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Synthesis and Characterization of Derivatives and Dimers of 4,5-Dicyanoimidazole

Eric C. Coad, Hui Liu, and Paul G. Rasmussen*

Contributions from The Willard H. Dow Laboratories, Department of Chemistry,
and the Macromolecular Research Center, The University of Michigan,
Ann Arbor, MI 48109-1055

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Abstract: *Synthesis of 1-methyl-2-fluoro-4,5-dicyanoimidazole was accomplished by halogen exchange between 1-methyl-2-bromo-4,5-dicyanoimidazole and potassium fluoride with catalytic 18-crown-6 ether in diglyme. Halogen exchange between 1-methyl-2-bromo-4,5-dicyanoimidazole and lithium chloride in N-methylpyrrolidinone at 150°C yielded 1-methyl-2-chloro-4,5-dicyanoimidazole, while additional heating to 210°C resulted in the subsequent demethylation to yield 2-chloro-4,5-dicyanoimidazole. The nucleophilic aromatic substitution reactions of various imidazole nucleophiles with 1-methyl-2-fluoro-4,5-dicyanoimidazole resulted in several derivatives of 2-(4',5'-dicyano-1'-imidazoyl)-4,5-dicyanoimidazole. The pKa, UV, and electronic properties are reported.*

Introduction

Although examples of C-N connectivity between imidazole rings are relatively rare, there are a few cases of such 1,2'-dimers reported. Syntheses which link imidazole and benzimidazole ring systems this way have been carried out using NAS reactions on 2,4,5-trichloroimidazole,[1] 2-chlorobenzimidazoles,[2] and 1-methyl-2-methylsulphonyl-5-nitro imidazole.[3] Some of these dimer systems have been examined specifically for their pharmaceutical applications.[4] For dicyanoimidazoles, one approach to synthesizing 2-substituted compounds has been through the use of the 2-diazo intermediates.[5]

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In recent years our group has developed several alternative routes to functionalized 4,5-dicyanoimidazoles which avoid the 2-diazo intermediate. Our previous work has shown that control of functionality at the 1- and 2- positions of 4,5-dicyanoimidazole can lead to a number of useful compounds,[6] and that there was a particular need for better leaving groups at both the 1- and 2- positions.[7]

We describe here the fluorination and chlorination of the 2-position of 4,5-dicyanoimidazole in order to prepare a good substrate for nucleophilic aromatic substitution (NAS) which may be used to establish 1,2'-connectivity between imidazole rings. The synthesis of 1-methyl-2-fluoro-4,5-dicyanoimidazole (**2**) provides a new substrate for the synthesis of 1,2'-connectivity between imidazole rings. The synthesis of 2-(4',5'-dicyano-1'-imidazolyl)-4,5-dicyanoimidazoles from the NAS of 1-methyl-2-fluoro-4,5-dicyanoimidazole (**2**) with various 4,5-dicyanoimidazole nucleophiles will be discussed, as well as the further functionalization of 2-(4',5'-dicyano-1'-imidazolyl)-4,5-dicyano imidazoles.

Results and Discussion

Previously, 1-methyl-2-bromo-4,5-dicyanoimidazole (**1**) had been used to accomplish nucleophilic aromatic substitution reactions with a variety of amines and other moderately strong nucleophiles. However, the 2-bromo derivative fails to react with weak nucleophiles. To attain enhanced reactivity at the 2-position of 4,5-dicyanoimidazole derivatives, the 2-fluoro and 2-chloro derivatives were prepared.

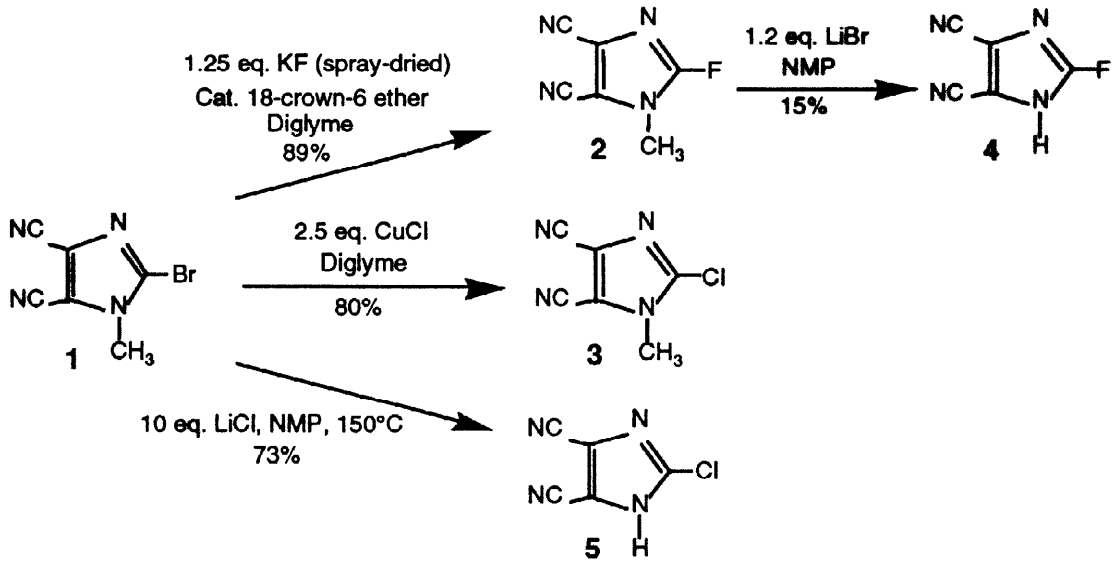
Transhalogenation reactions provide an alternative method of halogenation when one halogenated compound of a series is readily available and analogous derivatives are not readily obtained by similar methods. For example, fluorination of aryl bromides has been accomplished by transhalogenation.[8] We have adapted this method to imidazoles and 1-methyl-2-bromo-4,5-dicyanoimidazole (**1**) was fluorinated using potassium fluoride and a catalytic amount of 18-crown-6 ether in diglyme (Scheme 1).

Transhalogenation has been used to obtain chlorinated compounds from aryl bromides.[9] Similarly, 1-methyl-2-chloro-4,5-dicyanoimidazole (**3**) was obtained by transhalogenation of (**1**) with cuprous chloride in diglyme (Scheme 1).

We have demonstrated previously the dealkylation of imidazole substrates with lithium chloride in N-methyl pyrrolidinone (NMP). However, attempted dealkylation of 1-methyl-2-fluoro-4,5-dicyanoimidazole (**2**) with lithium chloride resulted in the formation of 2-chloro-4,5-dicyanoimidazole (**5**) due to the good leaving tendencies of fluorine. The dealkylation was successfully carried out using lithium bromide in NMP at reflux (Scheme 1). However due to difficulties in isolation, the yields were low.

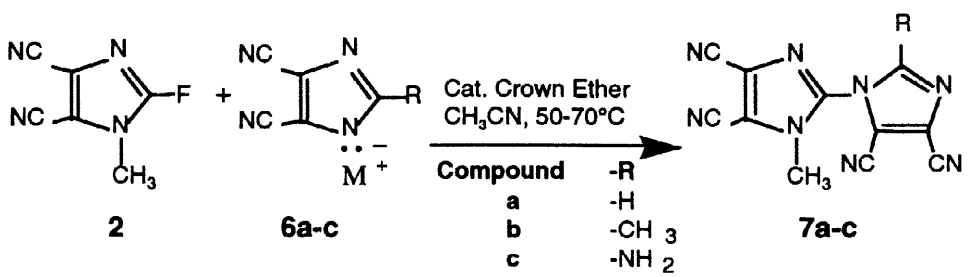
In the dealkylation of 1-methyl-2-bromo-4,5-dicyanoimidazole (**1**) with lithium chloride in NMP, the starting material first undergoes transhalogenation when heated at 150°C for a few hours to form 1-methyl-2-chloro-4,5-dicyanoimidazole (**3**) (Scheme 1). Additional heating of the reaction mixture at reflux leads to dealkylation and the formation of 2-chloro-4,5-dicyanoimidazole (**5**).

Scheme 1



A potentially straightforward route to difunctionalized dimer derivatives of 4,5-dicyanoimidazole would use a nucleophilic aromatic substitution (NAS) reaction by the anion of 2-bromo-4,5-dicyanoimidazole on 1-methyl-2-bromo-4,5-dicyanoimidazole (**1**). However, these reactions require fairly harsh conditions and lead to substantial transalkylation and almost no dimer product. Previous attempts to accomplish NAS reactions using imidazole or imidazole derivatives on 1-methyl-2-bromo-4,5-dicyanoimidazole (**1**) have only been successful with stronger nucleophiles.

Scheme 2



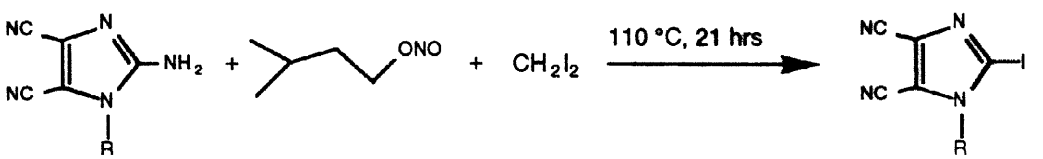
M^+	-R	Crown Ether	Yield	Product
K^+	-H	18-crown-6	73 %	**7a**
Li^+	$-CH_3$	12-crown-4	54 %	**7b**
K^+	$-NH_2$	18-crown-6	81 %	**7c**

Use of fluoro derivatives takes advantage of the good leaving group characteristics of fluorine when activating groups such as cyano are present on an aromatic ring.[10] Synthesis of dimeric compounds using 1-methyl-2-fluoro-4,5-dicyanoimidazole (**2**) has proven effective with the salts of 4,5-dicyanoimidazole (**6a**), 2-methyl-4,5-dicyanoimidazole (**6b**), and 2-amino-4,5-dicyanoimidazole (**6c**) (Scheme 2).

In all above cases, the nucleophile has either an electron donating group (-NH_2 or - CH_3) or a neutral group (-H) at the 2- position. On the other hand, if an electron withdrawing group (-Cl, -Br, or -I) is placed at the 2- position instead, the resulting nucleophile is not strong enough to react with 1-methyl-2-fluoro-4,5-dicyanoimidazole (**2**). No reactions were observed when the salt of 2-halo-4,5-dicyanoimidazole and 1-methyl-2-fluoro-4,5-dicyanoimidazole (**2**) were refluxed together in DMSO with 18-crown-6 ether catalyst for several days.

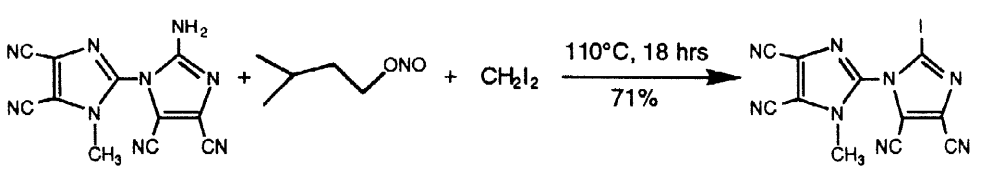
To obtain these substituted dimers, a different synthetic route was necessary. When the dimer, 1-methyl-2-(2'-amino-4',5'-dicyano-1'-imidazoyl)-4,5-dicyanoimidazole (**7c**), was treated with isoamyl nitrite in a halogen atom donating solvent (such as CH_2I_2, $CHBr_3$ or CCl_4) at 110 °C for a few hours, the corresponding 2'-halogen substituted dimer was isolated. In these reactions, 1-substituted 2-imidazolyl free radicals are apparently produced by the homolysis of the intermediate 2-diazonium salt, which forms in the first step, and these radicals subsequently abstract halogen atoms from the solvent.[11]

Scheme 3



8a-b **9a-b**

Starting Material	-R	Product	Yield
8a	-CH3	**9a**	40%
8b	-H	**9b**	33%



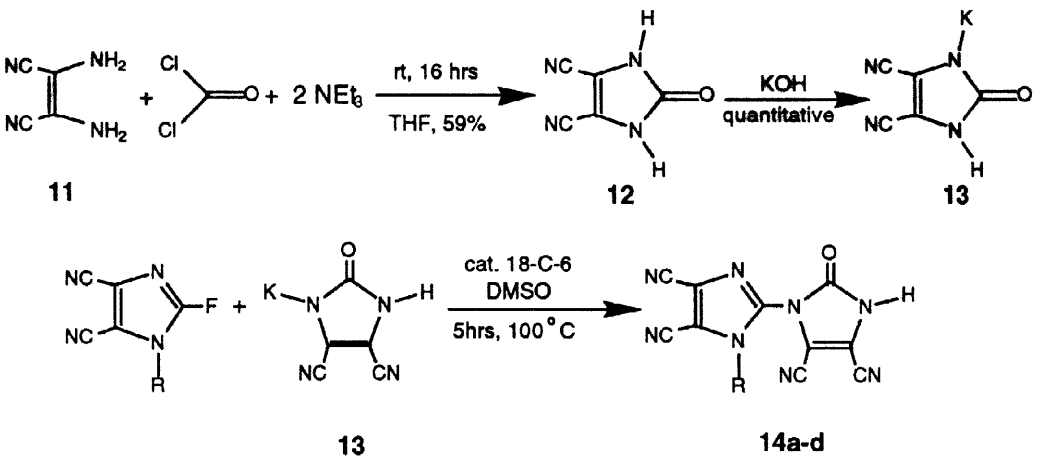
7c **10**

By this method, 1-methyl-2-amino-4,5-dicyanoimidazole (**8a**), 2-amino-4,5-dicyanoimidazole (**8b**), and 1-methyl-2-(2'-amino-4',5'-dicyano-1'-imidazoyl)-4,5-dicyanoimidazole (**7c**) were converted to the iodo substituted products in moderate yields (Scheme 3).

However, in the cases of bromination and chlorination, serious competition between halogen abstraction and hydrogen abstraction was observed. In the case of bromination, several different reagents were tried as bromine atom donors: cuprous bromide[12] did not give any desired products, and only starting material was recovered; NBS led to mostly hydrogen abstracted products, and minor bromine substituted products; $CHBr_3$ produced roughly equal amounts of bromine and hydrogen substituted products. In the case of chlorination using CCl_4 as the solvent, only a small amount of the desired products was formed, but major hydrogen abstracted side products were found. These results are consistent with the C-Cl and C-Br bond energies (79 and 66 kcal/mol, respectively) compared with the C-H bond energy of 96-99 kcal/mol, whereas C-I has a smaller bond energies (52 kcal/mol).[11]

In addition to the imidazole nucleophiles, we have used several other nucleophiles in NAS reactions with 1-methyl-2-fluoro-4,5-dicyanoimidazole (**2**) to demonstrate the enhanced reactivity of the fluorinated derivatives. For example, a series of 1-(1'-alkyl-4',5'-dicyano-2'-imidazoyl)-4,5-dicyano-2-imidazolone

Scheme 4

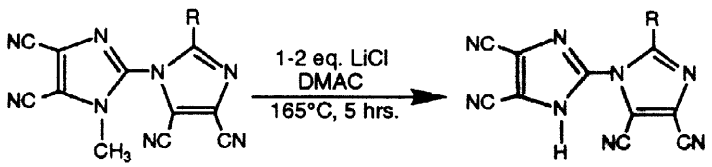


R	Product	Yield
Methyl	**14a**	78%
Isopropyl	**14b**	62%
n-Propyl	**14c**	79%
Isobutyl	**14d**	82%

dimers (**14a-d**) were synthesized in good yields by reacting 1-alkyl-2-fluoro-imidazole with the potassium salt of 4,5-dicyano-2-imidazolone (**13**) in the presence of a catalytic amount of 18-crown-6 (Scheme 4). The precursor, 4,5-dicyano-2-imidazolone (**12**), was prepared by reaction of DAMN (diaminomaleonitrile) (**11**) with phosgene using published procedures.[13]

Demethylation of 1-methyl-4,5-dicyanoimidazole substrates has been carried out previously with lithium chloride in NMP. The 1-methyl-2-(4',5'-dicyano-1'-imidazolyl)-4,5-dicyanoimidazole dimer derivatives (**7**) are easily demethylated to **15** using LiCl and DMAC (Scheme 5). Application of reagents used for demethylation of ethers[14] on the 1-methyl-dimer derivatives has demonstrated their general use.

Scheme 5

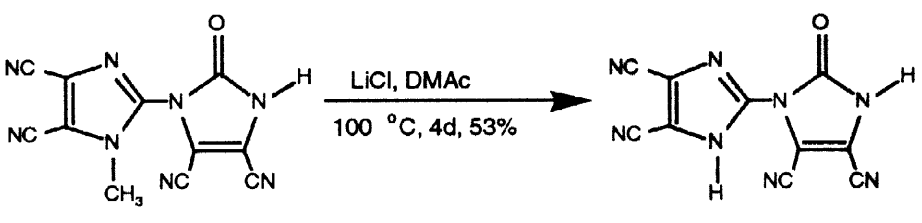


7a,7c **15a, 15c**

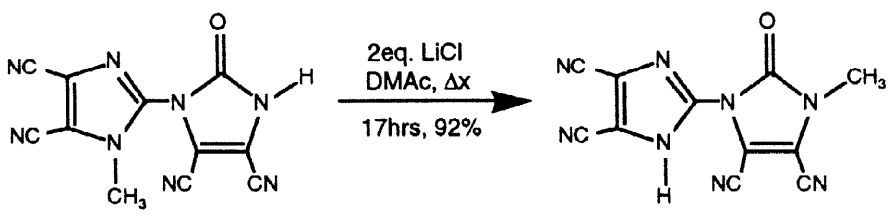
Starting Material	-R	Product	Yield
7a	-H	15a	88 %
7c	$-NH_2$	15c	88 %

Demethylation of 1-(1'-methyl-4',5'-dicyano-2'-imidazoyl)-4,5-dicyano-2-imidazolone (**14a**) successfully yielded **16** on small scale reactions (~200mg) using a procedure similar to that described above.

Scheme 6



14a **16**



14a **17**

In small scale reactions methyl chloride can apparently escape the reaction mixture but in large scale reactions, the 3'-position is alkylated before the methyl chloride can be evolved, resulting in 1-(4',5'-dicyano-2'-imidazoyl)-3-methyl-4,5-dicyano-2-imidazolone (**17**) (Scheme 6).

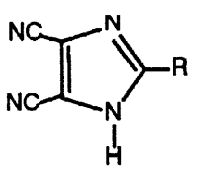
In general, the demethylation of the dimer derivatives occurs much more rapidly than the demethylation of the 1-methyl-4,5-dicyanoimidazole derivatives. Interestingly, no cleavage of the 1,2 ring connection was observed during the dealkylation process.

Properties

The pK_a values we determined for compounds **4**, **5**, and **9b**, and others reported recently are shown in Table 1. The pK_a values of compounds 2-amino-4,5-dicyanoimidazole (**8b**), 4,5-dicyanoimidazole (**18**), 2-bromo-4,5-dicyanoimidazole (**19**), and 2,4,5-tricyano imidazole (**20**) are also shown in Table 1 for comparison.

The data in Table 1 shows the trend expected for electron withdrawing and electron donating groups. The data are also in good accord with our observations regarding the relative nucleophilicity in the NAS reactions. The electron withdrawing effect of the second ring connected at the two position to the first is seen in compound **15c**.

Table 1. pK_a Values of Selected 4,5-Dicyanoimidazole Derivatives



Compound	-R	pK_a
8b	$-NH_2$	6.2†
18	-H	5.5†
9b	-I	3.0
19	-Br	2.7‡
5	-Cl	2.6
4	-F	2.4
15c	2-amino-imidazoyl	2.4
20	-CN	2.2†

† Reference 5d, ‡ Reference 5c

The UV-visible spectroscopic data for compounds **1**, **2**, **3**, **4**, **5**, and **19** indicate λ_{max} values between 247-256 nm, indicating only a few nm difference between the 1-methyl-4,5-dicyanoimidazoles and the 4,5-dicyanoimidazoles.

The UV-visible spectroscopy data for **7a**, **7b**, and **15a** show λ_{max} values between 249-258 nm, indicating only a few nm difference for these 2-(4',5'-dicyano-1'-imidazolyl)-4,5-dicyanoimidazole derivatives. Compounds **7c** and **15c** show λ_{max} values which are similar to the other compounds with peaks at 247 nm and 243 nm. Compounds **7c** and **15c** also show λ_{max} values which are typical of 2-amino-4,5-dicyanoimidazole derivatives (1-methyl-2-amino-4,5-dicyanoimidazole, λ_{max} = 301 nm) at 297 nm and 306 nm respectively. Direct comparison of the wavelength and intensity data for single ring and 1,2-coupled biimidazoles suggests rather little ring-ring interaction. However, several of the dimers exhibited strong visible fluorescence when illuminated with UV light. This fluorescence was never observed with single ring imidazoles.

The cyclic voltammograms of a number of 4,5-dicyanoimidazole derivatives were recorded to examine the electrochemical behavior of these compounds. The reduction potentials in Table 2 were assigned according to the following rules:

1) Samples that show strong anodic currents are called quasi reversible. Those that show very little re-oxidation are termed slightly reversible. When no re-oxidation is observed, waves are designated as irreversible.

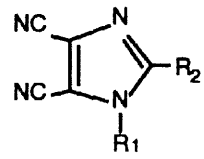
2) When there are two cathodic waves, two values for E_{red}(V) are reported.

3) When the waves show reversible behavior (or quasi reversibility) the value reported for E_{red}(V) is one-half the sum of the potentials at the peak of the cathodic and anodic waves. If the waves show irreversible behavior (or only slight reversibility) the value reported is the potential of the cathodic peak at half height.

Compounds **1**, **2**, and **3** (Table 2) all have irreversible reduction potentials from -2.18V to -2.34V, but the trend in the data is opposite to what would be expected. The expected order for electron withdrawing groups may be reversed due to changes in the solvation energy or because of differences in the relative planarity of the biimidazole ring system.

Compounds **7a**, **7b**, and **7c** (Table 2) all showed irreversible first reduction potentials from -1.84V to -2.06V, showing the trend expected for the electron withdrawing groups. Compounds **7a** and **7b** showed irreversible second reduction potentials of -2.50V and -2.46V respectively, while compound **7c** showed a quasi reversible second reduction potential of -2.44V.

Table 2. Cyclic Voltametric Properties of 4,5-Dicyanoimidazole Derivatives



Compound	-R1	-R2	E_{red}(V)*
1	-CH_3	-Br	-2.18 (irr)†
3	-CH_3	-Cl	-2.24 (irr)
2	-CH_3	-F	-2.34 (irr)
7a	4,5-DC-1-Me-2-I	-H	-1.93 (irr), -2.50 (irr)
7b	4,5-DC-1-Me-2-I	-CH_3	-2.02 (irr), -2.46 (irr)
7c	4,5-DC-1-Me-2-I	-NH_2	-2.06 (irr), -2.44 (quasi)

*Measured in CH_3CN vs Ag/Ag^+ with 0.10M Et_4NBF_4 as electrolyte. Ferrocene was used as standard. Scan rate = 1V/sec., start potential = 0.00 V, irr = irreversible, quasi = quasi-reversible, 4,5-DC-1-Me-2-I = (4,5-dicyano-1-methyl-2-imidazoyl), †data taken from reference.

Conclusions

The synthesis of 1-methyl-2-fluoro-4,5-dicyanoimidazole (2) was accomplished by halogen exchange between 1-methyl-2-bromo-4,5-dicyanoimidazole (1) and potassium fluoride with catalytic 18-crown-6 ether in diglyme. Halogen exchange between 1-methyl-2-bromo-4,5-dicyanoimidazole (1) and lithium chloride in N-methylpyrrolidinone at 150 °C yielded 1-methyl-2-chloro-4,5-dicyanoimidazole (3), while additional heating to 210 °C resulted in the subsequent demethylation to yield 2-chloro-4,5-dicyanoimidazole (5). The nucleophilic aromatic substitution reactions of various imidazole nucleophiles with 1-methyl-2-fluoro-4,5-dicyanoimidazole (2) resulted in the synthesis of several derivatives of 2-(4',5'-dicyano-1'-imidazoyl)-4,5-dicyanoimidazole.

Acknowledgment We thank Professor Richard G. Lawton (of The University of Michigan Chemistry Department) for many helpful discussions. PGR is grateful for support from the donors of the Petroleum Research Fund administered by the American Chemical Society.

Experimental

Melting points were recorded on a Mel-Temp apparatus and are uncorrected. Thin layer chromatography was done on Eastman Kodak silica gel sheets containing fluorescent indicator. Column chromatography was done using 220-400 mesh silica gel from Aldrich. Infrared spectra were recorded on a Nicolet 5-DX FTIR spectrophotometer. UV-visible spectroscopy was done on a Shimadzu UV-160 UV-visible Spectrophotometer. NMR spectra were recorded on a Bruker AM-200 (^{1}H NMR (200.1 MHz), ^{13}C NMR (50.3 MHz)), or Bruker AM-300 (^{1}H NMR (300.1 MHz), ^{13}C NMR (75.5 MHz)), or Bruker AM-360 (^{1}H NMR (360.1 MHz), ^{13}C NMR (90.6 MHz)) spectrophotometer. Chemical shift values are relative to tetramethylsilane in the appropriate solvent. ^{13}C NMR were done under broad band proton decoupling. GC-MS were recorded on a Finnigan model 4021 mass spectrometer. Nominal and high resolution mass spectra were recorded on a VG model 70-250S mass spectrometer. Elemental analyses were done at the University of Michigan on a Perkin-Elmer 2400 CHN analyzer or by Oneida Research Services, Inc., Whitesboro, NY

The 4, 5-dicyanoimidazole was obtained from Nippon Soda Co. Ltd., recrystallized from H_2O and dried prior to use. The 1-methyl-2-bromo-4,5-dicyanoimidazole (1) was prepared as previously reported.[6b] THF was distilled from sodium benzophenone ketyl. Acetonitrile was distilled from CaH_2. DMSO and triethylamine were distilled from BaO. DMAC and NMP were distilled from BaO or from phthalic anhydride. Spray-dried KF was purchased from Aldrich.

Cyclic voltammetry was done using a Princeton Applied Research (PAR) potentiostat/ galvanostat, model 173, a PAR universal programmer, model 175, and a PAR digital coulometer, model 179. For cyclic voltammetry, acetonitrile (HPLC grade) was distilled immediately prior to use. Et_4NBF_4 (99%, Aldrich) was recrystallized twice from freshly distilled acetonitrile and dried under vacuum prior to use. The electrolyte solution was 0.1M Et_4NBF_4 in acetonitrile. Samples were 0.003-0.005M in electrolyte solution. The reference solution was 0.010M $AgNO_3$ in electrolyte solution. All solvents and solutions were degassed prior to use. Working and reference electrodes were platinum wires and the counter electrode was a platinum foil.

1-Methyl-2-fluoro-4,5-dicyanoimidazole (2). In a dry-box, 1-methyl-2-bromo-4,5-dicyanoimidazole (1) (80.0 g, 0.38 mol), 1.25 equivalents of spray-dried potassium fluoride, a catalytic amount of 18-crown-6 ether, and approximately 100 mL of freshly distilled diglyme were placed in a round-bottomed flask equipped with magnetic stirrer, N_2 inlet, and reflux condenser. The mixture was heated at reflux for 12 hours, after which it was yellow-brown with a white salt precipitate (KBr / KF). The yellow-brown liquid was decanted and the salt was washed with acetone (3X150mL). The decanted liquid and acetone washes were combined. The acetone was removed under vacuum and the diglyme was distilled from the reaction at 50-60 °C under reduced pressure. The resulting brown oil was vacuum distilled twice, bp 95-110 °C at 0.02-0.03 mm, yielding 50.0 g (89%) of product **2**. The white solid: TLC EtOAc R_f 0.64; Mp 46-48 °C; IR(KBr) 2243, 1595, 1513, 1411, 1174 cm^{-1}; UV-vis(CH_3CN) $\lambda_{max}(\varepsilon)$ 250(12100); ^{1}H NMR (300.1 MHz, $CDCl_3$, ppm) δ 3.73 (s, 3H);

^{13}C NMR (75.5 MHz, $CDCl_3$, ppm) δ 150.0 (d, J = 252.1 Hz), 117.3 (d, J = 12.7 Hz), 110.7, 110.4 (d, J = 3.9 Hz), 107.0, 31.4; MS (E/I) m/z (relative intensity) 151 (M+1, 8), 150 (M^+, 100%), 149 (20), 135 (2), 122 (5), 109 (5); HRMS (EI with DCI probe) m/z calcd. for $C_6H_3N_4F$ 150.0342, obsd. 150.0338; Anal. calcd for $C_6H_3N_4F$: C, 48.02; H, 2.00; N, 37.32. Found: C, 47.96; H, 1.85; N, 37.15.

1-Methyl-2-chloro-4,5-dicyanoimidazole (3). In a dry box, 10.00 g (47.0 mmol) of 1-methyl-2-bromo-4,5-dicyanoimidazole (**1**), 11.67 g (118.0 mmol) of CuCl and 100 mL of freshly distilled diglyme were placed in a 250 mL round-bottomed flask equipped with magnetic stirrer, N_2 inlet, and reflux condenser. The mixture was heated at reflux for 12 hrs. The diglyme solution was filtered and the resulting brown residue (CuBr, CuCl) was washed with CH_2Cl_2 (3X100 mL). The CH_2Cl_2 was removed under vacuum and the diglyme solution was added. The diglyme was removed under vacuum, producing yellow-brown crystals. The yellow-brown crystals were dissolved in absolute ethanol, treated with carbon, and recrystallized twice yielding 2.97 g (38%) of product **3** as a white solid: TLC EtOAc R_f 0.66; Mp 114-116 °C; IR(KBr) 2243, 1473, 1214, 1121 cm^{-1}; UV-vis(CH_3CN) $\lambda_{max}(\varepsilon)$ 256(9240); ^1H NMR ($CDCl_3$, ppm) δ 3.81 (s, 3H); ^{13}C NMR ($CDCl_3$, ppm) δ 138.6, 121.5, 114.2, 110.7, 107.3, 33.9; MS (E/I) m/z (relative intensity) 168 (M+2, 41.4), 166 (M^+, 100.0), 131 (15.4), 125 (34.0); HRMS (EI with DCI probe) m/z calcd. for $C_5H_3N_4{}^{35}Cl$ 166.0046, obsd. 166.0044.

2-Fluoro-4,5-dicyanoimidazole (4). In a dry box, 4.0 g (27.0 mmol) of 1-methyl-2-fluoro-4,5-dicyanoimidazole (**2**), 2.9 g (33.0 mmol) of LiBr and 200 mL of freshly distilled NMP were placed in a 250 mL round-bottomed flask equipped with magnetic stirrer, N_2 inlet and reflux condenser. The mixture was heated at reflux 18 h and then cooled. The NMP was distilled from the reaction mixture under vacuum. The resulting lithium salt was boiled with 600 mL $CHCl_3$ and filtered. The salt was dissolved in 20 mL 10% HCl and extracted with ethyl acetate (3X50 mL). The organic layers were combined, the solution dried with Na_2SO_4, and the ethyl acetate removed under vacuum. The resulting off-white solid was recrystallized twice with H_2O yielding 0.53 g (15%) of product **4**. as an off-white solid: TLC 5/1 EtOAc/MeOH R_f 0.92; Mp 141-143°C; IR(KBr) 2250, 1590, 1472, 1312, 1072 cm^{-1}; UV-vis(CH_3CN) $\lambda_{max}(\varepsilon)$ 247(11200); ^1H NMR ((acetone-d_6, ppm) δ 10.27 (br s, 1H); ^{13}C NMR (acetone-d_6, ppm) δ 151.5 (d, J=248.9 Hz), 113.6 (d, J=4.5 Hz), 110.4; MS (EI with DCI probe) m/z (relative intensity) 253 (19.4), 252 (100.0), 200 (49.9), 137 (M+1, 5.8), 136 (M^+, 39.7), 109 (15.8); HRMS (EI with DCI probe) m/z (M^+) calcd. for $C_5H_1N_4F$ 136.0185, obsd 136.0185.

2-Chloro-4,5-dicyanoimidazole (5). In a dry box, 20.0 g (0.094 mol.) of 1-methyl-2-bromo-4,5-dicyanoimidazole (**1**), 40.0 g (0.943 mol.) of LiCl and 200 ml of freshly distilled NMP were placed in a 500 ml round-bottomed flask equipped with magnetic stirring, N_2 inlet and reflux condenser. The mixture was heated at 160-165 °C for 24 h, and then at reflux for 2 h. The NMP was distilled from the reaction mixture under vacuum. The resulting lithium salt was dried overnight at 100 °C. It was boiled in 600 mL $CHCl_3$, filtered, and dried. It was dissolved in 100 mL 10% HCl and extracted with ethyl acetate (3X100 mL). The organic layers

were combined, the solution was dried with Na_2SO_4, and the ethyl acetate removed under vacuum. The resulting off-white solid **5** was recrystallized twice with H_2O producing 10.4 g (72%) of product. The white solid **5**: TLC 5/1 EtOAc/ MeOH R_f 0.82; Mp 144-146°C; IR(KBr): 2247, 1573, 1493, 1409, 1293, 1006 cm^{-1}; UV-vis(CH_3CN) $\lambda_{max}(\varepsilon)$ 253(9700); ^1H NMR (acetone-d_6, ppm) δ 9.61(br s, 1H); ^{13}C NMR (DMSO-d_6, ppm) δ 137.5, 116.5, 110.7; MS (EI with DCI probe) m/z (relative intensity) 154 (m+2, 33.7), 152 (m+, 100.0), 127 (18.0), 125 (50.5); HRMS (EI with DCI probe) m/z calcd. for $C_5HN_4{}^{35}Cl$ 151.9890, obsd. 151.9893. Anal. calcd. for C_5HN_4Cl: C, 39.38; H, 0.66; N, 36.72. Found: C, 39.10; H, 0.56; N, 36.46.

1-Methyl-2-(4',5'-dicyano-1'-imidazolyl)-4,5-dicyanoimidazoles

General procedure

In a dry box, 1 equivalent of 1-methyl-2-fluoro-4,5-dicyanoimidazole (**2**), 1.5 equivalents of the indicated salt of a 4,5-dicyanoimidazole, a catalytic amount of crown ether and 20 mL of CH_3CN per 3 g of 1-methyl-2-fluoro-4,5-dicyanoimidazole (**2**) were placed in a round-bottomed flask equipped with magnetic stirrer, N_2 inlet, and reflux condenser. After the indicated reaction time, the CH_3CN was removed under vacuum. The resulting solids were dissolved in ethyl acetate and were extracted with 10% NH_4OH to remove the excess 4,5-dicyanoimidazole starting material. The organic layer was treated with brine, dried with Na_2SO_4, and treated with carbon. The solvent was removed under vacuum to produce a solid.

1-Methyl-2-(4',5'-dicyano-1'-imidazolyl)-4,5-dicyanoimidazole (7a). The 30.0 g (200 mmol) of compound **2**, with a catalytic amount of 18-crown-6 ether, were refluxed 37 h with 46.8 g (300 mmol) of the potassium salt of 4,5-dicyanoimidazole, the work up was as indicated above. The solid was recrystallized from absolute ethanol yielding 35.3 g (73%) of product **7a**. as a white solid: TLC EtOAc R_f 0.62; Mp 189-192°C; IR(KBr) 3131, 2245, 1540, 1463, 1363, 1297, 1218 cm^{-1}; UV-vis(CH_3CN) $\lambda_{max}(\varepsilon)$ 249(58300); ^1H NMR (acetone-d_6, ppm) δ 8.72 (s, 1H), 4.13 (s, 3H); ^{13}C NMR (acetone-d_6, ppm) δ 143.3, 138.3, 125.4, 121.1, 116.5, 114.5, 111.8, 111.6, 108.0, 107.7, 35.0; MS (EI with DCI probe) m/z (relative intensity) 249 (17.6), 248 (M^+, 100.0), 247 (7.6), 221 (28.5), 196 (10.2); HRMS (EI/w DCI probe) m/z (M^+) calcd 248.0559, obsd 248.0552; Anal. calcd for $C_{11}H_4N_8$: C, 53.21; H, 1.63; N, 45.16. Found: C, 53.02; H, 1.80; N, 45.15.

1-Methyl-2-(2'-methyl-4',5'-dicyano-1'-imidazolyl)-4,5-dicyanoimidazole (7b). The reaction was carried out using 0.5 g (3.0 mmol) of compound **2** with a catalytic amount of 12-crown-4 ether. After 37 h at reflux with 0.69 g (5.0 mmol) of the lithium salt of 2-methyl-4,5-dicyanoimidazole, the reaction mixture was worked up as indicated above. The solid was recrystallized from H_2O/acetone yielding 0.23 g (54%) of product **7b** as a white solid: TLC EtOAc R_f 0.59; Mp 224-226°C; IR(KBr) 3022, 2247, 1550, 1486, 1386, 1317, 1044 cm^{-1}; UV-vis(CH_3CN) $\lambda_{max}(\varepsilon)$ 250(63520); ^1H NMR (DMSO-d_6, ppm) δ 2.68(s, 3H), 1.31 (s, 3H); ^{13}C NMR (DMSO-d_6, ppm) δ 153.5, 136.1, 123.2, 119.6, 116.8, 113.6, 111.7, 111.5, 107.9, 107.6, 34.4, 13.5;

MS (EI with DCI probe) m/z (relative intensity) 264 (4.1), 263 (36.0), 262 (M^+, 100.0), 261 (31.5), 221 (33.5), 158 (9.7), 157 (16.7), 132 (17.4); HRMS (EI/w DCI probe) m/z (M^+) calcd 262.0715, obsd 262.0702; Anal. calcd for $C_{12}H_6N_8$: C, 54.96; H, 2.31; N, 42.73. Found: C, 55.25; H, 2.44; N, 42.48.

1-Methyl-2-(2'-amino-4',5'-dicyano-1'-imidazolyl)-4,5-dicyanoimidazole (7c). The reaction was carried out using 40.0 g (270 mmol) of **2** with a catalytic amount of 18-crown-6 ether. After 8 h at 50°C with 68.4 g (400 mmol) of the potassium salt of 2-amino-4,5-dicyanoimidazole, the mixture was worked up as above. The solid was recrystallized from acetonitrile/H_2O yielding 57g (81%) of product **7c** as a white solid: TLC EtOAc R_f 0.62; Mp 288-290°C; IR(KBr) 3424, 3364, 2248, 2230, 1643, 1487, 1421, 1255 cm^{-1}; UV-vis(CH_3CN) $\lambda_{max}(\varepsilon)$ 247(22670) 297(19020); ^1H NMR (DMSO-d_6, ppm) δ 7.73 (s, 2H), 3.77 (s, 3H); ^{13}C NMR (DMSO-d_6, ppm) δ 153.1, 136.2, 123.3, 119.4, 115.7, 112.1, 111.3, 108.5, 107.7, 106.9, 34.0; MS (EI with DCI probe) m/z (relative intensity) 265 (5.6), 264 (45.2), 263 (M^+, 100.0), 236 (10.1), 158 (29.3), 132 (43.6); HRMS (EI/w DCI probe) m/z (M^+) calcd 263.0668, obsd 263.0650.

1-Methyl-2-iodo-4,5-dicyanoimidazole (9a). A mixture of 0.51 g 1-methyl-2-amino-4,5-dicyanoimidazole (3.4 mmol), 4.5 mL isoamyl nitrite (10 eq.), and 6.0 mL diiodomethane (22 eq.) was placed in a 25 mL 3-neck round-bottom flask equipped with stirrer, N_2 inlet, and reflux condenser. The solution was heated to 110 °C for 21 hrs, and the solvent was removed by distillation. The residue was separated by column chromatography using 10% EtOAc in hexanes to give pure product as a yellow powder: 0.35g (40%). TLC EtOAc/hexanes (1:1) R_f = 0.62; Mp 180 °C; IR (KBr) 2920, 2240, 1454, 1353, 1329, 1210, 1098 cm^{-1}; ^1H NMR (acetone-d_6) δ 3.97 (s, 3H); MS (EI/w DCI probe) m/z (relative intensity) 258 (100), 131 (32), 101 (9), 79 (15), 67 (17), 43 (21); HRMS (EI/w DCI probe) m/z (M^+) calcd for $C_6N_4H_3I$: 257.9402, obsd: 257.9413. The 2-Iodo-4,5-dicyanoimidazole and 1-methyl-2-(2'-iodo-4',5'-dicyano-1'-imidazoyl) -4,5-dicyanoimidazole were synthesized by similar procedures, and their characterizations are as follows:

2-Iodo-4,5-dicyanoimidazole (9b). Yield: 33%. TLC EtOAc R_f = 0.07; Mp 176-178 °C; IR (KBr) 3203, 2241, 1754, 1370, 1275, 1264 cm^{-1}; No signals detected by ^1H NMR; MS (EI/w DCI probe) m/z (relative intensity) 244 (100), 117 (60), 71 (25), 53 (27), 43 (36); HRMS (EI/w DCI probe) m/z (M^+) calcd for C_5N_4HI: 243.9246, obsd: 243.9239.

1-Methyl-2-(2'-iodo-4',5'-dicyano-1'-imidazoyl)-4,5-dicyano imidazole (10). Yield: 71%. TLC EtOAc/hexanes (1:1) R_f = 0.28; Mp 208-210 °C; IR (KBr) 2247, 1527, 1489, 1417, 1407, 1355, 1319, 1272, 1004 cm^{-1}; ^1H NMR δ 3.81 (s, 3H, in $CDCl_3$); 3.85 (S, 3H, in DMSO-d_6); 4.12 (S, 3H, in acetone-d_6); MS (EI/w DCI probe) m/z (relative intensity) 374 (82), 247 (100), 221 (33), 195 (11), 154 (20), 102 (16), 67 (42); HRMS (EI/w DCI probe) m/z (M^+) calcd for $C_{11}N_8H_3I$: 373.9525, obsd: 373.9532.

1-(1'-Methyl-4',5'-dicyano-2'-imidazoyl)-4,5-dicyano-2-imidazolone (14a). In a 25 mL 3-neck round-bottom flask equipped with stirrer, addition funnel, N_2 inlet, and reflux condenser were placed 0.40 g

(2.3 mmol) of the potassium salt of 4,5-dicyano-2-imidazolone (**13**), catalytic amount of 18-crown-6, and 5 mL distilled DMSO. A solution of 0.35 g (2.3 mmol) of 1-methyl-2-fluoro-4,5-dicyanoimidazole in 5 mL DMSO was added dropwise to the flask while the reaction mixture was stirred at 100 °C in an oil bath under N_2. The reaction mixture was stirred for 5 hrs, and it was then poured into 20 mL acidified water (pH = 5). After stirring for 20 min., a yellow precipitate formed, and was removed by filtration. The precipitate was recrystallized from 25 mL water/acetone (2:1). Yield 0.48 g (78%) yellow fine powder. TLC EtOAc R_f = 0; Mp 262-265 °C; IR (KBr) 3252, 2246, 1748, 1536, 1430, 1360 cm^{-1}; ^1H NMR (acetone-d_6) δ 4.02 (s, 3H); ^{13}C NMR (acetone-d_6) δ 149.04, 138.69, 120.71, 116.01, 112.08, 109.60, 108.65, 108.45, 108.05, 107.30, 35.27; MS (EI/w DCI probe) m/z (relative intensity) 264 (100), 237 (12), 209 (8), 132 (15), 67 (60), 53 (20), 44 (22); HRMS (EI/w DCI probe) m/z (M^+) calcd for $C_{11}H_4N_8O$: 264.0508, obsd 264.0498.

The other 1-(1'-alkyl-4',5'-dicyano-2'-imidazoyl)-4,5-dicyano-2-imidazolone dimers were synthesized by similar procedures, and their characterizations are given below.

1-(1'-Isopropyl-4',5'-dicyano-2'-imidazoyl)-4,5-dicyano-2-imidazolone (14b). Yield: 62%. TLC EtOAc R_f = 0; Mp 237-240 °C; IR (KBr) 3005, 2240, 1742, 1522, 1378, 1363, 1333, 1220, 1080 cm^{-1}; ^1H NMR (acetone-d_6) δ 4.92 (m, 1H), 1.75 (d, 6H); ^{13}C NMR (acetone-d_6) δ 149.3, 136.0, 121.7, 111.3 111.0, 110.0, 108.7, 108.4, 107.9, 105.3, 52.8, 21.5; MS (EI/w DCI probe) m/z (relative intensity) 292 (17), 250 (100), 223 (15), 53 (14), 43 (98); HRMS (EI/w DCI probe) m/z (M^+) calcd for $C_{13}N_8H_8O$: 292.0821, obsd: 292.0815.

1-(1'-Propyl-4',5'-dicyano-2'-imidazoyl)-4,5-dicyano-2-imidazolone (14c). Yield: 79%. TLC EtOAc R_f = 0; Mp 240 °C; IR (KBr) 3324, 2242, 1735, 1526, 1314 cm^{-1}; ^1H NMR (acetone-d_6) δ 4.32 (t, 2H), 2.00 (m, 2H), 0.93 (t, 3H); MS (EI/w DCI probe) m/z (relative intensity) 292 (40), 277 (10), 264 (20), 250 (100), 223 (20), 208 (20), 43 (89); HRMS (EI/w DCI probe) m/z (M^+) calcd for $C_{13}N_8H_8O$: 292.0821, obsd: 292.0813.

1-(1'-Isobutyl-4',5'-dicyano-2'-imidazoyl)-4,5-dicyano-2-imidazolone (14d). Yield: 82%. TLC EtOAc R_f = 0; Mp 250-252 °C; IR (KBr) 3194, 2249, 2239, 1746, 1533, 1480, 1361, 1316 cm^{-1}; ^1H NMR (acetone-d_6) δ 4.21 (d, 2H), 2.25 (m, 1H), 0.95 (d, 6H); ^{13}C NMR (acetone-d_6) δ 149.2, 136.9, 120.2, 114.1, 111.3, 110.8, 108.8, 107.9, 107.8, 104.6, 54.2, 28.5, 19.0; MS (EI/w DCI probe) m/z (rel. int.) 306 (14), 264 (12), 250 (27), 149 (8), 57 (71), 43 (100); HRMS (EI/w DCI) m/z (M^+) calcd for $C_{14}N_8H_{10}O$: 306.0978, obsd: 306.0993.

2-(4,5-dicyano-1-imidazolyl)-4,5-dicyanoimidazole (15a). In a dry box, 26.0 g (105 mmol) of 1-methyl-2-(4,5-dicyano-1-imidazolyl)-4,5-dicyanoimidazole (**7a**), 4.49 g (106 mmol, 1 eq) of lithium chloride, and 20 mL of DMAC were placed in a 50 mL round-bottomed flask equipped with magnetic stirrer, N_2 inlet, and reflux condenser. After 9 h of reflux, the solvent was removed under vacuum and the lithium salt of the product was boiled in chloroform (3X50 mL) to remove the DMAC. The product was then dissolved in 10% HCl (30 mL) and extracted with EtOAc (5X50 mL). The EtOAc layers of the solution were combined, washed with brine, and dried with $MgSO_4$. The EtOAc was removed under vacuum. The solid was dissolved in acetonitrile and

treated with carbon. The solvent was removed under vacuum and the off-white solid was dried at 100°C, yield, 3.33 g (88%), **15a**. IR(KBr) 3229-2962(br), 2244, 1726, 1540, 1510, 1487, 1360, 1255, 1215, 1170 cm^{-1}; UV-vis(CH_3CN) $\lambda_{max}(\varepsilon)$ 258(62010); ^1H NMR (acetone-d_6, ppm) δ 8.64 (S, 1H); ^{13}C NMR (acetone-d_6, ppm) δ 141.6, 139.3, 125.3, 116.9, 112.4, 111.8, 110.6, 107.9; MS (EI/w DCI) m/z (rel. int.) 235 (17.4), 234 (M^+, 90.8), 208 (7.9), 207 (61.4), 182 (8.2); HRMS (EI/w DCI) m/z (M+) calcd 234.0402, obsd 234.0383.

2-(2-Amino-4,5-dicyano-1-imidazolyl)-4,5-dicyanoimidazole (15c). In a dry box, 10.0 g (38.0 mmol) of 1-methyl-2-(2-amino-4,5-dicyano-1-imidazolyl)-4,5-dicyanoimidazole (**7c**), 3.20 g (76.0 mmol, 2 eq) of lithium chloride, and 30 mL of DMAC were placed in a 100 mL round-bottomed flask with magnetic stiring, N_2 inlet, and reflux condenser. After 4 h at 165°C, the solvent was removed under vacuum and the lithium salt of the product was boiled in chloroform (3X50 mL) to remove the DMAC. It was dissolved in 10% HCl (100 mL) and extracted with EtOAc (8X100 mL). The EtOAc layers were combined and the solution was washed with brine, and dried with $MgSO_4$. The EtOAc was removed under vacuum. The solid was dissolved in acetonitrile and treated with carbon producing an off-white solid. The acetonitrile was removed under vacuum and the product dried at 100°C. The yield was 8.34 g (88%) of off-white solid **15c**: TLC 5/1 EtOAc/MeOH R_f 0.80; Mp ~200°C darkened to tan, ~220°C turned dark brown, ~340°C melted to a dark brown oil; IR(KBr) 3360, 3182, 3168, 2231, 1655, 1580, 1534, 1329 cm^{-1}; UV-vis(CH_3CN) $\lambda_{max}(\varepsilon)$ 243(12500) 306(12130); ^1H NMR (DMSO-d_6, ppm) δ 9.73 (br, s, 2H); ^{13}C NMR (DMSO-d_6 ppm) δ 151.7, 146.9, 121.7, 117.6, 115.2, 113.5, 110.8, 104.6; MS (EI/w DCI) m/z (rel. int.) 250 (8.3), 249 (M^+, 52.7), 222 (11.0), 149 (12.8), 144 (14.7), 120 (27.6), 118 (20.9); HRMS (EI/w DCI probe) m/z (M^+) calcd 249.0511, obsd 249.0509.

1-(4',5'-Dicyano-2'-imidazoyl)-4,5-dicyano-2-imidazolone (16). In a dry box, 0.20 g (0.76 mmol) of 1-(1'-methyl-4',5'-dicyano-2'-imidazoyl)-4,5-dicyano-2-imidazolone (**14a**) and 0.19 g (4.5 mmol) of LiCl, and 4 mL DMAc were placed in a 25 mL 3-neck round-bottom flask equipped with stirrer, N_2 inlet, and reflux condenser. The reaction mixture was stirred at 100 °C under N_2. After 4 days, the reaction was complete as shown by TLC. The mixture was cooled to room temperature, and precipitated from 20 mL of acidified water (pH = 5) twice. Yield 0.10 g (53%) yellow solid. TLC EtOAc R_f = 0; Mp 300 °C (decomposed); IR (KBr) 3521, 3243, 2244, 1756, 1576, 1543, 1473, 1367, 1308, 1178 cm^{-1}; No signals were detected by ^1H NMR. MS (EI/w DCI probe) m/z (relative intensity) 268 (30), 250 (100), 223 (75), 208 (52), 143 (40), 118 (42), 90 (26), 64 (32), 53 (72); HRMS (EI/w DCI probe) m/z (M^+) calcd for $C_{10}OH_2N_8$: 250.0352, obsd 250.0350.

1-(4',5'-dicyano-2'-imidazoyl)-3-methyl-4,5-dicyano-2-imidazolone (17). In a dry box, 0.40 g (1.5 mmol) of 1-(1'-methyl-4',5'-dicyano-2'-imidazoyl)-4,5-dicyano-2-imidazolone (**14a**), 0.13 g (3 mmol) LiCl, and 5 mL DMAc were placed in a 25 mL 3-neck round-bottom flask with magnetic stiring, N_2 inlet, and reflux condenser. The mixture was refluxed at 165 °C in an oil bath under N_2. The mixture turned black in 1 hr. After reflux for 17 hrs, it was allowed to cool and poured into 40 mL acidified water (pH = 5). After stirring

for 20 min., a yellow precipitate was filtered off and dried in vacuum oven. Yield: 0.35 g (92%). TLC EtOAc $R_f = 0.19$; Mp 264-266 °C; IR (KBr): 2242, 1760, 1618, 1572, 1457, 1393, 1162 cm^{-1}; ^1H NMR (acetone-d_6) δ 3.57 (s, 3H); MS (EI/w DCI probe) m/z (relative intensity) 264 (100), 237 (12), 224 (10), 209 (8), 132 (15), 67 (60), 53 (20), 44 (22), HRMS (EI/w DCI probe) m/z (M^+) calcd for $C_{11}OH_4N_8$: 264.0508, obsd 264.0515.

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