C–C activation |*Hot Paper*|

Cu-Catalyzed Cyanation of Arylboronic Acids with Acetonitrile: A Dual Role of TEMPO**

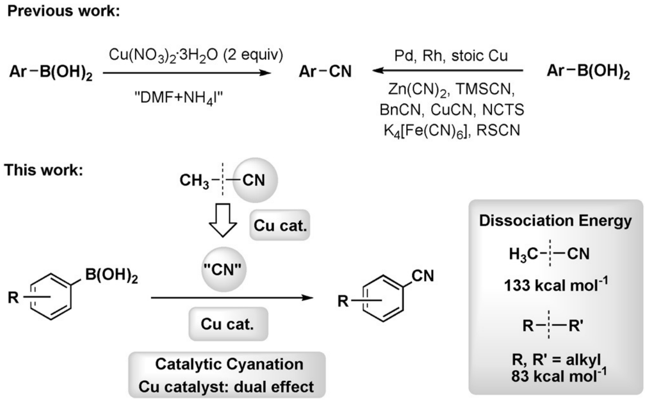
Yamin Zhu, Linyi Li, and Zengming Shen*[a]

Abstract: The cyanation of arylboronic acids by using acetonitrile as the “CN” source has been achieved under a Cu(cat.)/TEMPO system (TEMPO = 2,2,6,6-tetramethylpiperidine *N*-oxide). The broad substrate scope includes a variety of electron-rich and electron-poor arylboronic acids, which react well to give the cyanated products in high to excellent yields. Mechanistic studies reveal that TEMPO–CH_2CN, generated in situ, is an active cyanating reagent, and shows high reactivity for the formation of the CN^- moiety. Moreover, TEMPO acts as a cheap oxidant to enable the reaction to be catalytic in copper.

Introduction

The activation of C–C bonds is an appealing, yet challenging, strategy in modern organic chemistry that provides a novel and direct process for cross-coupling.[1] Acetonitrile is a common solvent that shows weak coordination to metal centers and is typically inert in transition-metal-catalyzed coupling reactions owing to a high CH_3–CN bond dissociation energy (133 kcal mol^{-1}), relative to alkane C–C bonds (ca. 83 kcal mol^{-1}) (Scheme 1). Consequently, catalytic activation of the acetonitrile C–CN bond by transition metals has rarely been explored.[2] A few examples of cyanation by employing the relatively safe acetonitrile as the cyano source have been documented by Cheng, Li, Zhu, Shen, and others.[3,4] Recently, we disclosed the Cu-catalyzed cyanation of aromatic C–H bonds through CH_3–CN bond cleavage, in which disilane plays a crucial role in promoting acetonitrile cleavage.[4] Herein, we describe the catalytic cyanation of boronic acids by using acetonitrile as an attractive cyano source. This strategy avoids the use of highly toxic metal cyanides and occurs through a novel mechanism for cross-coupling.

Arylboronic acids are readily available and easy-to-handle coupling partners in metal-catalyzed coupling reactions.[5–8] However, to the best of our knowledge, there are only a few examples regarding the transformation of arylboronic acids into aryl nitriles, which use Pd,[9a–b] Rh,[9c] or Cu[10] catalysts or stoichiometric promoters. In these procedures, metal cyanides (e.g., $Zn(CN)_2$, $K_4[Fe(CN)_6]$, CuCN, CuSCN) or specific organic cyanides (e.g., TMSCN, BnCN, NCTS, RSCN) were used as the cyanating agent. Identifying ways to generate “CN” in situ from simple and readily available reagents by a combination process is a highly attractive strategy. Since Chang’s pioneering discovery, there have been notable advances in this area;[8d,11–14] however, the main problem with these procedures is that superstoichiometric amounts of copper species were required. In 2012, Chang and co-workers developed a procotol for the cyanation of arylboronic acids by using a NH_4I/DMF combination;[10c] wherein, stoichiometric amounts of $Cu(NO_3)_2\cdot 3H_2O$ were needed (Scheme 1). More recently, advances have been made by Li,[3b] Zhu,[3c] and Chang,[11d] in the catalytic cyanation of aryl iodides and arenes by using a catalytic Cu species combined with a stoichiometric oxidant, Ag_2O or Ag_2CO_3. Although, silver salts are generally more expensive than copper species.



Scheme 1. Catalytic cyanation strategy using acetonitrile as the “CN” source.

As an alternative to metal oxidants, TEMPO (2,2,6,6-tetramethylpiperidine *N*-oxide) is a persistent nitroxide radical that has found widespread application in organic synthesis. Along with its use as a radical trapping reagent, TEMPO has been used as a mild oxidant in transition-metal-catalyzed coupling reactions.[15] Recently, we revealed that TEMPO can be used as

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[**] *TEMPO = 2,2,6,6-tetramethylpiperidine* N-oxide

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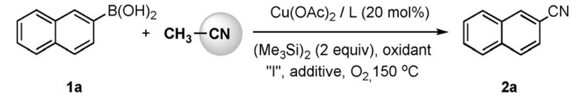
an oxidant in the cyanation reaction to allow the use of catalytic amounts of the Cu species.[4b] All of these studies inspired us to achieve the Cu-catalyzed cyanation of arylboronic acids by using CH_3CN as the "CN" source. Subsequent mechanistic studies have gained insight into the activation of the C–C bond in acetonitrile.

Results and Discussion

To test the Cu-catalyzed cyanation of arylboronic acids with acetonitrile, we used 2-naphthyl boronic acid (**1a**) as a model substrate. Based on conditions that we previously optimized for the cyanation of C–H bonds by using CH_3CN,[4] compound **1a** was first treated with $Cu(OAc)_2$/bathophenanthroline (**L2**) (20 mol%) and $(Me_3Si)_2$ (2 equiv) in CH_3CN under an oxygen atmosphere at 150 °C, but none of the desired product **2a** was observed (Table 1, entry 1). In contrast, the fast protonolysis of **1a** occurred to yield the deboronated naphthalene product. To avoid this side reaction, we envisioned a strategy that involved a sequential iodination/cyanation of arylboronic acids in one pot. Therefore, a wide range of oxidants were examined in the presence of I_2.[16] To our delight, TEMPO was the best oxidant, which gave the corresponding cyanated product **2a** in 50% yield (Table 1, entry 8). In contrast, Ag_2CO_3 only gave 19% yield of **2a** (Table 1, entry 2), and oxone, BQ, TBHP, and benzoic peroxyanhydride showed even poorer reactivity (Table 1, entries 3–6). With TEMPO as an oxidant, we switched from I_2 to NIS, and observed the yield **2a** increase to 65% (Table 1, entry 9). To further enhance the yield, various additives were tested. Gratifyingly, an 88% yield of **2a** was observed when using *i*Pr_2NH as an additive (Table 1, entry 11). Other additives, such as Cs_2CO_3, TMEDA, DBU, and H_2O, also efficiently gave the product **2a** in 59–80% yield (Table 1, entries 10, 12–14). When *i*Pr_2NH and H_2O were used as additives, we considered that they might combine with the boronic compound that is released from substrate **1a**, which would drive the cyanation reaction forward and result in a higher yield of the product. By varying the ligand, we found that the use of catalyst $Cu(OAc)_2$/1,10-phenanthroline (1,10-phen, **L4**) in acetonitrile afforded optimal results (Figure 1). Under these conditions, the cyanated product **2a** was formed in quantitative yield. Other copper complexes, such as $Cu(ClO_4)_2{\cdot}6H_2O$, $Cu(NO_3)_2{\cdot}3H_2O$, and $Cu(OTf)_2$, also worked well as catalysts for this transformation, which gave **2a** in 88, 92, and 78% yields, respectively. In addition, a series of control experiments were carried out, which suggest that disilane is essential for the C–CN cleavage (see the Supporting Information, Table S1).

Next, we investigated the scope of the reaction by varying the substituent on the arylboronic acid (Table 2). A variety of arylboronic acids **1b–g** with electron-donating groups (R = Me, OMe, OBn, *t*Bu, respectively) on the aryl ring furnished the corresponding products **2b–g** in 71–97% yields (Table 2, entries 1–6). More electron-rich boronic acids **1o–1q**, which contained two electron-donating substituents, worked more efficiently to give the products **2o–q** in 81–99% yields (Table 2, entries 14–16). Additionally, it was observed that electron-withdrawing substituents (R = 4-OCF_3, 4-CF_3, 4-COOMe, 4-F) were tolerated under the reaction conditions; however, the corresponding products **2j–l,r** were afforded in lower yields (Table 2, entries 9–11 and 17). Notably, the substrate **1n**, which contained a strongly electron-withdrawing NO_2 group, per-

Table 1. Optimization of conditions for arylboronic acid cyanation using CH_3CN.[a]



1a
2a

Entry	[I] source	Additive (1 equiv)	Oxidant	*t* [h]	Yield [%][b]
1	none	–	–	48	–
2	I_2 (0.6 equiv)	–	Ag_2CO_3 (1 equiv)	72	19
3	I_2 (0.6 equiv)	–	oxone (1 equiv)	72	13
4	I_2 (0.6 equiv)	–	BQ (1 equiv)	72	33
5	I_2 (0.6 equiv)	–	TBHP (1 equiv)	72	2
6	I_2 (0.6 equiv)	–	benzoic peroxy anhydride (1 equiv)	72	3
7[c]	I_2 (0.6 equiv)	–	TEMPO (2 equiv)	72	34
8	I_2 (0.6 equiv)	–	TEMPO (2 equiv)	72	50
9	NIS (1.1 equiv)	–	TEMPO (2 equiv)	58	65[d]
10	NIS (1.1 equiv)	Cs_2CO_3	TEMPO (2 equiv)	48	59
11	NIS (1.1 equiv)	*i*Pr_2NH	TEMPO (2 equiv)	48	88
12	NIS (1.1 equiv)	TMEDA	TEMPO (2 equiv)	48	78
13	NIS (1.1 equiv)	DBU	TEMPO (2 equiv)	48	78
14	NIS (1.1 equiv)	H_2O	TEMPO (2 equiv)	48	80

[a] Conditions: **1a** (0.2 mmol), $Cu(OAc)_2$ (20 mol%), **L2** (20 mol%), iodine source, $(Me_3Si)_2$ (2 equiv), TEMPO (2 equiv), additive, O_2, 150 °C. [b] Yield of isolated product **2a**. [c] Using **L1** as the ligand (20 mol%). [d] GC yield using dodecane as internal standard.

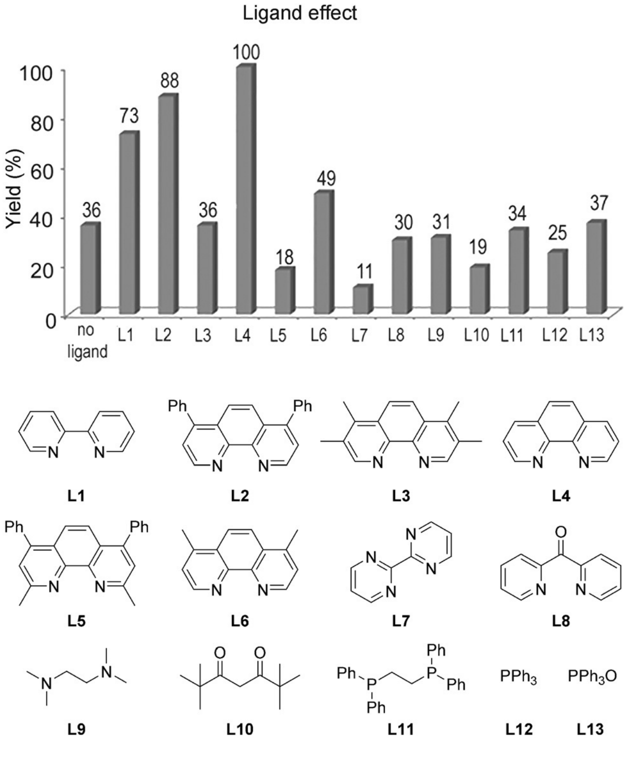
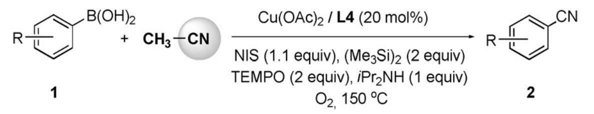
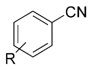
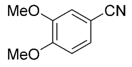
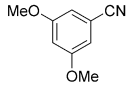
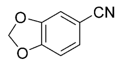
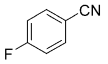
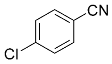
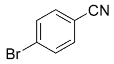
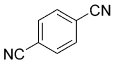
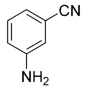
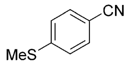
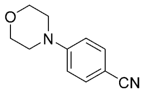
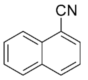
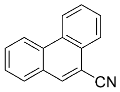


Figure 1. Effect of ligands in the cyanation of arylboronic acids by using CH_3CN.

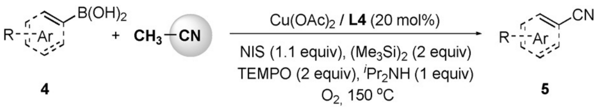
Table 2. Scope of substrates in the Cu-catalyzed arylboronic acid cyanation using CH_3CN.[a]

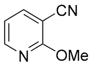


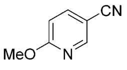
Entry	Arylnitrile		Yield [%][b]
1	 R = 4-Me	(**2b**)	74
2	R = 2-OMe	(**2c**)	85
3	R = 3-OMe	(**2d**)	85
4	R = 4-OMe	(**2e**)	96
5	R = 4-OBn	(**2f**)	71
6	R = 4-*t*-Bu	(**2g**)	97
7	R = 4-vinyl	(**2h**)	58
8	R = 4-phenyl	(**2i**)	86
9	R = 4-OCF_3	(**2j**)	53
10	R = 4-CF_3	(**2k**)	29
11	R = 4-COOMe	(**2l**)	53
12	R = 4-CN	(**2m**)	78
13	R = 3-NO_2	(**2n**)	>99
14		(**2o**)	>99
15		(**2p**)	81
16		(**2q**)	86
17		(**2r**)	46
18		(**2s**)	74
19		(**2t**)	21[c]
20		(**2m**)	90[d]
21		(**2u**)	48
22		(**2v**)	97
23		(**2w**)	57
24		(**2x**)	87
25		(**2y**)	90

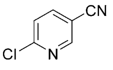
[a] Conditions: **1** (0.2 mmol), $Cu(OAc)_2$ (20 mol%), **L4** (20 mol%), NIS (1.1 equiv), $(Me_3Si)_2$ (2 equiv), TEMPO (2 equiv), *i*Pr_2NH (1 equiv), O_2, 150 °C, 2–3 days. [b] Yield of isolated product **2**. [c] Using (4-bromophenyl)boronic acid **1t** as substrate; 66% yield of **2m** was obtained in this reaction through the change of bromide to iodide. [d] Using (4-iodophenyl)boronic acid as substrate, TEMPO (4 equiv).

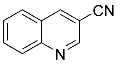
Table 3. Scope of heteroarylboronic acids in the Cu-catalyzed cyanation using CH_3CN.[a,b]

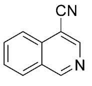


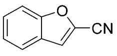

63% (**5a**)

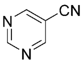

81% (**5b**)

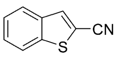

56% (**5c**)

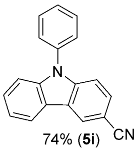

88% (**5d**)

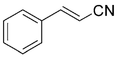

52% (**5e**)


25% (**5f**)


10% (**5g**)


58% (**5h**)


74% (**5i**)


62% (**5j**)

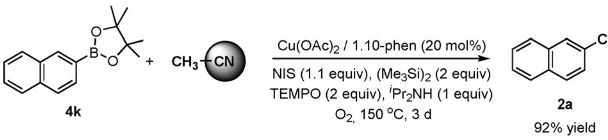
[a] Conditions: **4** (0.2 mmol), $Cu(OAc)_2$ (20 mol%), **L4** (20 mol%), NIS (1.1 equiv), $(Me_3Si)_2$ (2 equiv), TEMPO (2 equiv), *i*Pr_2NH (1 equiv), O_2, 150 °C, 2–3 days. [b] Yield of isolated product **5**.

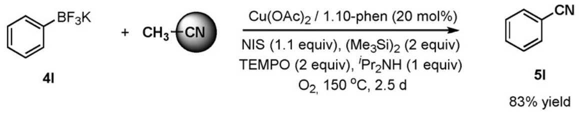
formed well and underwent complete conversion to the product **2n** (>99% yield, Table 2, entry 13). The versatile 4-CN (**1m**) and 4-Cl (**1s**) functional groups were well-tolerated and can be used as synthetic handles for various applications (Table 2, entries 12 and 18). The compatibility of this reaction was further extended to free vinyl (**1h**), NH_2 (**1u**), sulfide (**1v**), and morpholine (**1w**) functional groups on the aromatic ring, which gave the desired products in 48–97% yields (Table 1, entries 7 and 21–23). Fused phenanthrene-based boronic acid **1y** produced the corresponding product **2y** in 90% yield (Table 2, entry 25).

Encouraged by the broad scope of substituted phenyl boronic acid substrates in this reaction, we tested various heteroarylboronic acids under the Cu/TEMPO catalytic conditions with acetonitrile. As shown in Table 3, 3-pyridyl boronic acids **4a–c**, which contain 2-OMe, 6-OMe, and 6-Cl substituents, respectively, gave 3-cyano pyridines **5a–c** in good yields. Other heterocyclic boronic acids, including quinoline (**4d**), isoquinoline (**4e**), pyrimidine (**4f**), benzofuran (**4g**), benzothiophene (**4h**), and 9-phenyl-9*H*-carbazole (**4i**), reacted under these conditions to furnish the corresponding products in 10-88% yields. In addition, alkenyl boronic acid **4j** could smoothly reacted to give the cinnamonitrile **5j** in 62% yield.

Besides arylboronic acids, arylboronic esters and borate salts, such as potassium trifluoroborates, are both attractive classes of air-stable and easy-to-handle coupling reagents.[5] Under the optimal reaction conditions, widely-used boronic ester **4k** and borate salt **4l** were smoothly transformed into the corresponding cyanated products **2a** and **5l** in 92 and 83% yields, respectively [Eq. (1)–(2)]. In addition, 2-iodonaphthalene **3a** was subjected to the standard reaction conditions to test the reactivity of aryl iodide substrates in this cyanation reaction, and the corresponding cyanated product **2a** was afforded in 92% yield [Eq. (3)]. Overall, these results demonstrate that this methodology is a general and suitable approach for the cyanation of arylboronic acids, arylboronic esters, borate salts, and aryl iodides.

Next, we tested pentanenitrile (1 °CN), isobutyronitrile (2 °CN), and pivalonitrile (3 °CN) as alternative cyano sources





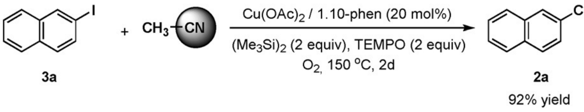
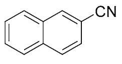
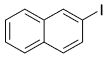
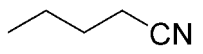
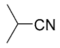
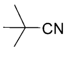


Table 4. Other alkylnitriles as "CN" source.[a]

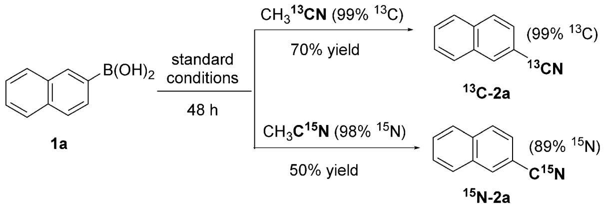
Other nitriles	Product yield [%]	
	 **2a**	 **3a**
	53	43
	27	75
	trace	80

[a] Under the standard conditions.

(Table 4). The experimental results revealed that the long chain primary nitrile, pentanenitrile, gave the cyanated product **2a** with an efficiency comparable to acetonitrile. Whereas, the secondary nitrile, isobutyronitrile, had lower efficiency in this system, and the more bulky tertiary nitrile, pivalonitrile, hardly reacted under the standard conditions. This trend indicates that the steric demand of the nitrile has a critical effect on the C–CN bond scission.

Isotope labeling study

To understand the mechanism of the Cu/TEMPO system for catalytic arylboronic acid cyanation, a series of mechanistic studies were executed. Labeling experiments were performed with both $CH_3{}^{13}CN$ and $CH_3C^{15}N$, and in both cases nearly complete isotopic incorporation into the cyano moiety of the product was observed (Scheme 2). This result indicates that the cyano group in product **2a** originates from the acetonitrile through C–CN bond cleavage.



Scheme 2. Isotope labeling experiments.

Reaction profile

A reaction profile was obtained for the Cu-catalyzed cyanation of **1a** under the standard conditions. We found that the iodination product **3a** was formed in almost quantitative yield within 30 min.[16] Subsequently, the cyanated product **2a** was gradually produced from **3a** over 48 h (Figure 2). Therefore, the iodination strategy plays a significant role in the cyanation of arylboronic acids.

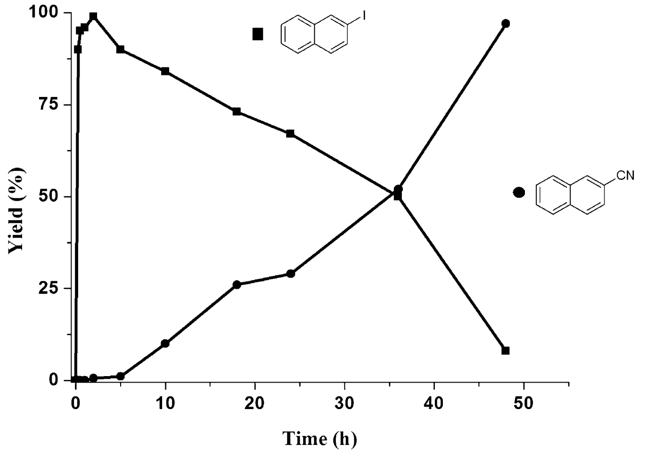


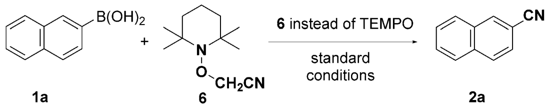
Figure 2. Reaction profile using **1a** as the model substrate.

Investigating the role of TEMPO

A key intermediate, TEMPO–CH_2CN (**6**), was isolated and confirmed by NMR spectroscopy and HRMS. Consequently, a series of experiments, which employed **6** in place of TEMPO, were executed. As displayed in Table 5, naphthalen-2-ylboronic acid **1a** reacted with **6** smoothly to give the cyanated product **2a** in 98% yield under O_2 and 95% yield under N_2 (Table 5, entries 1 and 4). In contrast, during optimization of the reaction conditions (Table S1, entry 7), we found that oxygen was essential for the cyanation of arylboronic acids with acetonitrile. Therefore, we propose that oxygen most likely enables the formation of **6**. Next, an experiment was designed to test the hypothesis that **6** is the active cyanating agent: the reaction was carried out in 1,4-dioxane, and **6** was used instead of TEMPO (Table 5, entry 2). Incredibly, a 33% yield of cyanated product **2a** was obtained. These studies support the proposal that intermediate **6** is indeed the direct supplier of the "CN" unit as well as being the oxidant for catalytic cyanation. Accordingly, TEMPO exhibits a dual role in this reaction: firstly, in the generation of the active cyanating agent, and secondly, as an oxidant in this catalytic cyanation. However, 2 equivalents of **6** are necessary for this reaction because **6** appears to decompose to other compounds (Table 5, entry 3).

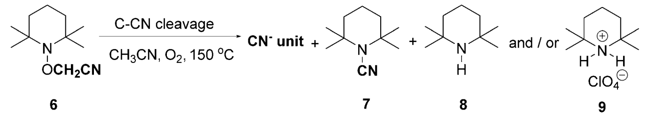
Subsequently, we investigated the C–CN cleavage[17] in TEMPO–CH_2CN (**6**) (Table 6). As aforementioned, other copper salts can be used as efficient catalysts for this transformation.

Table 5. Cyanation using **6** instead of TEMPO.



Entry	Conditions	Yield **2a** [%]
1	2 equiv **6** under O_2	98
2	2 equiv **6** using 1,4-dioxane as sol. under O_2	33
3	1 equiv **6** under O_2	55
4	2 equiv **6** under N_2	95

Table 6. Detection of CN^- by using indicator paper.[a]



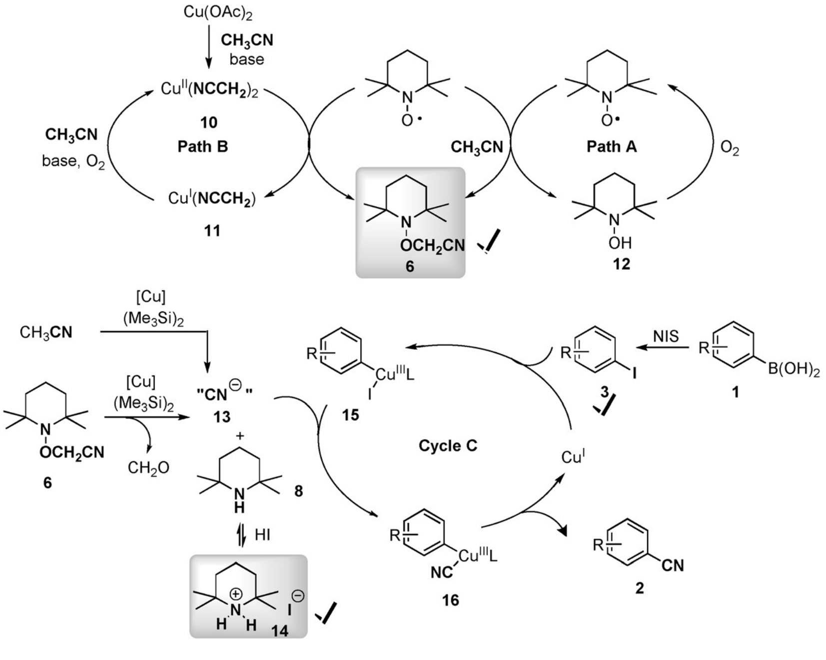
Entry	[Cu]/1,10-phen	$(Me_3Si)_2$	CN^-
1[b]	none	none	no
2	$Cu(OAc)_2$/1,10-phen (20 mol%)	none	yes
3	$Cu(NO_3)_2 \cdot 3H_2O$/1,10-phen (20 mol%)	none	yes
4	$Cu(OTf)_2$/1,10-phen (20 mol%)	none	yes
5	$Cu(ClO_4)_2 \cdot 6H_2O$/1,10-phen (20 mol%)	none	yes
6	$Cu(OAc)_2$/1,10-phen (20 mol%)	1 equiv	yes
7	$Cu(ClO_4)_2 \cdot 6H_2O$/1,10-phen (20 mol%)	1 equiv	yes
8	$Cu(ClO_4)_2 \cdot 6H_2O$/1,10-phen (1 equiv)	1 equiv	yes
9	none	1 equiv	yes

[a] CN^- was detected according to the reported procedure by Sukbok Chang[10c] and Jiang Cheng[11f]. [b] Starting material was stable without any conversion during 48 h.

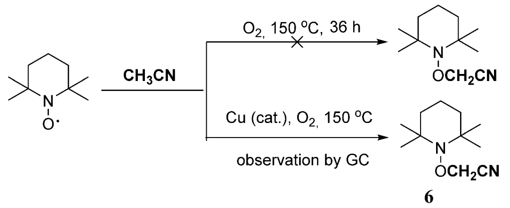
Consequently, we tested these copper complexes in the C–CN cleavage of **6** and found that catalytic amounts of $Cu(OAc)_2$, $Cu(NO_3)_2 \cdot 3H_2O$, $Cu(OTf)_2$, and $Cu(ClO_4)_2$ with 1,10-phenanthraline could efficiently cleave the C–CN bond in compound **6**. In all cases, the cyanide anion derived from **6** could be detected by indicator paper[10c, 11f] (Table 6, entries 2–5). Incidentally, compound **6** was stable in CH_3CN under O_2 at 150 °C in the absence of the copper salt and silane (Table 6, entry 1); however, in the presence of disilane alone, the cyanide anion could also be detected (Table 6, entry 9). These studies suggest that cleavage of the C–CN bond of TEMPO–CH_2CN (**6**) proceeds easily in the presence of a Cu^{II} complex and/or $(Me_3Si)_2$. It should be mentioned that the reaction in the presence of both the copper complex and silane proceeded faster than that with the Cu^{II} complex or $(Me_3Si)_2$ alone.

Whilst investigating the C–CN bond cleavage step of TEMPO–CH_2CN (**6**), we observed that these reactions (Table 6, entries 2–8) afforded multiple products, which were detected by GC. To elucidate their structure, the reaction in entry 7 was further analyzed by GC-MS (see the Supporting Information, Figure S8). One product was determined to be 2,2,6,6-tetramethylpiperidine (**8**) by MS (MW: 141.1). When $Cu(ClO_4)_2 \cdot 6H_2O$ was used as the catalyst, compound **8** could be converted into the $R_2NH_2ClO_4$ salt **9**, which was confirmed by single-crystal X-ray analysis. 2,2,6,6-Tetramethylpiperidine-1-carbonitrile (**7**) (M_W: 166.1) was also identified by NMR spectroscopy and HRMS, and we wondered whether it would act as a cyanating agent because N–CN compounds are often used as cyano sources in reported cyanation reactions.[18] However, by carrying out a control experiment, we excluded this possibility (see the Supporting Information, Scheme S2). Accordingly, these results indicated that not only the C–CN bond but also the N–O bond has been cleaved in compound **6**. Incidentally, during N–O bond cleavage, TEMPO might serve as an oxidant as well.[15, 19]

On the basis of the above mechanistic studies, we have proposed a catalytic cycle for the Cu/TEMPO system (Scheme 3). Two pathways for the formation of TEMPO–CH_2CN (**6**) are possible. In path A, TEMPO directly abstracts a hydrogen atom from acetonitrile to form the $^{\bullet}CH_2CN$ radical, which is trapped by a second molecule of TEMPO to yield TEMPO–CH_2CN (**6**) and TEMPOH (**12**)[19, 20b] (detected by GC, see the Supporting Information, for details). In path B, owing to the coordination ability of the nitrile group onto the Cu species, acetonitrile is selectively activated and deprotonated by base to generate the active Cu intermediate **10**,[21] which reacts with TEMPO to form TEMPO–CH_2CN (**6**) and $Cu(NCCH_2)$ (**11**). Species **11** can be oxidized by O_2 to regenerate the Cu^{II} complex; thus, oxygen is crucial for the generation of **6**. To the best of our knowledge, there is only one early report that demonstrated hydrogen abstraction from acetonitrile with a photochemically excited TEMPO to furnish compound **6**.[20a] To investigate this process, two control experiments were carried out in CH_3CN at 150 °C under oxygen with and without the copper catalyst (Scheme 4). Analysis of the two reactions by GC determined that compound **6** was only formed in the presence of the copper catalyst (see the Supporting Information, for details). Therefore, under thermal conditions, we reason that path B is more likely for the formation of the compound **6**.



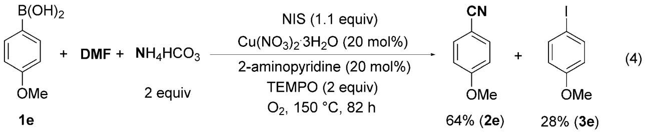
Scheme 3. Proposed mechanism for Cu(cat.)/TEMPO cyanation.



Scheme 4. Control experiments for "TEMPO".

In the reaction mechanism, TEMPO–CH$_2$CN (**6**) may then react with Cu^I, with the assistance of (Me$_3$Si)$_2$, to produce the "CN" species **13** and R$_2$NH **8** through C–CN and N–O bond cleavage. Notably, the R$_2$NH$_2$I salt **14** was also isolated and confirmed by single-crystal X-ray analysis. In this cleavage step, **6** also acts as an oxidant. However, the direct cleavage of acetonitrile to form the cyanide anion cannot be ruled out because the cyanated product was still obtained in the absence of TEMPO, albeit with low 20% yield (see the Supporting Information, Table S1). The cyanide anion **13** can then take part in the subsequent cyanation as a "CN" source. In cycle C, the initial iodination of arylboronic acids with NIS occurs. The generated aryl iodide **3** then reacts with the Cu–CN species to yield the desired aryl nitrile **2**. Accordingly, cheap acetonitrile efficiently acts as a "CN" source for the cyanation of arylboronic acids, and TEMPO allows this reaction to be catalytic in copper.

To probe the generality of this system, we wondered whether our Cu/TEMPO system would be efficient for a combined "CN" source (DMF and NH$_4^+$ salt).[10c] Surprisingly, the reaction of **1e** proceeded smoothly using our copper catalyzed conditions to furnish the cyanated product **2e** in 64% yield [Eq. (4)]. In contrast, a stoichiometric amount of the copper species was essential in Chang's report on the cyanation of arylboronic acids. This result indicates that TEMPO enables the reaction to be catalytic in Cu when using a combined "CN" source.



Conclusion

We have reported the Cu(cat.)/TEMPO system for the cyanation of arylboronic acids by using acetonitrile as the "CN" source. The reaction has a broad substrate scope: a variety of electron-rich and electron-poor arylboronic acids are tolerated well with high to excellent yields of the cyanated products being observed. Heteroaromatic nitriles can also be synthesized by using this approach. Mechanistic investigation revealed that TEMPO plays a significant role in promoting this transformation, and it allows the reaction to be catalytic in copper. Moreover, TEMPO–CH$_2$CN (**6**) is formed in situ and acts as the active cyanating reagent. Disilane is also necessary for this C–CN bond cleavage. Further investigation of new reactions using CH$_3$CN as a "CN" source is ongoing in our laboratory.

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Keywords: arylboronic acid · C–C activation · copper · cyanides · TEMPO

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