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# Palladium-Catalyzed Sequential Acylation/Cyanation of Aryl Iodides: A Regiospecific Synthesis of 2-Cyanoaryl Ketones

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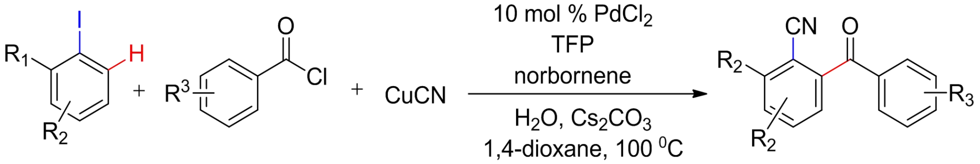
**ABSTRACT:** A palladium-catalyzed, norbornene-mediated acylation/cyanation reaction of iodobenzene was developed by the use of acyl chlorides as acylation reagents and cuprous cyanide. The reaction gave the 2-cyanoaryl ketones efficiently by using readily available starting materials.



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## INTRODUCTION

Palladium-catalyzed coupling reactions, including Heck, Suzuki, and Sonogashira couplings using commercially available organic halides or pseudo halides as the substrates, have become the classical protocols for C-C bond formations in pharmaceutical and material science.[1,2] The protocol allows one C-C bond formation through one C-halide bond. Although sequential double couplings of dihaloarene may result in difunctionalization of arenes, the availability of the starting materials is limited.[3] Transition-metal-catalyzed direct C-H bond functionalization represents one of the most promising procedures to produce C-C or C-heteroatom bonds.[4] The combination of C-halide and C-H activation would result in simultaneous double functionalization. Such step-economic transformations are urgently needed.[5]

The Catellani reaction allows the introduction of two different groups in one pot from aryl halides leading to poly-substituted aromatic compounds and fused aromatic rings using palladium/norbornene as a catalyst.[6] The method has been employed for the synthesis of cyclic or acyclic benzonitriles, helical alkenes, annulated indole derivatives, diaryl derivatives etc.[7] The Catellani reaction is usually limited to *ortho*-alkylation and arylation. Recently, palladium-catalyzed *ortho* C-H amination of aryl iodides was reported, providing amination products exclusively at the *ortho*-position instead of *ipso*.[8] Such a synthetic strategy has been extended to tandem C-H amination and C-I alkenylation,[9a,9b] arylation,[9c] borylation,[9d] alkynylation[9e,9f] etc. for the synthesis of poly-substituted aromatic compounds. Most recently, palladium/norbornene catalyzed *ortho* acylation of aryl iodides was reported leading to diaryl ketones and aryl alkyl ketones.[10]

Aryl ketones are very important compounds widely used in pharmaceutical, fragrance, dye, and agrochemical industries.[11] Traditional synthetic methods of aryl ketones rely primarily on Friedel-Crafts acylation in the presence of Lewis acids or Brønsted acid[12] or the reaction of activated carboxylic acid derivatives with organometallic reagents.[13] Although transition-metal catalyzed direct C-H bond activation/acylation of aromatic compounds offers an atom economic and environmentally friendly alternative strategy to aromatic ketones, the regioselective acylation is limited due to the directing groups.[14,15]

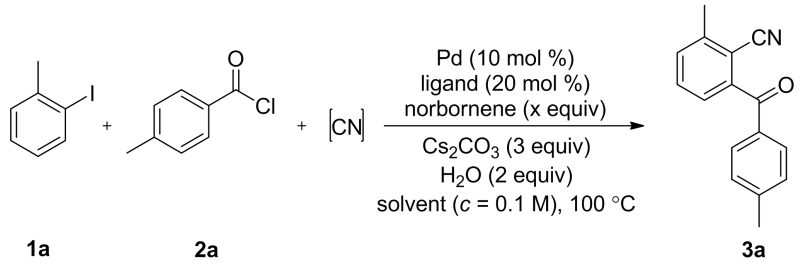
We have recently reported the synthesis of 2-alkynylanilines through palladium/norbornene catalyzed tandem C-H amination and C-I alkynylation.[9f] As a continuation, herein we report a palladium/norbornene catalyzed sequential acylation/cyanation reaction of aryl iodide with acyl chlorides and cuprous cyanide, which selectively leads to a series of aromatic ketones in moderate to good yields.

## RESULTS AND DISCUSSION

The three-component reaction of 2-iodotoluene (**1a**), 4-methyl-benzoyl chloride (**2a**) and potassium ferrocyanide [$K_4Fe(CN)_6 \cdot 3H_2O$] was initially chosen as the model reaction to optimize the reaction conditions. The combination of palladium chloride/tri(2-furyl)phosphine (TFP)/norbornene was used as the catalyst in the presence of $Cs_2CO_3$ in toluene at 100 ˚C. The selected results are summarized in Table 1. The desired product **3a** was obtained in 26 % yield (Table 1, entry 1). Further investigation of various solvents revealed that the yield was slightly improved when toluene was replaced by 1,4-dioxane (entry 2). More polar solvents such as DMF and $CH_3CN$ were found to be ineffective for this reaction (entries 3 and 4). The effect of other monodentate phosphine ligands was examined. Only a trace amount of product was detected when $PPh_3$ and $(3\text{-ClPh})_3P$ were employed, and $(C_6F_5)_3P$ was totally inactive (entries 7-9). Different palladium catalysts, including Pd(II) and Pd(0) catalysts, were surveyed, and it was found that $Pd(OAc)_2$, $[Pd(C_3H_5)Cl]_2$, and $Pd_2(dba)_3 \cdot CHCl_3$ cannot catalyze this reaction (entries 10 and 12). In addition, the variation of the amount of norbornene did not show a significant influence on the formation of the target product. Finally, we screened a series of cyanation reagents, including CuCN, TMSCN, and $Zn(CN)_2$. The yield of the target product was dramatically increased to 72% when CuCN was used (entry 13). Surprisingly, employment of TMSCN and $Zn(CN)_2$ did not result in any cyanation products (entries 14 and 15). We found that water is essential to the acylation reaction, and no desired product was observed when the reaction was conducted in strictly anhydrous dioxane (entry 16). The reaction did not occur below 80 °C, and higher temperature than

100 °C resulted in decrease of the yield (entries 17 and 18). The screening of bases showed that $K_2CO_3$ and $Na_2CO_3$ are not effective (entries 19-20). Further investigation revealed that none of the product was detected without palladium catalyst (entry 21).

**Table 1**. Optimization of the reaction conditions[a]



| entry | [Pd] | ligand | solvent | [CN] | x | yield (%) |
|---|---|---|---|---|---|---|
| 1 | $PdCl_2$ | TFP | toluene | $K_4Fe(CN)_6·3H_2O^b$ | 2 | 26 |
| 2 | $PdCl_2$ | TFP | dioxane | $K_4Fe(CN)_6·3H_2O^b$ | 2 | 30 |
| 3 | $PdCl_2$ | TFP | DMF | $K_4Fe(CN)_6·3H_2O^b$ | 2 | trace |
| 4 | $PdCl_2$ | TFP | $CH_3CN$ | $K_4Fe(CN)_6·3H_2O^b$ | 2 | trace |
| 5 | $PdCl_2$ | TFP | dioxane | $K_4Fe(CN)_6·3H_2O^b$ | 1 | 13 |
| 6 | $PdCl_2$ | TFP | dioxane | $K_4Fe(CN)_6·3H_2O^b$ | 3 | 32 |
| 7 | $PdCl_2$ | $PPh_3$ | dioxane | $K_4Fe(CN)_6·3H_2O^b$ | 2 | trace |
| 8 | $PdCl_2$ | $(3\text{-}ClC_6H_4)_3P$ | dioxane | $K_4Fe(CN)_6·3H_2O^b$ | 2 | trace |
| 9 | $PdCl_2$ | $(C_6F_5)_3P$ | dioxane | $K_4Fe(CN)_6·3H_2O^b$ | 2 | N.D. |
| 10 | $Pd(OAc)_2$ | TFP | dioxane | $K_4Fe(CN)_6·3H_2O^b$ | 2 | trace |
| 11 | $[Pd(C_3H_5)Cl]_2$ | TFP | dioxane | $K_4Fe(CN)_6·3H_2O^b$ | 2 | trace |
| 12 | $Pd_2(dba)_3·CHCl_3$ | TFP | dioxane | $K_4Fe(CN)_6·3H_2O^b$ | 2 | trace |
| 13 | $PdCl_2$ | TFP | dioxane | $CuCN^c$ | 2 | 72 |
| 14 | $PdCl_2$ | TFP | dioxane | $TMSCN^d$ | 2 | N.D. |
| 15 | $PdCl_2$ | TFP | dioxane | $Zn(CN)_2^e$ | 2 | N.D. |
| 16 | $PdCl_2$ | TFP | dioxane | $CuCN^f$ | 2 | N.D. |
| 17 | $PdCl_2$ | TFP | dioxane | $CuCN^g$ | 2 | N.D. |
| 18 | $PdCl_2$ | TFP | dioxane | $CuCN^h$ | 2 | 56 |
| 19 | $PdCl_2$ | TFP | dioxane | $CuCN^i$ | 2 | trace |
| 20 | $PdCl_2$ | TFP | dioxane | $CuCN^j$ | 2 | N.D. |
| 21 | -- | TFP | dioxane | CuCN | 2 | N.D. |

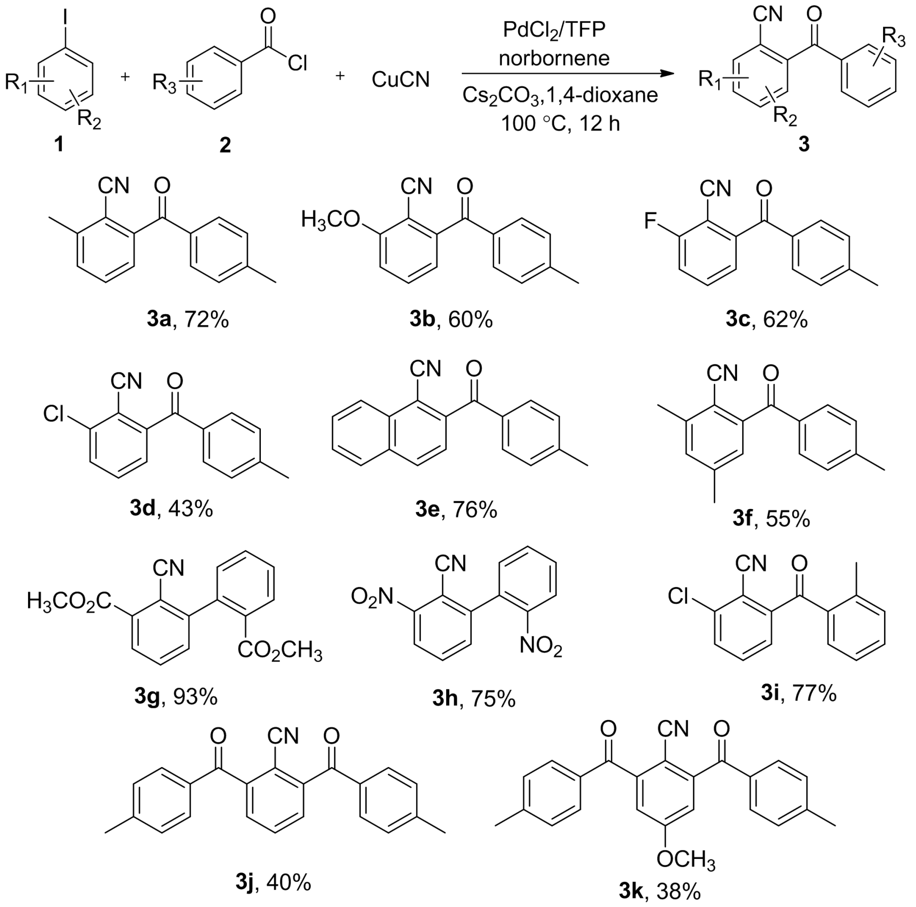
[a] **1a** (0.3 mmol, 1.0 equiv), **2a** (0.9 mmol, 3.0 equiv), CuCN (0.36 mmol, 1.2 equiv), Pd (10 mol %), ligand (20

mol %), norbornene (0.6 mmol, 2.0 equiv), $Cs_2CO_3$ (0.9 mmol, 3.0 equiv), $H_2O$ (0.6 mmol, 2.0 equiv), solvent (3.0 mL), 100 ˚C, 12 h. [b] 4 equiv; [c] 1.2 equiv; [d] TMSCN (2 equiv), CsF (3 equiv); [e] $Zn(CN)_2$ (2 equiv); [f] without $H_2O$; [g] 80 °C; [h] 120 °C; [i] $K_2CO_3$ (3.0 equiv); [j] $Na_2CO_3$ (3.0 equiv).

Under the optimized reaction conditions, the scope of aryl iodides was examined (Table 2). Generally, aryl iodides containing electron-donating and electron-withdrawing groups were both tolerated under the reaction conditions, providing the corresponding diaryl ketones **3a**-**3k** in moderate to good yields (Table 2). The inherent electronic nature of aryl iodides plays an important effect on this reaction. Aryl iodides **1a** and **1b**, bearing electronic-donating *ortho*-substitutents, reacted smoothly, giving **3a** and **3b** in *ca*. 70% yields. However, when 2-chloroiodobenzene was reacted with 4-methylbenzoyl chloride **2a** and CuCN, low yield of the desired product **3d** was obtained under the standard conditions. Notably, the substrate **1c** containing a *ortho*-fluoride substitutent could work well in this transformation, and the corresponding product **3c** was isolated in 62% yield. 1-Iodonaphthalene also worked well, providing the diaryl ketone **3e** in good yield (76%). When aryl iodides with strong electron-withdrawing groups were employed in the reaction, the desired products could not be obtained at all. Instead, the cross-coupling products of two molecules of aryl iodides were isolated. Homocoupling products, diethyl 2'-cyano-[1,1'-biphenyl]-2,3'-dicarboxylate **3g** and 2',3-dinitro-[1,1'-biphenyl]-2-carbonitrile **3h** were isolated in 93% and 75% yields, respectively. This result might indicate that the reaction is strongly influenced by the substituents of iodobenzene. Aryl iodides with strong electron-withdrawing groups are more reactive than acid anhydrous with respect to oxidative addition towards palladium. For aryl iodides without *ortho* substituents, diketones **3j** and **3k** were obtained in *ca*. 40% yields under the standard conditions. Unlike 2-iodotoluene, the reaction of 3-iodotoluene with 4-methylbenzoyl chloride and CuCN gave a complicated mixture. Under the similar conditions, 2-bromotoluene and 2-chlorotoluene were not reactive probably because C-Br bond and C-Cl bonds are more inert than C-I bond.

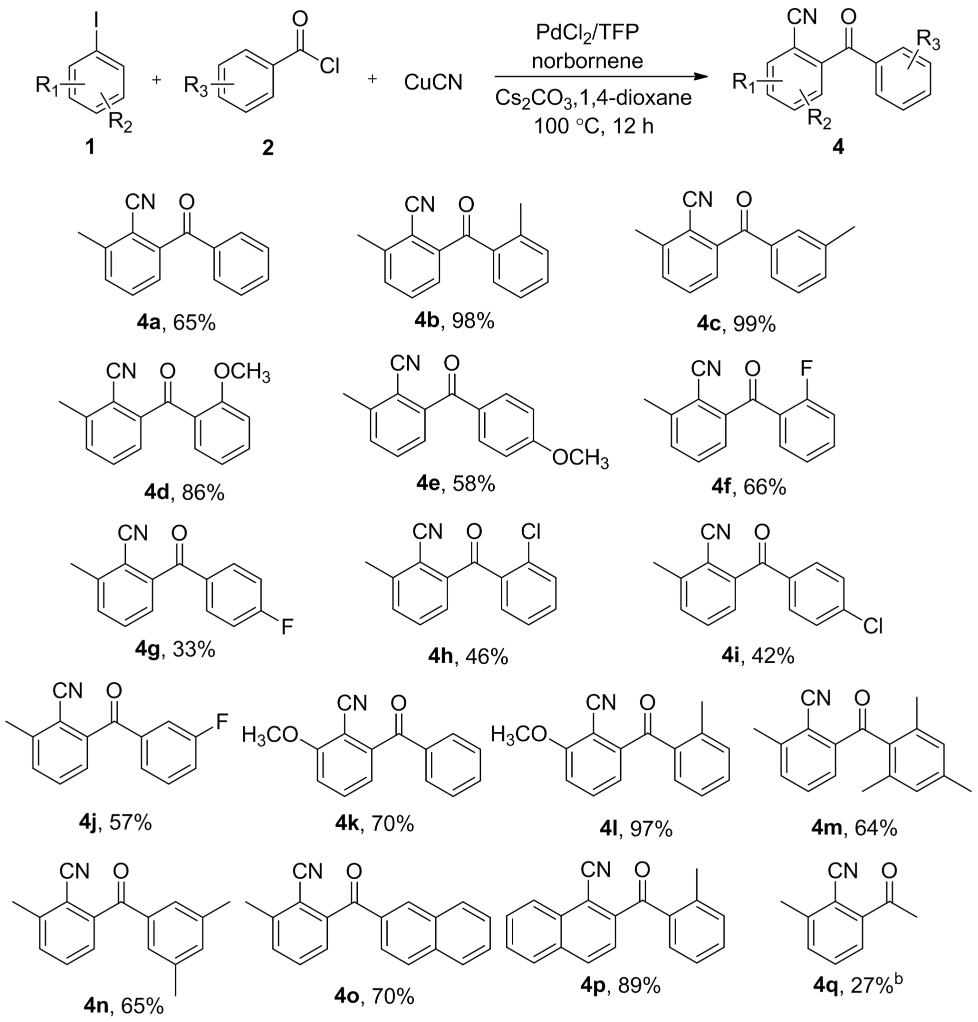
The scope of this reaction with a number of functionalized benzoyl chlorides **2** was subsequently explored. *Ortho*-, *para*-, and *meta*-substituted benzoyl chlorides were all good coupling partners in these reactions, and target ketones were afforded in moderate to good yields (Table 3, **4a**-**4p**). Generally, benzoyl chlorides with *ortho*-substituted groups work better in this reaction than the ones with *para*-substituted groups.[16] The reactions of 2-methylbenzoyl chloride and 3-methylbenzoyl chloride with 2-iodotoluene yielded the corresponding ketons **4b** and **4c** almost quantitatively. Similarly, 2-methoxybenzoyl chloride also afforded **4d** in 86% yield. The structure of **4d** was confirmed by X-ray single-crystal diffraction, and the molecular structure was given in supporting information. For benzoyl chlorides bearing electron-withdrawing *ortho*-substituents, the yields of the corresponding products **4f** and **4h** are much lower. Benzoyl chlorides having either electron-donating or electron-withdrawing *para*-substituents showed relatively lower activities than unsubstituted benzoyl chloride, and their corresponding products **4e**, **4g**, and **4i** were obtained in moderate yields. When 2,4,6-trimethylbenzoyl chloride was applied, **4m** was obtained in 64% yield, illustrating that the steric hindrance did not play a critical role in the reaction. 2-Furoyl chloride is not a suitable substrate, and no desired furoyl derivatives were obtained. The acetylation reaction was not successful in the cases of acetyl chloride or cyclohexanecarbonyl chloride. However, we were able to isolate 2-acetyl-6-methylbenzonitrile **4q** in 27% yield when acetic anhydride was applied under anhydrous conditions.

**Table 2.** The substrate scope of aryl iodide [a]



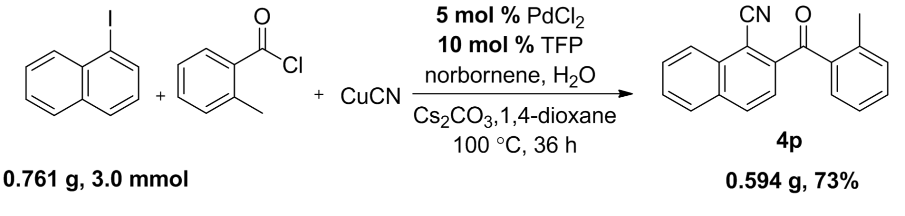
[a] Reaction conditions: **1a** (0.3 mmol, 1.0 equiv), **2a** (3.0 equiv), CuCN (1.2 equiv), $PdCl_2$ (10 mol %), TFP (20 mol %), norbornene (2.0 equiv), $Cs_2CO_3$ (3.0 equiv), $H_2O$ (2.0 equiv), 1,4-dioxane (3.0 ml), 100 ˚C, 12h.

**Table 3.** The substrates scope of benzoyl chloride [a]



[a] Reaction conditions: **1a** (0.3 mmol, 1.0 equiv), **2a** (3.0 equiv), CuCN (1.2 equiv), $PdCl_2$ (10 mol %), TFP (20 mol %), norbornene (2.0 equiv), $Cs_2CO_3$ (3.0 equiv), $H_2O$ (2.0 equiv), 1,4-dioxane (3 ml), 100 ˚C, 12 h; [b] acetic anhydride (5 equiv).

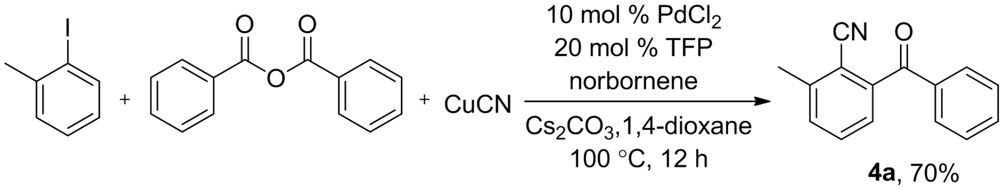
***Gram Scale***



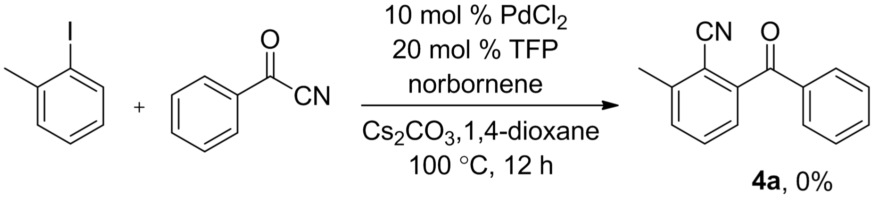
(1)

It is noteworthy that this sequential acylation/cyanation can be performed on the gram scale, and the loading of palladium catalyst can be lowered to 5 mol % (eq 1). We used 1-iodonaphthalene and 2-methylbenzoyl chloride as the substrates. The reaction of 1-iodonaphthalene (3 mmol, 0.761 g) and 2-methylbenzoyl chloride (9 mmol, 1.386 g) was performed in the presence of 0.15 mmol of palladium, 0.3 mmol of ligand, 6 mmol of $H_2O$ and 9 mmol of $Cs_2CO_3$ at 100 °C. The desired product **4p** was isolated in 73% yield within 36 h.

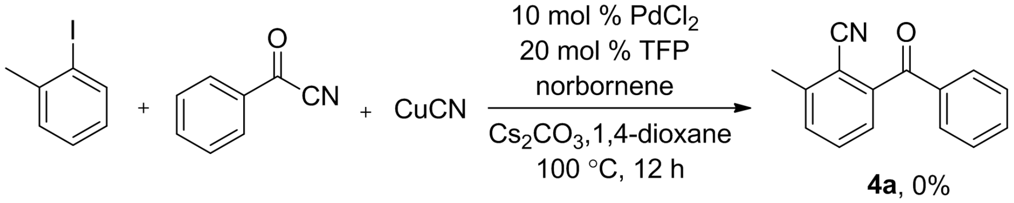
***Control Experiments***



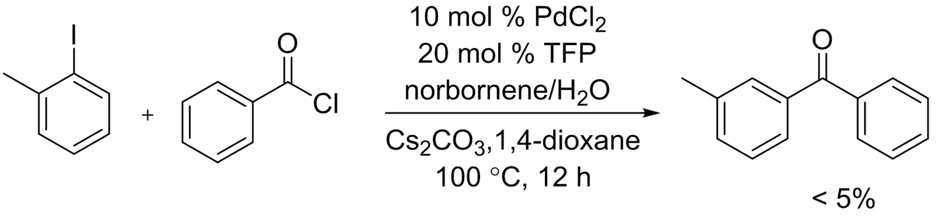
(2)



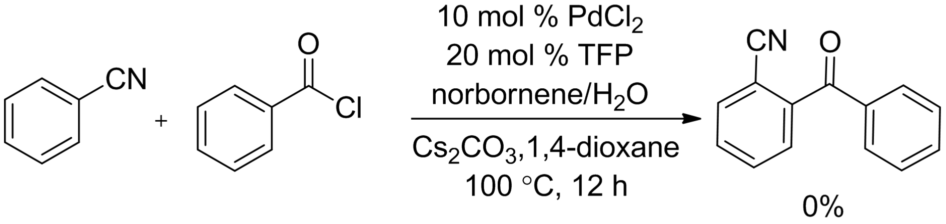
(3)



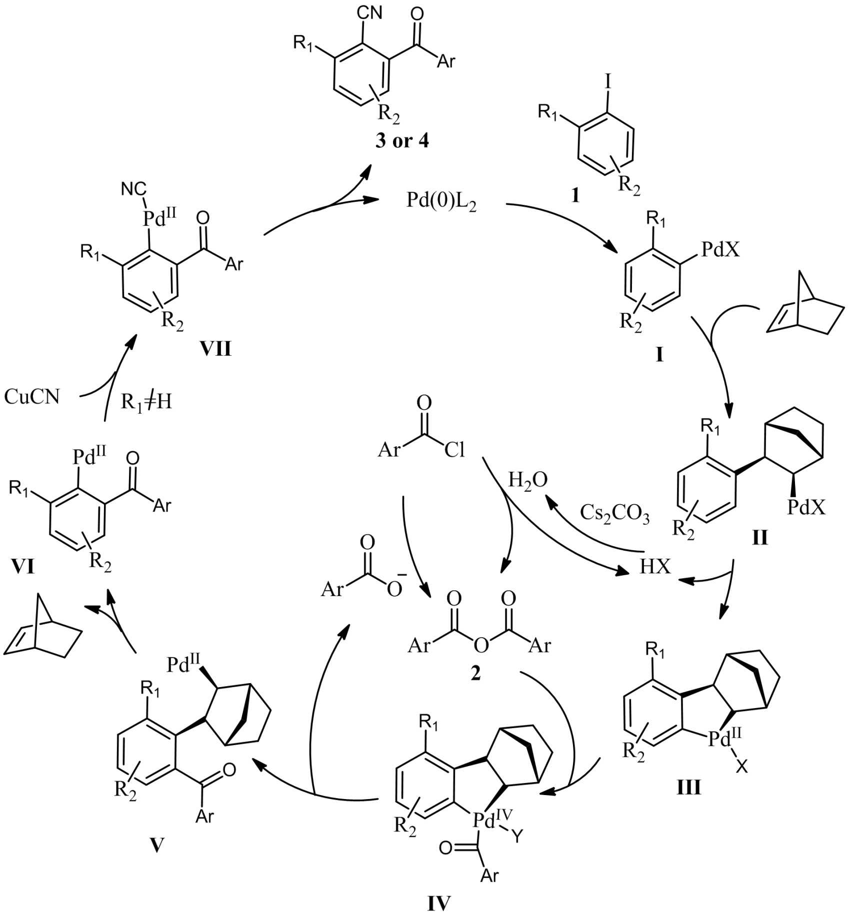
(4)



(5)



(6)



**Scheme 1.** Possible catalytic cycle

To gain mechanistic insights of this reaction, two control experiments were performed and the conversion was calculated according to the isolated products [eqs 2-6]. When benzoic anhydride was employed other than benzoyl chloride under anhydrous conditions, **4a** was isolated in up to 70 % yield (eq 2). When benzoyl chloride and CuCN were replaced by benzoyl cyanide, the reaction did not occur under the standard reaction conditions (eq 3). Further addition of CuCN did not initiate the reaction of 2-iodotoluene (eq 4). We also found that benzoylation of 2-iodotuluene and benzonitrile with benzoyl chloride was not successful under the present reaction conditions (eqs 5 and 6). In the eaction of 2-iodotoluene with benzoyl chlorides, only trace amount of expected 3-methylphenylphenone was observed, and a significant amount of di(*o*-tolyl) ether, 2-(*o*-tolyl)bicyclo[2.2.1]hept-2-ene, 5,9-dimethyl-1,2,3,4,4*a*,12*b*-hexahydro-1,4-methanotriphenylene were formed. These experiments may indicate that the acylation/cyanation product is not formed via acylation of benzonitrile.

Based on the above experimental results and previous reports,[6-10] a plausible mechanism is proposed in Scheme 1. The reaction is initiated by oxidative addition of substrate **1** to Pd(0) complex to generate aryl-Pd(II) complex **I**. A five-membered palladacycle intermediate **III** would be produced through norbornene insertion to the C-Pd bond and subsequent intramolecular C-H activation reaction via intermediate **II**. This palladacycle undergoes oxidative addition with acid anhydride, *in situ* generated from hydrolysis of benzoyl chloride. The palladium(IV) species **IV** undergoes a reductive elimination to give species **V**. After de-insertion of norbornene from **V**, a new aryl-Pd(II) species is formed with norbornene exclusion. At last, intermediate **VII**, formed by the transmetallation of species **VI** with CuCN, yield the desired product **3** or **4** and regenerate Pd(0) catalyst after reductive elimination.

## CONCLUSION

In conclusion, a palladium-catalyzed site-selective C-H bond acylation/C-I acyanation of aryl iodides with commercially available benzoyl choloride was reported. The reaction provides a straightforward and practical way to prepare a series of *ortho*-cyano aryl ketones in good to high yields. The development of further applications of this transformation is in progress in our laboratory.

## EXPERIMENTAL SECTION

**General procedure for the sequential acylation/cyanation reaction between aryl iodides 1, acyl chlorides 2, and CuCN.** To a 25 mL of Schlenk tube equipped with a Teflon-coated magnetic stir bar was charged with aryl iodide (0.3 mmol, 1.0 equiv), benzoyl chloride (126 mg, 0.9 mmol, 3.0 equiv), CuCN (32.2 mg, 0.36 mmol, 1.1 equiv), $PdCl_2$ (5.3 mg, 0.03 mmol, 10 mol %), TFP (13.9 mg, 0.06 mmol, 20 mol %), $Cs_2CO_3$ (293 mg, 0.9 mmol, 3.0 equiv), norbornene (56 mg, 0.6 mmol, 2.0 equiv), $H_2O$ (10.8 mg, 0.6 mmol, 2.0 equiv) and 1,4-dioxane (3.0 mL). The resulting light yellow suspension was stirred at room temperature for 5 min under $N_2$, and then heated to 100 °C overnight. Upon completion of the reaction as monitored by TLC, the reaction was allowed to cool to room temperature, diluted with ethyl acetate (5 ml) and water (15 mL), and extracted with ethyl acetate (10 mL x 3). The organic phase was collected and washed with brine, dried over anhydrous $Na_2SO_4$, then filtered and concentrated. The crude residue was purified by flash column chromatography on silica gel using petroleum ether/ethyl acetate as eluent to give the corresponding products.

**2-methyl-6-(4-methylbenzoyl)benzonitrile (3a):** Light yellow oil (50 mg, 72% yield). $^1$H NMR (400 MHz, $CDCl_3$): δ 2.44 (s, 3H), 2.64 (s, 3H), 7.29 (d, $J$ = 7.6 Hz, 2H), 7.41 (dd, $J$ = 0.8, 7.6 Hz, 1H), 7.49 (d, $J$ = 7.2 Hz, 1H), 7.55 (t, $J$ = 7.6 Hz, 1H), 7.72 (d, $J$ = 8.0 Hz, 2H). $^{13}$C{H} NMR (100 MHz, $CDCl_3$): δ 20.8, 21.8, 111.8, 116.1, 127.0, 129.4, 130.6, 131.6, 132.3, 133.5, 142.5, 143.7, 144.9, 193.9. HR MS (TOF MS, EI+) m/z calcd. for $C_{16}H_{13}NO$: 235.0997; found: 235.0993.

**2-methoxy-6-(4-methylbenzoyl)benzonitrile (3b):** Light yellow solid (45 mg, 60% yield); melting point: 101-103 ˚C. $^1$H NMR (400 MHz, $CDCl_3$): δ 2.44 (s, 3H), 3.99 (s, 3H), 7.12-7.16 (m, 2H), 7.28 (d, $J$ = 8.0 Hz, 2H), 7.59-7.63 (m, 1H), 7.72 (d, $J$ = 8.4 Hz, 2H). $^{13}$C{H} NMR (100 MHz, $CDCl_3$): δ 21.8, 56.5, 100.7, 113.3, 114.3, 121.3, 129.4, 130.5, 133.4, 133.5, 143.9, 145.1, 162.1, 193.4. HR MS (TOF MS, EI+) m/z calcd. for $C_{16}H_{13}NO_2$: 251.0946; found: 251.0944.

**2-fluoro-6-(4-methylbenzoyl)benzonitrile** (**3c**): Yellow oil (44 mg, 62% yield). $^1$H NMR (400 MHz, $CDCl_3$) δ 2.46 (s, 3H), 7.31 (d, $J$ = 7.6 Hz, 2H), 7.39-7.44 (m, 2H), 7.67-7.73 (m, 3H). $^{13}$C{H} NMR (100 MHz, $CDCl_3$) δ 21.9, 101.0 (d, $^2J_{C\text{-}F}$ = 16.2 Hz), 111.9, 118.6 (d, $^2J_{C\text{-}F}$ = 19.5 Hz), 125.5 (d, $^3J_{C\text{-}F}$ = 3.9 Hz), 129.6, 130.5, 132.9, 134.1 (d, $^3J_{C\text{-}F}$ = 8.8 Hz), 143.6, 145.5, 164.0 (d, $^1J_{C\text{-}F}$ = 260.0 Hz), 192.1 (d, $^4J_{C\text{-}F}$ = 1.9 Hz). HR MS (TOF MS, EI+) m/z calcd. for $C_{15}H_{10}FNO$: 239.0746; found: 239.0748.

**2-chloro-6-(4-methylbenzoyl)benzonitrile** (**3d**): White solid (33 mg, 43% yield); melting point: 134-136 ˚C. $^1$H NMR (400 MHz, $CDCl_3$): δ 2.45 (s, 3H), 7.31 (d, $J$ = 8.0 Hz, 2H), 7.51 (dd, $J$ = 1.2, 7.6 Hz, 1H), 7.62 (t, $J$ = 7.6 Hz, 1H), 7.68-7.72 (m, 3H). $^{13}$C{H} NMR (100 MHz, $CDCl_3$): δ 21.9, 112.4, 114.0, 127.5, 129.6, 130.6, 131.8, 132.8, 132.9, 138.8, 144.4, 145.6, 192.4. HR MS (TOF MS, EI+) m/z calcd. for $C_{15}H_{10}ClNO$: 255.0451; found: 255.0455.

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**2-(4-methylbenzoyl)-1-naphthonitrile (3e)**: Light yellow oil (62 mg, 76% yield). $^1$H NMR (400 MHz, CDCl$_3$) δ 2.44 (s, 3H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.64 (d, *J* = 8.4 Hz, 1H), 7.69-7.79 (m, 4H), 7.99 (d, *J* = 8.0 Hz, 1H), 8.14 (d, *J* = 8.4 Hz, 1H), 8.37 (d, *J* = 8.0 Hz, 1H). $^{13}$C{H} NMR (100 MHz, CDCl$_3$) δ 21.9, 109.3, 115.8, 124.9, 126.1, 128.7, 128.8, 129.5, 130.7, 132.5, 132.6, 133.5, 133.6, 142.4, 145.2, 194.2. HR MS (TOF MS, EI+) m/z calcd. for $C_{19}H_{13}NO$: 271.0997; found: 271.0994.

**2,4-dimethyl-6-(4-methylbenzoyl)benzonitrile (3f)**: Yellow oil (41 mg, 55% yield). $^1$H NMR (400 MHz, CDCl$_3$) δ 2.42 (s, 3H), 2.44 (s, 3H), 2.59 (s, 3H), 7.21 (s, 1H), 7.28 (s, 1H), 7.30 (d, *J* = 0.8 Hz, 2H), 7.71 (d, *J* = 8.4 Hz, 2H). $^{13}$C{H} NMR (100 MHz, CDCl$_3$) δ 20.7, 21.7, 21.8, 108.8, 116.4, 127.7, 129.4, 130.5, 132.9, 133.7, 142.6, 142.7, 143.4, 144.9, 194.2. HR MS (TOF MS, EI+) m/z calcd. for $C_{17}H_{15}NO$: 249.1154; found: 249.1156.

**dimethyl 2'-cyano-[1,1'-biphenyl]-2,3'-dicarboxylate (3g)**: Yellow oil (41 mg, 93% yield). $^1$H NMR (400 MHz, CDCl$_3$) δ 3.71 (s, 3H), 4.00 (s, 3H), 7.31 (dd, *J* = 1.2, 7.6 Hz, 1H), 7.52-7.58 (m, 2H), 7.62-7.70 (m, 2H), 7.12-7.15 (m, 2H). $^{13}$C{H} NMR (100 MHz, CDCl$_3$) δ 52.2, 52.9, 112.4, 116.1, 129.1, 129.3, 129.7, 130.9, 131.0, 131.5, 132.4, 132.6, 133.1, 139.5, 148.4, 164.9, 166.6. HR MS (TOF MS, EI+) m/z calcd. for $C_{17}H_{13}NO_4$: 295.0845; found: 295.0841.

**2',3-dinitro-[1,1'-biphenyl]-2-carbonitrile (3h)**: Yellow solid (30 mg, 75% yield); melting point: 188-190 ˚C. $^1$H NMR (400 MHz, CDCl$_3$): δ 7.45 (dd, *J* = 1.4, 7.8 Hz, 1H), 7.69-7.76 (m, 2H), 7.80-7.89 (m, 2H), 8.30 (dd, *J* = 1.0, 8.2 Hz, 1H), 8.37 (dd, *J* = 1.2, 8.4 Hz, 1H). $^{13}$C{H} NMR (100 MHz, CDCl$_3$) δ 107.6, 113.3, 124.8, 125.6, 131.0, 131.8, 131.9, 133.1, 134.1, 134.2, 146.2, 147.4, 149.3. HR MS (TOF MS, EI+) m/z calcd. for $C_{13}H_7N_3O_4$: 269.0437; found:269.0432.

**2-chloro-6-(2-methylbenzoyl)benzonitrile (3i)**: Yellow solid (59 mg, 77% yield); melting point: 110-112 ˚C. $^1$H NMR (400 MHz, CDCl$_3$): δ 2.52 (s, 3H), 7.23-7.31 (m, 2H), 7.35 (d, *J* = 7.6, 1H), 7.45-7.50 (m, 2H), 7.59 (t, *J* = 8.0 Hz, 1H), 7.70 (dd, *J* = 1.2, 8.0 Hz, 1H). $^{13}$C{H} NMR (100 MHz, CDCl$_3$): δ 20.9, 112.5, 113.9, 125.6, 128.6, 130.8, 132.0, 132.4, 132.5, 132.8, 135.7, 139.3, 139.6, 144.4, 194.5. HR MS (TOF MS, EI+) m/z calcd. for $C_{15}H_{10}ClNO$: 255.0451; found: 255.0456.

**2,6-bis(4-methylbenzoyl)benzonitrile (3j)**: Light yellow solid (41 mg, 40% yield); melting point: 164-166 ˚C. $^1$H NMR (400 MHz, CDCl$_3$): δ 2.45 (s, 6H), 7.31 (d, *J* = 8.0 Hz, 4H), 7.71-7.79 (m, 7H). $^{13}$C{H} NMR (100 MHz, CDCl$_3$): δ 21.9, 110.0, 114.7, 129.6, 130.6, 131.5, 133.1, 143.9, 145.5, 193.2. HR MS (TOF MS, EI+) m/z calcd. for $C_{23}H_{17}NO_2$: 339.1259; found:339.1263.

**4-methoxy-2,6-bis(4-methylbenzoyl)benzonitrile (3k)**: White solid (42 mg, 38% yield); melting point: 166-168 ˚C. $^1$H NMR (400 MHz, CDCl$_3$): δ 2.44 (s, 6H), 3.91 (s, 3H), 7.18 (s, 2H), 7.30 (d, *J* = 8.0 Hz, 4H), 7.75 (d, *J* = 8.0 Hz, 4H). $^{13}$C{H} NMR (100 MHz, CDCl$_3$): δ 21.9, 56.2, 101.3, 114.9, 116.2, 129.6, 130.6, 132.9, 145.6, 145.8, 161.6, 193.1. HR MS (TOF MS, EI+) m/z calcd. for $C_{24}H_{19}NO_3$: 369.1365; found: 369.1362.

**2-benzoyl-6-methylbenzonitrile (4a)**: Light yellow oil (43 mg, 65% yield). $^1$H NMR (400 MHz, CDCl$_3$): δ 2.65 (s, 3H), 7.43 (dd, *J* = 1.2, 7.2 Hz, 1H), 7.48-7.58 (m, 4H), 7.62-7.66 (m, 1H), 7.81 (m, 2H). $^{13}$C{H} NMR (100 MHz, CDCl$_3$): δ 20.8, 111.8, 116.0, 127.2, 128.6, 130.4, 131.6, 132.6, 133.8, 136.1, 142.1, 143.8, 194.2. HR MS (TOF MS, EI+) m/z calcd. for $C_{15}H_{11}NO$: 221.0841; found: 221.0843.

**2-methyl-6-(2-methylbenzoyl)benzonitrile (4b)**: Yellow oil (69 mg, 98% yield). $^1$H NMR (400 MHz, CDCl$_3$): δ 2.46 (s, 3H), 2.62 (s, 3H), 7.21 (t, *J* = 7.4 Hz, 1H), 7.27-7.31 (m, 2H), 7.35-7.37 (m, 1H), 7.42 (td, *J* = 7.6, 1.6 Hz, 1H), 7.48-7.52 (m, 2H). $^{13}$C{H} NMR (100 MHz, CDCl$_3$): δ 20.7, 20.9, 111.9, 116.1, 125.4, 128.3, 130.5, 131.6, 131.7, 131.9, 133.2, 136.6, 139.1, 142.4, 144.1, 196.1. HR MS (TOF MS, EI+) m/z calcd. for $C_{16}H_{13}NO$: 235.0997; found: 235.0994.

**2-methyl-6-(3-methylbenzoyl)benzonitrile (4c)**: Orange yellow oil (70 mg, 99% yield). $^1$H NMR (400 MHz, CDCl$_3$) δ 2.41 (s, 3H), 2.64 (s, 3H), 7.35-7.45 (m, 3H), 7.50-7.58 (m, 3H), 7.66 (s, 1H). $^{13}$C{H} NMR (100 MHz, CDCl$_3$): δ 20.8, 21.4, 111.8, 116.1, 127.1, 127.8, 128.5, 130.7, 131.6, 132.5, 134.7, 136.1, 138.6, 142.3, 143.7, 194.4. HR MS (TOF MS, EI+) m/z calcd. for $C_{16}H_{13}NO$: 235.0997; found: 235.0992.

**2-(2-methoxybenzoyl)-6-methylbenzonitrile (4d)**: Light yellow oil (65 mg, 86% yield). $^1$H NMR (400 MHz, CDCl$_3$): δ 2.63 (s, 3H), 3.65 (s, 3H), 6,97 (d, *J* = 8.4 Hz, 1H), 7.05-7.09 (m, 1H), 7.39-7.58 (m, 5H). $^{13}$C{H} NMR (100 MHz, CDCl$_3$): δ 20.8,

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55.6, 111.1, 111.7, 116.3, 120.9, 127.3, 127.6, 131.1, 131.5, 132.7, 134.0, 143.0, 143.5, 158.5, 194.0. HR MS (TOF MS, EI+) m/z calcd. for $C_{16}H_{13}NO_2$: 251.0946; found: 251.0948.

**2-(4-methoxybenzoyl)-6-methylbenzonitrile** (**4e**): Yellow oil (43 mg, 58% yield). $^1$H NMR (400 MHz, $CDCl_3$): δ 2.64 (s, 3H), 3.89 (s, 3H), 6.94-6.98 (m, 2H), 7.40 (d, $J$ = 7.6 Hz, 1H), 7.49 (d, $J$ = 7.2 Hz, 1H), 7.55 (t, $J$ = 7.6 Hz, 1H), 7.79-7.83 (m, 2H). $^{13}$C{H} NMR (100 MHz, $CDCl_3$) δ 20.8, 55.6, 111.7, 113.9, 116.1, 126.7, 128.9, 131.6, 132.0, 132.9, 142.9, 143.6, 164.2, 192.9. HR MS (TOF MS, EI+) m/z calcd. for $C_{16}H_{13}NO_2$: 251.0946; found: 251.0949.

**2-(2-fluorobenzoyl)-6-methylbenzonitrile** (**4f**): Light yellow oil (47 mg, 66% yield). $^1$H NMR (400 MHz, $CDCl_3$): δ 2.65 (s, 3H), 7.12-7.17 (m, 1H), 7.31 (td, $J$ = 1.2, 7.6 Hz, 1H), 7.46-7.48 (m, 1H), 7.52-7,55 (m, 2H), 7.57-7.63 (m, 1H), 7.73 (td, $J$ = 1.6, 7.6 Hz, 1H). $^{13}$C{H} NMR (100 MHz, $CDCl_3$): δ 20.8, 111.2, 116.0, 116.5 (d, $^2J_{C\text{-}F}$ = 21.7 Hz), 124.7 (d, $^3J_{C\text{-}F}$ = 3.8 Hz), 125.6 (d, $^2J_{C\text{-}F}$ = 13.2 Hz), 127.6 (d, $^4J_{C\text{-}F}$ = 2.1 Hz), 131.5 (d, $^4J_{C\text{-}F}$ = 2.0 Hz), 131.8, 133.4, 135.0 (d, $^3J_{C\text{-}F}$ = 8.4 Hz), 142.0, 143.9, 161.0 (d, $^1J_{C\text{-}F}$ = 253.1 Hz), 191.2. HR MS (TOF MS, EI+) m/z calcd. for $C_{15}H_{10}FNO$: 239.0746; found: 239.0745.

**2-(4-fluorobenzoyl)-6-methylbenzonitrile** (**4g**): Yellow oil (24 mg, 33% yield). $^1$H NMR (400 MHz, $CDCl_3$): δ 2.65 (s, 3H), 7.15-7.20 (m, 2H), 7.42 (d, $J$ = 7.6 Hz, 1H), 7.52-7.60 (m, 2H), 7.84-7.88 (m, 2H). $^{13}$C{H} NMR (100 MHz, $CDCl_3$): δ 20.8, 111.8, 115.9 (d, $^2J_{C\text{-}F}$ = 22.2 Hz), 115.9, 126.9, 131.7, 132.5 (d, $^3J_{C\text{-}F}$ = 3.0 Hz), 132.6, 133.0 (d, $^3J_{C\text{-}F}$ = 9.9 Hz), 141.9, 143.9, 166.2 (d, $^1J_{C\text{-}F}$ = 255.9 Hz), 192.7. HR MS (TOF MS, EI+) m/z calcd. for $C_{15}H_{10}FNO$: 239.0746; found: 239.0746.

**2-(2-chlorobenzoyl)-6-methylbenzonitrile** (**4h**): Light yellow solid (35 mg, 46% yield); melting point: 108-110 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ 2.66 (s, 3H), 7.39-7.57 (m, 7H). $^{13}$C{H} NMR (100 MHz, $CDCl_3$): δ 20.9, 111.7, 116.0, 127.1, 128.8, 130.4, 130.4, 131.8, 132.2, 132.5, 134.1, 137.3, 140.4, 144.6, 193.2; HR MS (TOF MS, EI+) m/z calcd. for $C_{15}H_{10}ClNO$: 255.0451; found: 255.0448.

**2-(4-chlorobenzoyl)-6-methylbenzonitrile** (**4i**): Light yellow solid (32 mg, 42% yield); melting point: 158-160 ˚C; $^1$H NMR (400 MHz, $CDCl_3$): δ 2.65 (s, 3H), 7.41

(d, *J* = 7.2 Hz, 1H), 7.48 (d, *J* = 8.4 Hz, 2H), 7.52-7.59 (m, 2H), 7.76 (d, *J* = 8.4 Hz, 2H). $^{13}$C{H} NMR (100 MHz, CDCl$_3$): δ 20.8, 111.8, 115.9, 127.0, 129.1, 131.7, 132.7, 134.4, 140.5, 141.6, 144.0, 193.0. HR MS (TOF MS, EI+) m/z calcd. for $C_{15}H_{10}ClNO$: 255.0451; found: 255.0450.

**2-(3-fluorobenzoyl)-6-methylbenzonitrile (4j)**: Light yellow oil (40 mg, 57% yield). $^1$H NMR (400 MHz, CDCl$_3$): δ 2.66 (s, 3H), 7.32-7.37 (m, 1H), 7.42 -7.60 (m, 6H). $^{13}$C{H} NMR (100 MHz, CDCl$_3$): δ 20.8, 111.9, 115.9, 116.8 (d, $^2J_{C\text{-}F}$ = 22.7 Hz), 120.9 (d, $^2J_{C\text{-}F}$ = 20.9 Hz), 126.3 (d, $^4J_{C\text{-}F}$ = 2.5 Hz), 127.2, 130.3 (d, $^3J_{C\text{-}F}$ = 6.4 Hz), 131.7, 132.9, 138.1 (d, $^3J_{C\text{-}F}$ = 6.4 Hz), 141.4, 144.1, 162.7 (d, $^1J_{C\text{-}F}$ = 247.5 Hz), 192.9 (d, $^4J_{C\text{-}F}$ = 3.2 Hz). HR MS (TOF MS, EI+) m/z calcd. for $C_{15}H_{10}FNO$: 239.0746; found: 239.0749.

**2-benzoyl-6-methoxybenzonitrile (4k)**: Yellow oil (49 mg, 70% yield). $^1$H NMR (400 MHz, CDCl$_3$): δ 4.01 (s, 3H), 7.15-7.18 (m, 2H), 7.47-7.51 (m, 2H), 7.60-7.65 (m, 2H), 7.81-7.83 (m, 2H). $^{13}$C{H} NMR (100 MHz, CDCl$_3$): δ 56.5, 100.8, 113.5, 114.2, 121.4, 128.6, 130.4, 133.5, 133.9, 135.9, 143.5, 162.1, 193.7. HR MS (TOF MS, EI+) m/z calcd. for $C_{15}H_{11}NO_2$: 237.0790; found: 237.0788.

**2-methoxy-6-(2-methylbenzoyl)benzonitrile (4l)**: Yellow oil (73 mg, 97% yield). $^1$H NMR (400 MHz, CDCl$_3$): δ 2.49 (s, 3H), 3.99 (s, 3H), 7.12 (dd, *J* = 0.8, 7.6 Hz, 1H), 7.17 (dd, *J* = 0.4, 8.4 Hz, 1H), 7.23 (t, *J* = 7.6 Hz, 1H), 7.30-7.33 (m, 2H), 7.44 (td, *J* = 1.2, 7.2 Hz, 1H), 7.56-7.60 (m, 1H). $^{13}$C{H} NMR (100 MHz, CDCl$_3$): δ 20.8, 56.5, 100.8, 114.2, 122.5, 125.4, 130.7, 131.8, 132.0, 133.5, 136.5, 139.2, 143.8, 162.4, 195.6. HR MS (TOF MS, EI+) m/z calcd. for $C_{16}H_{13}NO_2$: 251.0946; found: 251.0946.

**2-methyl-6-(2,4,6-trimethylbenzoyl)benzonitrile (4m)**: White solid (50 mg, 64% yield); melting point: 192-194 °C. $^1$H NMR (400 MHz, CDCl$_3$): δ 2.10 (s, 6H), 2.33 (s, 3H), 2.67 (s, 3H), 6.90 (s, 2H), 7.35 (dd, *J* = 0.6, 7.6 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 1H), 7.54 (dd, *J* = 0.6, 7.6 Hz, 2H). $^{13}$C{H} NMR (100 MHz, CDCl$_3$): δ 19.6, 20.9, 21.2, 111.2, 116.4, 128.7, 129.1, 132.0, 134.4, 134.8, 135.8, 139.5, 140.4, 145.1, 198.1. HR MS (TOF MS, EI+) m/z calcd. for $C_{18}H_{17}NO$: 263.1310; found: 263.1311.

**2-(3,5-dimethylbenzoyl)-6-methylbenzonitrile (4n)**: Light yellow oil (48 mg, 65% yield). $^1$H NMR (400 MHz, CDCl$_3$): δ 2.36 (d, *J* = 4.0 Hz, 6H), 2.65 (s, 3H), 7.26 (s,

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1H), 7.39-7.40 (m, 3H), 7.49-7.57 (m, 2H): $^{13}C\{H\}$ NMR (100 MHz, $CDCl_3$) δ 20.8, 21.2, 111.8, 116.0, 127.0, 128.2, 131.5, 132.3, 135.6, 136.2, 138.3, 142.6, 143.7, 194.6. HR MS (TOF MS, EI+) m/z calcd. for $C_{17}H_{15}NO$: 249.1154; found: 249.1158.

**2-(2-naphthoyl)-6-methylbenzonitrile (4o)**: Light yellow solid (57 mg, 70% yield); melting point: 184-186 ˚C. $^1H$ NMR (400 MHz, $CDCl_3$): δ 2.67 (s, 3H), 7.48-7.65 (m, 5H), 7.88-8.01 (m, 4H), 8.20 (s, 1H). $^{13}C\{H\}$ NMR (100 MHz, $CDCl_3$): δ 20.9, 111.9, 116.1, 125.1, 127.0, 127.2, 127.9, 128.8, 129.1, 129.7, 131.6, 132.2, 132.5, 133.1, 133.4, 135.9, 142.4, 143.9, 194.2. HR MS (TOF MS, EI+) m/z calcd. for $C_{19}H_{13}NO$: 271.0997; found: 271.0998.

**2-(2-methylbenzoyl)-1-naphthonitrile (4p)**: Yellow oil (72 mg, 89% yield). $^1H$ NMR (400 MHz, $CDCl_3$): δ 2.54 (s, 3H), 7.22-7.25 (m, 1H), 7.32-7.37 (m, 2H), 7.45-7.49 (m, 1H), 7.64 (d, $J$ = 8.4 Hz, 1H), 7.69-7.79 (m, 2H), 7.98 (d, $J$ = 7.2 Hz, 1H), 8.11 (d, $J$ = 8.4 Hz, 1H), 8.40 (d, $J$ = 8.8 Hz, 1H). $^{13}C\{H\}$ NMR (100 MHz, $CDCl_3$): δ 20.9, 109.9, 115.6, 125.5, 126.4, 128.6, 129.1, 130.9, 131.8, 132.2, 132.6, 133.9, 136.6, 139.3, 142.2, 196.3. HR MS (TOF MS, EI+) m/z calcd. for $C_{19}H_{13}NO$: 271.0997; found: 271.0997.

**2-acetyl-6-methylbenzonitrile (4q)[17]**: White solid (13 mg, 27% yield); melting point: 94-96 °C. $^1H$ NMR (400 MHz, $CDCl_3$): δ 2.63 (s, 3H), 2.68 (s, 3H), 7.52 (d, $J$ = 7.2 Hz, 1H), 7.57 (t, $J$ = 7.6 Hz, 1H), 7.74 (d, $J$ = 7.2 Hz, 1H). $^{13}C\{H\}$ NMR (100 MHz, $CDCl_3$): δ 20.9, 28.0, 110.8, 116.8, 127.1, 131.9, 133.8, 140.6, 144.6, 196.7.

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### Notes

The authors declare no competing financial interest.

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## ASSOCIATED CONTENT

**Supporting Information**. Spectra of $^1$H NMR, $^{13}$C NMR for new products and crystallographic data for **4d**. This material is available free of charge via the Internet at http://pubs.acs.org.

## REFERENCES

[1] a) Seechurn C. C. C. J.; Kitching M. O.; Colacot T. J.; Snieckus V. *Angew. Chem. Int. Ed.* **2012**, *51*, 5062. b) Leenders S. H. A. M.; Gramage-Doria R.; Bruin B. Reek J. N. H. *Chem. Soc. Rev.* **2015**, *44*, 433. c) Gandeepan P.; Cheng C.-H. *Chem. Asian J.* **2015**, *10*, 824. d) Denmark S. E.; Ambrosi A. *Org. Process Res. Dev.* **2015**, *19*, 982.

[2] a) Hartwig J. F. *Acc. Chem. Res.* **2008**, *41*, 1534. b) Seidel G.; Fürstner A. *Chem. Commun.* **2012**, *48*, 2055. c) de Vries J. G. *Top Organomet Chem.* **2012**, *42*, 1.

[3] Zhang X.; Liu A. Chen W. *Org. Lett.* **2008**, *10*, 3849.

[4] a) Rouquet G.; Chatani N. *Angew. Chem. Int. Ed.* **2013**, *52*, 11726. b) Zhang S.-Y.; Zhang F.-M.; Tu Y.-Q. *Chem. Soc. Rev.* **2011**, *40*, 1937.

[5] Wender P. A.; Verma V. A.; Paxton T. J.; Pillow T. H. *Acc. Chem. Res.* **2008**, *41*, 40.

[6] a) Catellani M.; Frignani F.; Rangoni A. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 119. b) Catellani M.; Motti E.; Minari M. *Chem. Comm.* **2000**, 157. c) Faccini F.; Motti E.; Catellani M. *J. Am. Chem. Soc.* **2004**, *126*, 78. d) Ferraccioli R.; Carenzi D.; RombolàO.; Catellani M. *Org. Lett.* **2004**, *6*, 4759. e) Maestri G.; Della Cá N.; Catellani M. *Chem. Comm.* **2009**, 4892. f) Della Ca´ N.; Maestri G.; Malacria M.; Derat E.; Catellani M. *Angew. Chem. Int. Ed.* **2011**, *50*, 12257. g) Motti E.; Della Ca´ N.; Xu D.; Piersimoni A.; Bedogni E.; Zhou Z.-M.; Catellani M. *Org. Lett.* **2012**, *14*, 5792.

[7] a) Lautens M.; Piguel S. *Angew. Chem. Int. Ed.* **2000**, *39*, 1045. b) Bressy C.; Alberico D.; Lautens M. *J. Am. Chem. Soc.* **2005**, *127*, 13148. c) Mariampillai B.;

Alberico D.; Bidau V.; Lautens M. *J. Am. Chem. Soc.* **2006**, *128*, 14436. d) Mariampillai B.; Alliot J.; Li M.; Lautens M. *J. Am. Chem. Soc.* **2007**, *129*, 15372. e) Gericke K. M.; Chai D. I.; Bieler N.; Lautens M. *Angew. Chem. Int. Ed.* **2009**, *48*, 1447. f) Martins A.; Candito D. A.; Lautens M. *Org. Lett.* **2010**, *12*, 5186. g) Jiao L.; Bach T. *J. Am. Chem. Soc.* **2011**, *133*, 12990. h) Wu X.; Zhou P.; Wang L.; Xu P.; Liang Y. *Chem. Commun.* **2014**, *50*, 3882. i) Zhang H.; Chen P.; Liu G. *Angew. Chem. Int. Ed.* **2014**, *53*, 10174. j) Wang X.-C.; Gong W.; Fang L.-Z.; Zhu R.-Y.; Li S.; Engle K. M.; Yu J.-Q. *Nature* **2015**, *519*, 334. k) Dong Z.; Wang J.; Dong G. *J. Am. Chem. Soc.* **2015**, *137*, 5887.

[8] Dong Z.; Dong G.-B. *J. Am. Chem. Soc.* **2013**, *135*, 18350.

[9] a) Chen Z.-Y.; Ye C.-Q.; Zhu H.; Zeng X.-P.; Yuan J.-J. *Chem. Eur. J.* **2014**, *20*, 4237. b) Zhou P.-X.; Ye Y.- Y.; Ma J.-W.; Zheng L.; Tang Q.; Qiu Y.-F.; Song B.; Qiu Z.-H.; Xu P.-F.; Liang Y.-M. *J. Org. Chem.* **2014**, *79*, 6627. c) Ye C.; Zhu H.; Chen Z. *J. Org. Chem.* **2014**, *79*, 8900. d) Shi H.; Babinski D. J.; Ritter T. *J. Am. Chem. Soc.* **2015**, *137*, 3775. e) Sun F.; Gu Z. *Org. Lett.* **2015**, *17*, 2222. f) Pan S.; Ma X.; Zhong D.; Chen W.; Liu M.; Wu H. *Adv. Synth. Catal.* **2015**, *357*, 3052.

[10] a) Dong Z.; Wang J.; Ren Z.; Dong G. *Angew. Chem. Int. Ed.* **2015**, *54*, 12664. b) Huang Y.; Zhu R.; Zhao K.; Gu Z. *Angew. Chem. Int. Ed.* **2015**, *54*, 12669. c) Zhou P.-X.; Ye Y.-Y.; Liu C.; Zhao L.-B.; Hou J.-Y.; Chen D.-Q.; Tang Q.; Wang A.-Q.; Zhang J.-Y.; Huang Q.-X.; Xu P.-F.; Liang Y.-M. *ACS Catal.* **2015**, *5*, 4927.

[11] a) Karen R. R.; George A. F.; Lee T. S.; Jill R. C.; Steve S. G.; Jeffrey H. T.; Clarence W. A.; David K. S.; Richard J. H.; Robert G. F.; Steven A. S.; Joseph H. C.; Lawrence R. B. *J. Med. Chem.* **2006**, *49*, 727. b) Helfried N.; Anne B.; Matthias B. *Chem. Eur. J.* **2008**, *14*, 3645. c) Lampe J. W.; Biggers C. K.; Defauw J. M.; Foglesong R. J.; Hall S. E.; Heerding J. M.; Hollinshead S. P.; Hu H.; Hughes P. F.; Jagdmann G. E.; Johnson M. G.; Lai Y.-S.; Lowden C. T.; Lynch M. P.; Mendoza J. S.; Murphy M. M.; Wilson J. W.; Ballas L. M.; Carter K.; Darges J. W.; Davis J. E.; Hubbard F. R.; Stamper M. L. *J. Med. Chem.* **2002**, *45*, 2624. d) Deng Y.; Chin Y.-W.; Chai H.; Keller W. J.; Kinghorn A. D. *J. Nat. Prod.* **2007**, *70*, 2049. e) Harrington P. J.; Lodewijk E. *Org. Process Res. Dev.* **1997**, *1*, 72.

[12] a) Sartori G.; Maggi R. *Chem. Rev.* **2006**, *106*, 1077. b) Chevallier F.; Blin T.; Nagaradja E.; Lassagne F.; Roisnel T.; Halauko Y. S.; Matulis V. E.; Ivashkevich O. A.; Mongin F. *Org. Biomol. Chem.* **2012**, *10,* 4878.

[13] Nahm S.; Weinreb S. M. *Tetrahedron Lett.* **1981**, *22*, 3815.

[14] a) Jia X.; Zhang S.; Wang W.; Luo F.; Cheng J. *Org. Lett.* **2009**, *11*, 3120. b) Sharma S.; Park J.; Park E.; Kim A.; Kim M.; Kwak J. H.; Jung Y. H.; Kim I. S. *Adv. Synth. Catal.* **2013**, *355*, 332. c) Lu J.; Zhang H.; Chen X.; Liu H.; Jiang Y.; Fu H. *Adv. Synth. Catal.* **2013**, *355*, 529. d) Park J.; Park E.; Kim A.; Lee Y.; Chi K.-W.; Kwak J. H.; Jung Y. H.; Kim I. S. *Org. Lett.* **2011**, *13*, 4390. e) Tlili A.; Schranck J.; Pospech J.; Neumann H.; Beller M. *Angew. Chem. Int. Ed.* **2013**, *52*, 6293. f) Pi C.; Cui X.; Liu X.; Guo M.; Zhang H.; Wu Y. *Org. Lett.* **2014**, *16*, 5164.

[15] Ko S.; Kang B.; Chang S. *Angew. Chem. Int. Ed.* **2005**, *44*, 455.

[16] a) Grainger R.; Cornella J.; Blakemore D. C.; Larrosa L.; Campanera J. M. *Chem. Eur. J.* **2014**, *20*, 16680. b) Konovalov A. I.; Lishchynskyi A.; Grushin V. V. *J. Am. Chem. Soc.* **2014**, *136*, 13410.

[17] Mangas-Sánchez J.; Busto E.; Gotor-Fernández V.; Gotor V. *Org. Lett.* **2012**, *14*, 1444.