DDQ-Mediated Oxidative Coupling: An Approach to 2,3-Dicyanofuran (Thiophene)

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Supporting Information



ABSTRACT: A facile oxidative coupling of α -carbonyl radicals to 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) for the synthesis of 2,3-dicyanofurans and thiophenes starting from readily available β -diketones, simple ketones, and β -keto thioamides in up to 95% yield in one step was developed. Mechanistic investigations revealed that a radical process could be involved in this transformation, and a water promoted C–C bond cleavage pathway is proposed for the formation of 2,3-dicyanofurans and thiophenes.

INTRODUCTION

The possibility of direct C–H functionalization, especially oxidative coupling, to form C–C bonds represents a significant challenge,¹ and application of these strategies to construct polysubstituted furans is especially attractive.^{11–n} Generally, electrophilic substrates in these transformations feature either aryl/vinyl groups^{2,3} or heteroatoms (such as N, O, and S)^{2,4} adjacent to the C(sp³)–H being activated (Scheme 1, eq a–c). Although great progress has already been made in this area, there is still a requirement to develop highly efficient and environmentally benign synthetic methods via oxidative coupling strategies due to the increasing demands of structural

Scheme 1. Strategies for C-H Functionalization



novelty and diversity in both material science and drug discovery.

Therefore, we envisaged an oxidative coupling protocol utilizing $C(sp^3)$ -H nucleophiles, such as ketones instead of the aforementioned electrophiles, providing electrophilic α -carbonyl radicals (Scheme 1, eq d). Electrophilic radicals, typically characterized by adjacent carbonyl groups, can be conveniently generated by transition metal-mediated oxidation of acidic ketones.⁵ Mn(OAc)₃ and cerium(IV) ammonium nitrate (CAN) are most commonly used as stoichiometric oxidants for the oxidative activation of ketones to generate α -carbonyl radicals, which can subsequently react with a variety of nucleophilic alkenes.^{6,7} Consequently, a mild and metal-free process for oxidative activation of $C(sp^3)$ -H bonds of nucleophiles is still a highly desirable goal.

We recently reported the first successful example of a DDQmediated coupling of a terminal allylic $C(sp^3)$ to a $C(sp^2)$ of styrene via an unconventional reaction mode.⁸ We wished to investigate the possibility of oxidative coupling of α - $C(sp^3)$ -H bonds of a carbonyl compound to styrene via DDQ-mediated formation of an α -carbonyl radical.⁹ Hence, we initially performed a reaction employing methyl acetoacetate **1a** and styrene in the presence of DDQ (1.5 equiv) in CH₃CN at room temperature. Unexpectedly, 2,3-dicyanofuran **2a** was obtained in 22% yield [eq 1]. From inspection of the structure of **2a**, it is clear that the 2,3-dicyanofuran backbone partly derives from

Received: November 22, 2013



DDQ molecule and not from styrene. This implies that a DDQmediated α -carbonyl radical formation may occur, and resulting α -carbonyl radical can further react with DDQ via an unconventional reaction pathway to afford 2,3-dicyanofuran 2a.^{10,11}

Notably, dicyanoaryl (heteroaryl) compounds have been successfully used for preparation of phthalocyanines, which show various practical applications such as dyes, pigments, photoelectric materials and other applications.^{12,13} In view of the unconventional formation of 2,3-dicyanofuran and its potential utility as a building block for the synthesis of phthalocyanines, we further explored this unconventional reaction system and reported the preliminary result in a Chinese patent application with limited substrate scope.¹⁴

Herein, we would like to describe in full detail the facile reaction of the in situ generated α -carbonyl radicals with DDQ itself, constructing not only 2,3-dicyanofurans but also 2,3-dicyanothiophenes in excellent yields under metal-free conditions. In addition, a hypothetical radical involved oxidative coupling and water-promoted C–C bond cleavage pathway was also discussed on the basis of both NMR spectroscopy studies and radical trapping experiments.

RESULTS AND DISCUSSION

With the encouragement of our interesting finding of 2,3dicyanofuran formation via presumably an unconventional reaction pathway [eq 1], we then further explored the reaction conditions (Table 1). The combination of substrate 1a (1.0

Table 1. Optimization of Reaction Conditions

	CN + CN + 1a	o solvent o	CN CN 2a
entry ^a	solvent	DDQ (equiv)	yield (%) ^d
1	CH ₃ NO ₂	2.0	22
2	CH ₃ NO ₂	2.0	23 ^b
3	DCE	2.0	26
4	toluene	2.0	15
5	CH ₃ CN	2.0	62
6	DMSO	2.0	7
7	DMF	2.0	9
8	DCM	2.0	29
9	CHCl ₃	2.0	22
10	THF	2.0	56
11	EtOAc	2.0	60
12	CH ₃ CN	3.0	93
13	CH ₃ CN	4.0	92
14	CH ₃ CN	3.0	86 ^c

^{*a*}Reaction conditions: Methyl acetoacetate 1a (0.2 mmol) and DDQ (0.6 mmol) in dry solvent (2.0 mL) at rt under N₂, which was stirred until the reaction was complete, as judged by TLC. ^{*b*}The reaction was performed at 60 °C. ^{*c*}The solvent was not dried. ^{*d*}Yields of isolated products.

equiv) and DDQ (3.0 equiv) in CH_3CN at room temperature were found to be the optimal reaction conditions (Table 1, entry 12), providing 2,3-dicyanofuran **2a** in 93% yield.

In order to understand the generality and scope of this highly efficient 2,3-dicyanofuran formation process, a number of 1,3dicarbonyl compounds were investigated, as shown in Scheme 2. It was found that ethyl, isopropyl, *tert*-butyl, and benzyl





^aYields of the isolated products. ^b5.0 equiv of DDQ was used.

acetoacetates all reacted smoothly affording the 2,3-dicyanofuran products in excellent yields (Scheme 2, 2b-2e). Nevertheless, the treatment of ethyl 4-chloroacetoacetate with DDQ under these standard conditions resulted in the formation of products 2b and 2f in 18 and 65% yields, respectively. Compound 2b might be generated through reduction of 2f by in situ formed DDQH₂. Interestingly, when using 5.0 equiv of DDQ in this reaction, only 2f was obtained, in good yield (85%). The reaction of ethyl trifluoroacetoacetate with DDQ delivered 2,3-dicyanofuran 2g in 69% yield. Subtle change to the acetyl group of 1 to propionyl and isobutyryl led to the formation of both 2h and 2i in comparable yields. However, use of methyl pivaloylacetate led to 2j in only moderate yield, probably due to the steric hindrance imparted by the tert-butyl group. A substrate with a benzyloxy group underwent this reaction to afford the corresponding product 2k in 82% yield. In addition, symmetric β -diketones 11 and 1m as well as 3oxobutanenitrile 1n can also be transformed to corresponding 2,3-dicyanofurans 2l, 2m, and 2n in excellent yields.

Next, we further extended the scope to aryl substrates (Scheme 3). Most of the aryl substrates tried gave the desired products (Scheme 3, 4a-4l) in good yields (62-92%). Although substrate 3j, bearing an electron-donating methoxy substituent on the aryl ring, gave a mixture of furan 4j and p-methoxybenzoic acid in 41 and 30% yields, respectively. Unsymmetrical β -diketone 3c was found to give a 1:2 mixture of two regioisomeric products 4c in 62% yield (Scheme 3). Single crystal X-ray diffraction analysis of 4k confirmed the 2,3-dicyanofuran structure (CCDC 943604). Moreover, substrates containing furan, thiophene, and pyridine moieties could also be used in this transformation affording the corresponding

Scheme 3. Substrate Scope for Oxidative Coupling of Carbonyl Compounds 3 with DDQ^{a}



^aYields of the isolated products. ^bThe ratio of two regioisomeric products was determined by ¹H NMR spectroscopy. ^cp-Methoxybenzoic acid was obtained in 30% yield.

furan-containing scaffold in moderate to excellent yields (Scheme 3, 4m-4o).

All of the products contain the 2,3-dicyano unit derived from DDQ itself, which indicated that an oxidative radical coupling pathway might be involved. Interestingly, DDQ has rarely been reported as electrophile in reactions with carbonyl nucleophiles.^{9c} Therefore, we proposed the tentative reaction pathway for this unexpected transformation shown in Figure 1. A single electron transfer (SET) from carbonyl compound **1a** to DDQ generates radicals **B** and **C**, which then selectively cross couple to each other to form a DDQ-substrate adduct **D**, probably due to the persistent radical effect (PRE).¹⁵ The adduct **D** is then subjected to a DDQ-mediated hydride abstraction due to the

absence of an adjacent proton and then cyclization and subsequent deprotonation to form the key intermediate G, ^{11,16} which was found to be quite stable in anhydrous CD₃CN in an NMR tube. The carbonyl group of **G** is then attacked by H₂O (water is actually introduced by opening the reaction flask to air during the workup) and leads to the ring-opening¹⁷ forming the free acid **I**. Intermediate **I** can then easily cyclize to form 2,3-dichloromaleic anhydride, which is accompanied by the release of dihydrofuran **K**. Finally, a third equivalent of DDQ is consumed in the aromatization of **K** to afford 2,3-dicyanofuran **2a**. However, the formation of **2a** from the key intermediate **G** via a retro-Diels–Alder pathway may also be possible.^{14b,c}

In order to further test our hypothesis, we needed to answer the following questions: (1) Is this really a radical-mediated process? (2) Is intermediate **G** involved in the reaction? (3) Does water promote the reaction affording 2,3-dichloromaleic anhydride? First, the reaction of **3b** was repeated with the addition of 3.0 equiv of TEMPO, providing a trace of **4b** and vicinal tricarbonyl compound **3bb** in 91% yield [eq 2]. This

$$\begin{array}{c} 0 & 0 \\ \hline \\ \hline \\ 0 \\ \hline \\ 0 \\ \hline \\ CH_3CN, N_2, rt, 12 h, 91\% \end{array} \xrightarrow{\begin{array}{c} 0 & 0 \\ \hline \\ 0 \\ \hline \hline \\ 0 \\ \hline \\ 0 \\ \hline \hline \\ 0 \\ \hline \\ 0 \\ \hline \hline \\ 0 \\ \hline \\ 0 \\ \hline \hline 0 \\ \hline \hline \\ 0 \\ \hline 0 \\ \hline \hline 0 \\ \hline 0 \\ \hline \hline 0 \\ \hline 0$$

observation implies that an α -carbonyl radical does form since it can be easily trapped by TEMPO to afford **3bb**, after further DDQ oxidation. Furthermore, electron paramagnetic resonance (EPR) experiments using **1a** and **3h** as model substrates revealed signals corresponding to radicals (see the Supporting Information, Figures S1 and S2).¹⁸

Next, to prove the formation of intermediate **G** and 2,3dichloromaleic anhydride, a series of NMR spectroscopy experiments in situ were also performed. It is notable that attempts to monitor and purify intermediate **G** by TLC and silica gel chromatography were not successful, although treatment of substrate **1a** with DDQ in CD₃CN afforded a new unidentified product, presumably the intermediate **G**, after 5 min, by analysis of the ¹H NMR spectra (Scheme 4, (2)). Interestingly, the NMR signal corresponding to this unidentified product gradually increased as substrate **1a** was consumed,



Figure 1. Proposed reaction pathway for oxidative radical addition.

Scheme 4. Reactions Were Monitored by ¹H NMR Spectroscopy^a



^{*a*}Reaction conditions: Carbonyl compound **1a** (0.1 mmol) was added to a solution of DDQ (0.3 mmol) in CD₃CN (1.0 mL) at room temperature under N₂. The resulting mixture was monitored by ¹H NMR spectroscopy with time. (1) Substrate **1a**; (2) after 5 min; (3) after 30 min; (4) after 1 h; (5) after 2 h; (6) addition of 1.0 equiv of H₂O for additional 1 h.

accompanied by the formation of a small amount of 2a after 30 min, which gradually increased over 2 h. The ¹H NMR spectra (Scheme 4, (5)) did not change further, even if the reaction time was further prolonged to 5 h. Therefore, it is sensible to conclude that a new product, possibly the proposed intermediate G, gradually converted to product 2a. Attempts to chromatographically isolate this intermediate have so far proved unsuccessful, suggesting that this new unidentified intermediate may be not stable and prone to hydrolysis by trace water in the solvent used for NMR spectroscopy, as proposed in Figure 1.

Recently, it was reported that the [2 + 2] cycloadducts of DDQ and 2-ethynylpyrroles are stable at room temperature, although a ring-opening reaction was found at higher temperature in the presence of MeOH affording rearrangement products.^{17,19} However, in our case, intermediate **G** was completely converted into product **2a** within one hour of addition of 1 equiv of H₂O to the sample in an NMR tube (Scheme 4, (5)). Furthermore, we also analyzed the ¹³C NMR spectra of the same reaction, and both DDQH₂ and 2,3-dichloromaleic anhydride (as judged by comparison of the ¹³C NMR spectra of authentic samples) were found following addition of 1.0 equiv of H₂O after an additional hour (Scheme 5, (3)). These NMR spectra provide supporting evidence consistent with the proposed mechanism.

On the basis of our reaction pathway hypothesis, we believed that simple ketones **5** could be useful in this system as long as the formation of an α -carbonyl radical in the presence of DDQ is possible. Despite the fact that successful formation of α carbonyl radicals has been reported through transition metalmediated oxidation for simple ketones,²⁰ only one example of a DDQ-mediated α -carbonyl radical formation from simple ketones has been reported.²¹ With this in mind, we initially used a challenging tetralone **5a** as a substrate under the described optimal conditions. This substrate could also form an enone via a well-known DDQ-mediated dehydrogenation.^{9b,14b,22} No reaction occurred upon treatment of **5a** with DDQ at room temperature in CH₃CN. To our delight, treatment of **5a** with DDQ under reflux successfully delivered the corresponding 2,3-dicyanofuran **6a**, instead of a dehydro-



 $^{a}(1)$ After 1 h; (2) after 2 h; (3) after 1.0 equiv of H₂O for additional 1 h; (4) product **2a**; (5) DDQH₂; (6) 2,3-dichloromaleic anhydride.

genation product, in 61% yield and accompanied by 10% of **6aa**, an oxidative aromatization product from **6a**. It was found that 6-methoxy tetralone **5b** also reacted smoothly affording **6b** in 40% yield, and **6bb** in 28% yield, respectively (Scheme 6).

Scheme 6. Substrate Scope for Oxidative Coupling of Carbonyl Compounds 5 to $DDQ^{a,b}$



^{*a*}Reaction conditions: Carbonyl compounds **5** (0.2 mmol) and DDQ (0.6 mmol) in dry CH₃CN (2.0 mL) at reflux under N₂, which was stirred until the reaction was complete, as judged by TLC. ^{*b*}Yields of isolated products. Yield when using 5.0 equiv of DDQ in the parentheses.

Use of 5.0 equiv of DDQ in reactions with **5a** and **5b** gave **6aa** and **6bb** only in 70 and 66% yields, respectively. Simple cyclic ketones **5c–5f** also showed good reactivity to giving 2,3-dicyanofurans in moderate to good yields (Scheme 6, **6c–6f**). However, acetophenone was found unsuitable for this reaction, presumably because of the difficulty in the formation of α -carbonyl radical; an electron-rich 2-methoxy acetophenone **5g** was found to give the corresponding furan **6g** in moderate yield (Scheme 6). In addition, treatment of 2-methoxy acetophenone **5g** and DDQ with LDA in THF failed to give any **6g**, which provided evidence that a Michael addition process could be ruled out in this system.

Following the successful reactions of β -diketones and simple ketones, we next turned our attention to the β -keto thioamide

substrates. According to our hypothesis, DDQ-substrate adduct **D** will undergo a DDQ-mediated hydride abstraction and subsequent cyclization. It is reasoned that, due to the stronger nucleophilicity of the thiocarbonyl group, the sulfur should dominate over the carbonyl's oxygen atom in the cyclization step, thus affording a thiophene unit. Therefore, a number of β -keto thioamide substrates 7 were employed, as shown in Scheme 7. It was found that methyl, ethyl, *tert*-butyl and benzyl





^{*a*}Reaction conditions: β -keto thioamides 7 (0.2 mmol) and DDQ (0.6 mmol) in dry EtOAc (2.0 mL) at rt under N₂, which was stirred until the reaction was complete as judged by TLC. ^{*b*}Yields of isolated products.

3-(dimethylamino)-3-thioxopropanoate all reacted smoothly giving the 2,3-dicyanothiophene products in excellent yields (Scheme 7, 8a–8d). The dimethyl thioamide motif was replaced with diethyl, morpholine and monomethyl functionalities, leading to the formation of 8e, 8f and 8g in good yields. In addition, β -keto thioamide substrates 7h–7k as well as 2cyano-*N*,*N*-dimethylethanethioamide 71 also showed good reactivity giving 2,3-dicyanothiophenes in moderate to good yields (Scheme 7, 8h–81). Single crystal X-ray diffraction analysis of 8j, confirmed the 2,3-dicyanothiophene structure.²³

Furthermore, 2,3-dicyanofuran 2a was selectively transformed to imidate 9 in 99% yield [eq 3],²³ which might be of interest in future biological activity studies.



CONCLUSION

In conclusion, we have demonstrated a facile oxidative coupling of α -carbonyl radicals to DDQ for the synthesis of 2,3dicyanofurans and thiophenes from readily available β diketones, simple ketones, and β -keto thioamides in up to 95% yield in one step. Mechanistic studies revealed that DDQmediated radical formation is involved in the initial step for all substrates, and then the DDQ-substrate adduct **D** undergoes a DDQ-mediated hydride abstraction and subsequent cyclization to form the key intermediate **G**. The existence of **G** was supported by the NMR spectroscopy studies; however, it was unstable and prone to an unconventional ring-opening promoted by trace amounts of H_2O and a subsequent ring-contraction to release the dihydrofuran **K**. From a synthetic point of view, this protocol represents a powerful, simple, and efficient approach to the construction of 2,3-dicyanofurans and thiophene units, which might be useful in biological scenarios. Further studies extending substrate scope of this oxidative coupling of α -carbonyl radicals and application of 2,3-dicyanofuran and thiophene derivatives to multistep syntheses are currently underway.

EXPERIMENTAL SECTION

General Information. Melting points were obtained in open capillary tubes using a melting point microapparatus, which were uncorrected. Mass spectra were recorded on TOF mass spectrometer. ¹H nuclear magnetic resonance (NMR) spectra were recorded using CDCl₃ (δ = 7.26 ppm), (CD₃)₂SO (δ = 2.50 ppm), and CD₃CN (δ = 1.94 ppm) as solvent at ambient temperature on 400 MHz spectrometer. Data are presented as follows: chemical shift (in ppm), integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet), coupling constant (J/Hz), and interpretation. ¹³C NMR spectra were recorded by broadband spin decoupling for CDCl₃ (δ = 77.2 ppm), (CD₃)₂SO ($\dot{\delta}$ = 39.5 ppm), and CD_3CN (δ = 118.3 ppm) at ambient temperatures on 100 MHz spectrometer. Chemical shift values are reported in ppm on the scale. Infrared spectra were recorded as thin films. Absorbtion frequencies are given in wave numbers (cm^{-1}) . Thin layer chromatography (TLC)was performed using commercially prepared 100-400 mesh silica gel plates, and visualization was effected at 254 or 365 nm. Unless otherwise noted, all reagents and solvents were used as purchased. Acetonitrile was dried and distilled from calcium hydride under nitrogen. Toluene and tetrahydrofuran were dried and distilled from sodium/benzophenone under nitrogen.

General Procedure for Synthesis of Polysubstituted Furans 2a-2n, 4a-4o and Thiophenes 8. Carbonyl compounds (0.2 mmol) were added to a solution of DDQ (137 mg, 0.6 mmol) in dry CH₃CN or EtOAc (2 mL) at room temperature under an atmosphere of N₂. The resulting mixture was stirred until the reaction was complete as judged by TLC. Then the resulting yellow solid was removed by filtration, and the solvent was evaporated to dryness, which was further purified by column chromatography on 100–200 mesh silica gel to afford pure polysubstituted furans 2a-2n, 4a-4o, and 8.

Methyl 4,5-dicyano-2-methylfuran-3-carboxylate (2a). A white solid (35 mg, 93%, yield): $R_f = 0.22$ (petroleum ether/ethyl acetate = 7:1); mp 70–72 °C; ¹H NMR (400 MHz, CDCl₃) δ 3.96 (s, 3H), 2.73 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 165.1, 160.1, 130.4, 115.1, 108.9, 108.8, 107.9, 52.7, 14.3; HRMS (EI-TOF) calcd. for C₉H₆N₂O₃ [M]⁺ 190.0378, found 190.0376; IR (KBr) 2957, 2249, 2235, 1722, 1561, 1457, 1419, 1311, 1228, 1127, 1088, 992 cm⁻¹.

Ethyl 4,5-dicyano-2-methylfuran-3-carboxylate (2b). A yellowish viscous oil (37 mg, 91%, yield): $R_f = 0.23$ (petroleum ether/ ethyl acetate = 7:1); ¹H NMR (400 MHz, CDCl₃) δ 4.41 (q, *J* = 7.1 Hz, 2H), 2.72 (s, 3H), 1.42 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 165.0, 159.6, 130.3, 115.2, 108.9, 107.9, 62.2, 14.2, 13.9; HRMS (EI-TOF) calcd. for C₁₀H₈N₂O₃ [M]⁺ 204.0535, found 204.0536; IR (KBr) 2987, 2249, 2236, 1717, 1600, 1444, 1308, 1227, 1132, 1088, 1025 cm⁻¹.

Isopropyl 4,5-dicyano-2-methylfuran-3-carboxylate (2c). A red viscous oil (38 mg, 88%, yield): $R_f = 0.28$ (petroleum ether/ethyl acetate = 20:1); ¹H NMR (400 MHz, CDCl₃) δ 5.24 (septet, J = 6.3 Hz, 1H), 2.71 (s, 3H), 1.40 (d, J = 6.3 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 164.8, 159.1, 130.2, 115.5, 109.0, 108.9, 108.0, 70.5, 21.7, 14.2; HRMS (EI-TOF) calcd. for C₁₁H₁₀N₂O₃ [M]⁺ 218.0691, found

218.0689; IR (film) 2986, 2938, 2238, 1728, 1600, 1554, 1434, 1304, 1258, 1238, 1128, 1104, 1084 cm⁻¹.

tert-Butyl 4,5-dicyano-2-methylfuran-3-carboxylate (2d). A light yellow viscous oil (40 mg, 86%, yield): $R_f = 0.30$ (petroleum ether/ethyl acetate = 20:1); ¹H NMR (400 MHz, CDCl₃) δ 2.69 (s, 3H), 1.60 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 164.6, 158.7, 129.9, 116.3, 109.1, 109.1, 108.1, 84.4, 28.0, 14.1; HRMS (EI-TOF) calcd. for C₁₂H₁₂N₂O₃ [M]⁺ 232.0848, found 232.0850; IR (film) 2982, 2934, 2236, 1726, 1598, 1554, 1415, 1371, 1312, 1258, 1121, 1085, 842 cm⁻¹.

Benzyl 4,5-dicyano-2-methylfuran-3-carboxylate (2e). A white solid (46 mg, 86%, yield): $R_f = 0.27$ (petroleum ether/ethyl acetate = 10:1); mp 123–125 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.47–7.45 (m, 2H), 7.42–7.34 (m, 3H), 5.39 (s, 2H), 2.70 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 165.2, 159.4, 134.6, 130.4, 128.8, 128.8, 128.6, 115.1, 108.9, 108.9, 107.9, 67.7, 14.4; HRMS (EI-TOF) calcd. for C₁₅H₁₀N₂O₃ [M]⁺ 266.0691, found 266.0693; IR (KBr) 2921, 2244, 1723, 1595, 1556, 1422, 1307, 1259, 1234, 1124, 1083, 778, 737 cm⁻¹.

Ethyl 2-(chloromethyl)-4,5-dicyanofuran-3-carboxylate (2f). A light yellow viscous oil (40 mg, 85%, yield): $R_f = 0.21$ (petroleum ether/ethyl acetate = 20:1); ¹H NMR (400 MHz, CDCl₃) δ 4.91 (s, 2H), 4.45 (q, J = 7.2 Hz, 2H), 1.43 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 160.4, 158.5, 131.8, 117.1, 108.9, 108.3, 107.4, 63.0, 33.9, 13.9; HRMS (EI-TOF) calcd. for C₁₀H₇ClN₂O₃ [M]⁺ 238.0145, found 238.0144; IR (film) 2987, 2242, 1728, 1554, 1432, 1310, 1244, 1122, 1062,737, 686 cm⁻¹.

Ethyl 4,5-dicyano-2-(trifluoromethyl)furan-3-carboxylate (2g). A light yellow viscous oil (36 mg, 69%, yield): $R_f = 0.24$ (petroleum ether/ethyl acetate = 30:1); ¹H NMR (400 MHz, CDCl₃) δ 4.48 (q, J = 7.1 Hz, 2H), 1.43 (t, J = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 156.3, 147.5 (q, J = 45.5 Hz), 132.3, 120.9 (q, J = 2.2 Hz), 116.6 (q, J = 270.7 Hz), 110.0, 107.1, 106.5, 63.7, 13.6; HRMS (EI-TOF) calcd. for C₁₀H₅F₃N₂O₃ [M]⁺ 258.0252, found 258.0253; IR (film) 2990, 2922, 2251, 1744, 1608, 1419, 1315, 1249, 1204, 1159, 1032, 790, 723 cm⁻¹.

Methyl 4,5-dicyano-2-ethylfuran-3-carboxylate (2h). A light yellow viscous oil (36 mg, 89%, yield): $R_f = 0.25$ (petroleum ether/ ethyl acetate = 20:1); ¹H NMR (400 MHz, CDCl₃) δ 3.94 (s, 3H), 3.11 (q, J = 7.5 Hz, 2H), 1.30 (t, J = 7.5 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 169.8, 160.0, 130.4, 114.2, 109.0, 108.8, 108.0, 52.7, 21.7, 11.4; HRMS (EI-TOF) calcd. for C₁₀H₈N₂O₃ [M]⁺ 204.0535, found 204.0537; IR (film) 2987, 2958, 2236, 1729, 1553, 1447, 1307, 1252, 1119, 1030, 784 cm⁻¹.

Methyl 4,5-dicyano-2-isopropylfuran-3-carboxylate (2i). A white solid (38 mg, 87%, yield): $R_f = 0.26$ (petroleum ether/ethyl acetate = 20:1); mp 55–57 °C; ¹H NMR (400 MHz, CDCl₃) δ 3.94 (s, 3H), 3.84 (septet, J = 7.0 Hz, 1H), 1.31 (d, J = 7.0 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 173.0, 160.0, 130.3, 113.2, 109.0, 108.8, 108.1, 52.7, 28.0, 20.2; HRMS (EI-TOF) calcd. for C₁₁H₁₀N₂O₃ [M]⁺ 218.0691, found 218.0692; IR (KBr) 2988, 2958, 2244, 2235, 1724, 1552, 1448, 1294, 1226, 1115, 1038, 816 cm⁻¹.

Methyl 2-*tert***-butyl-4,5-dicyanofuran-3-carboxylate (2j).** A white solid (22 mg, 48%, yield): $R_f = 0.28$ (petroleum ether/ethyl acetate = 30:1); mp 72–74 °C; ¹H NMR (400 MHz, CDCl₃) δ 3.96 (s, 3H), 1.46 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 174.0, 159.9, 129.0, 114.5, 110.2, 109.2, 108.0, 52.8, 35.9, 27.8; HRMS (EI-TOF) calcd. for C₁₂H₁₂N₂O₃ [M]⁺ 232.0848, found 232.0846; IR (KBr) 2987, 2961, 2233, 1718, 1437, 1305, 1249, 1113, 1023, 808, 791 cm⁻¹.

Ethyl 2-(benzyloxymethyl)-4,5-dicyanofuran-3-carboxylate (2k). A light yellow viscous oil (51 mg, 82%, yield): $R_f = 0.24$ (petroleum ether/ethyl acetate = 20:1); ¹H NMR (400 MHz, CDCl₃) δ 7.35–7.32 (m, 5H), 4.87 (s, 2H), 4.64 (s, 2H), 4.40 (q, J = 7.0 Hz, 2H), 1.40 (t, J = 7.0 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 162.8, 158.9, 136.8, 131.5, 128.6, 128.3, 128.0, 117.1, 108.7, 108.6, 107.8, 73.9, 62.6, 62.4, 13.9; HRMS (EI-TOF) calcd. for C₁₇H₁₄N₂O₄ [M]⁺ 310.0954, found 310.0955; IR (film) 2986, 2868, 2239, 1728, 1553, 1432, 1308, 1247, 1123, 1067, 743, 700 cm⁻¹.

4-Acetyl-5-methylfuran-2,3-dicarbonitrile (2l). A white solid (32 mg, 93%, yield): $R_f = 0.18$ (petroleum ether/ethyl acetate = 10:1);

mp 96–98 °C; ¹H NMR (400 MHz, CDCl₃) δ 2.71 (s, 3H), 2.63 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 189.7, 164.4, 130.4, 122.2, 109.8, 107.9, 107.8, 29.9, 15.1; HRMS (EI-TOF) calcd. for C₉H₆N₂O₂ [M]⁺ 174.0429, found 174.0427; IR (KBr) 3000, 2920, 2240, 1679, 1553, 1413, 1298, 1075, 963, 625 cm⁻¹.

4-Oxo-4,5,6,7-tetrahydrobenzofuran-2,3-dicarbonitrile (**2m**). A white solid (31 mg, 84%, yield): $R_f = 0.19$ (petroleum ether/ ethyl acetate = 2:1); mp 107–109 °C; ¹H NMR (400 MHz, (CD₃)₂SO) δ 2.92 (t, J = 6.2 Hz, 2H), 2.44 (t, J = 7.0 Hz, 2H), 2.08– 2.02 (m, 2H); ¹³C NMR (100 MHz, (CD₃)₂SO) δ 191.9, 172.7, 131.6, 120.0, 110.0, 109.3, 104.8, 37.4, 23.4, 21.6; HRMS (EI-TOF) calcd. for C₁₀H₆N₂O₂ [M]⁺ 186.0429, found 186.0428; IR (KBr) 2948, 2241, 1689, 1550, 1456, 1407, 1011, 672 cm⁻¹.

5-Methylfuran-2,3,4-tricarbonitrile (2n). A white solid (29 mg, 91%, yield): $R_f = 0.25$ (petroleum ether/ethyl acetate = 3:1); mp 50–52 °C; ¹H NMR (400 MHz, CDCl₃) δ 2.66 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 167.1, 130.8, 109.3, 108.5, 107.2, 107.0, 98.3, 14.0; HRMS (EI-TOF) calcd. for C₈H₃N₃O [M]⁺ 157.0276, found 157.0278; IR (KBr) 2245, 1696, 1597, 1565, 1416, 1170, 1083 cm⁻¹.

Methyl 4,5-dicyano-2-phenylfuran-3-carboxylate (4a). A white solid (42 mg, 83%, yield): $R_{\rm f} = 0.21$ (petroleum ether/ethyl acetate = 20:1); mp 124–126 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.95–7.93 (m, 2H), 7.60–7.50 (m, 3H), 3.96 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 162.5, 159.8, 132.3, 130.7, 129.2, 128.8, 126.1, 114.3, 110.4, 109.0, 108.0, 52.9; HRMS (EI-TOF) calcd. for C₁₄H₈N₂O₃ [M]⁺ 252.0535, found 252.0534; IR (KBr) 2956, 2237, 1734, 1532, 1489, 1438, 1307, 1269, 1219, 1098, 1017, 771, 692 cm⁻¹.

Ethyl 4,5-dicyano-2-phenylfuran-3-carboxylate (4b). A white solid (45 mg, 84%, yield): $R_f = 0.23$ (petroleum ether/ethyl acetate = 20:1); mp 108–110 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.96–7.94 (m, 2H), 7.60–7.50 (m, 3H), 4.42 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 162.3, 159.3, 132.3, 130.6, 129.2, 128.7, 126.2, 114.5, 110.6, 109.1, 108.1, 62.6, 13.8; HRMS (ESI-TOF) calcd. for C₁₅H₉N₂O₃ [M – H]⁺ 265.0613, found 265.0616; IR (KBr) 2979, 2926, 2237, 1711, 1546, 1427, 1307, 1230, 1123, 1021, 771, 699 cm⁻¹.

4-Acetyl-5-phenylfuran-2,3-dicarbonitrile; 4-Benzoyl-5-methylfuran-2,3-dicarbonitrile (4c). Ratio of the two isomers was 1:2. A light yellow viscous oil (29 mg, 62%, yield): $R_f = 0.23$ (petroleum ether/ethyl acetate = 10:1); ¹H NMR (400 MHz, CDCl₃) δ 7.76–7.75 (m, 4H), 7.70–7.66 (m, 4H), 7.63–7.59 (m, 1H), 7.56–7.53 (m, 6H), 2.49 (s, 6H), 2.46 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 190.2, 186.8, 162.6, 161.3, 136.3, 134.5, 132.4, 131.1, 130.4, 129.3, 129.1, 129.1, 126.4, 123.0, 122.3, 109.4, 109.1, 108.8, 108.0, 30.0, 14.5. MS(EI-TOF) *m*/*z* 236.1 [M]⁺.

5-Phenylfuran-2,3,4-tricarbonitrile (4d). A white solid (40 mg, 92%, yield): $R_f = 0.21$ (petroleum ether/ethyl acetate = 20:1); mp 149–151 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.04 (d, *J* = 7.4 Hz, 2H), 7.69–7.59 (m, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 164.0, 133.7, 130.1, 129.9, 126.7, 124.6, 111.0, 109.7, 107.3, 107.2, 94.1; HRMS (EI-TOF) calcd. for C₁₃H₃N₃O [M]⁺ 219.0433, found 219.0434; IR (KBr) 2237, 1543, 1488, 1450, 1407, 778, 706, 687 cm⁻¹.

Methyl 2-(2-bromophenyl)-4,5-dicyanofuran-3-carboxylate (4e). A white solid (51 mg, 78%, yield): $R_f = 0.22$ (petroleum ether/ethyl acetate = 10:1); mp 90–92 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.73–7.70 (m, 1H), 7.48–7.43 (m, 3H), 3.84 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 161.3, 159.1, 133.4, 133.1, 132.2, 131.5, 127.8, 127.5, 123.5, 117.4, 109.2, 108.7, 107.8, 53.0; HRMS (EI-TOF) calcd. for $C_{14}H_7BrN_2O_3$ [M]⁺ 329.9640, found 329.9647; IR (KBr) 2954, 2239, 1730, 1441, 1308, 1233, 1132, 1013, 779 cm⁻¹.

Methyl 2-(3-bromophenyl)-4,5-dicyanofuran-3-carboxylate (4f). A white solid (55 mg, 83%, yield): $R_f = 0.23$ (petroleum ether/ ethyl acetate = 10:1); mp 101–103 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.11 (t, J = 1.8 Hz, 1H), 7.92–7.90 (m, 1H), 7.70–7.68 (m, 1H), 7.40 (t, J = 8.0 Hz, 1H), 3.97 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 160.4, 159.5, 135.2, 131.9, 131.1, 130.3, 127.8, 127.8, 122.7, 115.1, 110.4, 108.8, 107.8, 53.2; HRMS (EI-TOF) calcd. for C₁₄H₇BrN₂O₃ [M]⁺ 329.9640, found 329.9642; IR (KBr) 3107, 2234, 1736, 1530, 1466, 1309, 1216, 1104, 1024, 779 cm⁻¹. **Methyl 2-(4-bromophenyl)-4,5-dicyanofuran-3-carboxylate** (**4g**). A white solid (56 mg, 85%, yield): $R_f = 0.25$ (petroleum ether/ethyl acetate = 20:1); mp 151–153 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.85 (d, J = 7.6 Hz, 2H), 7.65 (d, J = 7.6 Hz, 2H), 3.97 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 161.3, 159.6, 132.1, 130.9, 130.5, 127.3, 124.9, 114.7, 110.5, 108.9, 107.9, 53.1; HRMS (EI-TOF) calcd. for C₁₄H₇BrN₂O₃ [M]⁺ 329.9640, found 329.9638; IR (KBr) 2961, 2239, 1727, 1542, 1485, 1314, 1231, 1101, 838, 782 cm⁻¹.

Methyl 2-(4-chlorophenyl)-4,5-dicyanofuran-3-carboxylate (**4h**). A white solid (51 mg, 89%, yield): $R_f = 0.21$ (petroleum ether/ethyl acetate = 20:1); mp 141–143 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.94 (d, J = 8.4 Hz, 2H), 7.50 (d, J = 8.4 Hz, 2H), 3.97 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 161.2, 159.6, 138.8, 130.8, 130.5, 129.2, 124.5, 114.6, 110.5, 108.8, 107.9, 53.0; HRMS (EI-TOF) calcd. for C₁₄H₇ClN₂O₃ [M]⁺ 286.0145, found 286.0146; IR (KBr) 2962, 2239, 1727, 1485, 1313, 1233, 1104, 1089, 846, 781 cm⁻¹.

Methyl 4,5-dicyano-2-*p***-tolylfuran-3-carboxylate (4i).** A white solid (40 mg, 76%, yield): $R_f = 0.24$ (petroleum ether/ethyl acetate = 10:1); mp 137–139 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.84 (d, J = 8.3 Hz, 2H), 7.32 (d, J = 8.3 Hz, 2H), 3.95 (s, 3H), 2.44(s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 162.7, 159.9, 143.2, 130.4, 129.5, 129.1, 123.3, 113.7, 110.4, 109.1, 108.1, 52.9, 21.7; HRMS (EI-TOF) calcd. for C₁₅H₁₀N₂O₃ [M]⁺ 266.0691, found 266.0692; IR (KBr) 2956, 2924, 2233, 1739, 1499, 1308, 1214, 1095, 830, 780 cm⁻¹.

Methyl 4,5-dicyano-2-(4-methoxyphenyl)furan-3-carboxylate (4j). A white solid (23 mg, 41%, yield): $R_f = 0.22$ (petroleum ether/ethyl acetate = 10:1); mp 112–114 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.96 (d, J = 7.8 Hz, 2H), 7.01 (d, J = 7.8 Hz, 2H), 3.96 (s, 3H), 3.89 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 162.8, 162.7, 160.0, 131.0, 130.0, 118.5, 114.2, 112.7, 110.5, 109.2, 108.2, 55.6, 52.8; HRMS (EI-TOF) calcd. for C₁₅H₁₀N₂O₄ [M]⁺ 282.0641, found 282.0644; IR (KBr) 2956, 2845, 2230, 1741, 1607, 1499, 1308, 1264, 1180, 1095, 812, 781 cm⁻¹.

Methyl 4,5-dicyano-2-(2-(4-methylbenzyloxy)phenyl)furan-3-carboxylate (4k). A white solid (57 mg, 77%, yield): $R_f = 0.18$ (petroleum ether/ethyl acetate = 10:1); mp 137–139 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.55–7.47 (m, 2H), 7.20–7.15 (m, 4H), 7.12–7.08 (m, 2H), 5.05 (s, 2H), 3.72 (s, 3H), 2.37 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 160.2, 159.5, 157.1, 138.2, 133.6, 132.8, 131.1, 130.8, 129.3, 127.3, 120.9, 116.7, 116.2, 113.4, 109.3, 109.0, 108.2, 71.0, 52.5, 21.2; HRMS (ESI-TOF) calcd. for C₂₂H₁₆N₂O₄Na [M + Na]⁺ 395.1008, found 395.1013; IR (KBr) 2958, 2930, 2232, 1729, 1451, 1262, 1247, 1015, 809, 755 cm⁻¹.

Methyl 4,5-dicyano-2-(naphthalen-2-yl)furan-3-carboxylate (4). A white solid (54 mg, 89%, yield): $R_f = 0.21$ (petroleum ether/ ethyl acetate = 10:1); mp 181–183 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.57 (s, 1H), 7.97–7.89 (m, 4H), 7.65–7.57 (m, 2H), 3.99 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 162.5, 159.9, 134.7, 132.4, 130.7, 130.6, 129.2, 128.8, 128.5, 127.8, 127.3, 124.5, 123.3, 114.4, 110.5, 109.1, 108.1, 53.0; HRMS (EI-TOF) calcd. for C₁₈H₁₀N₂O₃ [M]⁺ 302.0691, found 302.0693; IR (KBr) 2952, 2232, 1740, 1535, 1200, 1094, 825, 784 cm⁻¹.

Methyl 4,5-dicyano-2,2'-bifuran-3-carboxylate (4m). Recrystallization of the crude product afforded a white solid (17 mg, 35%, yield): $R_f = 0.20$ (petroleum ether/ethyl acetate = 20:1); mp 134–136 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.86 (d, J = 3.7 Hz, 1H), 7.70 (d, J = 1.2 Hz, 1H), 6.66 (dd, J = 3.7, 1.7 Hz, 1H), 4.00 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 159.3, 152.8, 146.7, 141.5, 130.0, 119.3, 113.0, 111.6, 110.0, 108.8, 108.0, 52.9; HRMS (EI-TOF) calcd. for C₁₂H₆N₂O₄ [M]⁺ 242.0328, found 242.0329; IR (KBr) 3148, 2233, 1718, 1597, 1533, 1318, 1250, 1011, 782 cm⁻¹.

Methyl 2-(5-chlorothiophen-2-yl)-4,5-dicyanofuran-3-carboxylate (4n). Recrystallization of the crude product afforded a yellowish solid (44 mg, 75%, yield): $R_f = 0.29$ (petroleum ether/ethyl acetate = 20:1); mp 160–162 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.92 (d, J = 4.2 Hz, 1H), 7.03 (d, J = 4.2 Hz, 1H), 4.00 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 159.9, 156.4, 138.9, 132.5, 129.8, 127.4, 125.8, 111.4, 110.1, 108.7, 107.9, 53.1; HRMS (EI-TOF) calcd. for $C_{12}H_5ClN_2O_3S$ [M]⁺ 291.9709, found 291.9711; IR (KBr) 3098, 2231, 1719, 1555, 1494, 1443, 1238, 1219, 1069, 815, 785 cm⁻¹. **Methyl 4,5-dicyano-2-(pyridin-2-yl)furan-3-carboxylate (40).** A white solid (46 mg, 90%, yield): $R_f = 0.25$ (petroleum ether/ethyl acetate = 4:1); mp 97–99 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.76 (d, J = 4.3 Hz, 1H), 8.07 (d, J = 8.1 Hz, 1H), 7.88 (t, J = 7.8 Hz, 1H), 7.47 (t, J = 6.1 Hz, 1H), 3.95 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 159.6, 159.4, 150.3, 144.9, 136.9, 131.3, 126.0, 125.1, 116.7, 109.9, 108.7, 107.8, 53.2; HRMS (EI-TOF) calcd. for C₁₃H₇N₃O₃ [M]⁺ 253.0487, found 253.0484; IR (KBr) 2955, 2242, 1747, 1534, 1218, 1116, 1026, 786 cm⁻¹.

Methyl 4,5-dicyano-2-(dimethylamino)thiophene-3-carboxylate (8a). A white solid (45 mg, 95%, yield): $R_f = 0.20$ (petroleum ether/ethyl acetate = 3:1); mp 60–62 °C; ¹H NMR (400 MHz, CDCl₃) δ 3.90 (s, 3H), 3.13 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 167.0, 160.9, 121.6, 112.3, 111.9, 108.4, 100.6, 52.3, 45.6; HRMS (EITOF) calcd. for C₁₀H₉N₃O₂S [M]⁺ 235.0415, found 235.0417.

Ethyl 4,5-dicyano-2-(dimethylamino)thiophene-3-carboxylate (8b). A white solid (47 mg, 94%, yield): $R_f = 0.24$ (petroleum ether/dichloromethane = 1:1); mp 112–114 °C; ¹H NMR (400 MHz, CDCl₃) δ 4.36 (q, J = 7.1 Hz, 2H), 3.13 (s, 6H), 1.39 (t, J = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 166.9, 160.5, 121.7, 112.3, 111.9, 108.7, 100.5, 61.9, 45.6, 14.0; HRMS (EI-TOF) calcd. for C₁₁H₁₁N₃O₂S [M]⁺ 249.0572, found 249.0573.

tert-Butyl 4,5-dicyano-2-(dimethylamino)thiophene-3-carboxylate (8c). A white solid (51 mg, 92%, yield): $R_f = 0.30$ (petroleum ether/dichloromethane = 1:1); mp 121–123 °C; ¹H NMR (400 MHz, CDCl₃) δ 3.11 (s, 6H), 1.59 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 166.3, 160.0, 121.6, 112.5, 112.1, 110.6, 100.0, 83.7, 45.4, 28.0; HRMS (EI-TOF) calcd. for C₁₃H₁₅N₃O₂S [M]⁺ 277.0885, found 277.0887.

Benzyl 4,5-dicyano-2-(dimethylamino)thiophene-3-carboxylate (8d). A white solid (54 mg, 86%, yield): $R_f = 0.30$ (petroleum ether/dichloromethane = 1:1.5); mp 120–122 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.48 (d, J = 7.1 Hz, 2H), 7.39–7.31 (m, 3H), 5.35 (s, 2H), 3.09 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 167.2, 160.3, 135.0, 129.0, 128.6, 121.5, 112.4, 111.9, 108.3, 100.7, 67.6, 45.6; HRMS (EI-TOF) calcd. for $C_{16}H_{13}N_3O_2S$ [M]⁺ 311.0728, found 311.0727.

Methyl 4,5-dicyano-2-(diethylamino)thiophene-3-carboxylate (8e). A white solid (45 mg, 85%, yield): $R_f = 0.27$ (petroleum ether/dichloromethane = 1:1); mp 80–82 °C; ¹H NMR (400 MHz, CDCl₃) δ 3.89 (s, 3H), 3.46 (q, *J* = 7.1 Hz, 4H), 1.24 (t, *J* = 7.1 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 165.2, 161.3, 121.5, 112.4, 111.9, 109.7, 100.9, 52.4, 50.2, 12.0; HRMS (EI-TOF) calcd. for C₁₂H₁₃N₃O₂S [M]⁺ 263.0728, found 263.0729.

Methyl 4,5-dicyano-2-morpholinothiophene-3-carboxylate (8f). A light yellow solid (29 mg, 53%, yield): $R_f = 0.33$ (petroleum ether/dichloromethane = 1:2); mp 144–146 °C; ^IH NMR (400 MHz, CDCl₃) δ 3.91 (s, 3H), 3.89 (t, J = 4.7 Hz, 4H), 3.35 (t, J = 4.7 Hz, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 168.2, 160.3, 121.5, 112.5, 112.1, 111.3, 104.5, 65.9, 53.4, 52.5; HRMS (EI-TOF) calcd. for $C_{12}H_{11}N_3O_3S$ [M]⁺ 277.0521, found 277.0511.

Methyl 4,5-dicyano-2-(methylamino)thiophene-3-carboxylate (8g). A white solid (19 mg, 43%, yield): $R_f = 0.32$ (petroleum ether/dichloromethane = 1:1); mp 211–213 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.26 (s, 1H), 3.91 (s, 3H), 3.09 (d, J = 5.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 167.8, 163.6, 120.0, 112.0, 112.0, 103.3, 98.6, 52.2, 33.9; HRMS (EI-TOF) calcd. for C₉H₇N₃O₂S [M]⁺ 221.0259, found 221.0261.

4-Acetyl-5-(dimethylamino)thiophene-2,3-dicarbonitrile (**8h**). A white solid (34 mg, 77%, yield): $R_f = 0.25$ (petroleum ether/ dichloromethane = 1:2); mp 118–120 °C; ¹H NMR (400 MHz, CDCl₃) δ 3.06 (s, 6H), 2.64 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 191.0, 166.7, 119.9, 119.4, 112.9, 111.9, 101.0, 46.0, 30.3; HRMS (EI-TOF) calcd. for C₁₀H₉N₃OS [M]⁺ 219.0466, found 219.0463.

5-(Dimethylamino)-4-propionylthiophene-2,3-dicarbonitrile (8i). A white solid (32 mg, 68%, yield): $R_f = 0.30$ (petroleum ether/ dichloromethane = 1:2); mp 140–142 °C; ¹H NMR (400 MHz, CDCl₃) δ 3.04 (s, 6H), 2.99 (q, J = 7.3 Hz, 2H), 1.21 (t, J = 7.3 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 195.4, 166.1, 119.5, 119.0, 112.9, 112.0, 100.7, 45.8, 36.0, 8.8; HRMS (EI-TOF) calcd. for C₁₁H₁₁N₃OS [M]⁺ 233.0623, found 233.0625. **4-Benzoyl-5-(dimethylamino)thiophene-2,3-dicarbonitrile** (8j). A light yellow solid (41 mg, 73%, yield): $R_f = 0.21$ (petroleum ether/ethyl acetate = 3:1); mp 176–178 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.82 (d, *J* = 7.4 Hz, 2H), 7.65 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.7 Hz, 2H), 3.00 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 188.7, 164.5, 137.6, 134.3, 129.8, 129.0, 121.2, 116.5, 112.0, 111.6, 99.3, 45.2; HRMS (EI-TOF) calcd. for C₁₅H₁₁N₃OS [M]⁺ 281.0623, found 281.0620; IR (KBr) 2928, 2604, 2496, 2205, 1644, 1544, 1410, 1397, 1352, 1035, 804 cm⁻¹.

4-(4-Bromobenzoyl)-5-(diethylamino)thiophene-2,3-dicarbonitrile (8k). A light yellow solid (47 mg, 61%, yield): $R_f = 0.32$ (petroleum ether/dichloromethane = 1:2); mp 90–92 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.69 (d, J = 8.5 Hz, 2H), 7.64 (d, J = 8.5 Hz, 2H), 3.27 (q, J = 7.1 Hz, 4H), 1.09 (t, J = 7.1 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 187.8, 162.9, 135.6, 132.4, 131.3, 129.7, 120.8, 117.0, 112.0, 111.7, 99.9, 50.1, 11.7; HRMS (EI-TOF) calcd. for C₁₇H₁₄BrN₃OS [M]⁺ 387.0041, found 387.0042.

5-(Dimethylamino)thiophene-2,3,4-tricarbonitrile (8l). A white solid (18 mg, 45%, yield): $R_f = 0.20$ (petroleum ether/ethyl acetate = 2:1); mp 170–172 °C; ¹H NMR (400 MHz, CDCl₃) δ 3.37 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 165.9, 122.4, 113.3, 110.8, 110.5, 99.3, 85.1, 44.0; HRMS (EI-TOF) calcd. for C₉H₆N₄S [M]⁺ 202.0313, found 202.0314.

General Procedure for Synthesis of Polysubstituted Furans **6a–6g.** Carbonyl compounds (0.2 mmol) were added to a solution of 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) (137 mg, 0.6 mmol) in dry CH₃CN (2 mL) at room temperature under an atmosphere of N₂. The resulting mixture was stirred under reflux until the reaction was complete, as judged by TLC. Then the solvent was evaporated to dryness, and the residue was purified by column chromatography on 100–200 mesh silica gel to afford pure polysubstituted furans **6a–6g**.

4,5-Dihydronaphtho[**1,2-***b***]furan-2,3-dicarbonitrile (6a).** A white solid (27 mg, 61%, yield): $R_f = 0.21$ (petroleum ether/ethyl acetate = 10:1); mp 167–169 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.58–7.56 (m, 1H), 7.37–7.31 (m, 2H), 7.30–7.27 (m, 1H), 3.09 (t, J = 7.9 Hz, 2H), 2.90 (t, J = 7.9 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 155.9, 136.0, 130.4, 128.9, 128.7, 127.6, 124.5, 121.3, 120.6, 109.7, 109.3, 109.0, 27.8, 19.3; HRMS (EI-TOF) calcd. for C₁₄H₈N₂O [M]⁺ 220.0637, found 220.0639; IR (KBr) 2950, 2925, 2241, 2223, 1620, 1530, 1447, 1432, 766, 714 cm⁻¹.

Naphtho[1,2-*b*]furan-2,3-dicarbonitrile (6aa). A white solid (4 mg, 10%, yield): $R_f = 0.22$ (petroleum ether/ethyl acetate = 10:1); mp 198–200 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.35–8.33 (m, 1H), 8.04–8.02 (m, 1H), 7.93 (d, J = 8.8 Hz, 1H), 7.79–7.71 (m, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 152.4, 133.8, 131.2, 128.8, 128.4, 128.0, 120.6, 120.5, 120.4, 116.8, 109.6, 109.1, 105.4; HRMS (ESI-TOF) calcd. for C₁₄H₇N₂O [M + H]⁺ 219.0558, found 219.0556; IR (KBr) 2922, 2852, 2232, 1556, 1459, 1379, 1261, 1147, 810, 756 cm⁻¹.

7-Methoxy-4,5-dihydronaphtho[**1,2-***b***]furan-2,3-dicarbonitrile (6b).** A white solid (20 mg, 40%, yield): $R_f = 0.22$ (petroleum ether/ethyl acetate = 15:1); mp 150–152 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.51 (d, J = 8.3 Hz, 1H), 6.85–6.82 (m, 2H), 3.85 (s, 3H), 3.05 (t, J = 7.8 Hz, 2H), 2.89–2.85 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 161.4, 156.2, 138.4, 128.1, 123.0, 118.5, 117.6, 114.8, 112.5, 110.0, 109.7, 109.0, 55.5, 28.2, 19.3; HRMS (EI-TOF) calcd. for C₁₅H₁₀N₂O₂ [M]⁺ 250.0742, found 250.0744; IR (KBr) 2963, 2913, 2243, 2219, 1618, 1595, 1498, 1448, 1431, 1272, 1248, 1035, 827 cm⁻¹.

7-Methoxynaphtho[1,2-*b*]furan-2,3-dicarbonitrile (6bb). A white solid (14 mg, 28%, yield): $R_f = 0.23$ (petroleum ether/ethyl acetate = 15:1); mp 176–178 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.14 (d, *J* = 8.9 Hz, 1H), 7.76 (d, *J* = 8.7 Hz, 1H), 7.59 (d, *J* = 8.7 Hz, 1H), 7.35 (dd, *J* = 8.9, 2.3 Hz, 1H), 7.29 (d, *J* = 2.1 Hz, 1H), 3.99 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 159.9, 152.5, 135.7, 130.3, 126.9, 122.2, 120.4, 118.6, 117.4, 115.0, 109.7, 109.3, 107.7, 105.3, 55.6; HRMS (EI-TOF) calcd. for C₁₅H₈N₂O₂ [M]⁺ 248.0586, found 248.0589; IR (KBr) 2937, 2229, 1634, 1598, 1474, 1461, 1370, 1266, 1249, 1169, 1028, 854, 814 cm⁻¹.

4,5,6,7-Tetrahydrobenzofuran-2,3-dicarbonitrile (6c). A colorless oil (9 mg, 25%, yield): $R_f = 0.25$ (petroleum ether/ethyl acetate

= 20:1); ¹H NMR (400 MHz, CDCl₃) δ 2.68 (t, *J* = 6.1 Hz, 2H), 2.56 (t, *J* = 5.6 Hz, 2H), 1.95–1.89 (m, 2H), 1.85–1.79 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 158.9, 128.8, 121.1, 110.1, 109.3, 108.8, 23.3, 21.9, 21.7, 20.5; HRMS (EI-TOF) calcd. for C₁₀H₈N₂O [M]⁺ 172.0637, found 172.0640; IR (KBr) 2949, 2863, 2230, 1616, 1540, 1444, 1425, 1279, 1170, 1099, 955, 938 cm⁻¹.

5,6,7,8-Tetrahydro-4*H***-cyclohepta**[*b*]**furan-2,3-dicarbonitrile** (**6d**). A colorless oil (31 mg, 82%, yield): $R_f = 0.33$ (petroleum ether/ ethyl acetate = 30:1); ¹H NMR (400 MHz, CDCl₃) δ 2.84 (t, *J* = 5.8 Hz, 2H), 2.59 (t, *J* = 5.7 Hz, 2H), 1.87–1.81 (m, 2H), 1.77–1.70 (m, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 160.4, 126.1, 123.7, 109.6, 109.1, 108.1, 29.0, 28.1, 26.3, 24.3, 23.1; HRMS (EI-TOF) calcd. for C₁₁H₁₀N₂O [M]⁺ 186.0793, found 186.0794; IR (KBr) 2932, 2854, 2241, 2226, 1602, 1539, 1446, 1281, 1209, 1070, 962, 810 cm⁻¹.

6,7-Dihydro-4H-thiopyrano[**4**,**3**-*b*]**furan-2,3-dicarbonitrile** (**6e**). A white solid (13 mg, 34%, yield): $R_f = 0.16$ (petroleum ether/ ethyl acetate = 6:1); mp 80–82 °C; ¹H NMR (400 MHz, CDCl₃) δ 3.63 (s, 2H), 2.99 (s, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 158.0, 128.7, 118.4, 109.3, 108.7, 108.2, 25.7, 25.1, 22.0; HRMS (EI-TOF) calcd. for C₉H₆N₂OS [M]⁺ 190.0201, found 190.0203; IR (KBr) 2935, 2923, 2907, 2227, 1606, 1538, 1437, 1415, 1330, 1196, 1083, 719 cm⁻¹.

6,7-Dihydro-4H-furo[**3**,2-*c*]**pyran-2,3-dicarbonitrile (6f).** A white solid (20 mg, 58%, yield): $R_f = 0.23$ (petroleum ether/ethyl acetate = 5:1); mp 88–90 °C; ¹H NMR (400 MHz, CDCl₃) δ 4.66 (t, J = 1.7 Hz, 2H), 4.03 (t, J = 5.5 Hz, 2H), 2.86 (tt, J = 1.7, 5.5 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 155.7, 129.8, 119.5, 109.2, 108.8, 105.9, 64.1, 62.0, 24.8; HRMS (EI-TOF) calcd. for C₉H₆N₂O₂ [M]⁺ 174.0429, found 174.0427; IR (KBr) 2997, 2928, 2877, 2242, 2227, 1613, 1534, 1462, 1443, 1428, 1325, 1287, 1110, 1083, 961, 938, 843, 755 cm⁻¹.

5-(2-Methoxyphenyl)furan-2,3-dicarbonitrile (6g). A white solid (11 mg, 25%, yield): $R_f = 0.21$ (petroleum ether/ethyl acetate = 20:1); mp 136–138 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.82 (d, J = 7.8 Hz, 1H), 7.45 (t, J = 7.5 Hz, 1H), 7.22 (s, 1H), 7.09 (t, J = 7.6 Hz, 1H), 7.04 (d, J = 8.5 Hz, 1H), 3.99 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 156.6, 156.5, 132.1, 128.7, 127.0, 121.2, 115.8, 111.5, 111.4, 110.4, 109.9, 109.1, 55.7; HRMS (EI-TOF) calcd. for C₁₃H₈N₂O₂ [M]⁺ 224.0586, found 224.0587; IR (KBr) 3153, 2944, 2230, 1603, 1529, 1491, 1453, 1282, 1254, 1165, 1017, 756 cm⁻¹.

Preparation of Compound 3bb. A solution of carbonyl compound 3b (39 mg, 0.2 mmol) and TEMPO (95 mg, 0.6 mmol) in dry CH₃CN (2 mL) was treated with 2,3-dichloro-5,6dicyanobenzoquinone (DDQ) (137 mg, 0.6 mmol) at room temperature under an atmosphere of N2. Then the resulting mixture was stirred until the reaction was complete, as judged by TLC. The solvent was evaporated to dryness to give 3bb (38 mg, ratio = 1:3, determined by ^îH NMR spectroscopy) as a light yellow oil in 91% yield after column chromatography (100-200 mesh silica gel, petroleum ether/ethyl acetate = 5:1 as eluent). The observed characterization data (¹H and ¹³C NMR spectra, HRMS, and IR) are consistent with that previously reported in the literature.²⁴ Ketone: ¹H NMR (400 MHz, CDCl₃) δ 7.98 (d, J = 7.7 Hz, 2H), 7.68 (t, J = 7.4 Hz, 1H), 7.52 (t, J = 7.5 Hz, 2H), 4.40 (q, J = 7.1 Hz, 2H), 1.35 (t, J = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 190.3, 183.8, 160.5,135.6, 131.5, 130.0, 129.2, 63.4, 13.9. Hydrate: ¹H NMR (400 MHz, CDCl₃) δ 8.07 (d, J = 7.8 Hz, 2H), 7.59 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.5 Hz, 2H), 5.54 (s, 2H), 4.18 (q, J = 7.1 Hz, 2H), 1.04 (t, J = 7.1 Hz, 2Hz), 1.04 (t, J = 7.1 Hz, 2Hz), 1.04 (t, J = 7.1 Hz, 2Hz), 1.04 (t, J = 7.1 Hz), 1.04 (t, J = 7.1 Hz7.1 Hz, 3H).¹³C NMR (100 MHz, CDCl₃) δ 191.7, 169.9, 134.6, 131.4, 130.2, 128.8, 91.8, 63.1, 13.6; HRMS (EI-TOF) calcd. for $C_{11}H_{10}O_4$ [M]⁺ 206.0579, found 206.0580; IR (KBr) 3443, 2986, 1752, 1700, 1233, 1130 cm⁻¹

Preparation of Methyl 4-cyano-5-(imino(methoxy)methyl)-2-methylfuran-3-carboxylate (9). NaOMe (0.1 mL, 0.6 mmol, 30% solution in MeOH) was added dropwise to a solution of 2,3dicyanofuran 2a (96 mg, 0.5 mmol) in MeOH (10 mL) at room temperature. The mixture was stirred for 5 min. Then the solvent was evaporated to dryness, giving 9 as a white solid after flash chromatography 100–200 mesh silica gel (25%, ethyl acetate/ petroleum ether) (110 mg, 99% yield): mp 137–139 °C; ¹H NMR

(400 MHz, CDCl₃) δ 8.18 (s, 1H), 3.97 (s, 3H), 3.91 (s, 3H), 2.66 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 161.7, 161.4, 157.5, 148.3, 115.3, 111.2, 97.7, 53.7, 52.3, 13.9; HRMS (EI-TOF) calcd. for C₁₀H₁₀N₂O₄ [M]⁺ 222.0641, found 222.0640; IR (KBr) 3290, 2245, 1720, 1658, 1554, 1444, 1273, 1130, 1102, 979 cm⁻¹.

Procedure for NMR Experiments. 1a (12.0 mg, 0.1 mmol) was added to a solution of 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) (70.0 mg, 0.3 mmol) in dry CD_3CN (1.0 mL) at room temperature under an atmosphere of N_2 . Then the resulting mixture was stirred and monitored by NMR spectroscopy with time.

ASSOCIATED CONTENT

S Supporting Information

Copies of ¹H, ¹³C NMR spectra of compounds **2**, **4**, **6**, **8**, **9**, and **3bb**, crystal data for compounds **4k** (CCDC 943604), **8j** (CCDC 943606), and **9** (CCDC 943605), NMR and EPR experiment details. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

The Fundamental Research Funds for the Central Universities, the Shanghai Committee of Science and Technology (No. 11DZ2260600), and the National Natural Science Foundation of China (No. 21172068) are thanked for support. W.P.D. and J.S.F. also thank the Catalysis and Sensing for our Environment (CASE) network and the Natural Science Foundation of China for young foreign scientists (No. 21050110426).

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