JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

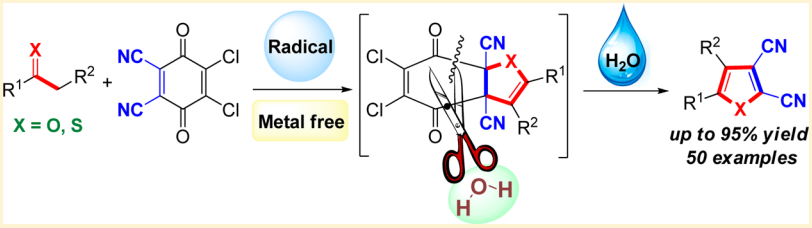
DDQ-Mediated Oxidative Coupling: An Approach to 2,3-Dicyanofuran (Thiophene)

Zheng-Lin Wang,[†] Hong-Liang Li,[†] Li-Shi Ge,[†] Xing-Lan An,[†] Zi-Gang Zhang,[†] Xiaoyan Luo,*[,†] John S. Fossey,[†,‡] and Wei-Ping Deng*[,†]

[†]Shanghai Key Laboratory of New Drug Design & School of Pharmacy, East China University of Science and Technology, 130 Meilong Road, Shanghai 200237, China

[‡]School of Chemistry, University of Birmingham, Edgbaston, Birmingham, B15 2TT, England, U.K.

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.

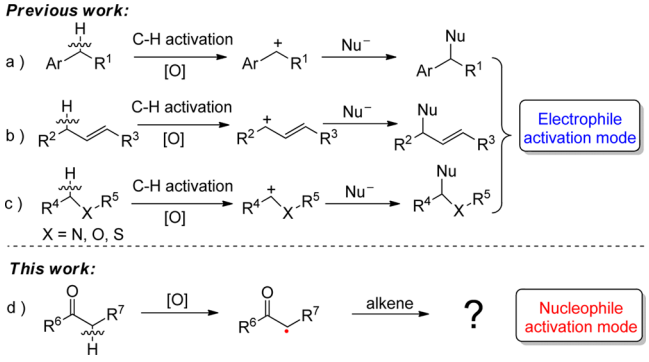
INTRODUCTION

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(sp^3)−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 novelty and diversity in both material science and drug discovery.

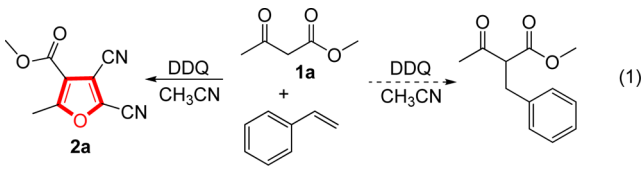
Therefore, we envisaged an oxidative coupling protocol utilizing C(sp^3)−H nucleophiles, such as ketones instead of the aforementioned electrophiles, providing electrophilic α-carbonyl radicals (Scheme 1, eq d). Electrophilic radicals, typically characterized by adjacent carbonyl groups, can be conveniently 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 DDQ-mediated 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 CH_3CN 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

Scheme 1. Strategies for C−H Functionalization



Received: November 22, 2013
Published: January 15, 2014



(1)

DDQ molecule and not from styrene. This implies that a DDQ-mediated 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.

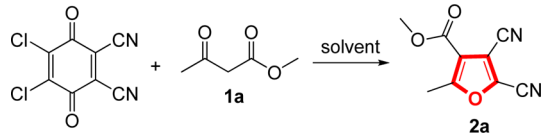
RESULTS AND DISCUSSION

With the encouragement of our interesting finding of 2,3-dicyanofuran 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 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 1,3-dicarbonyl compounds were investigated, as shown in Scheme 2. It was found that ethyl, isopropyl, *tert*-butyl, and benzyl 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 $DDQH_2$. 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 **1l** and **1m** as well as 3-oxobutanenitrile **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

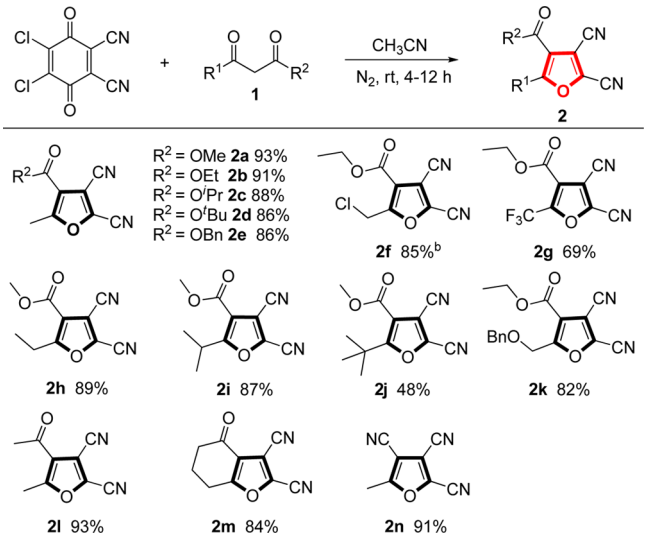
Table 1. Optimization of Reaction Conditions



entry[a]	solvent	DDQ (equiv)	yield (%)[d]
1	CH_3NO_2	2.0	22
2	CH_3NO_2	2.0	23[b]
3	DCE	2.0	26
4	toluene	2.0	15
5	CH_3CN	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_3CN**	**3.0**	**93**
13	CH_3CN	4.0	92
14	CH_3CN	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 N_2, 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.

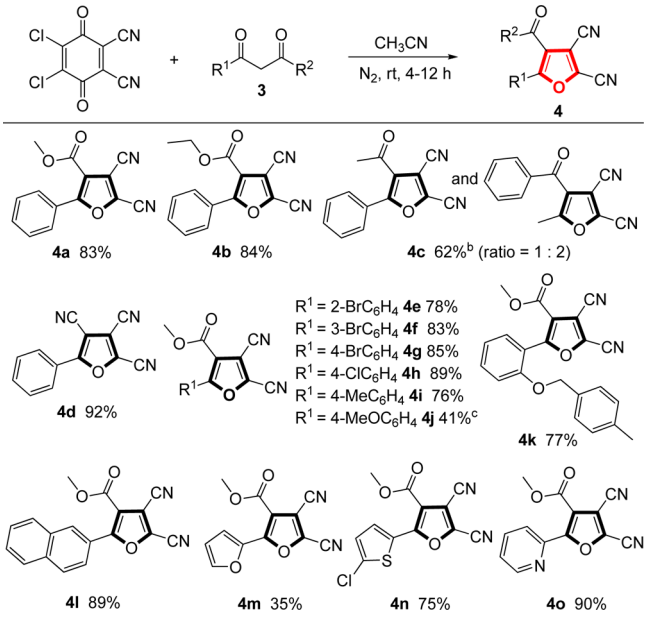
Scheme 2. Substrate Scope for Oxidative Coupling of Carbonyl Compounds 1 to DDQ[a]



[a]Yields of the isolated products. [b]5.0 equiv of DDQ was used.

dx.doi.org/10.1021/jo4026034 | J. Org. Chem. 2014, 79, 1156−1165

Scheme 3. Substrate Scope for Oxidative Coupling of Carbonyl Compounds 3 with DDQ[a]

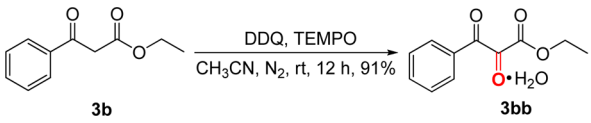


[a]Yields of the isolated products. [b]The ratio of two regioisomeric products was determined by ^{1}H NMR spectroscopy. [c]*p*-Methoxybenzoic acid was obtained in 30% yield.

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 CD_3CN in an NMR tube. The carbonyl group of **G** is then attacked by H_2O (water is actually introduced by opening the reaction flask to air during the workup) and leads to the ring-opening[17] 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



(2)

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 2,3-dichloromaleic 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 CD_3CN afforded a new unidentified product, presumably the intermediate **G**, after 5 min, by analysis of the ^{1}H NMR spectra (Scheme 4, (2)). Interestingly, the NMR signal corresponding to this unidentified product gradually increased as substrate **1a** was consumed,

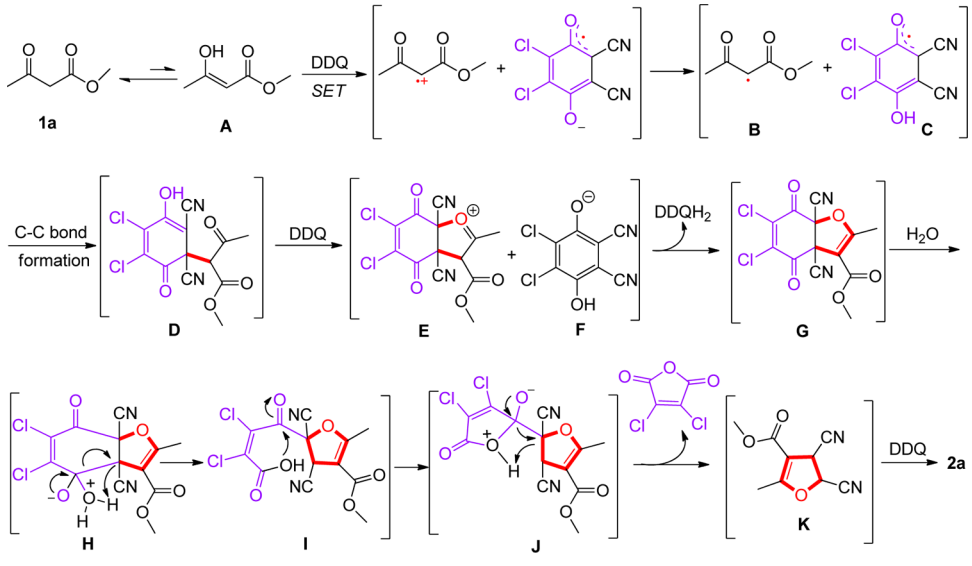
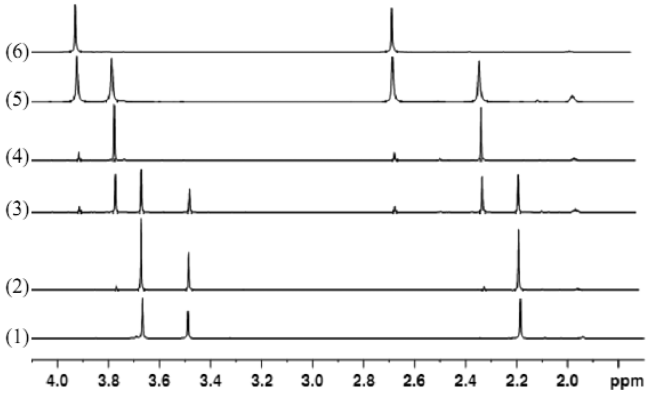


Figure 1. Proposed reaction pathway for oxidative radical addition.

dx.doi.org/10.1021/jo4026034 | J. Org. Chem. 2014, 79, 1156–1165

Scheme 4. Reactions Were Monitored by ^{1}H NMR Spectroscopy[a]



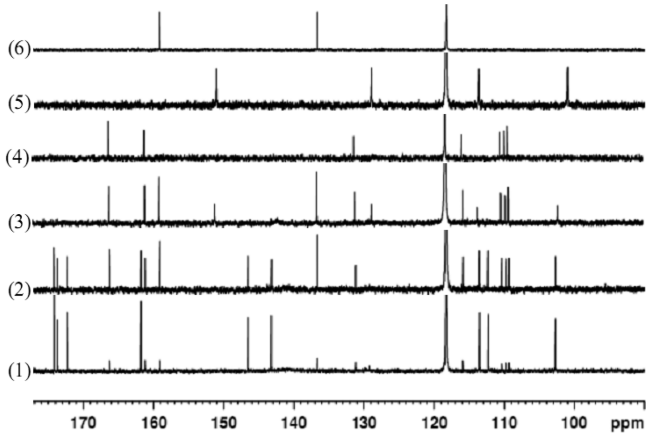
[a]Reaction conditions: Carbonyl compound **1a** (0.1 mmol) was added to a solution of DDQ (0.3 mmol) in CD_3CN (1.0 mL) at room temperature under N_2. The resulting mixture was monitored by ^{1}H NMR spectroscopy with time. (1) Substrate **1a**; (2) after 5 min; (3) after 30 min; (4) after 1 h; (5) after 2 h; (6) addition of 1.0 equiv of H_2O for additional 1 h.

accompanied by the formation of a small amount of **2a** after 30 min, which gradually increased over 2 h. The ^{1}H 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 H_2O to the sample in an NMR tube (Scheme 4, (5)). Furthermore, we also analyzed the ^{13}C NMR spectra of the same reaction, and both $DDQH_2$ and 2,3-dichloromaleic anhydride (as judged by comparison of the ^{13}C NMR spectra of authentic samples) were found following addition of 1.0 equiv of H_2O after an additional hour (Scheme 5, (3)). These NMR spectra provide supporting evidence consistent with the proposed mechanism.

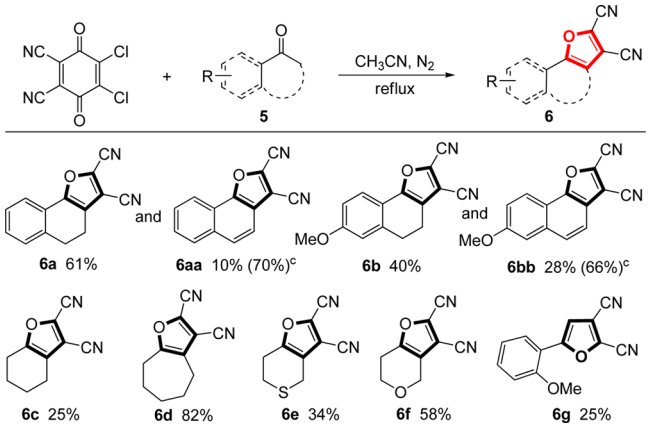
On the basis of our reaction pathway hypothesis, we believed that simple ketones **5** could be useful in this system as long as the formation of an α-carbonyl radical in the presence of DDQ is possible. Despite the fact that successful formation of α-carbonyl radicals has been reported through transition metal-mediated 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 CH_3CN. To our delight, treatment of **5a** with DDQ under reflux successfully delivered the corresponding 2,3-dicyanofuran **6a**, instead of a dehydrogenation 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 5. Reactions Were Monitored by ^{13}C NMR Spectroscopy[a]



[a](1) After 1 h; (2) after 2 h; (3) after 1.0 equiv of H_2O for additional 1 h; (4) product **2a**; (5) $DDQH_2$; (6) 2,3-dichloromaleic anhydride.

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 CH_3CN (2.0 mL) at reflux under N_2, which was stirred until the reaction was complete, as judged by TLC. [b]Yields of isolated products. [c]Yield when using 5.0 equiv of DDQ in the parentheses.

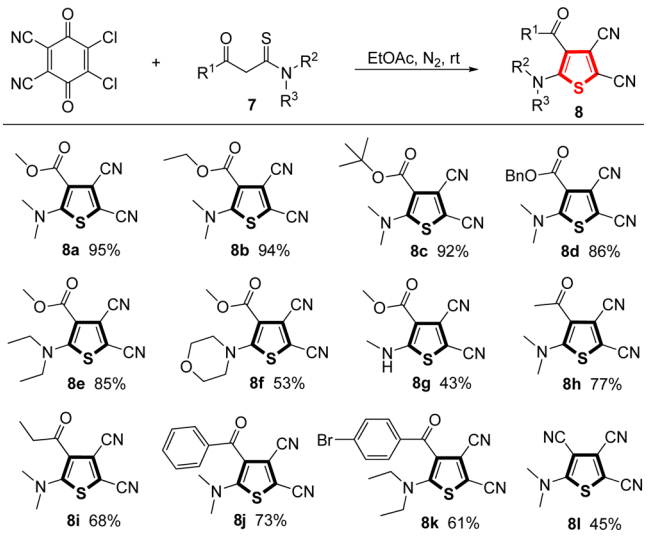
Use of 5.0 equiv of DDQ in reactions with **5a** and **5b** gave **6aa** and **6bb** only in 70 and 66% yields, respectively. Simple cyclic ketones **5c**−**5f** also showed good reactivity to giving 2,3-dicyanofurans in moderate to good yields (Scheme 6, **6c**−**6f**). However, acetophenone was found 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

dx.doi.org/10.1021/jo4026034 | J. Org. Chem. 2014, 79, 1156−1165

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

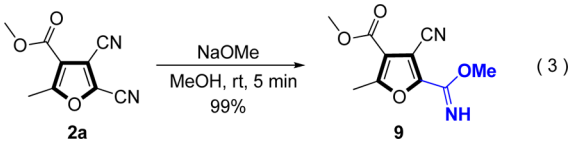
Scheme 7. Substrate Scope for Oxidative Coupling of *β*-Keto Thioamides 7 to DDQ[a,b]



[a]Reaction conditions: *β*-keto thioamides **7** (0.2 mmol) and DDQ (0.6 mmol) in dry EtOAc (2.0 mL) at rt under N_2, 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 2-cyano-*N*,*N*-dimethylethanethioamide **7l** also showed good reactivity giving 2,3-dicyanothiophenes in moderate to good yields (Scheme 7, **8h**–**8l**). 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 2,3-dicyanofurans 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 DDQ-mediated 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. ^{1}H nuclear magnetic resonance (NMR) spectra were recorded using $CDCl_3$ (δ = 7.26 ppm), $(CD_3)_2SO$ (δ = 2.50 ppm), and CD_3CN (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. ^{13}C NMR spectra were recorded by broadband spin decoupling for $CDCl_3$ (δ = 77.2 ppm), $(CD_3)_2SO$ (δ = 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 CH_3CN or EtOAc (2 mL) at room temperature under an atmosphere of N_2. 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; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.96 (s, 3H), 2.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 160.1, 130.4, 115.1, 108.9, 108.8, 107.9, 52.7, 14.3; HRMS (EI-TOF) calcd. for $C_9H_6N_2O_3$ $[M]^+$ 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); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.41 (q, J = 7.1 Hz, 2H), 2.72 (s, 3H), 1.42 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 159.6, 130.3, 115.2, 108.9, 107.9, 62.2, 14.2, 13.9; HRMS (EI-TOF) calcd. for $C_{10}H_8N_2O_3$ $[M]^+$ 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); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.24 (septet, J = 6.3 Hz, 1H), 2.71 (s, 3H), 1.40 (d, J = 6.3 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{11}H_{10}N_2O_3$ $[M]^+$ 218.0691, found

dx.doi.org/10.1021/jo4026034 | J. Org. Chem. 2014, 79, 1156–1165

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, $CDCl_3$) δ 2.69 (s, 3H), 1.60 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{12}H_{12}N_2O_3$ $[M]^+$ 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, $CDCl_3$) δ 7.47−7.45 (m, 2H), 7.42−7.34 (m, 3H), 5.39 (s, 2H), 2.70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{15}H_{10}N_2O_3$ $[M]^+$ 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, $CDCl_3$) δ 4.91 (s, 2H), 4.45 (q, J = 7.2 Hz, 2H), 1.43 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{10}H_7ClN_2O_3$ $[M]^+$ 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, $CDCl_3$) δ 4.48 (q, J = 7.1 Hz, 2H), 1.43 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{10}H_5F_3N_2O_3$ $[M]^+$ 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, $CDCl_3$) δ 3.94 (s, 3H), 3.11 (q, J = 7.5 Hz, 2H), 1.30 (t, J = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{10}H_8N_2O_3$ $[M]^+$ 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, $CDCl_3$) δ 3.94 (s, 3H), 3.84 (septet, J = 7.0 Hz, 1H), 1.31 (d, J = 7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{11}H_{10}N_2O_3$ $[M]^+$ 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, $CDCl_3$) δ 3.96 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{12}H_{12}N_2O_3$ $[M]^+$ 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, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{17}H_{14}N_2O_4$ $[M]^+$ 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, $CDCl_3$) δ 2.71 (s, 3H), 2.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.7, 164.4, 130.4, 122.2, 109.8, 107.9, 107.8, 29.9, 15.1; HRMS (EI-TOF) calcd. for $C_9H_6N_2O_2$ $[M]^+$ 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, $(CD_3)_2SO$) δ 2.92 (t, J = 6.2 Hz, 2H), 2.44 (t, J = 7.0 Hz, 2H), 2.08−2.02 (m, 2H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) 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 $C_{10}H_6N_2O_2$ $[M]^+$ 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, $CDCl_3$) δ 2.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 130.8, 109.3, 108.5, 107.2, 107.0, 98.3, 14.0; HRMS (EI-TOF) calcd. for $C_8H_3N_3O$ $[M]^+$ 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_f = 0.21 (petroleum ether/ethyl acetate = 20:1); mp 124−126 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.95−7.93 (m, 2H), 7.60−7.50 (m, 3H), 3.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{14}H_8N_2O_3$ $[M]^+$ 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, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{15}H_9N_2O_3$ $[M - H]^+$ 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, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) 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, $CDCl_3$) δ 8.04 (d, J = 7.4 Hz, 2H), 7.69−7.59 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{13}H_5N_3O$ $[M]^+$ 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, $CDCl_3$) δ 7.73−7.70 (m, 1H), 7.48−7.43 (m, 3H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 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, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{14}H_7BrN_2O_3$ $[M]^+$ 329.9640, found 329.9642; IR (KBr) 3107, 2234, 1736, 1530, 1466, 1309, 1216, 1104, 1024, 779 cm^{-1}.

dx.doi.org/10.1021/jo4026034 | J. Org. Chem. 2014, 79, 1156−1165

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; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 7.6 Hz, 2H), 7.65 (d, J = 7.6 Hz, 2H), 3.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{14}H_7BrN_2O_3$ $[M]^+$ 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; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 8.4 Hz, 2H), 7.50 (d, J = 8.4 Hz, 2H), 3.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{14}H_7ClN_2O_3$ $[M]^+$ 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; ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{15}H_{10}N_2O_3$ $[M]^+$ 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; ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{15}H_{10}N_2O_4$ $[M]^+$ 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; ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{22}H_{16}N_2O_4Na$ $[M + Na]^+$ 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 (4l). A white solid (54 mg, 89%, yield): R_f = 0.21 (petroleum ether/ethyl acetate = 10:1); mp 181−183 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 1H), 7.97−7.89 (m, 4H), 7.65−7.57 (m, 2H), 3.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{18}H_{10}N_2O_3$ $[M]^+$ 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; ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{12}H_6N_2O_4$ $[M]^+$ 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; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 4.2 Hz, 1H), 7.03 (d, J = 4.2 Hz, 1H), 4.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 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 (4o). A white solid (46 mg, 90%, yield): R_f = 0.25 (petroleum ether/ethyl acetate = 4:1); mp 97−99 °C; ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{13}H_7N_3O_3$ $[M]^+$ 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; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.90 (s, 3H), 3.13 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 160.9, 121.6, 112.3, 111.9, 108.4, 100.6, 52.3, 45.6; HRMS (EI-TOF) calcd. for $C_{10}H_9N_3O_2S$ $[M]^+$ 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; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.36 (q, J = 7.1 Hz, 2H), 3.13 (s, 6H), 1.39 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{11}H_{11}N_3O_2S$ $[M]^+$ 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; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.11 (s, 6H), 1.59 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{13}H_{15}N_3O_2S$ $[M]^+$ 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; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 7.1 Hz, 2H), 7.39−7.31 (m, 3H), 5.35 (s, 2H), 3.09 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) 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; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.89 (s, 3H), 3.46 (q, J = 7.1 Hz, 4H), 1.24 (t, J = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{12}H_{13}N_3O_2S$ $[M]^+$ 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; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.91 (s, 3H), 3.89 (t, J = 4.7 Hz, 4H), 3.35 (t, J = 4.7 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) 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; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (s, 1H), 3.91 (s, 3H), 3.09 (d, J = 5.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 163.6, 120.0, 112.0, 103.3, 98.6, 52.2, 33.9; HRMS (EI-TOF) calcd. for $C_9H_7N_3O_2S$ $[M]^+$ 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; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.06 (s, 6H), 2.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.0, 166.7, 119.9, 119.4, 112.9, 111.9, 101.0, 46.0, 30.3; HRMS (EI-TOF) calcd. for $C_{10}H_9N_3OS$ $[M]^+$ 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; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.04 (s, 6H), 2.99 (q, J = 7.3 Hz, 2H), 1.21 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{11}H_{11}N_3OS$ $[M]^+$ 233.0623, found 233.0625.

dx.doi.org/10.1021/jo4026034 | J. Org. Chem. 2014, 79, 1156−1165

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; ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{15}H_{11}N_3OS$ $[M]^+$ 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; ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{17}H_{14}BrN_3OS$ $[M]^+$ 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; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.37 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 122.4, 113.3, 110.8, 110.5, 99.3, 85.1, 44.0; HRMS (EI-TOF) calcd. for $C_9H_6N_4S$ $[M]^+$ 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 CH_3CN (2 mL) at room temperature under an atmosphere of N_2. 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; ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{14}H_8N_2O$ $[M]^+$ 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; ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.4, 133.8, 131.2, 128.8, 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 $C_{14}H_7N_2O$ $[M + H]^+$ 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; ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{15}H_{10}N_2O_2$ $[M]^+$ 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; ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{15}H_8N_2O_2$ $[M]^+$ 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); ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{10}H_8N_2O$ $[M]^+$ 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); ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{11}H_{10}N_2O$ $[M]^+$ 186.0793, found 186.0794; IR (KBr) 2932, 2854, 2241, 2226, 1602, 1539, 1446, 1281, 1209, 1070, 962, 810 cm^{-1}.

6,7-Dihydro-4*H*-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; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.63 (s, 2H), 2.99 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.0, 128.7, 118.4, 109.3, 108.7, 108.2, 25.7, 25.1, 22.0; HRMS (EI-TOF) calcd. for $C_9H_6N_2OS$ $[M]^+$ 190.0201, found 190.0203; IR (KBr) 2935, 2923, 2907, 2227, 1606, 1538, 1437, 1415, 1330, 1196, 1083, 719 cm^{-1}.

6,7-Dihydro-4*H*-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; ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.7, 129.8, 119.5, 109.2, 108.8, 105.9, 64.1, 62.0, 24.8; HRMS (EI-TOF) calcd. for $C_9H_6N_2O_2$ $[M]^+$ 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; ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{13}H_8N_2O_2$ $[M]^+$ 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 CH_3CN (2 mL) was treated with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) (137 mg, 0.6 mmol) at room temperature under an atmosphere of N_2. 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 ^{1}H 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 (^{1}H and ^{13}C NMR spectra, HRMS, and IR) are consistent with that previously reported in the literature.[24] Ketone: ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.3, 183.8, 160.5,135.6, 131.5, 130.0, 129.2, 63.4, 13.9. Hydrate: ^{1}H NMR (400 MHz, $CDCl_3$) 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, 3H).^{13}C NMR (100 MHz, $CDCl_3$) 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 2,3-dicyanofuran **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; ^{1}H NMR

dx.doi.org/10.1021/jo4026034 | J. Org. Chem. 2014, 79, 1156−1165

(400 MHz, $CDCl_3$) δ 8.18 (s, 1H), 3.97 (s, 3H), 3.91 (s, 3H), 2.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{10}H_{10}N_2O_4$ $[M]^+$ 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

Supporting Information

Copies of ^1H, ^{13}C 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.

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: xyluo@ecust.edu.cn.

*E-mail: weiping_deng@ecust.edu.cn.

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).

■ REFERENCES

(1) For selected reviews on oxidative coupling of C−H bonds, see: (a) Ashenhurst, J. A. *Chem. Soc. Rev.* **2010**, *39*, 540. (b) Shi, W.; Liu, C.; Lei, A. *Chem. Soc. Rev.* **2011**, *40*, 2761. (c) Cho, S. H.; Kim, J. Y.; Kwak, J.; Chang, S. *Chem. Soc. Rev.* **2011**, *40*, 5068. (d) Ramirez, T. A.; Zhao, B.; Shi, Y. *Chem. Soc. Rev.* **2012**, *41*, 931. (e) Shi, Z.; Zhang, C.; Tang, C.; Jiao, N. *Chem. Soc. Rev.* **2012**, *41*, 3381. (f) Song, G.; Wang, F.; Li, X. *Chem. Soc. Rev.* **2012**, *41*, 3651. (g) Li, B.-J.; Shi, Z.-J. *Chem. Soc. Rev.* **2012**, *41*, 5588. (h) Shang, X.; Liu, Z.-Q. *Chem. Soc. Rev.* **2013**, *42*, 3253. (i) Li, B.; Dixneuf, P. H. *Chem. Soc. Rev.* **2013**, *42*, 5744. (j) Le Bras, J.; Muzart, J. *Chem. Rev.* **2011**, *111*, 1170. (k) Liu, C.; Zhang, H.; Shi, W.; Lei, A. *Chem. Rev.* **2011**, *111*, 1780. (l) He, C.; Guo, S.; Ke, J.; Hao, J.; Xu, H.; Chen, H.-Y.; Lei, A. *J. Am. Chem. Soc.* **2012**, *134*, 5766. (m) Yamashita, K.; Yamamoto, Y.; Nishiyama, H. *J. Am. Chem. Soc.* **2012**, *134*, 7660. (n) Zheng, M.-F.; Huang, L.-B.; Wu, W.-Q.; Jiang, H.-F. *Org. Lett.* **2013**, *15*, 1838.

(2) For selected reviews on activation of sp^3 C−H bond, see: (a) Li, C.-J. *Acc. Chem. Res.* **2009**, *42*, 335 and the references therein. (b) Scheuermann, C. J. *Chem.—Asian J.* **2010**, *5*, 436. (c) Yoo, W. J.; Li, C.-J. *Top. Curr. Chem.* **2010**, *292*, 281. (d) Yeung, C. S.; Dong, V. M. *Chem. Rev.* **2011**, *111*, 1215. (e) Sun, C.-L.; Li, B.-J.; Shi, Z.-J. *Chem. Rev.* **2011**, *111*, 1293. (f) Zhang, S.-Y.; Zhang, F.-M.; Tu, Y.-Q. *Chem. Soc. Rev.* **2011**, *40*, 1937. (g) Zhang, C.; Tang, C.; Jiao, N. *Chem. Soc. Rev.* **2012**, *41*, 3464.

(3) For selected examples of activation of allylic, benzylic sp^3 C−H bonds, see: (a) Li, Z.; Li, C.-J. *J. Am. Chem. Soc.* **2006**, *128*, 56. (b) Li, Z.; Cao, L.; Li, C.-J. *Angew. Chem., Int. Ed.* **2007**, *46*, 6505. (c) Cheng, D.; Bao, W. *Adv. Synth. Catal.* **2008**, *350*, 1263. (d) Lin, S.; Song, C.-X.; Cai, G.-X.; Wang, W.-H.; Shi, Z.-J. *J. Am. Chem. Soc.* **2008**, *130*, 12901. (e) Li, Y.-Z.; Li, B.-J.; Lu, X.-Y.; Lin, S.; Shi, Z.-J. *Angew. Chem., Int. Ed.* **2009**, *48*, 3817. (f) Mo, H.; Bao, W. *Adv. Synth. Catal.* **2009**, *351*, 2845. (g) Qin, C.; Jiao, N. *J. Am. Chem. Soc.* **2010**, *132*, 15893. (h) Guo, C.; Song, J.; Luo, S.-W.; Gong, L.-Z. *Angew. Chem., Int. Ed.* **2010**, *49*, 5558. (i) Correia, C. A.; Li, C.-J. *Adv. Synth. Catal.* **2010**, *352*, 1446. (j) Xu, J.; Fu, Y.; Luo, D.-F.; Jiang, Y.-Y.; Xiao, B.; Liu, Z.-J.; Gong, T.-J.; Liu, L. *J. Am. Chem. Soc.* **2011**, *133*, 15300. (k) Wang, X.; Ye, Y.; Zhang, S.; Feng, J.; Xu, Y.; Zhang, Y.; Wang, J. *J. Am. Chem. Soc.* **2011**, *133*, 16410. (l) Hayashi, Y.; Itoh, T.; Ishikawa, H. *Angew. Chem., Int. Ed.* **2011**, *50*, 3920. (m) Chen, F.; Qin, C.; Cui, Y.; Jiao, N. *Angew. Chem., Int. Ed.* **2011**, *50*, 11487. (n) Qin, C.; Zhou, W.; Chen, F.; Ou, Y.; Jiao, N. *Angew. Chem., Int. Ed.* **2011**, *50*, 12595. (o) Qin, C.; Shen, T.; Tang, C.-H; Jiao, N. *Angew. Chem., Int. Ed.* **2012**, *51*, 6971. (p) Wang, T.; Zhou, W.; Yin, H.; Ma, J.-A.; Jiao, N. *Angew. Chem.* **2012**, *124*, 10981; *Angew. Chem., Int. Ed.* **2012**, *51*, 10823. (q) Cui, Y.; Floreancig, P. E. *Org. Lett.* **2012**, *14*, 1720. (r) Brizgys, G. J.; Jung, H. H.; Floreancig, P. E. *Chem. Sci.* **2012**, *3*, 438.

(4) For selected examples of activation of sp^3 C−H bond adjacent to heteroatoms, see: (a) Zhang, Y.; Li, C.-J. *J. Am. Chem. Soc.* **2006**, *128*, 4242. (b) Zhang, Y.; Li, C.-J. *Angew. Chem.* **2006**, *118*, 1983; *Angew. Chem., Int. Ed.* **2006**, *45*, 1949. (c) Li, Z.; Bohle, D. S.; Li, C.-J. *Proc. Natl. Acad. Sci. U. S. A.* **2006**, *103*, 8928. (d) Zhao, L.; Li, C.-J. *Angew. Chem., Int. Ed.* **2008**, *47*, 7075. (e) Tu, W.; Liu, L.; Floreancig, P. E. *Angew. Chem.* **2008**, *120*, 4252; *Angew. Chem., Int. Ed.* **2008**, *47*, 4184. (f) Li, Z.; Yu, R.; Li, H. *Angew. Chem., Int. Ed.* **2008**, *47*, 7497. (g) Zhao, L.; Baslé, O.; Li, C.-J. *Proc. Natl. Acad. Sci. U. S. A.* **2009**, *106*, 4106. (h) Volla, C. M. R.; Vogel, P. *Org. Lett.* **2009**, *11*, 1701. (i) Li, H.; He, Z.; Guo, X.; Li, W.; Zhao, X.; Li, Z. *Org. Lett.* **2009**, *11*, 4176. (j) Tu, W.; Floreancig, P. E. *Angew. Chem., Int. Ed.* **2009**, *48*, 4567. (k) Liu, L.; Floreancig, P. E. *Angew. Chem., Int. Ed.* **2010**, *49*, 3069; *Angew. Chem., Int. Ed.* **2010**, *49*, 5894. (l) Yang, F.; Li, J.; Xie, J.; Huang, Z.-Z. *Org. Lett.* **2010**, *12*, 5214. (m) Boess, E.; Sureshkumar, D.; Sud, A.; Wirtz, C.; Fares, C.; Klussmann, M. *J. Am. Chem. Soc.* **2011**, *133*, 8106. (n) Nishino, M.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2011**, *76*, 6447. (o) Alagiri, K.; Devadig, P.; Prabhu, K. R. *Chem.—Eur. J.* **2012**, *18*, 5160. (p) Han, X.; Floreancig, P. E. *Org. Lett.* **2012**, *14*, 3808. (q) Clausen, D. J.; Floreancig, P. E. *J. Org. Chem.* **2012**, *77*, 6574. (r) Zhang, G.; Wang, S.; Ma, Y.; Kong, W.; Wang, R. *Adv. Synth. Catal.* **2013**, *355*, 874. (s) Zhang, G.; Ma, Y.; Wang, S.; Kong, W.; Wang, R. *Chem. Sci.* **2013**, *4*, 2645.

(5) For selected reviews on transition metal-mediated oxidation of acidic ketones, see: (a) Nair, V.; Deepthi, A. *Chem. Rev.* **2007**, *107*, 1862. (b) Nair, V.; Balagopal, L.; Rajan, R.; Mathew, J. *Acc. Chem. Res.* **2004**, *37*, 21. (c) Nair, V.; Mathew, J.; Prabhakaran, J. *Chem. Soc. Rev.* **1997**, 127. (d) Snider, B. B. *Chem. Rev.* **1996**, *96*, 339. (e) Iqbal, J.; Bhatia, B.; Nayyar, N. K. *Chem. Rev.* **1994**, *94*, 519. (f) Linker, T. *J. Organomet. Chem.* **2002**, *661*, 159. (g) Pan, X.-Q.; Zou, J.-P.; Zhang, W. *Mol. Diversity* **2009**, *13*, 421. (h) Snider, B. B. *Tetrahedron* **2009**, *65*, 10738. (i) Nair, V.; Deepthi, A. *Tetrahedron* **2009**, *65*, 10745.

(6) For selected examples of $Mn(OA(c)_3$ as radical oxidant, see: (a) Tan, X.-H.; Chen, C. *Angew. Chem.* **2006**, *118*, 4451; *Angew. Chem., Int. Ed.* **2006**, *45*, 4345. (b) Wu, W.; Xu, J.; Huang, S.; Su, W. *Chem. Commun.* **2011**, *47*, 9660. (c) Keane, H. A.; Hess, W.; Burton, J. W. *Chem. Commun.* **2012**, *48*, 6496. (d) Bush, J. B., Jr.; Finkbeiner, H. *J. Am. Chem. Soc.* **1968**, *90*, 5905. (e) Heiba, E. I.; Dessau, R. M.; Rodewald, P. G. *J. Am. Chem. Soc.* **1974**, *96*, 7977. (f) Corey, E. J.; Kang, M. *J. Am. Chem. Soc.* **1984**, *106*, 5384. (g) Logan, A. W. J.; Parker, J. S.; Hallside, M. S.; Burton, J. W. *Org. Lett.* **2012**, *14*, 2940.

(7) For selected examples of CAN as radical oxidant, see: (a) Nicolaou, K. C.; Hale, C. R. H.; Ebner, C.; Nilewski, C.; Ahles, C. F.; Rhoades, D. *Angew. Chem.* **2012**, *124*, 4805; *Angew. Chem., Int. Ed.* **2012**, *51*, 4726. (b) Nicolaou, K. C.; Adsool, V. A.; Hale, C. R. H. *Angew. Chem., Int. Ed.* **2011**, *50*, 5149. (c) Linker, T.; Schanzenbach, D.; Elamparuthi, E.; Sommermann, T.; Fudickar, W.; Gyóllai, V.; Somsák, L.; Demuth, W.; Schmittel, M. *J. Am. Chem. Soc.* **2008**, *130*, 16003.

(8) (a) Liu, H.; Cao, L.; Sun, J.; Fossey, J. S.; Deng, W.-P. *Chem. Commun.* **2012**, *48*, 2674. (b) Li, Y.; Cao, L.; Luo, X.; Deng, W.-P. *Chin. J. Chem.* **2012**, *30*, 2834.

(9) DDQ-mediated formation of α-carbonyl radical from ketones, see: (a) Becker, H.-D. *J. Org. Chem.* **1965**, *30*, 989. (b) Walker, D.;

Hiebert, J. D. *Chem. Rev.* **1967**, *67*, 153. (c) Kucklaender, U.; Bollig, R.; Frank, W.; Gratz, A.; Jose, J. *Bioorg. Med. Chem.* **2011**, *19*, 2666. (d) Bhunia, S.; Ghosh, S.; Dey, D.; Bisai, A. *Org. Lett.* **2013**, *15*, 2426.

(10) For selected reviews on preparation of substituted furans, see: (a) Hou, X.-L.; Cheung, H.- Y.; Hon, T.-Y.; Kwan, P. L.; Lo, T.- H.; Tong, S. Y.; Wong, H. N. C. *Tetrahedron* **1998**, *54*, 1955. (b) Keay, B. A. *Chem. Soc. Rev.* **1999**, *28*, 209. (c) Jeevanandam, A.; Ghule, A.; Ling, Y. -C. *Curr. Org. Chem.* **2002**, *6*, 841. (d) Brown, R. C. D. *Angew. Chem., Int. Ed.* **2005**, *44*, 850. (e) Kirsch, S. F. *Org. Biomol. Chem.* **2006**, *4*, 2076. (f) D'Souza, D. M.; Müller, T. J. J. *Chem. Soc. Rev.* **2007**, *36*, 1095. (g) Balme, G.; Bouyssi, D.; Monteiro, N. *Herterocycles* **2007**, *73*, 87. (h) Cadierno, V.; Crochet, P. *Curr. Org. Synth.* **2008**, *5*, 343.

(11) For selected recent examples of preparation of substituted furans, see: (a) Fournier, J.; Arseniyadis, S.; Cossy, J. *Angew. Chem., Int. Ed.* **2012**, *51*, 7562. (b) Kramer, S.; Skrydstrup, T. *Angew. Chem., Int. Ed.* **2012**, *51*, 4681. (c) Lenden, P.; Entwistle, D. A.; Willis, M. C. *Angew. Chem., Int. Ed.* **2011**, *50*, 10657. (d) Zhang, M.; Jiang, H.-F.; Neumann, H.; Beller, M.; Dixneuf, P. H. *Angew. Chem., Int. Ed.* **2009**, *48*, 1681. (e) Jiang, H.-F.; Pan, X.-Y.; Huang, L.-B.; Zhao, J.; Shi, D.-B. *Chem. Commun.* **2012**, *48*, 4698. (f) Deng, Y.-Q.; Fu, C.-L.; Ma, S. *Chem.—Eur. J.* **2011**, *17*, 4976. (g) Hu, J.; Wei, Y.-B.; Tong, X.-F. *Org. Lett.* **2011**, *13*, 3068. (h) Yin, B.-L.; Zeng, G.-H.; Cai, C.-B.; Ji, F.-H.; Huang, L.; Li, Z.-R.; Jiang, H.-F. *Org. Lett.* **2012**, *14*, 616. (i) Rauniyar, V.; Wang, Z. J.; Burks, H. E.; Toste, F. D. *J. Am. Chem. Soc.* **2011**, *133*, 8486. (j) Vicente, R.; González, J.; Riesgo, L.; González, J.; López, L. A. *Angew. Chem., Int. Ed.* **2012**, *51*, 8063. (k) González, J.; González, J.; Pérez-Calleja, C.; López, L. A.; Vicente, R. *Angew. Chem., Int. Ed.* **2013**, *52*, 5853. (l) He, T.; Gao, P.; Zhao, S.-C.; Shi, Y.-D.; Liu, X.-Y.; Liang, Y.-M. *Adv. Synth. Catal.* **2013**, 355. (m) Cui, X.; Xu, X.; Wojtas, L.; Kim, M. M.; Zhang, X. P. *J. Am. Chem. Soc.* **2012**, *134*, 19981.

(12) (a) Mack, J.; Kobayashi, N. *Chem. Rev.* **2011**, *111*, 281. (b) Nemykin, V. N.; Polshyna, A. E.; Makarova, E. A.; Kobayashi, N.; Lukyanets, E. A. *Chem. Commun.* **2012**, *48*, 3650. (c) Luzyanin, K. V.; Kukushkin, V. Y.; Kopylovich, M. N.; Nazarov, A. A.; Galanski, M.; Pombeiro, A. J. L. *Adv. Synth. Catal.* **2008**, *350*, 135. (d) Shaabani, A.; Maleki-Moghaddam, R.; Maleki, A.; Rezayan, A. H. *Dyes Pigm.* **2007**, *74*, 279. (e) Muranaka, A.; Ohira, S.; Hashizume, D.; Koshino, H.; Kyotani, F.; Hirayama, M.; Uchiyama, M. *J. Am. Chem. Soc.* **2012**, *134*, 190. (f) Zhang, Y.; Ma, P.; Zhu, P.-H.; Zhang, X.-Y.; Gao, Y.-N.; Qi, D.-D.; Bian, Y.-Z.; Kobayashi, N.; Jiang, J.-Z. *J. Mater. Chem.* **2011**, *21*, 6515.

(13) (a) Knawby, D. M.; Swager, T. M. *Chem. Mater.* **1997**, *9*, 535. (b) Nemykin, V. N.; Polshina, A. E.; Kobayashi, N. *Chem. Lett.* **2000**, 1236. (c) Christie, R. M.; Freer, B. G. *Dyes Pigm.* **1997**, *33*, 107. (d) Buehrdel, G.; Beckert, R.; Birckner, E.; Grummt, U.-W.; Beyer, B.; Kluge, S.; Weston, J.; Goerls, H. *Eur. J. Org. Chem.* **2007**, 5404. (e) Cook, M. J.; Jafari-Fini, A. *Tetrahedron* **2000**, *56*, 4085. (f) Taraymovich, E. S.; Korzhenevskii, A. B.; Mitasova, Y. V.; Kumeev, R. S.; Koifman, O. I.; Stuzhin, P. A. *J. Porphyrins Phthalocyanines* **2011**, *15*, 54. (g) Miyazaki, E.; Kaku, A.; Mori, H.; Iwatania, M.; Takimiya, K. *J. Mater. Chem.* **2009**, *19*, 5913. (h) Dubinina, T. V.; Dyumaeva, D. V.; Trashin, S. A.; Sedova, M. V.; Dudnik, A. S.; Borisova, N. E.; Tomilova, L. G.; Zefirov, N. S. *Dyes Pigm.* **2013**, *96*, 699.

(14) (a) The initial results for the synthesis of 2,3-dicyanofurans has been filed as Chinese patent application with limited substrate scope: Deng, W.-P.; Wang, Z.-L.; Zhang, Z.-G.; Li, H.-C. CN 102516210 A, 2012. (b) One example has been reported on the formation of 2,3-dicyanofuran as byproduct in 8% yield in the presence of DDQ: Barrett, A. G. M.; Blaney, F.; Campbell, A. D.; Hamprecht, D.; Meyer, T.; White, A. J. P.; Witty, D.; Williams, D. J. *J. Org. Chem.* **2002**, *67*, 2735. (c) An example of similar reaction but with very limited substrates scope from other group was just reported after our patent application: Li, J.-S.; Xue, Y.; Li, Z.-W.; Liu, W.-D.; Lu, C.-H.; Zhao, P.-X. *Synlett* **2013**, *24*, 2003.

(15) (a) Bhattacharya, A.; DiMichele, L. M.; Dolling, U.-H.; Douglas, A. W.; Grabowski, E. J. J. *J. Am. Chem. Soc.* **1988**, *110*, 3318. (b) Bhattacharya, A.; DiMichele, L. M.; Dolling, U.-H.; Grabowski, E. J. J.; Grenda, V. J. *J. Org. Chem.* **1989**, *54*, 6118. (c) Fischer, H. *Chem. Rev.* **2001**, *101*, 3581. (d) Studer, A. *Chem.—Eur. J.* **2001**, *7*, 1159. (e) Studer, A.; Schulte, T. *Chem. Rec.* **2005**, *5*, 27.

(16) For DDQ-mediated hydride abstraction, see: Liu, W.-B.; Jiang, H.-F.; Zhang, M.; Qi, C.-R. *J. Org. Chem.* **2010**, *75*, 966.

(17) (a) Trofimov, B. A.; Sobenina, L. N.; Stepanova, Z. V.; Ushakov, I. A.; Mikhaleva, A. I.; Tomilin, D. N.; Kazheva, O. N.; Alexandrov, G. G.; Chekhlov, A. N.; Dyachenko, O. A. *Tetrahedron Lett.* **2010**, *51*, 5028. (b) Sobenina, L. N.; Stepanova, Z. V.; Ushakov, I. A.; Mikhaleva, A. I.; Tomilin, D. N.; Kazheva, O. N.; Alexandrov, G. G.; Dyachenko, O. A.; Trofimov, B. A. *Tetrahedron* **2011**, *67*, 4832.

(18) (a) Huang, Z.-L.; Jin, L.-Q.; Feng, Y.; Peng, P.; Yi, H.; Lei, A. *Angew. Chem., Int. Ed.* **2013**, *52*, 7151. (b) Polyakov, N. E.; Konovalov, V. V.; Leshina, T. V.; Luzina, O. A.; Salakhutdinov, N. F.; Konovalova, T. A.; Kispert, L. D. *J. Photochem. Photobiol., A* **2001**, *141*, 117.

(19) Trofimov, B. A.; Sobenina, L. N.; Stepanova, Z. V.; Ushakov, I. A.; Sinegovskaya, L. M.; Vakul'skaya, T. I.; Mikhaleva, A. I. *Synthesis* **2010**, 470.

(20) Heiba, E. I.; Dessau, R. M. *J. Am. Chem. Soc.* **1971**, *93*, 524; *J. Am. Chem. Soc.* **1972**, *94*, 2888.

(21) Ding, Y.; Huang, Z.-J.; Yin, J.; Lai, Y.-S.; Zhang, S.-B.; Zhang, Z.-G.; Fang, L.; Peng, S.-X.; Zhang, Y.-H. *Chem. Commun.* **2011**, *47*, 9495.

(22) (a) Jing, Y.; Xu, C.-G.; Ding, K.; Lin, J.-R.; Jin, R.-H.; Tian, W.-S. *Tetrahedron Lett.* **2010**, *51*, 3242. (b) Arslan, T.; Sadak, A. E.; Saracoglu, N. *Tetrahedron* **2010**, *66*, 2936.

(23) For X-ray structure of **4k**, **8j**, and **9** and the corresponding data, see the Supporting Information. CCDC 943604 (**4k**), CCDC 943606 (**8j**), and CCDC 943605 (**9**) contain the crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

(24) Mecinović, J.; Hamed, R. B.; Schofield, C. J. *Angew. Chem., Int. Ed.* **2009**, *48*, 2796.