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Chelation-Assisted Palladium-Catalyzed Cascade Bromination/Cyanation Reaction of 2-Arylpyridine and 1-Arylpyrazole C−H Bonds

Xiaofei Jia,[†] Dongpeng Yang,[†] Wenhui Wang,[†] Fang Luo,[†] and Jiang Cheng*[,†,‡]

[†]*College of Chemistry & Materials Engineering, Wenzhou University, Wenzhou 325027, P. R. China, and* [‡]*State Key Laboratory of Coordination Chemistry, Nanjing University, Nanjing 210093, P. R. China*

jiangcheng@wzu.edu.cn

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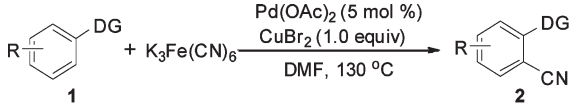

DG = 2-pyridinyl, 1-pyrazolyl 17 examples, 45-90% yield

A chelation-assisted palladium-catalyzed cascade bromination/cyanation reaction of 2-arylpyridine and 1-arylpyrazole C−H bonds has been developed. Notably, the reaction employs $K_3[Fe(CN)_6]$ as a safe and nontoxic cyanide source, providing aromatic nitriles in moderate to good yields in one-pot. The procedure tolerates methoxy, chloro, fluoro, cyano, trifluoromethyl, and carbomethoxy groups.

Introduction

Benzonitriles are of considerable interest in organic chemistry as integral ingredients of dyes, herbicides, natural products, agrochemicals, and pharmaceuticals.[1] In addition, they represent versatile intermediates for further transformations in synthetic organic chemistry.[2] The Rosenmund−von Braun reaction[3] (reaction of aryl halides with copper(I) cyanide) and the Sandmeyer reaction[4] (reaction of diazonium salts with copper(I) cyanide) are widely used in the preparation of benzonitriles. Compared to the classic methods, transition-metal-catalyzed cyanation of aryl halides is a mild and direct method to access benzonitriles.[5−7] However, prefunctionalization was required to achieve benzonitriles. Thus, development of a simple method is a highly desired goal in synthetic chemistry.

Transition-metal-catalyzed functionalization of aryl C−H bonds followed by C−C bond formation provides a promising

(1) Kleemann, A.; Engel, J.; Kutscher, B.; Reichert, D. *Pharmaceutical substances: syntheses, patents, applications*, 4th ed.; Georg Thieme: Stuttgart, 2001.

(2) Larock, R. C. *Comprehensive Organic Transformations: A guide to Functional Group Preparations*; VCH: New York, 1989.

(3) (a) Wöhler, F.; Liebig, J. *Justus Liebigs Ann. Chem.* **1832**, *3*, 267. (b) Friedrich, K.; Wallenfels, K. In *The Chemistry of the Cyano Group*; Wiley: New York, 1970; pp 77−86. (c) Friedrich, K. In *The Chemistry of Functional Groups, Supp. C*; Wiley: New York, 1970; pp 1345−1390.

(4) (a) Sandmeyer, T. *Ber. Dtsch. Chem. Ges.* **1884**, *17*, 1633. (b) Hodgson, H. H. *Chem. Rev.* **1947**, *40*, 251.

(5) For selected reports on palladium-catalyzed cyanation of aryl halides, see: (a) Sundermeier, M.; Zapf, A.; Beller, M. *Eur. J. Inorg. Chem.* **2003**, 3513 and references cited therein. (b) Zhang, A.; Neumeyer, J. L. *Org. Lett.* **2003**, *5*, 201. (c) Chidambaram, R. *Tetrahedron Lett.* **2004**, *45*, 1441. (d) Marcantonio, K. M.; Frey, L. F.; Liu, Y.; Chen, Y.; Strine, J.; Phenix, B.; Wallace, D. J.; Chen, C. Y. *Org. Lett.* **2004**, *6*, 3723. (e) Collibee, S. E.; Strivastava, R. R. *Tetrahedron Lett.* **2004**, *45*, 8895. (f) Schareina, T.; Zapf, A.; Beller, M. *Chem. Commun.* **2004**, 1388. (g) Williams, J. M.; Yang, C. Y. *Org. Lett.* **2004**, *6*, 2837. (h) Schareina, T.; Zapf, A.; Beller, M. *J. Organomet. Chem.* **2004**, *689*, 4576. (i) Stazi, F.; Palmisano, G.; Turconi, M.; Stantagostino, M. *Tetrahedron Lett.* **2005**, *46*, 1815. (j) Hatsuda, M.; Seki, M. *Tetrahedron* **2005**, *61*, 9908. (k) Hatsuda, M.; Seki, M. *Tetrahedron Lett.* **2005**, *46*, 1849. (l) Jensen, M. L.; Gajare, A. S.; Toyota, K.; Yoshijuji, M.; Ozawa, F. *Tetrahedron Lett.* **2005**, *46*, 8645. (m) Weissman, S. A.; Zewge, D.; Chen, C. *J. Org. Chem.* **2005**, *70*, 1508. (n) Lin, L. S.; Fors, B. P.; Chobanian, H. R. *Tetrahedron Lett.* **2006**, *47*, 3303. (o) Whittall, J.; Cormack, P. M.; Pitts, W. R. *Tetrahedron* **2006**, *62*, 4705. (p) Gelman, D.; Grossman, O. *Org. Lett.* **2006**, *8*, 1189. (q) Li, L.-H.; Pan, Z.-L.; Liang, Y.-M. *Synlett* **2006**, 2094. (r) Schareina, T.; Zapf, A.; Magerlein, W.; Muller, N.; Beller, M. *Tetrahedron Lett.* **2007**, *48*, 1087. (s) Buono, F. G.; Chidambaram, R; Mueller, R. H.; Waltermire, R. E. *Org. Lett.* **2008**, *10*, 5325. (t) Ren, Y.; Liu, Z.; He, S.; Zhao, S.; Wang, J.; Niu, R.; Yin, W. *Org. Process Res. Dev.* **2009**, *13*, 764. (u) Velmathi, S.; Leadbeater, N. E. *Tetrahedron Lett.* **2008**, *49*, 4693. (v) Nandurkar, N. S.; Bhanage, B. M. *Tetrahedron* **2008**, *64*, 3655. (w) Ryberg, P. *Org. Proc. Res. Dev.* **2008**, *12*, 540.

(6) For selected reports on copper-catalyzed cyanation of aryl halides, see: (a) Sundermeier, M.; Zapf, A.; Beller, M. *Angew. Chem., Int. Ed.* **2003**, *42*, 1661. (b) Ren, Y.; Liu, Z.; Zhao, S.; Tian, X.; Yin, W.; He, S.; Wang, J. *Catal. Commun.* **2009**, *10*, 768. (c) Schareina, T.; Zapf, A.; Mägerlein, W.; Müller, N.; Beller, M. *Tetrahedron Lett.* **2007**, *48*, 1087. (d) Anderson, B. A.; Bell, E. C.; Ginah, F. O.; Harn, N. K.; Pagh, L. M.; Wepsiec, J. P. *J. Org. Chem.* **1998**, *63*, 8224. (e) Zhang, Z.; Liebeskind, L. S. *Org. Lett.* **2006**, *8*, 4331. (f) Akita, Y.; Shimazaki, M.; Ohta, A. *Synthesis* **1981**, 974. (g) Dalton, J. R.; Regen, S. L. *J. Org. Chem.* **1979**, *44*, 4443. (h) Yang, C.; Williams, J. M. *Org. Lett.* **2004**, *6*, 2837. (i) Weissman, S. A.; Zewge, D.; Chen, C. *J. Org. Chem.* **2005**, *70*, 1508. (j) Cristau, H.-J.; Ouali, A.; Spindler, J.-F.; Taillefer, M. *Chem.—Eur. J.* **2005**, *11*, 2483. (k) Zanon, J.; Klapars, A.; Buchwald, S. *J. Am. Chem. Soc.* **2003**, *125*, 2890. (l) Wu, J. X.; Beck, B.; Ren, R. X. *Tetrahedron Lett.* **2002**, *43*, 387. (m) Ren, Y.; Wang, W.; Zhao, S.; Tian, X.; Wang, J.; Yin, W.; Cheng, L. *Tetrahedron Lett.* **2009**, *50*, 4595.

(7) For selected reports on nickel-catalyzed cyanation of aryl halides, see: (a) Cassar, L. *J. Organomet. Chem.* **1973**, *54*, 57. (b) Cassar, L.; Foà, M.; Montanari, F.; Marinelli, G. P. *J. Organomet. Chem.* **1979**, *173*, 335. (c) Sakaibara, Y.; Okuda, F.; Shimoyabashi, A.; Kirino, K.; Sakai, M.; Uchino, N.; Takagi, K. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 1985. (d) Sakaibara, Y.; Ido, Y.; Sakai, K.; Sakai, M.; Uchino, N. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 2776. (e) Percec, V.; Bae, J.-Y.; Hill, D. H. *J. Org. Chem.* **1995**, *60*, 6895. (f) Leadbeater, N. E.; Arvela, R. K. *J. Org. Chem.* **2003**, *68*, 9122.

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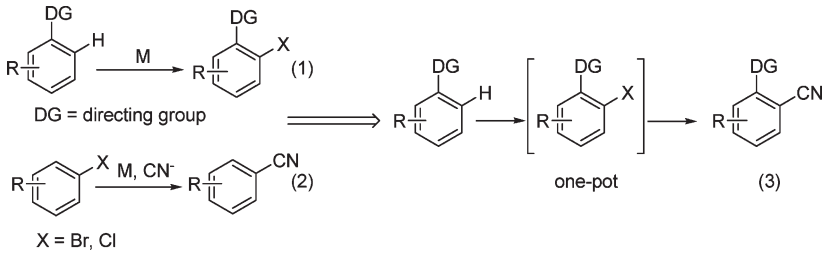
SCHEME 1. Path of Cascade Bromination/Cyanation Reaction

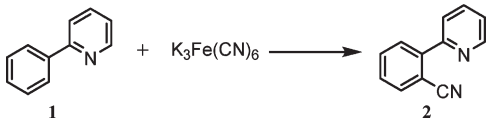


alternative to the standard coupling reactions. Over the past decades, extensive efforts have been directed toward C−C bond formation via C−H functionalization.[8] Nevertheless, to the best of our knowledge, few examples have been reported to access aromatic nitriles via C−H bond cleavage. In 2006, Yu developed the direct transformation of C−H bond to benzonitriles employing TMSCN or CH_3NO_2 as the cyanating reagent.[9] The application of NaCN in sp^3 C−H bond cyanation catalyzed by Ru was also demonstrated by Murahashi.[10] Recently, we reported a palladium-catalyzed direct cyanation of 2-arylpyridine C−H bonds with CuCN.[11] Considering the sensitivity of TMSCN to moisture and toxicity of MCN (M = Na, Cu), the use of less poisonous and easily handled cyanide sources in C−H bond cyanating reaction would be highly attractive. In light of the chelation-assisted transition-metal-catalyzed halogation of C−H developed by Sanford, Shi, and Yu[12] (Scheme 1, eq 1) and the transition-metal-catalyzed cyanation of aryl halides (Scheme 1, eq 2),[5−7] we envisioned accessing benzonitriles by a cascade halogation/cyanation of the C−H bond reaction using $K_3[Fe(CN)_6]$ (Scheme 1, eq 3). Herein, we report the chelation-assisted palladium-catalyzed cascade bromination/cyanation of 2-arylpyridine and 1-arylpyrazole C−H bonds employing $K_3[Fe(CN)_6]$ as a nontoxic and safe cyanating reagent.

Results and Discussion

Selected results for the cyanation of 2-phenylpyridine with $K_3[Fe(CN)_6]$ are shown in Table 1. During the screening of oxidants, we found that copper sources had a dramatic effect on the reaction. Among the Cu(II) tested, $CuBr_2$ was the best, and the yield was sharply increased to 90% by employing 1.0 equiv of $CuBr_2$ at 130 °C in DMF for 4 h (entry 3). Other oxidants, such as $CuSO_4$, $Cu(acac)_2$, Oxone, BQ, and $PhI(OAc)_2$, were almost totally ineffective for this transformation. No product could be detected in the absence of $Pd(OAc)_2$. The solvent also played an important role in the procedure. Other polar solvents such as DMSO and NMP, and low-polar solvents including toluene and xylene, inhibited the reaction (Table 1, entries 12−16). We reasoned that the concentration of CN^- in the solvent had a dramatic effect on the reaction, which caused the deactivation of the transition-metal catalyst by formation of too stable cyano complexes.[13] Importantly, due to the electron-withdrawing cyano group attached to the aryl ring, monocyanated product was obtained as a major product. The reaction conducted on a 1 mmol scale formed the cyanation product **2a** in 80% yield. Furthermore, this transformation is very practical as it does not require the use of strong bases or expensive ligands and the rigorous exclusion of air/moisture is not required.

TABLE 1. Optimization of Reaction Conditions[a]



1 2

entry	oxidant	solvent	yield(%)
1	CuF_2	DMF	< 5
2	$CuCl_2$	DMF	34
3	$CuBr_2$	DMF	90
4	$Cu(OAc)_2$	DMF	< 5
5	$Cu(OTf)_2$	DMF	22
6	$Cu(acac)_2$	DMF	< 5
7	$CuSO_4$	DMF	< 5
8	CuO	DMF	< 5
9	Oxone	DMF	< 5
10	BQ	DMF	< 5
11	$PhI(OAc)_2$	DMF	< 5
12	$CuBr_2$	DMSO	< 5
13	$CuBr_2$	DMP	< 5
14	$CuBr_2$	xylene	< 5
15	$CuBr_2$	toluene	< 5
16	$CuBr_2$	CH_3CN	11
17	$CuBr_2$	THF	13

[a] 2-Phenylpyridine (0.2 mmol), $K_3[Fe(CN)_6]$ (0.04 mmol), $Pd(OAc)_2$ (5 mol %), oxidant (1.0 equiv), dry solvent (1 mL), 130 °C, under air, 4 h.

With the optimized conditions in hand, the cyanations of 2-arylpyridines by $K_3[Fe(CN)_6]$ were tested, as shown in

(8) For selected reports on C−C bond formation via C−H functionalization, see: (a) Giri, R.; Yu, J.-Q. *J. Am. Chem. Soc.* **2008**, *130*, 14082. (b) Kalyani, D.; Deprez, N. R.; Desai, L. V.; Sanford, M. S. *J. Am. Chem. Soc.* **2005**, *127*, 7330. (c) Tsai, A. S.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2008**, *130*, 6316. (d) Norinder, J.; Matsumoto, A.; Yoshikai, N.; Nakamura, E. *J. Am. Chem. Soc.* **2008**, *130*, 5858. (e) Chiong, H. A.; Pham, Q.-N.; Daugulis, O. *J. Am. Chem. Soc.* **2007**, *129*, 9879. (f) Wen, J.; Zhang, J.; Chen, S.-Y.; Li, J.; Yu, X.-Q. *Angew. Chem., Int. Ed.* **2008**, *47*, 8897. (g) Wakui, H.; Kawasaki, S.; Satoh, T.; Miura, M.; Nomura, M. *J. Am. Chem. Soc.* **2004**, *126*, 8658. (h) Hennessy, E. J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2003**, *125*, 12084. (i) Ueda, S.; Nagasawa, H. *Angew. Chem., Int. Ed.* **2008**, *47*, 6411. (j) Deng, G. J.; Zhao, L.; Li, C.-J. *Angew. Chem., Int. Ed.* **2008**, *47*, 6278. (k) Seregin, I. V.; Ryabova, V.; Gevorgyan, V. *J. Am. Chem. Soc.* **2007**, *129*, 7742. (l) Kuninobu, Y.; Fujii, Y.; Matsuki, T.; Nishina, Y.; Takai, K. *Org. Lett.* **2009**, *11*, 2711. (m) Reddy, B. V. S.; Reddy, L. R.; Corey, E. J. *Org. Lett.* **2006**, *8*, 3391. (n) Lane, B. S.; Sames, D. *Org. Lett.* **2004**, *6*, 2897. (o) Jin, W.-W.; Yu, Z.-K.; He, W.; Ye, W.-J.; Xiao, W.-J. *Org. Lett.* **2009**, *11*, 1317.

(9) Chen, X.; Hao, X.-S.; Goodhue, C. E.; Yu, J.-Q. *J. Am. Chem. Soc.* **2006**, *128*, 6790.

(10) (a) Murahashi, S.-I.; Nakae, T.; Terai, H.; Komiya, N. *J. Am. Chem. Soc.* **2008**, *130*, 11005. (b) Murahashi, S.-I.; Komiya, N.; Terai, H. *Angew. Chem., Int. Ed.* **2005**, *44*, 6931.

(11) Jia, X.; Yang, D.; Zhang, S.; Cheng, J. *Org. Lett.* **2009**, *11*, 4716.

(12) (a) Kalyani, D.; Dick, A. R.; Anani, W. Q.; Sanford, M. S. *Org. Lett.* **2006**, *8*, 2523. (b) Wan, X. B.; Ma, Z. X.; Li, B. J.; Zhang, K. Y.; Cao, S. K.; Zhang, S. W.; Shi, Z. J. *J. Am. Chem. Soc.* **2006**, *128*, 7416. (c) Mei, T.-S.; Giri, R.; Maugel, N.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2008**, *47*, 5215.

(13) (a) Takagi, K.; Okamoto, T.; Sakakibara, Y.; Oka, S. *Chem. Lett.* **1973**, 471. (b) Sundermeier, M.; Zapf, A.; Mutyala, S.; Baumann, W.; Sans, J.; Weiss, S.; Beller, M. *Chem.—Eur. J.* **2003**, *9*, 1828. (c) See ref 5f.

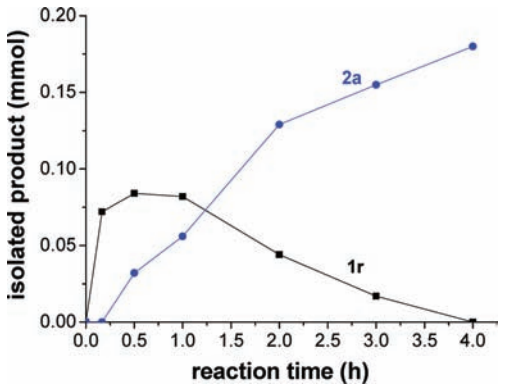


FIGURE 1. Distribution of the products along with the reaction time. Key: 2-Phenylpyridine (0.2 mmol), $K_3[Fe(CN)_6]$ (0.04 mmol), $Pd(OAc)_2$ (5 mol %), $CuBr_2$ (1.0 equiv), dry DMF (1 mL), 130 °C, under air. **2a**: 2-(pyridin-2-yl)benzonitrile. **1r**: 2-(2-bromophenyl)pyridine.

SCHEME 2. Preliminary Studies on the Mechanism

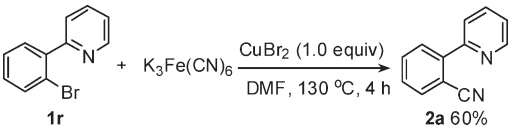
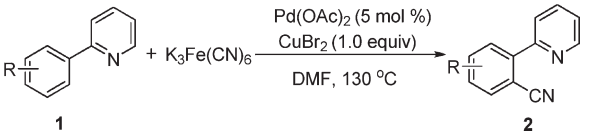


Table 2. As expected, a series of functional groups, including methoxy, chloro, fluoro, cyano, trifluoromethyl, and carbomethoxy, were compatible under this procedure, and the cyanation products were isolated in good yields (Table 2, entries 2−11). Generally, the reaction was not sensitive to the electronic properties of the substituents on the phenyl ring, as both electron-donating groups (Table 2, entries 2−6) and electron-withdrawing groups (Table 2, entries 7 and 9−11) could be employed in the reaction. Normally, the reaction could finish within 4−7 h for 2-arylpyridines. However, the hindrance on the aryl group of 2-arylpyridine had a slight effect on the reaction. For example, the *ortho*-substituted substrate **1d** delivered an 85% yield of **2d**, but prolonged time was required (4 days). Benzo[*h*]quinoline was subjected to the standard reaction condition, delivering the corresponding cyanation product in 54% yield. (Table 2, entry 12). 1-Arylpyrazoles were good reaction partners, and the cyanating products were isolated in moderate yields with elongated time, along with the recovered starting materials (Table 2, entries 13−17).

More experiments were carried out for better understanding of the mechanism. 2-(2-Bromophenyl)pyridine **1r** was detected during the reaction, and the molar quantities of **1r** and **2a** at different reaction times are outlined in Figure 1. 2-(2-Bromophenyl)pyridine **1r** may be the intermediate since the transformation of **1r** to **2a** was observed in Figure 1. In our previously reported direct cyanation of 2-arylpyridine C−H bonds, 24 h was required to ensure the completion of the reaction,[11] while 4 h was sufficient to finish the current reaction for 2-phenylpyridine. Further study revealed that $CuBr_2$ may facilitate reaction of **1r** with $K_3[Fe(CN)_6]$. The cyanating product **2a** was isolated in 60% yield even in the absence of palladium (Scheme 2). Moreover, during the screening of the optimized reaction conditions, $CuBr_2$, $CuCl_2$, and $Cu(OTf)_2$ also showed reactivity for the transformation,

(14) Yu, W.-Y.; Sit, W. N.; Lai, K.-M.; Zhou, Z.; Chan, A. S. C. *J. Am. Chem. Soc.* **2008**, *130*, 3304.

TABLE 2. Palladium-Catalyzed Bromination/Cyanation of 2-Arylpyridine and 1-Arylpyrazole C−H Bonds[a]



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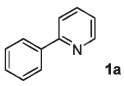
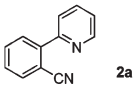
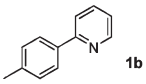
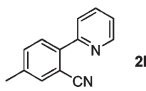
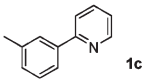
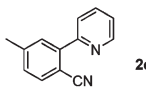
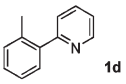
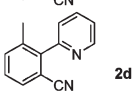
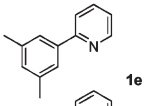
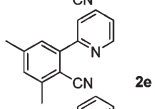
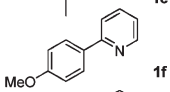
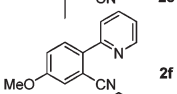
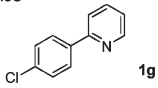
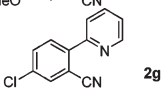
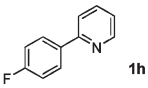
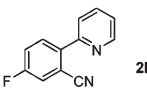
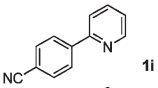
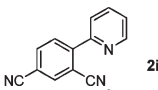
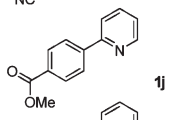
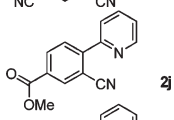
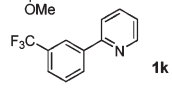
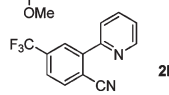
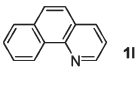
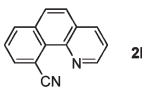
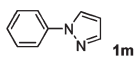
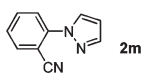
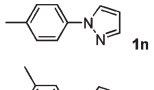
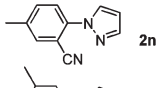
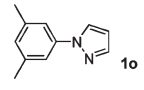
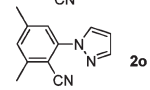
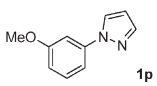
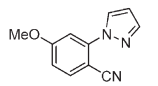
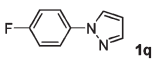
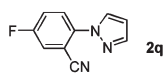
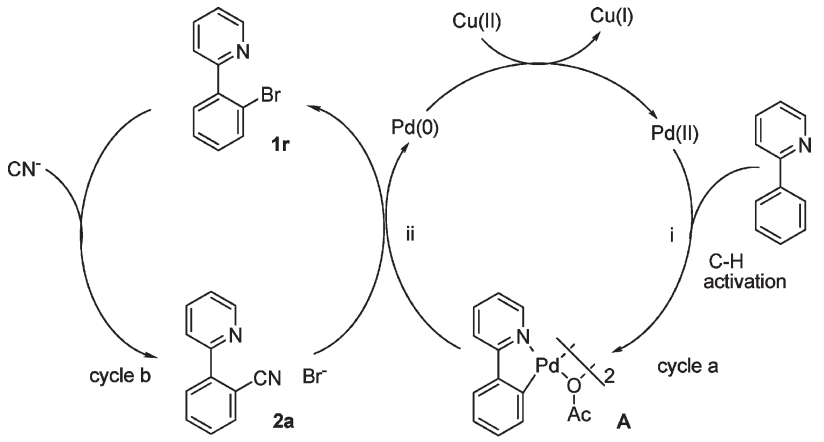
1	 1a	 2a	4 h	90
2	 1b	 2b	4 h	87
3	 1c	 2c	4 h	74
4	 1d	 2d	4 days	85
5	 1e	 2e	4 h	90
6	 1f	 2f	4 h	72
7	 1g	 2g	7 h	70
8	 1h	 2h	4 h	87
9	 1i	 2i	7 h	60
10	 1j	 2j	7 h	79
11	 1k	 2k	7 h	61
12	 1l	 2l	48 h	54
13	 1m	 2m	48 h	48
14	 1n	 2n	48 h	52
15	 1o	 2o	48 h	45
16	 1p	 2p	48 h	52
17	 1q	 2q	48 h	47

[a]Substrate **1** (0.2 mmol), $K_3[Fe(CN)_6]$ (0.04 mmol), $Pd(OAc)_2$ (5 mol %), $CuBr_2$ (1.0 equiv), dry DMF (1 mL), 130 °C.

SCHEME 3. Plausible Mechanism



ligand was omitted for clarity

while other Cu(II) sources and oxidants were totally ineffective. In the case of using $CuCl_2$ as the stoichiometric additive, the chlorination product 2-(2-chlorophenyl)pyridine was also detected. These results favored the possibility of a tandem C−H bond bromination/cyanation pathway.

On the basis of these experimental results, a plausible mechanism is outlined in Scheme 3. Step i in cycle a involves the chelate-directed C−H activation of 2-phenylpyridine to afford a cyclopalladated intermediate **A**.[14] Step ii of the proposed catalytic cycle involves carbon−bromine bond-formation via reductive elimination to deliver the bromination intermediate **1r** along with a Pd(0) species, which is oxidized to Pd(II) by Cu(II). In cycle b, the intermediate **1r** delivers the cyanation product catalyzed by copper and palladium. It should be noted that a mechanism of direct cyanation could not be completely excluded.

Conclusions

In conclusion, we have demonstrated an efficient palladium-catalyzed cascade bromination/cyanation reaction of 2-arylpyridine and 1-arylpyrazole C−H bonds. Importantly, the reaction employs $K_3[Fe(CN)_6]$ as an inexpensive and nontoxic cyanide source. Furthermore, this transformation is very practical, and a series of functional groups could be tolerated. As such, it represents a novel and simple method to access aromatic nitriles.

Experimental Section

General Procedure for the Bromination/Cyanation Reaction. A Schlenk reaction tube was charged with 2-arylpyridine (0.2 mmol), $K_3[Fe(CN)_6]$ (13.2 mg, 0.04 mmol), $Pd(OAc)_2$ (2.2 mg, 10 mol %), $CuBr_2$ (44.6 mg, 1.0 equiv), and dry DMF (1 mL). The mixture was allowed to stir at 130 °C in the sealed Schlenk tube. After completion of the reaction, as monitored by TLC, brine was added (10 mL), and the reaction mixture was extracted with ethyl acetate (3 × 5 mL). The ethyl acetate extracts were concentrated in vacuo, and the residue was purified by flash column chromatography on a silica gel (eluting with ethyl acetate, petroleum ether, and Et_3N) to give the product.

2-(Pyridin-2-yl)benzonitrile (2a):[9] colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.77 (d, J = 4.7 Hz, 1H), 7.84−7.75 (m, 4H), 7.71- 7.68 (m, 1H), 7.52−7.49 (m, 1H), 7.36−7.34 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 154.9, 149.6, 143.1, 136.6, 133.9, 132.6, 129.7, 128.5, 123.1, 122.9, 118.5, 110.7; R_f = 0.31, in 1:5:0.06 EA/PE/Et_3N.

5-Methyl-2-(pyridin-2-yl)benzonitrile (2b):[11] white solid; mp 62−63 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.76−8.74 (m, 1H), 7.81−7.72 (m, 3H), 7.59 (s, 1H), 7.50−7.47 (m, 1H), 7.33−7.32 (m, 1H), 2.43 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 155.2, 149.7, 140.6, 139.0, 136.7, 134.3, 133.7, 129.8, 123.0, 123.0, 118.8, 110.7, 20.8; R_f = 0.32, in 1:5:0.06 EA/PE/Et_3N.

4-Methyl-2-(pyridin-2-yl)benzonitrile (2c):[11] white solid; mp 54−55 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.76 (d, J = 4.5 Hz, 1H), 7.85−7.76 (m, 2H), 7.69−7.66 (m, 2H), 7.36−7.29 (m, 2H), 2.47 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 155.2, 149.7, 143.7, 143.2, 136.7, 133.8, 130.6, 129.4, 123.2, 123.1, 118.8, 107.8, 21.7. R_f = 0.36, in 1:5:0.06 EA/PE/Et_3N.

3-Methyl-2-(pyridin-2-yl)benzonitrile (2d):[11] colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.76 (d, J = 4.6 Hz, 1H), 7.84−7.81 (m, 1H), 7.60 (d, J = 7.7 Hz, 1H), 7.51 (d, J = 7.7 Hz, 1H), 7.50−7.34 (m, 3H), 2.23 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.0, 149.7, 143.5, 137.7, 136.6, 134.7, 130.5, 128.4, 124.5, 123.0, 118.1, 112.6, 20.0; R_f = 0.28, in 1:5:0.06 EA/PE/Et_3N.

2,4-Dimethyl-6-(pyridin-2-yl)benzonitrile (2e):[11] colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.74 (d, J = 4.8 Hz, 1H), 7.83−7.71 (m, 2H), 7.41 (s, 1H), 7.34−7.30 (m, 1H), 7.18 (s, 1H), 2.58 (s, 3H), 2.41 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 155.8, 149.6, 143.8, 143.0, 136.5, 130.7, 128.0, 123.4, 123.3, 123.0, 117.7, 108.0, 21.5, 20.8; R_f = 0.38, in 1:5:0.06 EA/PE/Et_3N.

5-Methoxy-2-(pyridin-2-yl)benzonitrile (2f):[11] white solid; mp 102−103 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.74 (d, J = 4.8 Hz, 1H), 7.80−7.73 (m, 3H), 7.32−7.19 (m, 3H), 3.88 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 159.5, 154.9, 149.7, 136.7, 136.0, 131.3, 122.8, 122.8, 119.3, 118.6, 118.4, 111.7, 55.7; R_f = 0.24, in 1:5:0.06 EA/PE/Et_3N.

5-Chloro-2-(pyridin-2-yl)benzonitrile (2g):[11] white solid; mp 165−166 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.77 (d, J = 4.8 Hz, 1H), 7.84−7.76 (m, 4H), 7.67−7.64 (m, 1H), 7.38−7.36 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 154.0, 150.0, 141.7, 136.9, 134.9, 133.5, 133.1, 131.2, 123.5, 123.0, 117.4, 112.3; R_f = 0.25, in 1:5:0.06 EA/PE/Et_3N.

5-Fluoro-2-(pyridin-2-yl)benzonitrile (2h):[11] white solid; mp 129−130 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.74 (d, J = 4.3 Hz, 1H), 7.85−7.72 (m, 3H), 7.49−7.46 (m, 1H), 7.39−7.35 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.4 (d, J_{C-F} = 250.2 Hz), 154.0, 149.8, 139.8, 136.9, 132.0 (d, J_{C-F} = 8.3 Hz), 123.2 (d, J_{C-F} = 25.3 Hz), 120.7 (d, J_{C-F} = 16.1 Hz), 120.5, 120.3, 117.4, 112.2; R_f = 0.31, in 1:5:0.06 EA/PE/Et_3N.

4-(Pyridin-2-yl)isophthalonitrile (2i):[11] white solid; mp 155−156 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.82 (d, J = 4.7 Hz, 1H), 8.09−7.84 (m, 5H), 7.46−7.44 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 153.2, 150.3, 147.0, 137.4, 137.2, 135.7, 131.0, 124.4, 123.4, 116.7, 116.6, 113.2, 112.5; R_f = 0.21, in 1:5:0.06 EA/PE/Et_3N.

Methyl 3-cyano-4-(pyridin-2-yl)benzoate (2j): white solid; mp 102−103 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.82−8.80 (m, 1H), 8.47 (d, J = 1.5 Hz, 1H), 8.34−8.31 (m, 1H), 7.97−7.94 (m, 1H), 7.88−7.85 (m, 2H), 7.43−7.41 (m, 1H), 3.99 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.9, 154.2, 150.0, 146.9, 136.9, 135.3, 133.4, 130.7, 130.2, 123.8, 123.3, 117.8, 111.4, 52.6; IR (prism, cm^{-1}) 2956, 2228, 1725, 1607, 1585, 1573, 1464, 1434; MS(EI) m/z 238 (M^+); HRMS calcd for $C_{14}H_{10}N_2NaO_2$ $(M + Na)^+$ 261.0640, found 261.0634; R_f = 0.21, in 1:5:0.06 EA/PE/Et_3N.

2-(Pyridin-2-yl)-4-(trifluoromethyl)benzonitrile (2k): white solid; mp 140−141 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.81 (d, J = 4.8 Hz, 1H), 8.06−8.01 (m, 2H), 7.95−7.82 (m, 3H), 7.44−7.40 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 151.9 (q, J_{C-F} = 269.2 Hz), 146.3, 137.2, 131.6, 131.0 (q, J_{C-F} = 3.9 Hz), 130.7 (q, J_{C-F} = 6.1 Hz), 129.5 (q, J_{C-F} = 3.5 Hz), 128.3, 124.4 (q, J_{C-F} = 44.2 Hz), 123.4, 121.1, 117.3, 111.9; IR (prism, cm^{-1}) 2923, 2230, 1610, 1585, 1460, 1426; MS(EI) m/z 248 (M^+); HRMS calcd for $C_{13}H_8F_3N_2$ $(M + H)^+$ 249.0640, found 249.0634; R_f = 0.21, in 1:5:0.06 EA/E/Et_3N.

Benzo[*h*]quinoline-10-carbonitrile (2l):[11] white solid; mp 132−133 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.11 (dd, J = 4.3, 1.7 Hz, 1H), 8.20 (d, J = 8.1 Hz, 1H), 8.12−8.08 (m, 2H), 7.79−7.71 (m, 3H), 7.63−7.61 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 148.4, 144.4, 136.2, 135.6, 134.0, 132.7, 130.7, 127.3, 127.2, 127.0, 126.9, 123.0, 120.7, 108.9; R_f = 0.26, in 1:5:0.06 EA/PE/Et_3N.

2-(1*H*-Pyrazol-1-yl)benzonitrile (2m):[15] colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.14 (d, J = 2.4 Hz, 1H), 7.82−7.77 (m, 3H), 7.73−7.71 (m, 1H), 7.46−7.43 (m, 1H), 6.56−6.54 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 142.2, 142.0, 134.4, 134.0, 129.5, 127.2, 124.2, 116.9, 108.4, 105.3; R_f = 0.42, in 1:5:0.06 EA/PE/Et_3N.

5-Methyl-2-(1*H*-pyrazol-1-yl)benzonitrile (2n):[11] white solid; mp 65−66 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.08 (d, J = 2.5 Hz, 1H), 7.79 (d, J = 1.5 Hz, 1H), 7.66 (d, J = 8.4 Hz, 1H), 7.56 (s, 1H), 7.49 (dd, J = 8.4, 1.5 Hz, 1H), 6.53 (t, J = 2.2 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 141.9, 139.9, 137.6, 134.8, 134.4, 129.5, 124.3, 117.0, 108.2, 105.2, 20.6; R_f = 0.4, in 1:5:0.06 EA/PE/Et_3N.

2,4-Dimethyl-6-(1*H*-pyrazol-1-yl)benzonitrile (2o): colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.08 (d, J = 2.5 Hz, 1H), 7.78 (d, J = 1.6 Hz, 1H), 7.38 (s, 1H), 7.12 (s, 1H), 6.52−6.51 (m, 1H), 2.58 (s, 3H), 2.42 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 144.5, 143.8, 142.4, 141.8, 129.8, 129.5, 122.7, 116.1, 107.9, 103.5, 21.6, 20.9; IR (prism, cm^{-1}) 2922, 2221, 1612, 1569, 1540, 1465; MS(EI) m/z 197 (M^+); HRMS (EI) calcd for $C_{12}H_{11}N_3$ (M^+) requires 197.0953, found 197.0953; R_f = 0.43, in 1:5:0.06 EA/PE/Et_3N.

3-Methoxy-2-(1*H*-pyrazol-1-yl)benzonitrile (2p): white solid; mp 66−67 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.20 (d, J = 2.5 Hz, 1H), 7.79 (d, J = 1.3 Hz, 1H), 6.66 (d, J = 8.7 Hz, 1H), 7.33 (d, J = 2.5 Hz, 1H), 6.92 (dd, J = 8.7, 2.5 Hz, 1H), 6.54−6.53 (m, 1H), 3.92 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 163.7, 143.8, 142.1, 135.6, 129.6, 117.5, 113.9, 109.2, 108.4, 96.4, 55.9; IR (prism, cm^{-1}) 2923, 2222, 1607, 1574, 1522, 1498; MS(EI) m/z 199 (M^+); HRMS (EI) calcd for $C_{11}H_9N_3O$ (M^+) requires 199.0746, found 199.0747; R_f = 0.38, in 1:5:0.06 EA/PE/Et_3N.

5-Fluoro-2-(1*H*-pyrazol-1-yl)benzonitrile (2q): white solid; mp 99−100 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.07 (d, J = 2.5 Hz, 1H), 7.81−7.75 (m, 2H),7.50−7.41 (m, 2H), 6.56−6.54 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 160.3 (d, J_{C-F} = 248.8 Hz), 142.3, 138.8, 129.6, 126.6 (d, J_{C-F} = 8.8 Hz), 121.6 (d, J_{C-F} = 22.5 Hz), 120.6 (d, J_{C-F} = 26.3 Hz), 115.6, 108.6, 106.8; IR (prism, cm^{-1}) 3039, 2922, 2232, 1527, 1495, 1442, 1404; MS(EI) m/z 187 (M^+); HRMS (EI) calcd for $C_{10}H_6FN_3$(M^+) requires 187.0546, found 187.0546; R_f = 0.41, in 1:5:0.06 EA/E/Et_3N.

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Supporting Information Available: Experimental procedures along with copies of spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

(15) Hoz, A. D. L.; Díaz-Ortiz, A.; Elguero, J.; Martínez, L. J.; Moreno, A.; Sánchez-Migallón, A. *Tetrahedron* **2001**, *57*, 4397.