-S. *RSC Adv.* **2012**, *2*, 10167. (e) Wang, X.; Pan, Y.-M.; Huang, X.-C.; Mao, Z.-Y.; Wang, H.-S. *Org. Biomol. Chem.* **2014**, *12*, 2028.

(10) Yao, P. *Appl. Organomet. Chem.* **2014**, *28*, 194.

(11) (a) Zhu, M.-K.; Zhao, J.-F.; Loh, T.-P. *Org. Lett.* **2011**, *13*, 6308. (b) Chen, Y.; Guo, S.; Li, K.; Qu, J.; Yuan, H.; Hua, Q.; Chen, B. *Adv. Synth. Catal.* **2013**, *355*, 711. (c) Peng, Z.; Hu, G.; Qiao, H.; Xu, P.; Gao, Y.; Zhao, Y. *J. Org. Chem.* **2014**, *79*, 2733. (d) Xu, W.; Hu, G.; Xu, P.; Gao, Y.; Yin, Y.; Zhao, Y. *Adv. Synth. Catal.* **2014**, *356*, 2948. (e) Zhao, Y.; Song, Q. *Chem. Commun.* **2015**, *51*, 13272.

(12) Ouyang, K.; Hao, W.; Zhang, W. X.; Xi, Z. *Chem. Rev.* **2015**, *115*, 12045.

(13) (a) Liu, J.-B.; Yan, H.; Chen, H.-X.; Luo, Y.; Weng, J.; Lu, G. *Chem. Commun.* **2013**, *49*, 5268. (b) Barluenga, J.; Valdés, C. *Angew. Chem., Int. Ed.* **2011**, *50*, 7486.

(14) (a) Roglans, A.; Pla-Quintana, A.; Moreno-Mañas, M. *Chem. Rev.* **2006**, *106*, 4622. (b) Zhao, X.; Zhang, Y.; Wang, J. *Chem. Commun.* **2012**, *48*, 10162. (c) Felpin, F. X.; Nassar-Hardy, L.; Le Callonnec, F.; Fouquet, E. *Tetrahedron* **2011**, *67*, 2815. (d) Taylor, J. G.; Moro, A. V.; Correia, C. R. D. *Eur. J. Org. Chem.* **2011**, *2011*, 1403.

(15) Rao, M. L.; Venkatesh, V.; Banerjee, D. *Tetrahedron* **2007**, *63*, 12917.

(16) Neumann, H.; Brennführer, A.; Beller, M. *Chem. - Eur. J.* **2008**, *14*, 3645.

(17) Ito, K.; Tamashima, H.; Iwasawa, N.; Kusama, H. *J. Am. Chem. Soc.* **2011**, *133*, 3716.

(18) Li, X.; Zou, G. *Chem. Commun.* **2015**, *51*, 5089.

(19) Zhou, Q.; Wei, S.; Han, W. *J. Org. Chem.* **2014**, *79*, 1454.

(20) Ekoue-Kovi, K.; Xu, H.; Wolf, C. *Tetrahedron Lett.* **2008**, *49*, 5773.

(21) Lerebours, R.; Camacho-Soto, A.; Wolf, C. *J. Org. Chem.* **2005**, *70*, 8601.

(22) Parella, R.; Naveen; Kumar, A.; Babu, S. A. *Tetrahedron Lett.* **2013**, *54*, 1738.

(23) Liu, Y.; Meng, G.; Liu, R.; Szostak, M. *Chem. Commun.* **2016**, *52*, 6841.

(24) O'Keefe, B. M.; Simmons, N.; Martin, S. F. *Org. Lett.* **2008**, *10*, 5301.

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