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Hydroxide-Initiated Conversion of Aromatic Nitriles to Imidazolines: Fullerenes vs TCNE

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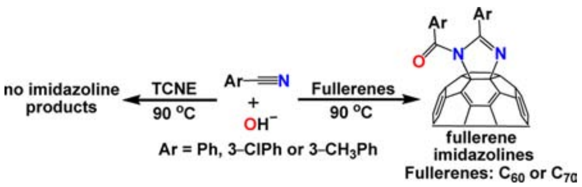
ABSTRACT

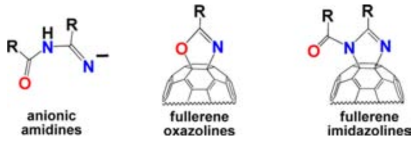


Transformation of aromatic nitriles to imidazolines has been achieved under basic conditions with the electron-deficient C_{60} and C_{70} fullerenes, but not with the electron-deficient olefin of tetracyanoethylene (TCNE). In situ UV−vis−NIR indicates that the ability of RC_{60}^- to undergo single-electron transfer (SET) to C_{60} is crucial for the reaction.

Organonitriles are a class of molecules widely used for conversion to various functionalities including amides, aldehydes, amines, carboxylic acids, ketones, hydrazones, lactams, imidates, and amidines.[1] Weak nucleophilic intermediates of anionic amidines with the negative charge located on the imine nitrogen atom (Scheme 1) are known to form via the base-mediated dimerization of aromatic nitriles,[2] which may in principle further react with electron-deficient olefins to form imidazolines. However, no such reaction has been reported so far.

Fullerenes, represented by C_{60} and C_{70}, are very electron-deficient molecules as evidenced by their ability to undergo six reversible one-electron reductions.[3] In the meantime, they are reactive in addition reactions and behave as electron-deficient olefins.[4] It is therefore of interest to explore the transformation reactions of organonitriles with fullerenes, which can serve as models to explore novel reactions.[5]

Scheme 1. Structural Illustrations of Anionic Amidines, Fullerene Oxazolines, and Imidazolines



Previous work has shown that OH^- can undergo nucleophilic addition to C_{60} to form a strong nucleophile $[C_{60}O]^{2-}$, which further reacts with benzonitrile to form fullerene oxazolines (Scheme 1) at rt.[6] However, it is intriguing that no fullerene product resulting from reactions involving OH^- with PhCN was isolated, since the base-mediated hydrolysis is one of the most conventional reactions for nitriles. Interestingly, by elevating the reaction temperature to 90 °C, new fullerene heterocycles of imidazolines (Scheme 1) are indeed formed via a multicomponent reaction of OH^- with nitriles and fullerenes. Such compounds have been reported recently by reactions of C_{60} with amidines.[7]

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Table 1. Screening of the Reaction Conditions and the Substrate Scope[a]

entry	ArCN	fullerenes	OH^- (equiv)	temp (°C)	product	yield[b] (%)
1	PhCN	C_{60}	3	rt	**1**	39
2	PhCN	C_{60}	9	rt	**1**	25
3	PhCN	C_{60}	3	90	**2a**	26
4	PhCN	C_{60}	6	90	**2a**	32
5	PhCN	C_{60}	9	90	**2a**	**43**
6	PhCN	C_{60}	9	90	**2a**	41[c]
7	PhCN	C_{60}	12	90	**2a**	32
8	PhCN	C_{60}	9	120	**2a**	40
9	3-ClPhCN	C_{60}	6	90	**2b**	37
10	3-CH_3PhCN	C_{60}	9	90	**2c**	36
11	PhCN	C_{70}	9	90	**3**	**41**

[a] Reaction conditions: TBAOH (tetra-*n*-butylammonium hydroxide, 1.0 M in MeOH) was added into ArCN (30 mL), and the mixture was stirred for 20 min at the preset temperature under argon. C_{60} or C_{70} (50 mg) was added, and the reaction was stirred for 30 min before quenching with I_2 (1 equiv to TBAOH). [b] Isolated yield. [c] The reaction was allowed to proceed for 90 min after adding C_{60}.

The reaction conditions and substrate scope were screened, and the results are listed in Table 1. Only fullerene oxazoline (**1**) was obtained at rt (entries 1 and 2). As the temperature was increased to 90 °C, 1′-benzoyl-2′-phenyl-2′-imidazolino[5′,4′:1,2][60]fullerene (**2a**) was obtained (entries 3−7). The increase in temperature to 120 °C did not improve the yield (entry 8). A molar ratio of 9:1 for OH^- to C_{60} is most appropriate for the reaction (entry 5); a smaller or larger amount of OH^- would result in a lower yield for the product (entries 4 and 7), where less C_{60} would react if less OH^- was used, while more toluene-insoluble materials would be formed if too much OH^- was used. Also, a prolonged reaction time would not improve the yield of imidazolines either (entry 6). Aromatic nitriles 3-ClPhCN and 3-CH_3PhCN can also result in the imidazoline products **2b** and **2c** with a similar yield as PhCN. Higher fullerene C_{70} also works as an effective substrate to achieve this transformation and results in compound **3**.

The structures of **2a** and **3** are identified by the single-crystal X-ray diffraction (Figure 1). As for **2a**, an imidazoline heterocycle, which consists of benzamide and benzonitrile units, is unambiguously shown with two N-atoms bonding to C_{60} at the [6,6] bond (Figure 1a). The sum of the bond angles of C62−C61−N2, C62−C61−N1, and N1−C61−N2 is 360°, indicating that C61 is an sp^2 carbon. The bond lengths of N1−C61 (1.399 Å) and C61−N2 (1.257 Å) are in good agreement with the C−N (1.47 Å) and C═N (1.28 Å) bond lengths,[8] indicating explicitly that an imidazoline heterocycle is formed on the C_{60} cage. The bond length of C68−O1 (1.221 Å) is consistent with the typical C═O bond length (1.20 Å),[8] demonstrating that **2a** is 1′-benzoyl-2′-phenyl-2′-imidazolino[5′,4′:1,2][60]fullerene.

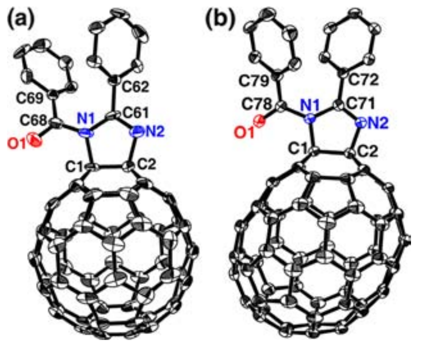

Figure 1. ORTEP diagrams of (a) **2a** and (b) **3** with 50% thermal ellipsoids. H-atoms and solvent molecules were omitted for clarity. Selected bond lengths (Å): (a) N1−C61 1.399(9), C61−N2 1.257(8), C68−O1 1.221(8); (b) N1−C71 1.414(4), C71−N2 1.272(5), C78−O1 1.211(4).

The same heterocycle is bonded to the C_{70} cage at the C1−C2 bond of compound **3** as shown in Figure 1b.[9] Due to the lower symmetry of C_{70} and the heterocycle, two 1,2-regioisomers can be formed in principle with the heterocycle orientated toward different directions.[10] However, only one regioisomer is obtained in the reaction, with the imine N bonded to the apical C2 carbon, while the amino N bonded to the C1 carbon. The exhibited regioselectivity for the heterocycle provides an important clue for the reaction mechanism as shown below.

The structures of **2a** and **3** are further supported by spectroscopic characterizations, where the protonated molecular ions of **2a** and **3** are shown in the HRMS (Figures S3 and S18), and resonances due to the aromatic protons are exhibited in the ^1H NMR spectra (Figures S4 and S19). The ^{13}C NMR spectrum of **2a** shows two weak resonances at 93.29 and 82.63 ppm (Figure S5), corresponding to the sp^3 fullerene carbons bonded to the imine[6,11] and amino[12] N-atoms respectively, and is consistent with the recently reported data for C_{60} imidazolines.[7] As for **3**, only one weak resonance corresponding to the sp^3 C_{70} carbon bonded to the amino nitrogen is shown at 78.22 ppm (Figure S20), while the one bonded to the imine nitrogen is missing probably due to the weak nature of this resonance as observed in **2a** and also C_{70} oxazolines.[13] Also, resonances for the carbonyl and the imine C-atoms of **2a** and **3** appear in the range 160−170 ppm. A total of 29 and 34 signals appear for the sp^2 carbons of the fullerene cage for **2a** and **3**, in agreement with the C_s symmetry of

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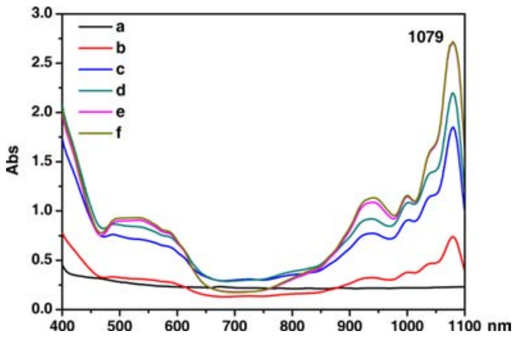
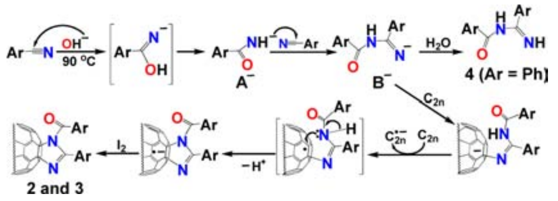


Figure 2. In situ vis−NIR spectra of (a) 625 μmol of TBAOH (1.0 M in MeOH, 625 μL) in PhCN (30 mL) after heating at 90 °C for 20 min; (b−f) after adding C_{60} (50 mg) into solution (a) for 3, 13, 23, 30, and 40 min respectively. All measurements were performed with a 1-mm cuvette under Ar.

Scheme 2. Proposed Mechanism for the Transformation of Nitriles to Fullerene Imidazolines[a]



[a] The negative charge, which is likely delocalized over a large area of fullerenes due to π-conjugation, is drawn in a hexagon of the fullerene cage for clarity.

the compounds as shown by the X-ray single-crystal structures. The UV−vis spectrum of **2a** (Figure S2) is similar to that of C_{60} oxazolines,[11a,c] while the spectrum of **3** (Figure S17) shows the typical absorptions for the C_{70} C1−C2 adducts.[13,14]

The reaction of TBAOH with PhCN and C_{60} was followed with the in situ vis−NIR spectroscopy (Figure 2). No absorption appears from 400 to 1100 nm during the reaction of TBAOH with PhCN (Figure 2a), while the strong characteristic absorption of $C_{60}^{\bullet-}$ appears at 1079 nm[15] (Figure 2b−f) after C_{60} is added, indicating that a significant amount of $C_{60}^{\bullet-}$ is generated during the formation of imidazolines. The results therefore imply that the C_{60} imidazolines are likely formed via a monoanion mechanism (RC_{60}^{-}) rather than a dianion mechanism (RC_{60}^{2-}), which was involved in the formation of C_{60} oxazolines,[6,16] since $C_{60}^{\bullet-}$ can be generated by RC_{60}^{-} via SET,[17] while C_{60}^{2-} (~ 950 nm) would be produced if there were RC_{60}^{2-} according to the relationships of reduction potentials of $C_{60}^{n-/(n+1)-}$ with those of $RC_{60}^{n-/(n+1)-}$ (n = 0 or 1).[3,18]

The absence of the dianionic intermediates during the reaction is further confirmed by the absence of absorption bands arising from the dianion of **2a**, which was produced via controlled-potential bulk electrolysis (see Experimental Section in the Supporting Information (SI) for details) and exhibits absorptions at 651, 724, and 975 nm (Figure S25). Notably, when the in situ spectrum of Figure 2f is overlaid with the spectrum of $C_{60}^{\bullet-}$ by normalizing the absorption at 1079 nm (Figure S26), the reaction mixture exhibits stronger absorptions than the pristine $C_{60}^{\bullet-}$ in the region below 1050 nm, implying the existence of other anionic species (likely RC_{60}^{-}) in the mixture.

A plausible reaction mechanism for the conversion of nitriles to fullerene imidazolines is shown in Scheme 2. The reaction is initiated by the attack of OH^{-} at the C-atom of the nitrile with the formation of intermediate $\mathbf{A}^{-}$ (amide anion), which further reacts with another nitrile molecule and results in intermediate $\mathbf{B}^{-}$ (amidine anion) with the negative charge on the imine N. Subsequently, the $\mathbf{B}^{-}$ would attack the electron-deficient fullerenes and afford $\mathbf{B}C_{2n}^{-}$ (n = 30 or 35), which would undergo an SET to a C_{2n} molecule, resulting in $\mathbf{B}C_{2n}^{\bullet}$ and $C_{2n}^{\bullet-}$. Intermediate $\mathbf{B}C_{2n}^{\bullet}$ would then undergo a ring-closure reaction with the formation of a new C_{2n}−N (amino) bond, accompanied with the loss of a proton, resulting in $\mathbf{2}^{\bullet-}$ or $\mathbf{3}^{\bullet-}$. The fullerene imidazolines are finally obtained by oxidation with I_2 to remove the negative charge from the fullerene cage. The formation of the intermediate $\mathbf{B}^{-}$ is unambiguously demonstrated by the isolation of compound **4** (*N*-benzoylbenzamidine) via protonation of the reaction mixture of PhCN and OH^{-} with water (see Experimental Section in the SI for details).

Previous work has shown that a heterocyclic rearrangement is involved during the formation of the fullerene oxazolines, which is driven by the formation of the more stable ring-opened dianionic intermediate.[6b,13] However, such a rearrangement is unlikely to occur during the formation of fullerene imidazolines, since only monoanionic intermediates are involved in the formation of fullerene imidazolines. Consequently, the formation of only one C_{70} imidazoline product (Figure 1b), in which the imine N is bonded to the C2, while the amino N is bonded to the C1, explicitly demonstrates that the negative charge is located on the imine N-atom of intermediate $\mathbf{B}^{-}$, since the C2 carbon is preferred as the first reaction site of C_{70} for reactions involving anionic species due to the favored formation of the 2−RC_{70}^{-} intermediate.[13,14c]

NBO calculations with Gaussian09 at the B3LYP/6-311G(d)//B3LYP/6-31G level for the charge distributions of $\mathbf{A}^{-}$ and $\mathbf{B}^{-}$ were performed. The calculations predict that the imine N-atom bears a charge of −0.882 and −0.701 for the intermediates of $\mathbf{A}^{-}$ and $\mathbf{B}^{-}$ respectively (Figure S30), implying that $\mathbf{B}^{-}$ is a weaker nucleophile as compared with $\mathbf{A}^{-}$, which may account for the incapability of $\mathbf{B}^{-}$ to further react with another nitrile molecule to form the trimeric intermediate.

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Since a novel transformation of aromatic nitriles to imidazolines was demonstrated under the basic conditions with the use of electron-deficient fullerenes, it was of interest to investigate whether such a transformation can be achieved with other typical electron-deficient alkenes. TCNE is an ideal substrate to study, since it is even more electron-deficient than C_{60} and C_{70} as evidenced by the more positive potential for the first reduction ($E_{1/2}$ vs SCE: 0.30 V for TCNE, −0.43 V for C_{60}, −0.42 V for C_{70}, Figure S29), and is capable of undergoing a nucleophilic addition reaction with nucleophiles including cyanide and Grignard reagents.[19]

Reactions of TCNE with OH^- and PhCN were carried out with a TCNE:OH^- molar ratio of 1:9, 1:6, 1:3, and 20:1, while other conditions remained similar to those when fullerenes were used (see Experimental Section in the SI for details). The reaction crude products were separated with a flash silica column. Surprisingly, no TCNE imidazoline product was obtained. Since the $\mathbf{BTCNE}^-$ is expected to form, as TCNE is more electron-deficient than fullerenes and capable of addition reactions with nucleophiles, it implies that the intermediates of anionic fullerene species ($\mathbf{BC}_{2n}^-$) may possess a unique character that is absent for the conventional anionic alkene species.

As shown in Scheme 2, an SET from $\mathbf{BC}_{2n}^-$ to C_{2n} to form the $\mathbf{BC}_{2n}^{\bullet}$ and $C_{2n}^{\bullet-}$ is required in order to form the second C_{2n}−N bond via a nucleophilic attack of amino N to the fullerene cage. Such an electron transfer is supported by the appearance of characteristic absorptions for $C_{60}^{\bullet-}$ in the in situ vis−NIR spectrum of the reaction mixture and has been proposed for the mechanochemical synthesis of C_{120} and the reaction of C_{60} with alkoxide ions.[17] However, it seems that no electron transfer occurs from $BTCNE^-$ to TCNE as indicated by the in situ UV−vis spectra of the reaction mixture of TCNE with OH^- and PhCN (Figure 3).

The in situ UV−vis spectra of the reaction mixture display absorption bands at 400 and 419 nm, which have been assigned to originate from the 1,1,2,3,3-pentacyanopropenyl anion ($PCNP^-$)[20] likely formed via an oligomerization initiated by nucleophilic attack of $RTCNE^-$ to neutral TCNE.[19c] Additional absorption bands are shown between 510 and 564 nm for the reaction mixture with a 1:20 molar ratio of OH^- to TCNE, which likely arise from the anionic species from further oligomerization due to a higher TCNE concentration. The most important information is that no absorptions due to $TCNE^{\bullet-}$ within 350−500 nm[21] (Figure S27) are shown in the spectra, indicating that the resulting $\mathbf{BTCNE}^-$ likely favors the nucleophilic attack to another TCNE and undergoes an oligomerization reaction,[19c] rather than undergoing an SET to neutral TCNE. Such a reactivity difference can be understood by the variation of electron delocalization between $\mathbf{BC}_{2n}^{\bullet-}$ and $\mathbf{BTCNE}^{\bullet-}$. Due to the effective π-delocalization of fullerene cages, the amount of the negative charge located at the individual fullerene C-atom of $\mathbf{BC}_{2n}^-$ is significantly reduced, while the C-atom in $\mathbf{BTCNE}^-$ may bear a greater negative charge due to a poorer delocalization, rendering $\mathbf{BTCNE}^-$ a better nucleophile compared with $\mathbf{BC}_{2n}^-$.

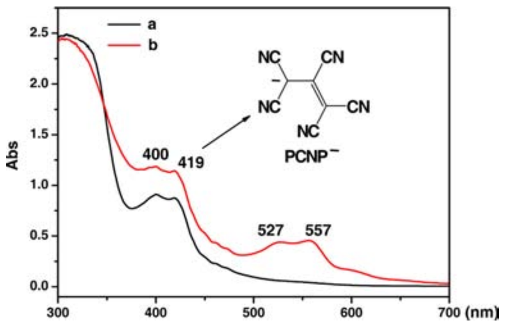

Figure 3. In situ UV−vis spectra of the reaction mixture of TBAOH (1.0 M in MeOH) and TCNE with a molar ratio of (a) 9:1 (2.2 mM for TCNE) and (b) 1:20 (9.2 mM for TCNE) in PhCN after heating at 90 °C for 30 min. See Experimental Section in the SI for details. All measurements were performed with a 1-mm cuvette under Ar.

The weaker nucleophilicity of $\mathbf{BC}_{2n}^-$ compared with $\mathbf{BTCNE}^-$ is further supported by DFT calculations with Gaussian09 at the B3LYP/6-311G(d)//B3LYP/6-31G level, which predict that the largest NBO negative charge is −0.163 for $\mathbf{BC}_{60}^-$, −0.141 for $\mathbf{BC}_{70}^-$, and a much greater value of −0.525 for $\mathbf{BTCNE}^-$, located at the C-atom adjacent to the one bonded to the amidine addend for $\mathbf{BC}_{2n}^-$ and $\mathbf{BTCNE}^-$ (Figure S30).

In summary, a novel transformation of aromatic nitriles to imidazolines has been achieved under basic conditions with the use of electron-deficient C_{60} and C_{70} fullerenes. The reaction mechanism is proposed on the basis of in situ vis−NIR spectral measurement and also the structures of the obtained C_{60} and C_{70} imidazolines. However, no such transformation is achieved when TCNE, an electron-deficient alkene, is used even though it is more electron-deficient than fullerenes and capable of nucleophilic additions. Such a difference is attributed to the distinction between RC_{2n}^- and $RTCNE^-$ in their ability of transferring electrons to the neutral counterparts, which is closely related to the intrinsic nature of the electron delocalization of the two types of molecules. This is a good example of employing fullerenes as models for exploring novel reactions.

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Supporting Information Available. Experimental and calculation details, crystallographic data (CIF), HPLC traces, and spectra of the new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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The authors declare no competing financial interest.