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PAPER

A highly efficient one-pot reaction of 2-(*gem*-dibromovinyl)phenols-(thiophenols) with $K_4Fe(CN)_6$ to 2-cyanobenzofurans(thiophenes)†

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2-Cyanobenzofurans and 2-cyanobenzothiophenes were prepared through an efficient one-pot Ullmann-reaction/cyanation reaction. In the presence of CuI/Na_2CO_3–$Pd(OAc)_2/PPh_3$ in DMF, the reaction of 2-(*gem*-dibromovinyl)phenols and 2-(*gem*-dibromovinyl)thiophenols with $K_4Fe(CN)_6$, as non-toxic and user-friendly cyanating reagent, proceeded smoothly to generate the corresponding 2-cyanobenzofurans and 2-cyanobenzothiophenes in good yields.

Introduction

Heteroaromatic cyanides, are not only structural skeletons that were widely found in dyes, agrochemicals, pharmaceutically active compounds, materials and natural products,[1] but also versatile building blocks in modern organic chemistry.[2] In addition, they are readily converted to a variety of other organic compounds, such as acids, esters, amides, amines, and aldehydes.[3] Therefore, it is important to develop efficient methods to introduce the cyano group into heteroaromatic compounds.

For the preparation of heteroaromatic cyanides, the traditional methods are Rosenmund–von Braun method,[4] and Sandmeyer reaction.[5] However, these reactions require a stoichiometric amount of CuCN and suffer from harsh reaction conditions and complicated workup procedures. Recently, transition-metal-catalyzed cyanation of aromatic and heteroaromatic halides with metal cyanides has received much attention.[6] In general, nucleophilic metal-catalyzed cyanations proceed in the presence of Cu, Pd, or Ni-complexes and various cyanation reagents, such as KCN and NaCN‡,[7] $Zn(CN)_2$,[8] CuCN,[9] $(CH_3)_2C(OH)CN$,[10] TMSCN,[11] and $K_4Fe(CN)_6$.[12] Compared with other cyanation reagents, $K_4Fe(CN)_6$ exhibits excellent properties of low-cost, non-toxic and handling without special precautions.

Representative methods for the preparation of heteroaromatic cyanides *via* the direct cyanation of heterocycles can be achieved from the corresponding heterocycles with a suitable cyanide agent. Methods for direct cyanation of pyridines,[13a] thiophenols,[13b,d] indoles,[13b,d,g] pyrroles,[13b,d] and 2-phenylpyridines[13c,e,f] have been reported in the literature. Most recently, the direct cyanation of 3-position of indoles and pyrroles,[14a–d] and 2-position of benzoxazoles, benzothiazoles, benzimidazoles, caffeines, and triazoles have been developed.[14e] However, the direct cyanation of benzofurans and benzothiophenes for the synthesis of 2-cyanobenzofurans and 2-cyanobenzothiophenes has not been described yet, to our knowledge because introduction of a cyano functionality into a benzofuran or benzothiophene ring is more difficult by using such an approach.

Over the past decade, *gem*-dihaloolefins have been received much attention owing to their high reactivity and easy preparation from the corresponding aldehydes.[15] Most importantly, 2-(*gem*-dibromovinyl)phenols, 2-(*gem*-dibromovinyl)thiophenols and 2-(*gem*-dibromovinyl)anilines were extensively used for the preparation of a variety of heterocycles, such as indoles,[16] benzothiophenes,[17] and benzofurans[16d,i,17b] *via* transition-metal-catalyzed one-pot Ullmann-type reaction/amination–Suzuki/Heck/Sonogashira coupling reactions with organoboron agents,[16a,i,17a] alkenes,[16c] or alkynes.[16d] Recently, Lautens *et al.* isolated 2-bromobenzofurans, 2-bromobenzothiophenes and 2-bromoindoles, as significant synthetic intermediates, which subsequently were used as electrophiles for further carbon–carbon bond formations *via* transition-metal-catalyzed cross-coupling reactions, from corresponding 2-(*gem*-dibromovinyl)phenols, 2-(*gem*-dibromovinyl)thiophenols[17b] and 2-(*gem*-dibromovinyl)anilines,[18] respectively *via* Cu- and Pd-catalyzed intramolecular cross-coupling reactions. Therefore, to expand the application scope of *gem*-dibromoolefins and provide a practical straightforward route to 2-substituted benzofused heterocycles is more and more essential.

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‡ KCN and NaCN are extremely toxic [LDL_0 (oral, human): 2.86 and 2.80 mg kg^{-1}, respectively] and develop HCN on contact with acidic water. $K_4[Fe(CN)_6]$ is nontoxic and is used in the food industry for metal precipitation in wine, it has also been used as an anti-agglutinating auxiliary for NaCl. It is soluble in water without decomposition.

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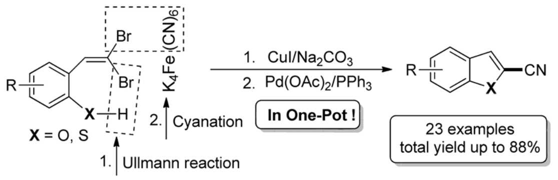
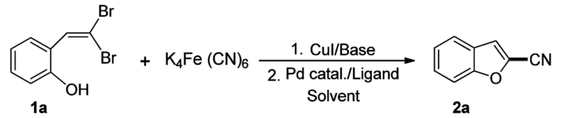


Scheme 1 One-pot reaction of 2-(*gem*-dibromovinyl)phenols(thiophenols) with $K_4Fe(CN)_6$.

In continuation of our efforts on the organic transformations of *gem*-dihaloolefins,[19] herein we report a novel one-pot reaction of 2-(*gem*-dibromovinyl)phenols and 2-(*gem*-dibromovinyl)thiophenols with $K_4Fe(CN)_6$ in the presence of CuI/Na_2CO_3–$Pd(OAc)_2/PPh_3$ in DMF. The reactions proceeded smoothly through a one-pot Ullmann-reaction/cyanation process and generated the corresponding 2-cyanobenzofurans and 2-cyanobenzothiophenes in good yields under mild and low-toxic reaction conditions (Scheme 1).

Results and discussion

Table 1 Optimization of the reaction conditions[a]

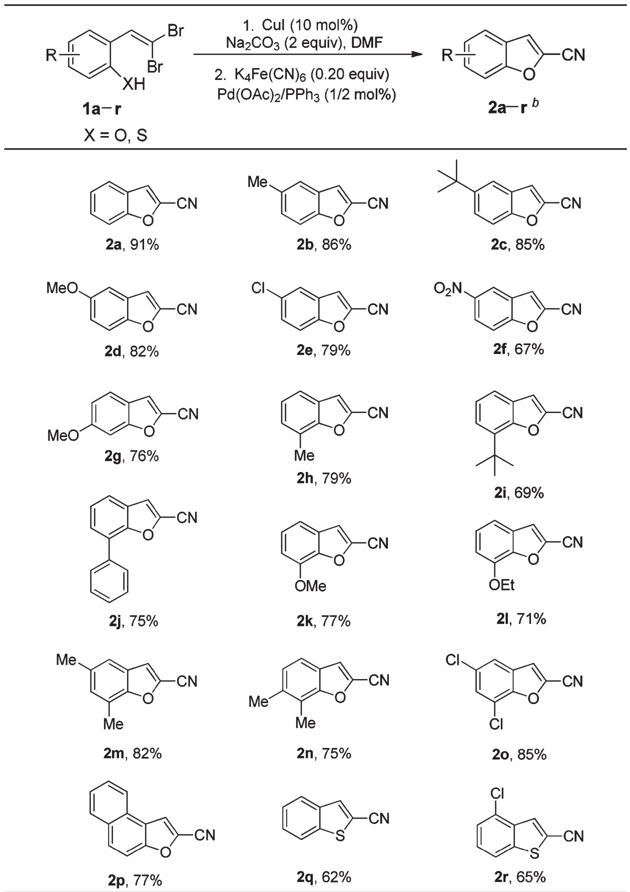


Entry	Base	Pd catal./ligand	Solvent	**2a**[b] (%)
1	Na_2CO_3	$Pd(OAc)_2/PPh_3$	DMF	92
2	*t*-BuOK	$Pd(OAc)_2/PPh_3$	DMF	86
3	$NaHCO_3$	$Pd(OAc)_2/PPh_3$	DMF	84
4	*t*-BuONa	$Pd(OAc)_2/PPh_3$	DMF	68
5	K_2CO_3	$Pd(OAc)_2/PPh_3$	DMF	62
6	Et_3N	$Pd(OAc)_2/PPh_3$	DMF	59
7	Cs_2CO_3	$Pd(OAc)_2/PPh_3$	DMF	NR
8	K_3PO_4	$Pd(OAc)_2/PPh_3$	DMF	NR
9	DMAP	$Pd(OAc)_2/PPh_3$	DMF	NR
10	DABCO	$Pd(OAc)_2/PPh_3$	DMF	NR
11	Na_2CO_3	$Pd(OAc)_2/PPh_3$	NMP	76
12	Na_2CO_3	$Pd(OAc)_2/PPh_3$	DMA	69
13	Na_2CO_3	$Pd(OAc)_2/PPh_3$	Glyme	54
14	Na_2CO_3	$Pd(OAc)_2/PPh_3$	DMSO	26
15	Na_2CO_3	$Pd(OAc)_2/PPh_3$	Toluene	NR
16	Na_2CO_3	$Pd(OAc)_2/PPh_3$	THF	NR
17	Na_2CO_3	$Pd(OAc)_2/PPh_3$	Dioxane	NR
18	Na_2CO_3	$PdCl_2/PPh_3$	DMF	85
19	Na_2CO_3	$Pd(PPh_3)_4$	DMF	78
20	Na_2CO_3	$Pd(PPh_3)_2Cl_2$	DMF	69
21	Na_2CO_3	$PdCl_2(CH_3CN)_2$	DMF	82
22	Na_2CO_3	$Pd(OAc)_2/PCy_3$	DMF	84
23	Na_2CO_3	$Pd(OAc)_2$/dppf	DMF	92
24	Na_2CO_3	$Pd(OAc)_2$/dppe	DMF	86
25	Na_2CO_3	$Pd(OAc)_2$	DMF	25
26	Na_2CO_3	PPh_3	DMF	NR
27	Na_2CO_3	$Pd(OAc)_2/PPh_3$	DMF	42[c]
28	Na_2CO_3	$Pd(OAc)_2/PPh_3$	DMF	27[d]
29	Na_2CO_3	$Pd(OAc)_2/PPh_3$	DMF	0[e]
30	Na_2CO_3	$Pd(OAc)_2/PPh_3$	DMF	92[f]
31	Na_2CO_3	$Pd(OAc)_2$/P*t*-Bu_3	DMF	38[g]

[a] Reaction conditions: **1a** (1.0 mmol), CuI (0.10 mmol), base (2.0 mmol), solvent (2.0 mL) at 80 °C, 6 h; then $K_4Fe(CN)_6$ (0.20 mmol), Pd catal. (0.01 mol), ligand (0.02 mmol) at 120 °C, 6 h. [b] Isolated yields. [c] K_3FeCN_6 (0.20 mmol). [d] CuCN (1.20 mmol). [e] TMSCN (1.20 mmol). [f] NaCN (1.20 mmol). [g] In the absence of CuI.

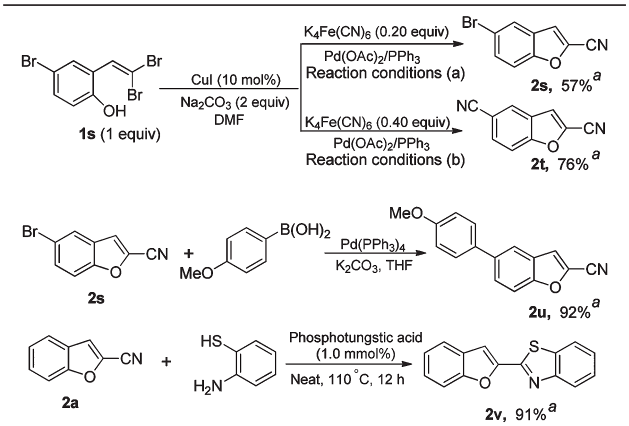
Our initial investigation was focused on the optimization of reaction conditions for the model reaction of 2-(*gem*-dibromovinyl) phenol (**1a**) with $K_4Fe(CN)_6$. As listed in Table 1, the base plays an important role in the one-pot reaction. Among the bases tested, Na_2CO_3 was the most suitable base. *t*-BuOK, $NaHCO_3$, *t*-BuONa, K_2CO_3, and Et_3N were subsequently inferior. However, no desired product **2a** was isolated and only the intermediate bromobenzofuran was formed when Cs_2CO_3, K_3PO_4, DMAP, or DABCO was used as base instead of Na_2CO_3 in the model reaction (Table 1, entries 1–10). The solvent also has a significant effect on the model reaction. When the reaction was carried out in the presence of CuI–$Pd(OAc)_2/PPh_3$ in DMF, 92% yield of **2a** was obtained, and 26–76% yields of **2a** was isolated when the reaction was performed in NMP, DMA, glyme, or DMSO. Unfortunately, no desired **2a** was detected and only bromobenzofuran was obtained as the reaction media was switched to toluene, THF or dioxane (Table 1, entries 11–17). For the effect of palladium catalyst on the model reaction, the one-pot reaction could occur in the presence of a catalytic amount (1.0 mol%) of palladium salt/*P*-ligand or palladium complex, such as $Pd(OAc)_2/PPh_3$, $PdCl_2/PPh_3$, $Pd(PPh_3)_4$, $Pd(PPh_3)_2Cl_2$, $PdCl_2(CH_3CN)_2$, $Pd(OAc)_2/PCy_3$, $Pd(OAc)_2$/dppf, or $Pd(OAc)_2$/dppe in DMF in the presence of CuI and Na_2CO_3, **2a** was obtained in 69–92% yields (Table 1, entries 1 and 18–24). To our delight, 92% yield of **2a** was isolated, representing the best results, when $Pd(OAc)_2/PPh_3$ or $Pd(OAc)_2$/dppf was used as catalyst system in the model reaction (Table 1, entries 1 and 23). It is obvious that palladium, as well as *P*-ligand are essential in the reaction (Table 1, entries 25 and 26). For the optimiztion of CN source, $K_4Fe(CN)_6$ displayed the highest reactivity in the reaction. Other CN sources, such as CuCN, K_3FeCN_6 and TMSCN exhitited the low reactivity to the reaction. Although NaCN displayed the comparable reactivity with $K_4Fe(CN)_6$, but it is a very toxic compound (Table 1, entries 27–30). However, the use of a single metal CuI or $Pd(OAc)_2$ for the one-pot reaction was not effective, even in the presence of P*t*-Bu_3 (Table 1, entries 26 and 31).[18] For the further optimization of reaction conditions, the sequential reaction of 2-(*gem*-dibromovinyl)phenol in the presence of CuI (10 mol%), Na_2CO_3 (2.0 equiv) in DMF at 80 °C for 6 h, then $K_4Fe(CN)_6$ (0.20 mmol) and $Pd(OAc)_2/PPh_3$ (1.0 mol%) were added to the reaction system and then the cyanation reaction was carried out at 120 °C for 6 h.

Under the optimized reaction conditions, the scope of substituted 2-(*gem*-dibromovinyl)phenols and 2-(*gem*-dibromovinyl) thiophenols with $K_4Fe(CN)_6$ in the one-pot Ullmann-reaction/cyanation reaction was investigated. The results are shown in Scheme 2. As can be seen from Scheme 2, the one-pot reactions of $K_4Fe(CN)_6$ with substituted 2-(*gem*-dibromovinyl)phenols (Scheme 2, **1a–o**) generated the corresponding products (**2a–o**) in good to excellent yields. A variety of 2-(*gem*-dibromovinyl)-phenols bearing substituents on the benzene rings were examined. The results in Scheme 2 indicated that a variety of functional groups, including electron-donating and electron-withdrawing ones were tolerated. 2-(*gem*-Dibromovinyl)phenols with an electron-donating group, such as Me, MeO, *t*-Bu, and a weak electron-withdrawing group, such as Cl, on the *para*-position of phenols, gave superior yields of the products (**2b–e**) to



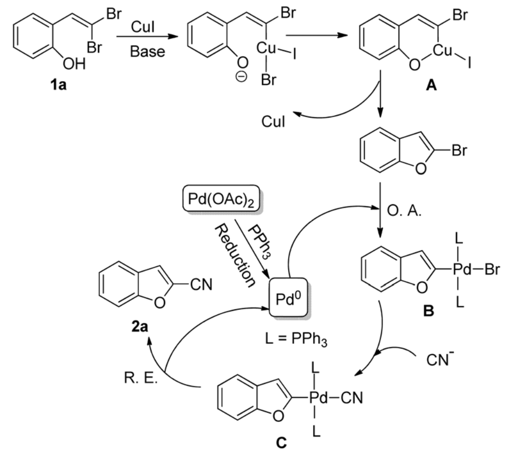
[a] Reaction conditions: **1** (1.0 mmol), CuI (0.10 mmol), Na_2CO_3 (2.0 mmol), DMF (2.0 mL) at 80 °C, 6 h; then $K_4Fe(CN)_6$ (0.20 mmol), $Pd(OAc)_2$ (0.01 mol), PPh_3 (0.02 mmol) at 120 °C, 6 h. [b] Isolated yields.

Scheme 2 Cu/Pd-catalyzed one-pot reactions of 2-(*gem*-dibromovinyl)-phenols(thiophenols) with $K_4Fe(CN)_6$ [a].



Reaction conditions (a): **1s** (1.0 mmol), CuI (0.10 mmol), Na_2CO_3 (2.0 mmol), DMF (2.0 mL) at 80 °C, 6 h; then $K_4Fe(CN)_6$ (0.20 mmol), $Pd(OAc)_2$ (0.05 mol), PPh_3 (0.02 mmol) at 100 °C, 6 h; (b): **1s** (1.0 mmol), CuI (0.10 mmol), Na_2CO_3 (2.0 mmol), DMF (2.0 mL) at 80 °C, 6 h; then $K_4Fe(CN)_6$ (0.40 mmol), $Pd(OAc)_2$ (0.05 mol), PPh_3 (0.02 mmol) at 120 °C, 6 h. [a] Isolated yields.

Scheme 3 The one-pot reaction of **1s** and the further transformation of **2s** and **2a**.

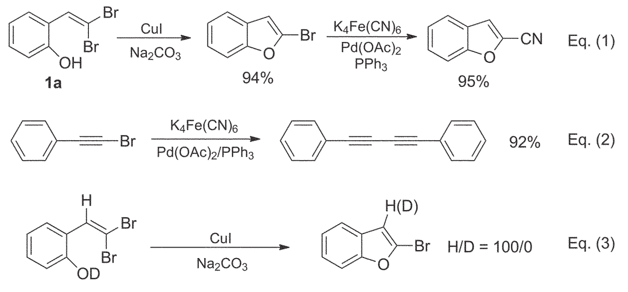


Scheme 4 Possible reaction mechanism.

that of **2f**, with a strong electron-withdrawing group, NO_2 on the *para*-position of phenols. It should be noted that 2-(*gem*-dibromovinyl)phenol with a strong electron-donating functionality, such as MeO on the *meta*-position of phenol generated 76% yield of the product **2g**. Meanwhile, the *ortho*-effect is not obvious for Me, MeO, and Ph groups on the *ortho*-position of phenols in the reactions (**2h**, **2j** and **2k**). However, a little *ortho*-effect was observed for relatively larger bulky groups, such as EtO and *t*-Bu groups (**2i** and **2l**). Disubstituted 2-(*gem*-dibromovinyl)phenols, such as **1m**, **1n**, and **1o**, also underwent the one-pot reaction smoothly with $K_4Fe(CN)_6$ under the present reaction conditions and afforded the corresponding products **2m–o** in 75–85% yields. Under the recommended reaction conditions, 1-(*gem*-dibromovinyl)-2-naphthalenol also underwent the reaction to generate the corresponding product **2p** in 77% yield. The present reaction conditions were also suitable for the synthesis of 2-cyanobenzothiophenes (**2q** and **2r**) from the corresponding 2-(*gem*-dibromovinyl)thiophenols (**1q** and **1r**) and $K_4Fe(CN)_6$ in one-pot.

When the reaction of 4-bromo-2-(*gem*-dibromovinyl)phenol (**1s**) and $K_4Fe(CN)_6$ with 5 : 1 molar ratio was performed under reaction conditions (a), a mono-cyanation product, 5-bromo-2-cyanobenzofuran **2s** was obtained in 57% yield (Scheme 3). On the other hand, when the reaction of **1s** and $K_4Fe(CN)_6$ with 2.5 : 1 molar ratio was performed under the reaction conditions (b), an Ullmann-type di-cyanation product, 2,5-dicyanobenzofuran **2t** was isolated in 76% yield (Scheme 3). These results indicated that the reactivity of Br at furan ring is more than that of Br in benzene ring of 2,5-dibromobenzofuran. When obtained **2s** was used as a starting material to react with 4-methoxyphenylboronic acid under the classic Suzuki reaction conditions, the corresponding Suzuki coupling product, 2-cyano-5-(4-methoxyphenyl)benzofuran (**2u**) was isolated in 92% yield. We also used **2a** as a starting material to react with 2-aminophenylthionol in the presence of phosphotungstic acid, and the di-heterocycle compound, 2-(benzofuran-2-yl)benzothiazole (**2v**) was obtained in 91% yield (Scheme 3).

Although the exact mechanism of this reaction is not clear, a possible pathway was proposed and shown in Scheme 4. The reaction occurs involving an intramolecualr Ullmann-type



Scheme 5 The formation of 2-bromobenzofuran and D-labelled experiment.

reaction of 2-(*gem*-dibromovinyl)phenol, and subsequently intermolecular cyanation reaction with $K_4Fe(CN)_6$. Initially, an elimination of HBr from 2-(*gem*-dibromovinyl)phenol (**1a**) *via* a classic Ullmann reaction to 2-bromobenzofuran taken place in the presence of CuI and Na_2CO_3.[20] The obtained 2-bromobenzofuran then underwent an oxidative addition with Pd(0) from the reduction of its precursor $Pd(OAc)_2$ in the presence of a reducing agent, such as PPh_3,[21] to generate intermediate **B**. The obtained **B** proceeded in a ligand exchange with CN^- to generate an Ar–Pd(II)–CN intermediate **C**, which subsequently underwent reductive elimination to form the corresponding product 2-cyanobenzofuran, **2a**, along with the generation of Pd(0), and finally the catalytic cycle was closed.

To verify the formation of 2-bromobenzofuran, **1a** was carried out in the presence of CuI (10 mol%) and Na_2CO_3 (2.0 equiv) in DMF and 2-bromobenzofuran was isolated in 94% yield. The obtained 2-bromobenzofuran then reacted with $K_4Fe(CN)_6$ in the presence of $Pd(OAc)_2/PPh_3$ to give **2a** in 95% yield (Scheme 5, eqn (1)). We also tried the reaction of 1-bromo-2-phenylacetylene with $K_4Fe(CN)_6$ under the present reaction conditions. However, no cyanation product was obtained, and a homo-coupling product was obtained in 92% yield (Scheme 5, eqn (2)). When 2-(*gem*-dibromovinyl)phenol-D, prepared from D_2O exchange, was carried out in the presence of CuI/Na_2CO_3, 2-bromobenzofuran was isolated in 93% yield without a D-rich element in the product (Scheme 5, eqn (3)). These results support the intermolecular reaction of **1a** through a key intermediate **A**.

Conclusion

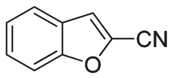
In conclusion, a novel and highly efficient synthetic method for the preparation of 2-cyanobenzofurans and 2-cyanobenzothiophenes has been developed. In the presence of CuI/Na_2CO_3–$Pd(OAc)_2/PPh_3$, 2-(*gem*-dibromovinyl)phenols and 2-(*gem*-dibromovinyl)thiophenols reacted with $K_4Fe(CN)_6$ smoothly to generated the corresponding products in good yields through an Ullmann reaction/cyanation reaction in one-pot. The extend investigation of this kind reaction and detail reaction mechanism are currently underway in our laboratory.

Experimental section

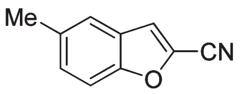
All the reactions of 2-(*gem*-dibromovinyl)phenols and 2-(*gem*-dibromovinyl)thiophenols with $K_4Fe(CN)_6$ were carried out under a nitrogen atmosphere. ^1H and ^{13}C NMR spectra were measured on a Bruker Avance 400 MHz NMR spectrometer with $CDCl_3$ as solvent and recorded in ppm relative to internal tetramethylsilane standard. High resolution mass spectroscopy data of the product were collected on a Waters Micromass GCT instrument. Solvents, and general chemicals were purchased from commercial suppliers and used without further purification. All the *gem*-dibromovinyl substrates were synthesized according to the reported procedures in the literatures.[17*b*,22]

Typical procedure for the one-pot reaction

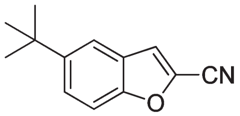
A sealable reaction tube equipped with a magnetic stirrer bar was charged with *gem*-dibromovinyl substrate (1.0 mmol), CuI (0.10 mmol), Na_2CO_3 (2.0 mmol) and DMF (2.0 mL). The rubber septum was then replaced by a Teflon-coated screw cap, and the reaction vessel placed in an oil bath at 80 °C. After stirring of the mixture at this temperature for 6 h, it was cooled to room temperature and $K_4Fe(CN)_6$ (0.20 mmol), $Pd(OAc)_2$ (0.01 mmol) and PPh_3 (0.02 mmol) were added to the reaction system. Then the reaction vessel was placed in an oil bath at 120 °C for 6 h. It was cooled to room temperature after the reaction and diluted with ethyl acetate, washed with water and brine, dried with Mg_2SO_4. After the solvent was removed under reduced pressure, the residue was purified by column chromatography on silica gel (eluant: petroleum ether) to afford the corresponding product.



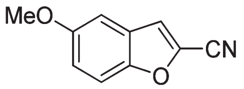
Benzofuran-2-carbonitrile, 2a. White solid, m.p. 36–38 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, J = 8.0 Hz, 1H), 7.57–7.50 (m, 2H), 7.46 (s, 1H), 7.40–7.36 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.59, 128.36, 127.22, 125.42, 124.48, 122.50, 118.37, 111.98, 111.74. IR (KBr, cm^{-1}): 2230 ($\nu_{C\equiv N}$). HRMS (EI) ($[M]^+$) Calcd for C_9H_5NO: 143.0371, Found: 143.0372.



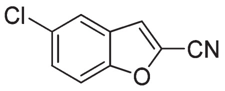
5-Methylbenzofuran-2-carbonitrile, 2b. White solid, m.p. 71–73 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.43–7.41 (m, 2H), 7.36 (s, 1H), 7.32–7.30 (m, 1H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.19, 134.27, 129.92, 127.24, 125.58, 121.96, 118.16, 111.92, 111.51, 21.19. IR (KBr, cm^{-1}): 2225 ($\nu_{C\equiv N}$). HRMS (EI) ($[M]^+$) Calcd for $C_{10}H_7NO$: 157.0528, Found: 157.0530.



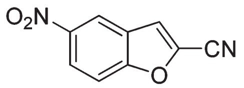
5-(*tert*-Butyl)benzofuran-2-carbonitrile, 2c. White solid, m.p. 58–60 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.64 (d, J = 2.0 Hz, 1H), 7.59–7.57 (m, 1H), 7.47 (d, J = 8.8 Hz, 1H), 7.41 (s, 1H), 1.38 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.05, 147.88, 127.28, 126.76, 125.27, 118.67, 118.36, 111.99, 111.40, 34.85, 31.60. IR (KBr, cm^{-1}): 2225 ($\nu_{C\equiv N}$). HRMS (EI) ([M]$^+$) Calcd for $C_{13}H_{13}NO$: 199.0997, Found: 199.0995.



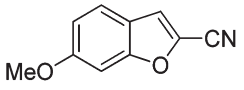
5-Methoxybenzofuran-2-carbonitrile, 2d. White solid, m.p. 89–91 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (d, J = 9.2 Hz, 1H), 7.37 (s, 1H), 7.12–7.09 (m, 1H), 7.05 (d, J = 2.8 Hz, 1H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.07, 150.77, 127.74, 126.05, 118.38, 118.35, 112.64, 111.82, 103.31, 55.83. IR (KBr, cm^{-1}): 2230 ($\nu_{C\equiv N}$). HRMS (EI) ([M]$^+$) Calcd for $C_{10}H_7NO_2$: 173.0477, Found: 173.0474.



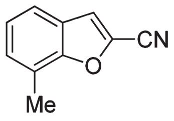
5-Chlorobenzofuran-2-carbonitrile, 2e. White solid, m.p. 123–125 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (dd, J = 2.0, 0.8 Hz, 1H), 7.51–7.45 (m, 2H), 7.40 (d, J = 0.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.96, 130.44, 128.85, 128.68, 126.77, 121.97, 117.68, 113.17, 111.22. IR (KBr, cm^{-1}): 2229 ($\nu_{C\equiv N}$). HRMS (EI) ([M]$^+$) Calcd for C_9H_4NOCl: 176.9981, Found: 176.9980.



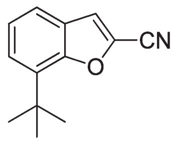
5-Nitrobenzofuran-2-carbonitrile, 2f. White solid, m.p. 117–119 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.82 (d, J = 2.4 Hz, 1H), 8.45–8.42 (m, 1H), 8.28 (d, J = 4.0 Hz, 1H), 8.02–7.99 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 158.00, 145.30, 129.65, 126.43, 124.33, 121.21, 120.49, 113.71, 111.60. IR (KBr, cm^{-1}): 2237 ($\nu_{C\equiv N}$). HRMS (EI) ([M]$^+$) Calcd for $C_9H_4N_2O_3$: 188.0222, Found: 188.0223.



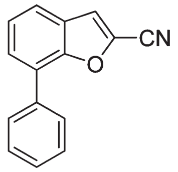
6-Methoxybenzofuran-2-carbonitrile, 2g. White solid, m.p. 78–80 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (d, J = 8.4 Hz, 1H), 7.38 (s, 1H), 7.01–6.97 (m, 2H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.20, 157.14, 126.30, 122.66, 118.61, 118.55, 114.88, 112.10, 95.44, 55.75. IR (KBr, cm^{-1}): 2218 ($\nu_{C\equiv N}$). HRMS (EI) ([M]$^+$) Calcd for $C_{10}H_7NO_2$: 173.0477, Found: 173.0475.



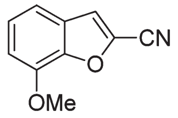
7-Methylbenzofuran-2-carbonitrile, 2h. White solid, m.p. 46–48 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (d, J = 7.2 Hz, 1H), 7.43 (s, 1H), 7.30–7.23 (m, 2H), 2.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.92, 129.05, 126.97, 125.02, 124.61, 122.53, 119.87, 118.69, 111.98, 14.82. IR (KBr, cm^{-1}): 2229 ($\nu_{C\equiv N}$). HRMS (EI) ([M]$^+$) Calcd for $C_{10}H_7NO$: 157.0528, Found: 157.0525.



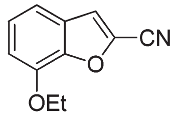
7-(*tert*-Butyl)benzofuran-2-carbonitrile, 2i. White solid, m.p. 101–103 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53–7.51 (m, 1H), 7.45 (s, 1H), 7.41–7.39 (m, 1H), 7.30–7.26 (m, 1H), 1.50 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.24, 135.96, 126.47, 126.11, 124.98, 124.61, 120.36, 118.47, 112.16, 34.43, 29.68. IR (KBr, cm^{-1}): 2227 ($\nu_{C\equiv N}$). HRMS (EI) ([M]$^+$) Calcd for $C_{13}H_{13}NO$: 199.0997, Found: 199.0995.



7-Phenylbenzofuran-2-carbonitrile, 2j. White solid, m.p. 116–118 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82–7.79 (m, 2H), 7.66–7.63 (m, 2H), 7.54–7.51 (m, 3H), 7.46–7.42 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.03, 134.93, 128.80, 128.52, 128.35, 127.72, 127.41, 126.51, 126.29, 125.13, 121.50, 118.62, 111.80. IR (KBr, cm^{-1}): 2228 ($\nu_{C\equiv N}$). HRMS (EI) ([M]$^+$) Calcd for $C_{15}H_9NO$: 219.0684, Found: 219.0681.

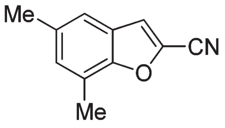


7-Methoxybenzofuran-2-carbonitrile, 2k. White solid, m.p. 102–104 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (s, 1H), 7.30–7.22 (m, 2H), 6.97 (dd, J = 7.6, 1.2 Hz, 1H), 4.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.65, 145.42, 127.39, 127.10, 125.35, 118.64, 114.23, 111.54, 109.74, 56.19. IR (KBr, cm^{-1}): 2228 ($\nu_{C\equiv N}$). HRMS (EI) ([M]$^+$) Calcd for $C_{10}H_7NO_2$: 173.0477, Found: 173.0476.

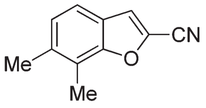


7-Ethoxybenzofuran-2-carbonitrile, 2l. White solid, m.p. 74–76 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (s, 1H), 7.27–7.20 (m, 2H), 6.96 (dd, J = 7.6, 1.6 Hz, 1H), 4.26 (q, J = 6.8 Hz, 2H), 1.52 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.57, 144.96, 127.28, 127.14, 125.32, 118.69, 114.07, 111.62, 110.74, 64.78, 14.69. IR (KBr, cm^{-1}): 2231

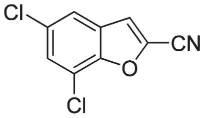
($\nu_{C\equiv N}$). HRMS (EI) ($[M]^+$) Calcd for $C_{11}H_9NO_2$: 187.0633, Found: 187.0636.



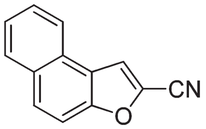
5,7-Dimethylbenzofuran-2-carbonitrile, 2m. White solid, m.p. 88–90 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.35 (s, 1H), 7.25 (d, J = 2.4 Hz, 1H), 7.11 (s, 1H), 2.48 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.50, 134.31, 130.69, 126.94, 125.15, 121.88, 119.28, 118.42, 112.12, 21.17, 14.76. IR (KBr, cm^{-1}): 2230 ($\nu_{C\equiv N}$). HRMS (EI) ($[M]^+$) Calcd for $C_{11}H_9NO$: 171.0684, Found: 171.0686.



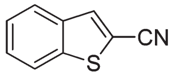
6,7-Dimethylbenzofuran-2-carbonitrile, 2n. White solid, m.p. 37–39 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.36 (d, J = 9.6 Hz, 2H), 7.15 (d, J = 8.0 Hz, 1H), 2.43 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.42, 137.24, 126.90, 126.42, 122.86, 120.63, 118.87, 118.78, 112.23, 19.32, 11.50. IR (KBr, cm^{-1}): 2226 ($\nu_{C\equiv N}$). HRMS (EI) ($[M]^+$) Calcd for $C_{11}H_9NO$: 171.0684, Found: 171.0680.



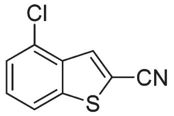
5,7-Dichlorobenzofuran-2-carbonitrile, 2o. White solid, m.p. 109–112 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.58 (d, J = 2.0 Hz, 1H), 7.51 (d, J = 1.6 Hz, 1H), 7.45 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.10, 130.72, 129.40, 128.54, 127.66, 120.55, 118.47, 118.08, 110.58. IR (KBr, cm^{-1}): 2234 ($\nu_{C\equiv N}$). HRMS (EI) ($[M]^+$) Calcd for $C_9H_3NOCl_2$: 210.9592, Found: 210.9595.



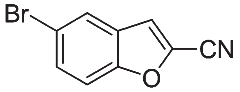
Naphtho[2,1-*b*]furan-2-carbonitrile, 2p. White solid, m.p. 88–90 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, J = 7.6 Hz, 1H), 7.94 (d, J = 8.0 Hz, 1H), 7.87 (d, J = 9.2 Hz, 1H), 7.82 (d, J = 0.8 Hz, 1H), 7.67–7.63 (m, 1H), 7.60–7.54 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.11, 130.57, 129.93, 128.98, 127.67, 127.22, 126.44, 125.87, 123.12, 121.36, 117.16, 112.03, 111.99. IR (KBr, cm^{-1}): 2224 ($\nu_{C\equiv N}$). HRMS (EI) ($[M]^+$) Calcd for $C_{13}H_7NO$: 193.0528, Found: 193.0529.



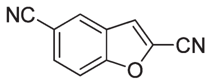
Benzothiophene-2-carbonitrile, 2q. Colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.91–7.83 (m, 3H), 7.54–7.44 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.21, 137.37, 134.90, 127.80, 125.66, 125.20, 122.29, 114.38, 109.59. IR (KBr, cm^{-1}): 2224 (ν_{CN}). HRMS (EI) ($[M]^+$) Calcd for C_9H_5NS:159.0143, Found: 159.0147.



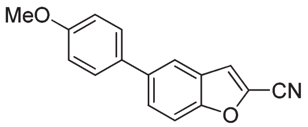
4-Chlorobenzothiophene-2-carbonitrile, 2r. White solid, m.p. 107–109 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.99 (s, 1H), 7.75–7.71 (m, 1H), 7.47–7.42 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.07, 135.99, 133.03, 130.24, 128.51, 125.58, 120.77, 113.75, 110.53. IR (KBr, cm^{-1}): 2226 ($\nu_{C\equiv N}$). HRMS (EI) ($[M]^+$) Calcd for C_9H_4NSCl: 192.9753, Found: 192.9756.



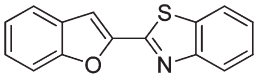
5-Bromobenzofuran-2-carbonitrile, 2s. White solid, m.p. 147–149 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, J = 2.0 Hz, 1H), 7.61 (dd, J = 8.8, 2.0 Hz, 1H), 7.45 (d, J = 8.8 Hz, 1H), 7.40 (d, J = 0.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.31, 131.48, 128.48, 127.35, 125.07, 117.75, 117.50, 113.55, 111.15. IR (KBr, cm^{-1}): 2228 ($\nu_{C\equiv N}$). HRMS (EI) ($[M]^+$) Calcd for C_9H_4NOBr: 220.9476, Found: 220.9474.



Benzofuran-2,5-dicarbonitrile, 2t. White solid, m.p. 171–173 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 8.09 (d, J = 1.2 Hz, 1H), 7.80 (dd, J = 8.8, 1.6 Hz, 1H), 7.70 (d, J = 8.8 Hz, 1H), 7.56 (d, J = 0.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.77, 131.44, 129.62, 127.85, 126.12, 118.08, 117.84, 113.51, 110.59, 109.05. IR (KBr, cm^{-1}): 2227 ($\nu_{C\equiv N}$), 2228 ($\nu_{C\equiv N}$). HRMS (EI) ($[M]^+$) Calcd for $C_{10}H_4N_2O$: 168.0324, Found: 168.0320.



5-(4-Methoxyphenyl)benzofuran-2-carbonitrile, 2u. White solid, m.p. 87–89 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.77 (d, J = 1.6 Hz, 1H), 7.69–7.67 (m, 1H), 7.58–7.47 (m, 4H), 7.02–6.98 (m, 2H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.34, 154.91, 138.03, 132.90, 128.41, 127.95, 127.73, 126.03, 120.09, 118.57, 114.37, 112.10, 111.78, 55.35. IR (KBr, cm^{-1}): 2226 ($\nu_{C\equiv N}$). HRMS (EI) ($[M]^+$) Calcd for $C_{16}H_{11}NO_2$:249.0790, Found: 249.0788.



2-(Benzofuran-2-yl)benzothiazole, 2v. Yellow solid,[23] m.p. 218–220 °C. ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.14 (d, J = 8.4 Hz, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.70 (d, J = 7.6 Hz, 1H), 7.64 (d, J = 8.4 Hz, 1H), 7.56–6.53 (m, 2H), 7.46–6.41 (m, 2H), 7.34–7.41 (m, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 157.58, 155.51, 153.86, 149.79, 134.70, 128.15, 126.67, 126.45, 125.64, 123.78, 123.51, 122.12, 121.66, 111.87, 107.55.

Acknowledgements

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