doi:10.1246/cl.2010.462

Photochemical Formal Alkadiene Insertion into an Aromatic C–CN Bond Using Cyanide Ion as a Catalyst

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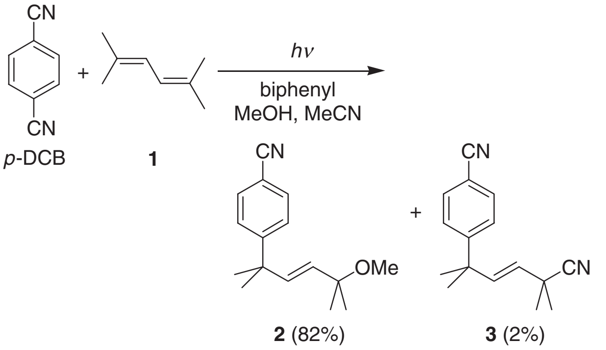
A reaction involving formal alkadiene insertion into a C–CN bond taking place via a catalytic photo-NOCAS mechanism was developed. The process involves photoirradiation of an acetonitrile solution containing 2,5-dimethyl-2,4-hexadiene (**1**), *p*-dicyanobenzene (*p*-DCB), phenanthrene (Phen), and a catalytic amount (20 mol %) of tetra-*n*-butylammonium cyanide. The reaction proceeds in the absence of noble metals and under mild conditions (ambient temperature without bases). This is the first example of a photo-NOCAS reaction in which a catalytic amount of nucleophilic species is employed to promote the process.

Activation of essentially unreactive chemical bonds such as aromatic C–CN bonds[1] has been actively studied in recent years but it remains a challenging task.[2–4] Reactions for this purpose often require severe conditions and noble metal catalysts. As a result, the development of C–CN bond cleavage reactions that proceed under mild and noble metal-free conditions is an important goal from the viewpoint of synthetic utility.

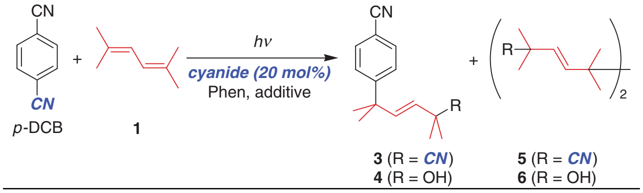
Photochemical reactions serve as promising methods to cleave inert bonds. Several years ago, Arnold and his co-workers described photo-NOCAS (nucleophile–olefin combination, aromatic substitution) reactions of *p*-dicyanobenzene (*p*-DCB, terephthalonitrile) and 2,5-dimethyl-2,4-hexadiene (**1**) in a methanolic solution, which proceed via photochemically induced *ipso*-substitution of aromatic cyano groups (eq 1).[5,6]



(1)

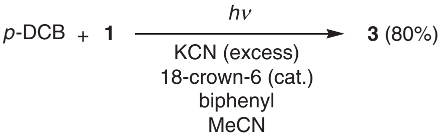
These workers noticed that not only the typical photo-NOCAS product **2** (82%) is produced in this reaction, but also the cyanide containing adduct **3** (2%) is formed. Further investigations demonstrated that when an excess of potassium cyanide is included in the reaction mixture **3** is generated in a high yield (80%) (eq 2). This finding suggests that photo-NOCAS reaction with free cyanide ion as a nucleophile is the true source of **3**. It has been proposed that cyanide ion, involved in the formation of **3** in methanol (eq 1), comes from *ipso*-substitution on the radical anion of *p*-dicyanobenzene ($p\text{-DCB}^{\bullet-}$). Based on this suggestion, we expected that incorporation of a catalytic amount of cyanide ion in the photo-NOCAS reaction mixture would enable the operation of a chain mechanism for formal alkadiene insertion into aromatic C–CN bonds.[7]

Table 1. Photochemical C–CN insertion reaction[a]



Entry	Cyanide	Additive	Solvent	Yields[b]/%			
				3	4	5	6
1	KCN	—	MeCN/ H_2O	19	28	3	8
2[c]	KCN	—	MeCN	0	0	0	0
3	KCN	18-crown-6[d]	MeCN	36	0	2	0
4	$n\text{-Bu}_4\text{N}^+\text{CN}^-$	—	MeCN	60	0	0	3
5	$n\text{-Bu}_4\text{N}^+\text{CN}^-$	MS4A[e]	MeCN	56	0	0	2

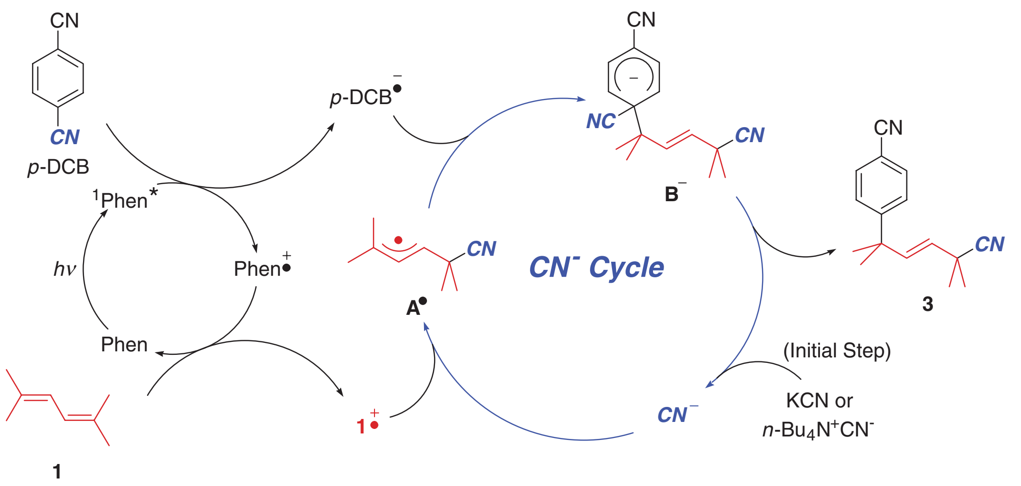
[a]Conditions: 300-W high-pressure mercury lamp, Pyrex filter, **1** (75 µmol), *p*-DCB (25 µmol), Phen (25 µmol), cyanide (5 µmol), in MeCN (4 mL)–H_2O (1 mL) or in MeCN (5 mL), under Ar, rt, 20 h. [b]Determined by ^{1}H NMR analysis based on the amount of *p*-DCB (for **3** and **4**) and **1** (for **5** and **6**) used. [c]Photoreaction was carried out in a suspension. [d]5 µmol. [e]100 mg.



$$p\text{-DCB} + \mathbf{1} \xrightarrow[\substack{\text{KCN (excess)}\\ \text{18-crown-6 (cat.)}\\ \text{biphenyl}\\ \text{MeCN}}]{h\nu} \mathbf{3}\ (80\%) \qquad (2)$$

In exploratory studies aimed at testing this proposal, an acetonitrile–water (4:1) solution containing **1**, *p*-DCB, phenanthrene (Phen),[8,9] and a catalytic amount (20 mol %) of potassium cyanide was photoirradiated for 20 h (Table 1, Entry 1). This process afforded a complex product mixture that contained the desired adduct **3** (19%) along with undesired products **4**–**6** (28, 3, and 8%, respectively).[10,11] Recognizing that products **4** and **6** arise by the addition of water (or formally hydroxide ion) to the cation radical of **1**, we assumed that photoreactions in solutions that did not contain water would increase the selectivity for production of **3**. However, potassium cyanide has a very low solubility in anhydrous acetonitrile. As a result, photoirradiation of a suspension of this cyanide salt in anhydrous acetonitrile did not lead to formation of any recognizable products, and only degradation of *p*-DCB was observed (Entry 2).

An optimal procedure for highly selective formation of the formal insertion product **3** was uncovered. At first, 18-crown-6 (equimolar to potassium cyanide) was employed as an additive



Scheme 1. Plausible mechanism for the formation of **3**.

to improve the solubility of potassium cyanide in dry acetonitrile (Entry 3). Despite the high selectivity observed for the photoreaction in the presence of the crown ether, the process might not be synthetically suitable because of the low yield (36%) of **3** formed and difficulties associated with separation of the crown ether. Use of an acetonitrile-soluble cyanide source, tetra-*n*-butylammonium cyanide, resolved this problem and led to an optimal method for carrying out the photo-NOCAS reaction. Thus, photoirradiation of a mixture of **1** and *p*-DCB in anhydrous acetonitrile, containing tetra-*n*-butylammonium cyanide, led to formation of **3** in a 60% yield (Entry 4).[13] When a powder form of molecular sieve (MS) 4A was included to remove trace amounts of water, no significant change in the product distribution was observed (Entry 5).

A typical photo-NOCAS mechanistic pathway is responsible for the formation of **3**.[5,6,10,12] The route is initiated by single electron transfer (SET) from the singlet excited state of Phen (^{1}Phen*) to *p*-DCB ($\Delta G_{\mathrm{et}} = -0.3\,\mathrm{eV}$), which is then followed by SET from **1** to Phen$^{\bullet+}$ (Scheme 1) to give $\mathbf{1}^{\bullet+}$ ($\Delta G_{\mathrm{et}} = -0.4\,\mathrm{eV}$).[8] Addition of cyanide ion to $\mathbf{1}^{\bullet+}$ affords the allylic radical intermediate $\mathbf{A}^{\bullet}$, which couples with *p*-DCB$^{\bullet-}$ to form $\mathbf{B}^{-}$. Regeneration of the aromatic ring affords the three-component adduct **3** and regenerates cyanide ion. The formation of the cyanide containing dimer **5** is a result of dimerization of $\mathbf{A}^{\bullet}$.[11] Alcohols **4** and **6** are formed by similar reaction mechanisms to those of **3** and **5**, respectively, with water or hydroxide ion serving as the nucleophile.

The process described above corresponds to a formal alkadiene insertion reaction into an aromatic C–CN bond. Importantly, it takes place under mild (ambient temperature and without base) and noble metal-free conditions. It also represents the first example of the use of a catalytic amount of nucleophilic species to promote photo-NOCAS reactions. We believe that this type of catalytic photoreaction can also be applied to the other photo-NOCAS reactions.[5]

This work was partially supported by Grant-in-Aids for Scientific Research on Priority Areas (429) (No. 16033252), Scientific Research (B) (Nos. 15350026 and 20044027), JSPS Fellows (No. 20-4975), and the Cooperation for Innovative Technology and Advanced Research in Evolutional Area (CITY AREA) program from the Ministry of Education, Culture, Sports, Science and Technology (MEXT) of Japan.

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