



# Studies on Synthetically Useful Carbon–Carbon Bond Forming Reactions via Photoinduced Electron Transfer

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**Studies on Synthetically Useful Carbon–Carbon Bond  
Forming Reactions via Photoinduced Electron Transfer**

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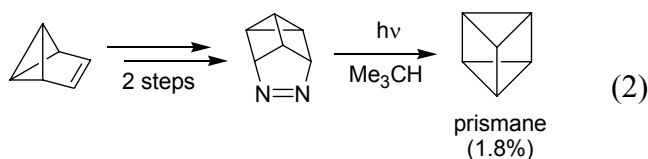
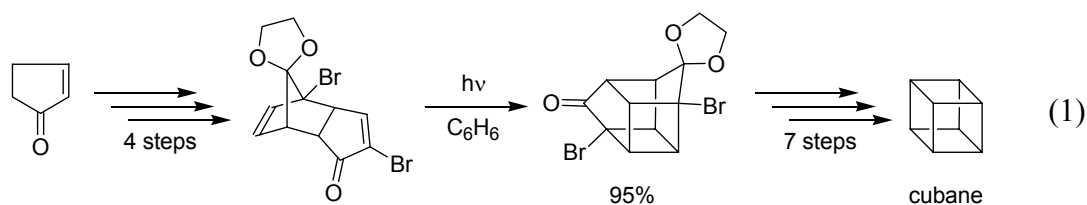
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## GENERAL INTRODUCTION

### *“Green and Sustainable Chemistry” and Photochemical Reactions*

Green and sustainable chemistry is one of the most urgent research topics in the field of chemistry.<sup>1</sup> Development and improvement of the processes, so that which can meet the principles of the green chemistry,<sup>1a</sup> is crucial for the survival of human beings and all other organisms on the earth.

Photochemical reaction is believed to be one of the most promising organic reactions to reduce the environmental load. It might be able to cleanly convert chemicals using light energy—like photosynthesis in chloroplast<sup>2</sup>—instead of fossil fuel combustion. In addition, highly distorted molecules such as cubane (eq. 1)<sup>3</sup> and prismane (eq. 2)<sup>4</sup> can be easily synthesized by the reaction that proceeds via high-energy species like electronically-excited molecules and radical ions.



The fact, however, is usually not so elegant as desired. The highly reactive intermediates often cause non-selective reactions and secondary reactions, including degradations, which results in the formation of complex mixture of photoproducts.

Many efforts have been made to improve the selectivity to develop synthetically

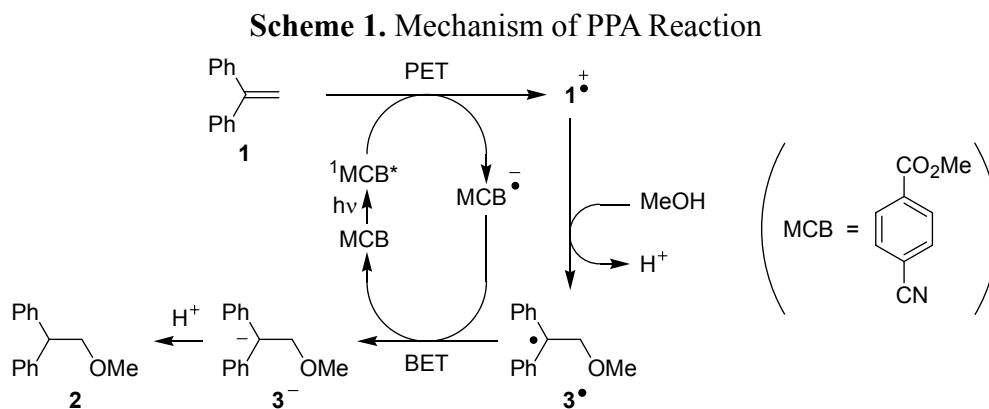
useful photochemical reactions. Among them, the author has noticed the following three photoinduced electron transfer (PET) reactions: photochemical polar addition (PPA), oxidative photodimerization, and photo-NOCAS (Nucleophile–Olefin Combination, Aromatic Substitution) reaction.

## Synthetically Useful Photoinduced Electron Transfer (PET) Reactions (1):

### Photochemical Polar Addition (PPA) Reaction

Photochemical polar addition (PPA), the addition of nucleophiles into photochemically-generated reactive species, is one of the most fundamental as well as synthetically-useful photoreactions.<sup>5</sup>

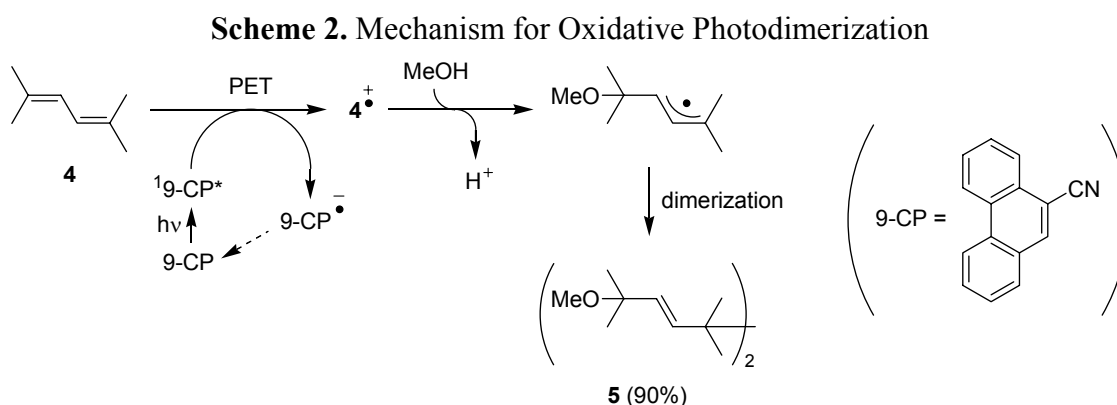
Arnold and his coworker first reported this type of photochemical reaction in 1973, in which methanol adds to **1** in *anti*-Markovnikov manner selectively to form **2** in the presence of methyl *p*-cyanobenzoate (MCB) (Scheme 1).<sup>6</sup> The reaction is initiated via PET process from **1** to the excited singlet state of MCB (<sup>1</sup>MCB\*), and the resulting **1**<sup>+</sup> is trapped by methanol to afford **3**<sup>•</sup>. The stability of the resulting benzylic radical over primary alkyl one is responsible for the *anti*-Markovnikov selectivity of the methanol addition. Back electron transfer (BET) from MCB<sup>•−</sup> to the benzylic radical **3**<sup>•</sup> followed by protonation complete the reaction to yield adduct **2**.<sup>7</sup>



## Synthetically Useful Photoinduced Electron Transfer (PET) Reactions (2):

### Oxidative Photodimerization Reactions

The PPA-type reaction also proceeds with aliphatic alkadiene **4**. In this photoreaction, the radical intermediate derived from **4** does not undergo BET pathway, but dimerizes (oxidative photodimerization). This type of photoreaction was first reported by Mizuno and coworkers, in which **4**<sup>+</sup> is trapped by methanol and then dimerizes to give **5** (Scheme 2).<sup>8</sup>



## Synthetically Useful Photoinduced Electron Transfer (PET) Reactions (3):

### Photo-NOCAS (Nucleophile–Olefin Combination, Aromatic Substitution)

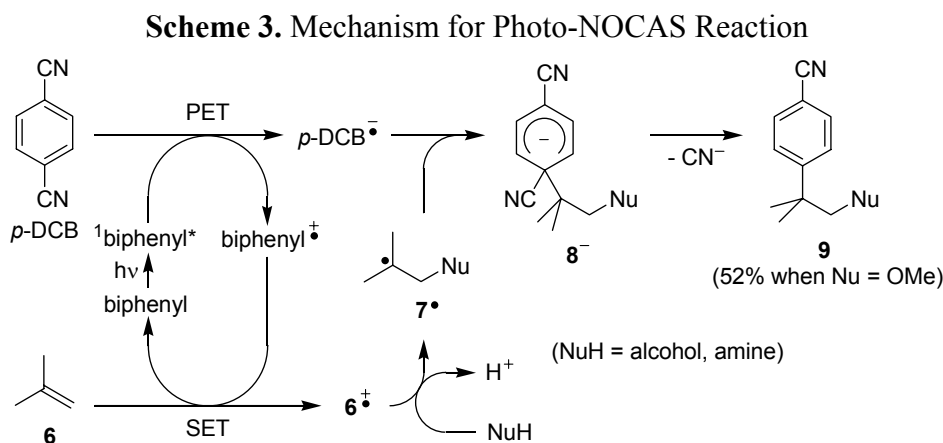
#### Reaction

In some cases, the electron acceptors such as polycyanobenzenes can be also included in the PPA products, which lead to one-step formation of more complicated compounds. The key step of this photoreaction is the *ipso*-attack of radical to the radical anion of polycyanobenzenes. It is called “photo-NOCAS (nucleophile–olefin combination, aromatic substitution)” reaction.<sup>9</sup>

Scheme 3 shows the general mechanism of the photo-NOCAS reaction. Photoexcitation of biphenyl causes tandem single-electron transfer, which results in the formation of radical ion pair, [**6**<sup>+</sup> ... *p*-DCB<sup>−</sup>].<sup>7</sup> The radical cation **6**<sup>+</sup> is trapped by a



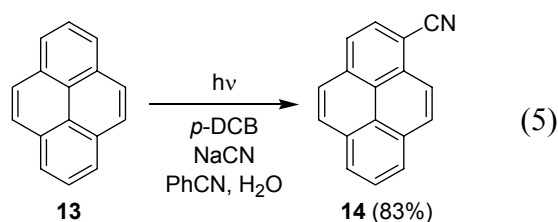
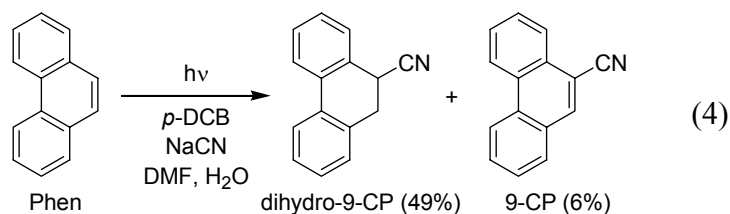
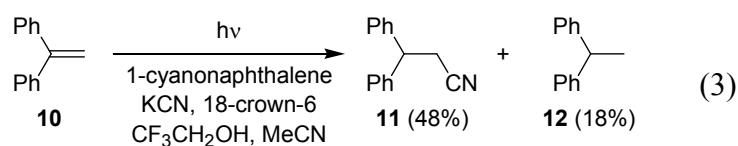
nucleophile such as an alcohol or an amine<sup>10</sup> and then the resulting radical **7**<sup>•</sup> couples with *p*-DCB<sup>-</sup> to form **8**<sup>-</sup>. The aromaticity of the benzene ring is regenerated by the elimination of cyanide ion<sup>11,12</sup> to form the *ipso*-substituted product **9**.



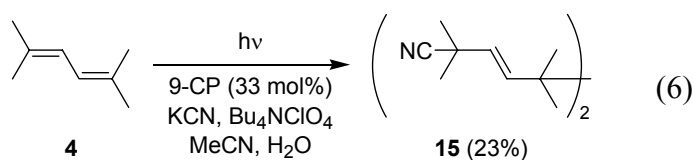
### Introduction of Carbon-Nucleophiles in the PET Reactions

The carbon–carbon bond forming reactions play key roles in organic syntheses, constructing carbon frameworks, and introducing functional groups to them. However, the introduction of carbanions in the above-mentioned PET reactions has been rarely reported so far.

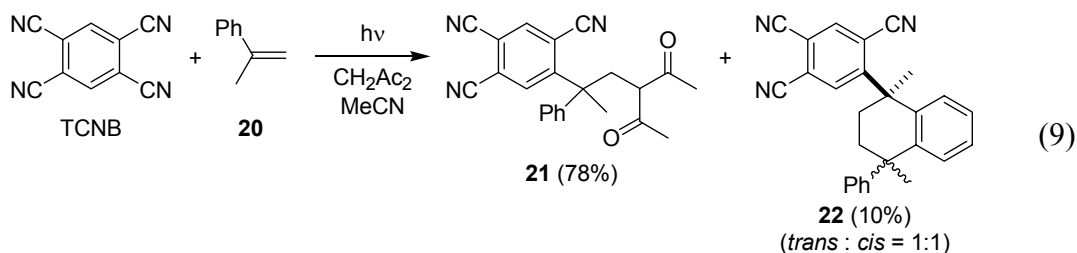
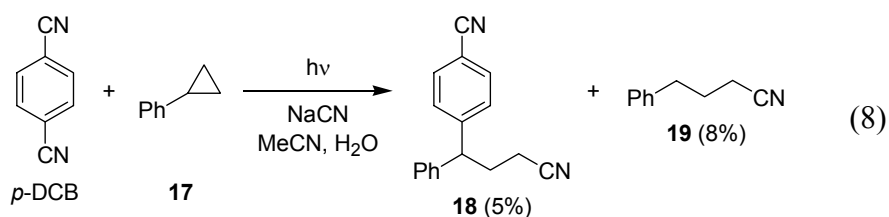
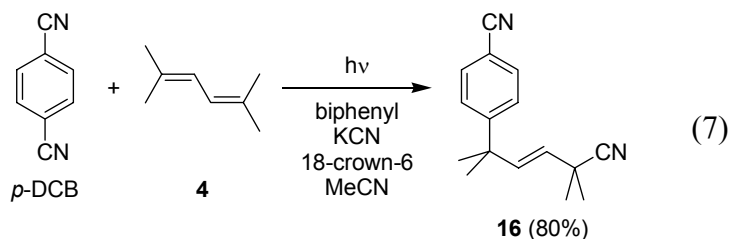
To the best of our knowledge, cyanide ion was the sole carbon-nucleophile to be used in PPA. As for aromatic alkenes, the addition of cyanide ion into **10** to form **11** was reported by Arnold and his coworkers (eq. 3).<sup>13</sup> Mizuno and coworkers also reported the hydrocyanations of phenanthrene (Phen) to yield 9-cyano-9,10-dihydrophenanthrene (dihydro-9-CP) and its rearomatized compound, 9-cyano-phenanthrene (9-CP) (eq. 4).<sup>14</sup> Kitamura and coworkers reported similar photoreaction of pyrene (**13**) in an oil-in-water emulsion system to obtain 1-cyanopyrene (**14**) in high yield of 83% (eq. 5).<sup>15</sup>



Recently, the author demonstrated in his master's thesis that cyanide ion can also be introduced to an aliphatic diene **4** (eq. 6),<sup>16</sup> which is the only known case for which carbanion takes part in oxidative photodimerization reaction.



As for photo-NOCAS reactions, again, only a few examples of introducing carbon-nucleophiles have been reported: the uses of cyanide ion and active methylene compounds. As for the former, Arnold and his coworker reported the use of diene **4** to give **16** (eq. 7).<sup>17</sup> Mizuno and his coworkers employed phenylcyclopropane **17** instead of olefins to obtain **18** (eq. 8).<sup>18</sup> The latter is a use of the enol forms of  $\beta$ -dicarbonyl compounds as nucleophiles in the presence of 1,2,4,5-tetracyanobenzene (TCNB), which is reported by Xu and coworkers (eq. 9).<sup>19</sup>



## Overview of the Thesis

In this thesis, the author has tried to employ the anions of various active methylene compounds<sup>20</sup> in the above three PET reaction systems to extend the synthetic usefulness of them. The dissertation consists of general introduction, four chapters, and conclusion.

Chapter 1 deals with the development of a novel synthetic method for  $\alpha$ -monoalkylation of active methylene compounds using PPA, and its application to the intramolecular reaction to produce cycloalkane derivatives.

Chapter 2 deals with the use of oxidative photodimerization reaction to synthesize active methylene compound-incorporated dimers.

Chapter 3 deals with the development of tandem  $\alpha$ -monoalkylation method for active methylene compounds by use of photo-NOCAS type three-component coupling

reaction.

Chapter 4 deals with more mechanistic aspects of PET reaction: the mechanism of the enhancement effects of magnesium salts on PET reaction is discussed through analyses of steady-state and time-resolved absorption spectra, fluorescence spectra and their quenching, and quantum chemical calculations.

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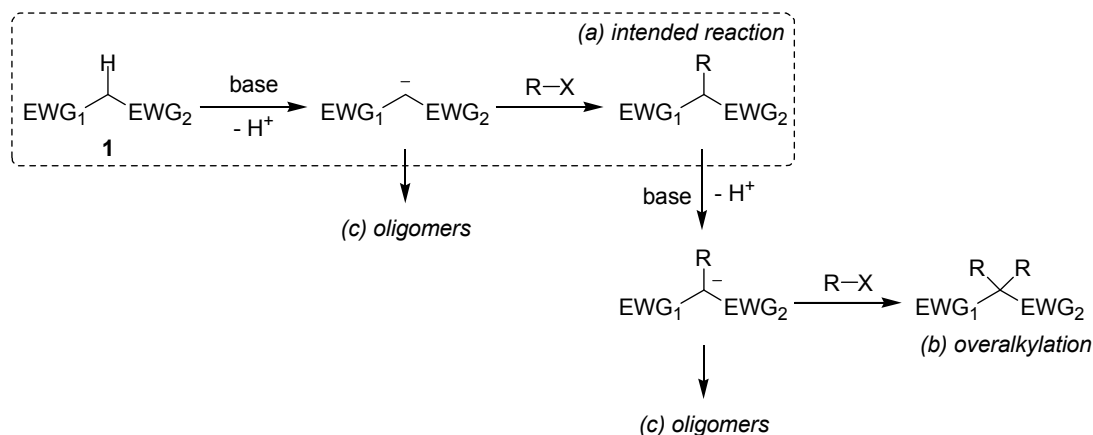
## CHAPTER 1. Synthesis of $\alpha$ -Monoalkylated Active Methylene Compounds by Use of Photochemical Polar Addition

### 1.1. Introduction

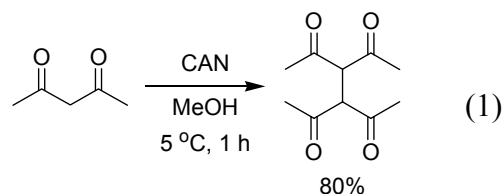
Processes that directly transform carbon–hydrogen bonds into carbon–carbon bonds are important synthetic methods.<sup>1</sup> However, from an ecological viewpoint,<sup>2</sup> most of these reactions are problematic owing to the fact that they rely on the use of noble metal catalysts. Among various substrates explored for these processes, active methylene compounds (**1**) including enolizable  $\beta$ -dicarbonyl compounds are perhaps the most prominent owing to the relatively high acidities of their methylene groups.<sup>3–5</sup> Treatment of these substances with strong bases, such as sodium hydride, results in the formation of the corresponding anions, which undergo C–C bond forming reactions with alkyl halides via nucleophilic substitution (Scheme 1, path *a*).<sup>6–8</sup> The use of  $\beta$ -ketoesters in this fashion comprise well-known synthetic methods to obtain methyl ketones (acetoacetic ester synthesis)<sup>4</sup> and carboxylic acids (malonic ester synthesis).<sup>5</sup>

The alkylation reactions, however, do not always afford the desired products in high yields owing to the intervention of side reactions. For example, over alkylation

**Scheme 1.** Conventional Monoalkylation Reactions of Active Methylene Compounds

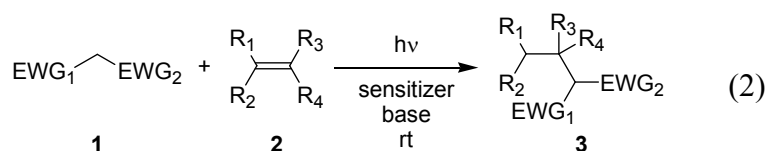


easily occurs to give undesirable symmetrically disubstituted products (Scheme 1, path *b*).<sup>6</sup> Also, the anions of active methylene compounds tend to oligomerize (path *c*).<sup>3</sup> Even the highly efficient dimerization of  $\beta$ -dicarbonyl compounds via one-electron oxidation by cerium(IV) ammonium nitrate (CAN) has been reported (eq. 1).<sup>9</sup>



Methods have been explored to circumvent problems inherent in base-promoted alkylation reactions of  $\beta$ -dicarbonyl compounds that are associated with the severe control of reaction conditions<sup>6</sup> and side reactions.<sup>10,11</sup>

In this chapter, the author describes the first photochemical method for direct alkylation of **1** to produce  $\alpha$ -monoalkylated propanedinitrile derivative **3** under mild conditions and in a highly regioselective manner (eq. 2).



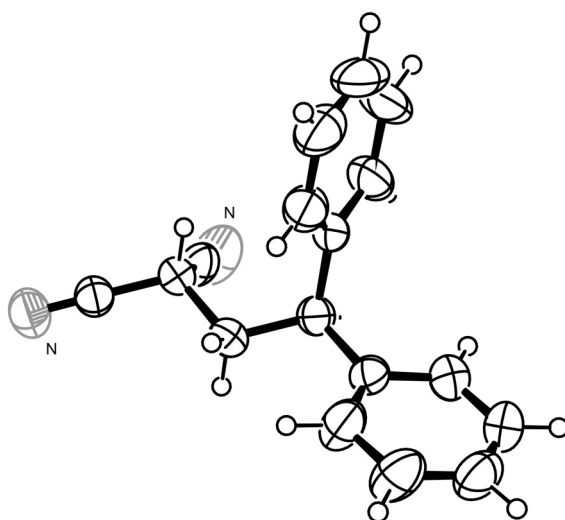


## 1.2. Results and Discussion

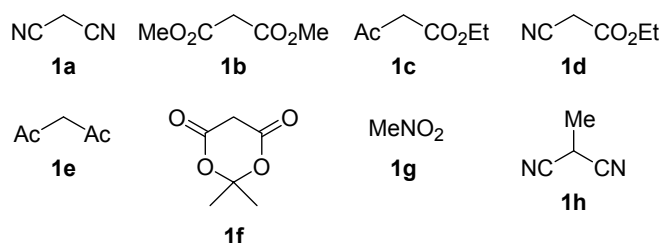
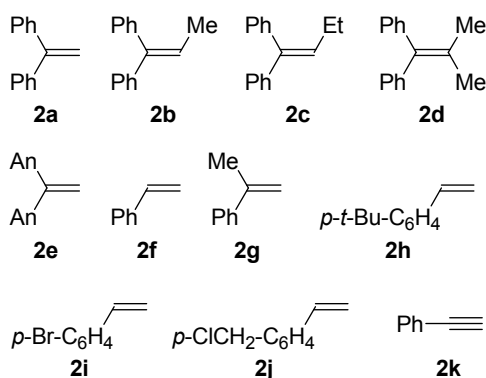
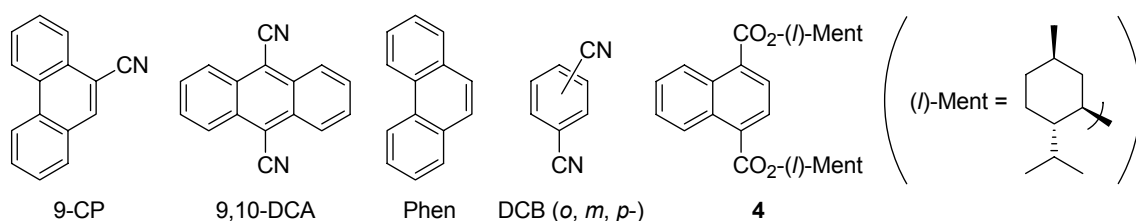
### 1.2.1. Photochemical $\alpha$ -Monoalkylation of Active Methylene Compounds

Photoirradiation of an aqueous acetonitrile solution containing propanedinitrile (**1a**, malononitrile), 1,1-diphenylethene (**2a**), lithium carbonate and a catalytic amount of 9-cyanophenanthrene (9-CP) leads to selective high yielding (91%) formation of the *anti*-Markovnikov photochemical polar addition (PPA) product,  $\alpha$ -monoalkylated propanedinitrile **3aa** (Table 1, entry 1).<sup>12</sup> Importantly, an  $\alpha,\alpha$ -dialkylated product is not generated in this process. The structure of **3aa** was determined by the analyses of <sup>1</sup>H- and <sup>13</sup>C-NMR, MS, HRMS, and IR spectra, and by a single-crystal X-ray crystallographic analysis. An ORTEP diagram for **3aa** is shown in Figure 1.

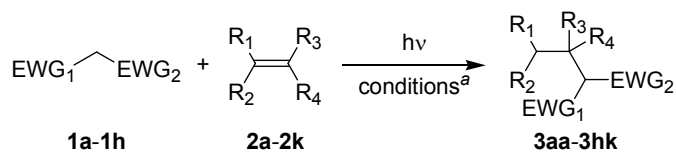
The reaction described above is a novel method for alkylation of **1**. It should find utility as a safe and environmentally friendly synthetic method, since it proceeds under mild (ambient temperature and in the presence of weak base) and halogen-free conditions, in contrast to the conventional S<sub>N</sub>2 alkylation.<sup>3–8</sup> Besides, it is also the first example of a process in which a nucleophilic carbon species other than cyanide anion<sup>13,14</sup> is used in PPA.<sup>12,15</sup>



**Figure 1.** ORTEP diagram for **3aa**

**Chart 1. Active Methylene Compounds (1a–1h)****Chart 2. Alkenes (2a–2k)****Chart 3. Photosensitizers**

The author has found that the efficiency of this reaction strongly depends on the base used. Specifically, lower yields of **3aa** are observed when heavier alkali metal carbonates are used (entries 2–5). In addition, strong bases, such as sodium hydroxide and potassium *tert*-butoxide, are not effective in promoting the reaction (entries 6 and 7). In the absence of a base, the photoreaction does not take place in aqueous acetonitrile (entry 8) but it does proceed in dry dimethyl sulfoxide (DMSO) in the presence of

**Table 1.** Photochemical Polar Addition of **1** into **2**

entry	active methylene compound	alkene	sensitizer(s)	base	product	yield <sup>b</sup> / %
1	<b>1a</b>	<b>2a</b>	9-CP	Li <sub>2</sub> CO <sub>3</sub>	<b>3aa</b>	91
2				Na <sub>2</sub> CO <sub>3</sub>		66
3				K <sub>2</sub> CO <sub>3</sub>		68
4				Rb <sub>2</sub> CO <sub>3</sub>		23
5				Cs <sub>2</sub> CO <sub>3</sub>		15
6				NaOH		13
7 <sup>c</sup>				KO- <i>t</i> -Bu		trace
8				none		0
9 <sup>d</sup>						31
10			9,10-DCA	Li <sub>2</sub> CO <sub>3</sub>		27
11			<i>o</i> -DCB, Phen			71
12			<i>m</i> -DCB, Phen			60
13			<i>p</i> -DCB, Phen			44
14			TCNB, Phen			3
15		<b>2b</b>	9-CP	Li <sub>2</sub> CO <sub>3</sub>	<b>3ab</b>	52
16		<b>2c</b>			<b>3ac</b>	19
17		<b>2d</b>			<b>3ad</b>	0
18		<b>2e</b>			<b>3ae</b>	46
19		<b>2f</b>			<b>3af</b>	40
20		<b>2g</b>			<b>3ag</b>	33
21		<b>2h</b>			<b>3ah</b>	38
22		<b>2i</b>			<b>3ai</b>	0
23		<b>2j</b>			<b>3aj</b>	0
24		<b>2k</b>			<b>3ak</b>	0
25	<b>1b</b>	<b>2a</b>	9-CP	Li <sub>2</sub> CO <sub>3</sub>	<b>3ba</b>	0
26				Cs <sub>2</sub> CO <sub>3</sub>		38
27 <sup>c</sup>				KO- <i>t</i> -Bu		100
28 <sup>c</sup>		<b>2b</b>		KO- <i>t</i> -Bu	<b>3bb</b>	12
29 <sup>c</sup>		<b>2f</b>			<b>3bf</b>	78
30 <sup>c</sup>		<b>2g</b>			<b>3bg</b>	77
31 <sup>c</sup>		<b>2h</b>			<b>3bh</b>	72
32	<b>1c</b>	<b>2a</b>	9-CP	NaOH	<b>3ca</b>	51

**Table 1.** (Continued)

33	<b>1d</b>	<b>2a</b>	9-CP	Na <sub>2</sub> CO <sub>3</sub>	<b>3da</b>	63
34		<b>2b</b>			<b>3db</b>	13 <sup>e</sup>
35 <sup>c</sup>	<b>1e</b>	<b>2a</b>	9-CP	KO- <i>t</i> -Bu	<b>3ea</b>	0
36 <sup>c</sup>	<b>1f</b>	<b>2a</b>	9-CP	KO- <i>t</i> -Bu	<b>3fa</b>	complex
37 <sup>c</sup>	<b>1g</b>	<b>2a</b>	9-CP	KO- <i>t</i> -Bu	<b>3ga</b>	0
38	<b>1h</b>	<b>2a</b>	9-CP	Na <sub>2</sub> CO <sub>3</sub>	<b>3ha</b>	22
39		<b>2b</b>			<b>3hb</b>	0

<sup>a</sup> Conditions: 300-W high-pressure mercury lamp, Pyrex filter, active methylene compound (2.5 mmol), alkene (75 μmol), sensitizer(s) (25 μmol each), base (1.25 mmol), in MeCN (4 mL)–H<sub>2</sub>O (1 mL), under Ar, rt, 20 h. <sup>b</sup> Determined by <sup>1</sup>H NMR based on the amount of **2** used. <sup>c</sup> In dry MeCN (5 mL). <sup>d</sup> In dry DMSO (5 mL) with MS4A (250 mg). <sup>e</sup> Mixture of diastereomers.

molecular sieves (MS) 4A. The author proposes that DMSO acts as the “base” in this case (entry 8).<sup>16</sup> While the use of 9-CP results in the highest yield of **3aa** (entry 1), other photosensitizers, including phenanthrene (Phen) which participates as a redox photosensitizer,<sup>17</sup> can be used for the reaction (entries 10–14).

The results of studies exploring the scope of alkenes that can be employed in the reaction showed that alkyl substituents on the vinylic positions of 1,1-diphenylethene lead to lower yields of the products **3ab–3ad** (entries 15–17). The dimethoxy derivative of 1,1-diphenylethene **2e**, styrene (**2f**), and its alkylated derivatives **2g** and **2h** also participate in reactions that form the corresponding photoproducts **3ae–3ah** (entries 18–21). On the other hand, reactions utilizing halogen-containing styrene derivatives (e.g., **2i** and **2j**) afford polymeric mixtures and none of the desired adducts (entries 22 and 23). Finally, alkyne **2k** does not react under the conditions employed (entry 24).

The photoinduced monoalkylation reaction takes place with a variety of active methylene compounds, but in each case a different base-dependence is observed. For example, 2,2-diphenylethylation of dimethyl malonate (**1b**) proceeds efficiently in the presence of stronger bases (entries 25–27), as exemplified by the formation of **3ba** in

quantitative yield when potassium *tert*-butoxide is used (entry 27). Other alkenes (**2b**, **2f–2h**) also react with **1b** (entries 28–31). Ethyl acetoacetate (**1c**) and ethyl cyanoacetate (**1d**), which react in a manner similar to **1a** and **1b** (entries 32–34), can be applied in mild photochemical  $\beta$ -ketoester (e.g., acetoacetic<sup>4</sup> and malonic<sup>5</sup> ester) synthetic procedures. However, adducts are not formed in reactions of acetylacetone (**1e**) and Meldrum's acid (**1f**)<sup>18</sup> (entries 35 and 36) and the active “methyl” compound nitromethane (**1g**) does not participate in this process (entry 37). While introduction of the second alkyl group into the active “methine” compound, 2-methylpropanedinitrile (**1h**) is accomplished in 22% yield by using **2a** as the alkene, reaction of **1h** with the more highly substituted alkene **2b** does not take place (entries 38 and 39).

### 1.2.2. Enantioselective Formation of $\alpha$ -Monoalkylated Propanedinitrile

The development of photosensitized (catalytic) stereoselective reactions that proceed via electron transfer pathways is a challenging research topic.<sup>11c,19–22</sup> A comprehensive study on enantiodifferentiating PPA reactions of alcohols with 1,1-diphenyl-1-alkenes has been carried out by Inoue et al.,<sup>20</sup> but knowledge is lacking on the use of carbon nucleophiles in these processes.

Here, the first enantiodifferentiating PPA of carbon nucleophile is shown in Table 2. A slight enantiomeric excess (*ee*) of 0.7% for the product **3ab** is observed in the product **3ab** of the PPA reaction of **1a** with **2b** photosensitized by the di-*l*-menthyl ester of 1,4-naphthalenedicarboxylic acid **4** (entry 2).<sup>20a</sup> A small increase of *ee* and a severe decrease of yield take places when a solvent system with lower polarity is employed (entry 3). This result suggests that lower solvent polarity causes an enhancement in the face selective complexation between the excited chiral photosensitizer **4** and the prochiral alkene **2b**.

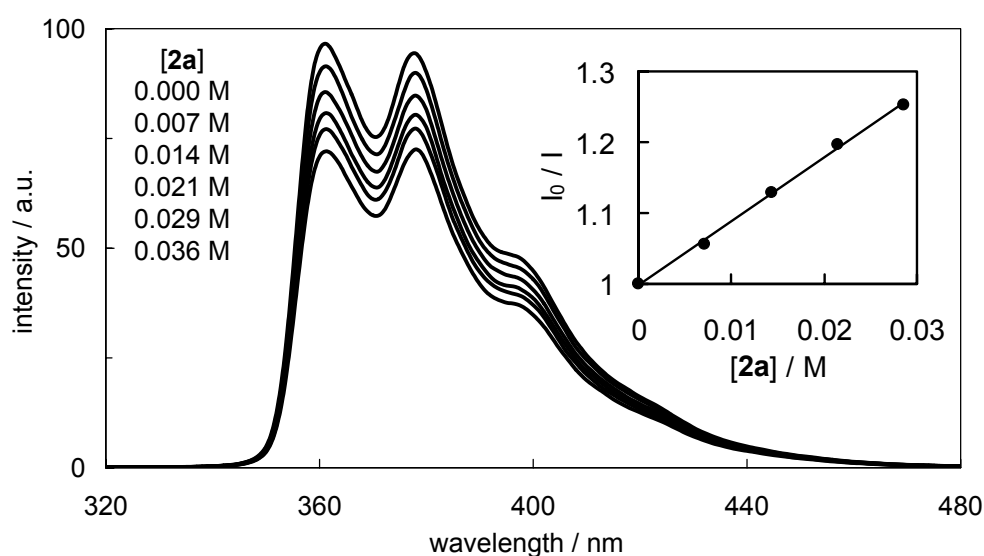
**Table 2.** Enantiodifferentiating Photochemical Polar Addition of **1a** into **2b**

entry	sensitizer	solvents	yield <sup>b</sup> / %	<i>ee</i> <sup>c</sup> / %
1	9-CP	MeCN/H <sub>2</sub> O = 4/1	38	—
2	<b>4</b>	MeCN/H <sub>2</sub> O = 4/1	25	0.7
3		PhH/MeCN = 3/1	0.8	4.2

<sup>a</sup> Conditions: 300-W high-pressure mercury lamp, Pyrex filter, **1a** (2.5 mmol), **2b** (75  $\mu$ mol), sensitizer (25  $\mu$ mol), Na<sub>2</sub>CO<sub>3</sub> (1.25 mmol), solvents (5 mL in total), under Ar, rt, 20 h. <sup>b</sup> Determined by <sup>1</sup>H NMR based on the amount of **2b** used. <sup>c</sup> Determined by chiral GC.

### 1.2.3. Fluorescence Quenching of 9-Cyanophenanthrene (9-CP) by 1,1-Diphenylethene (**2a**)

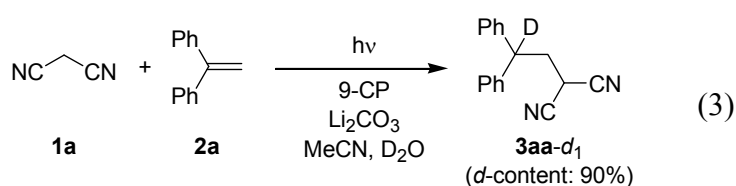
Fluorescence of 9-CP in acetonitrile was efficiently quenched by the addition of **2a** (Figure 2). No apparent rise of exciplex emission was observed during the addition. A Stern–Volmer plot<sup>23</sup> of the quenching at 361 nm showed linear correlation of the reciprocal of relative fluorescence intensity  $I_0/I$  with the concentration of **2a** with a gradient of  $9.0\text{ M}^{-1}$ , from which the quenching rate constant ( $k_q$ ) was determined as  $3.8 \times 10^8\text{ M}^{-1}\text{ s}^{-1}$ .<sup>24</sup> An electrochemical analysis was also performed to demonstrate that the photoinduced electron transfer (PET) from **2a** to the excited singlet state of 9-CP ( $^1\text{9-CP}^*$ ) occurs exergonically ( $\Delta G_{\text{PET}} = -0.29\text{ eV}$ ).<sup>25</sup> These results indicate that PET occurs from **2a** to  $^1\text{9-CP}^*$  at the initial stage of the photoreaction.



**Figure 2.** Fluorescence spectral change of 9-CP ( $1.04 \times 10^{-4}\text{ M}$ ,  $\lambda_{\text{ex}} = 311 \pm 2.5\text{ nm}$ ) in MeCN by the addition of **2a**. The inset is a Stern–Volmer plot at 361 nm.

#### 1.2.4. Plausible Mechanism

In mechanistic investigations, we observed that a deuterium was incorporated into the benzylic position of **3aa** with a *d*-content of 90% when deuterium oxide was used instead of water in the mixed solvent system for reaction of **1a** and **2a** (eq. 3). This result clearly shows that protonation of the anion intermediate proceeds at its benzylic position.

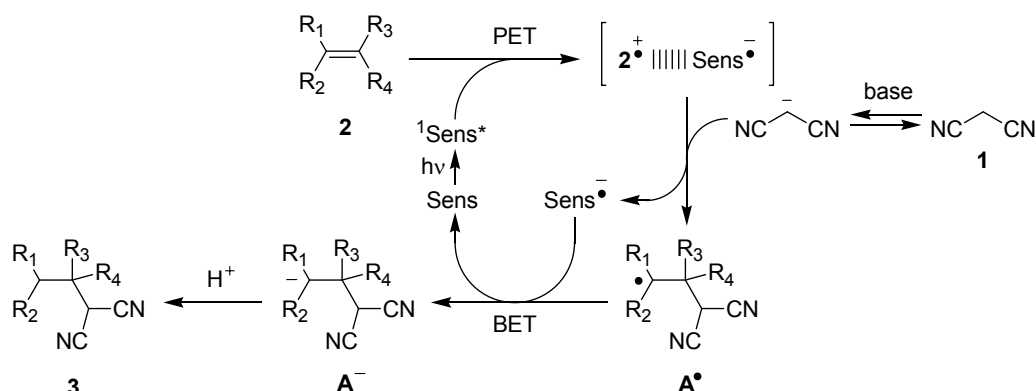


Based on this result, we propose that the reaction is promoted by PET from **2** to the excited singlet state of an electron-accepting photosensitizer (<sup>1</sup>Sens\*) (Scheme 2). This affords **2**<sup>+</sup>, which reacts with the anion of **1** to form benzylic radical intermediates **A**<sup>•</sup>. An alternative pathway might involve SET from the anion of **1** to Sens<sup>+</sup>, followed by a coupling of the resulting radical with **2** to form **A**<sup>•</sup> (Scheme 3). The back electron transfer (BET) from Sens<sup>•−</sup> to **A**<sup>•</sup> is highly exothermic (e.g., −1.45 eV with (U)B3LYP/6-31G\* when the reaction is initiated from **1a**, **2a**, and 9-CP) and fast, and the resulting anion **A**<sup>−</sup> is protonated to give an *anti*-Markovnikov adduct **3**. In the redox-photosensitized process,<sup>17</sup> Ph<sub>2</sub>C=CH<sub>2</sub> acts as an electron mediator between alkene and an electron-accepting cosensitizer and the resulting radical ion pair reacts in a similar manner as described above.

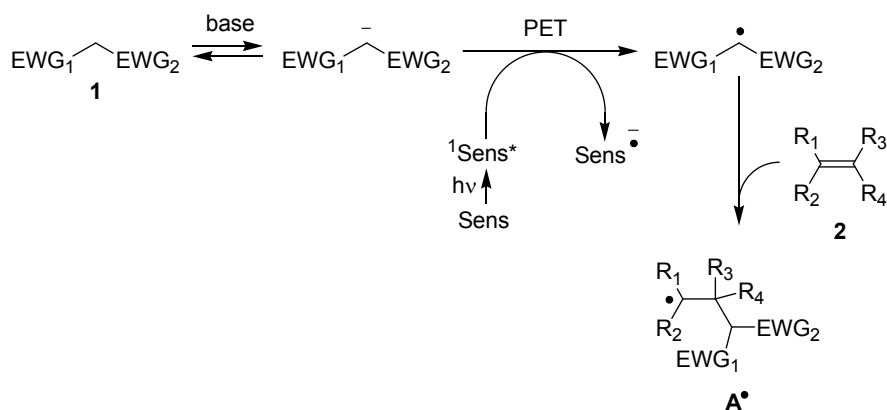
To elucidate whether PET occurs dominantly from **2** (Scheme 2) or from the anion of **1** (Scheme 3), the concentration of the anion of **1a** was estimated as follows. An ICP–AES (Inductively Coupled Plasma–Atomic Emission Spectrometry) analysis was performed to determine the solubility of lithium carbonate in acetonitrile as



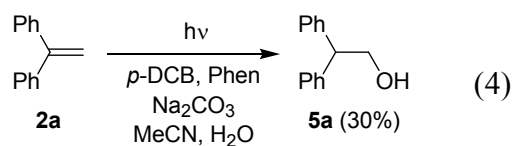
**Scheme 2.** Plausible Mechanism for the Formation of **3**



**Scheme 3.** Alternative Pathway for the Formation of **A<sup>•</sup>**



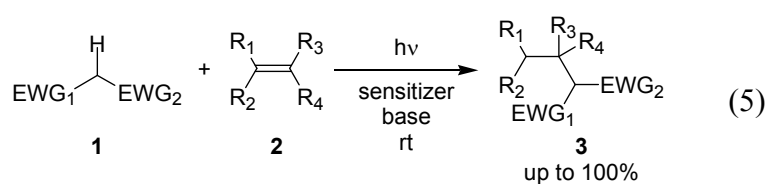
$1.0 \times 10^{-5}$  M. From this value and known  $pK_a$  values for the carbonate and **1a**,<sup>26</sup> the concentration of the anion of **1a** was calculated to be around  $5.2 \times 10^{-6}$  M. Since this concentration is about 2900 times lower than that of **2a** (15 mM) and efficient exergonic electron transfer is predicted for both paths,<sup>27</sup> we concluded that PET from **2** is the major path, although these pathways are in competition. In fact, the PET reaction occurs even in the absence of **1**, producing water adduct **5a** (eq. 4); that is, **2a<sup>+</sup>** formed by PET is captured by water (or formally hydroxide ion) as a weak nucleophile, and the resulting radical undergoes BET–protonation pathway to give **5a**.



The low concentration of the anion of **1** described above is the feature of this photoreaction system. Nucleophilic species usually have lower oxidation potential than that of alkenes. Therefore, their coexistence at similar concentration in the reaction mixture results in exclusive one-electron oxidation of nucleophiles, not alkenes, and the resulting radicals tend to dimerize or give complex product mixtures.<sup>3,9</sup> One of the solutions for this problem presented from electroorganic chemists is the separation of active sites, or control of concentration,<sup>28</sup> which uses, for example, adsorption of alkenes on anodes, diffusion of the alkene radical cations over a boundary of two liquid phases, or solid-supported nucleophiles to localize the existence of nucleophilic species. Our reaction system employs in situ generation of nucleophilic anion species by use of weak base, which can also be classified as an example of the active-site separation.

### 1.3. Conclusion

A novel, safe, and environmentally friendly synthetic method for the direct  $\alpha$ -monoalkylation of active methylene compounds, using PPA with electron-rich alkenes, has been developed (eq. 5). The enantiodifferentiating addition of propanedinitrile was also accomplished by the use of a chiral photosensitizer, although the enantiomeric excess of the photoproduct was low.



This reaction might be synthetically important since it proceeds in safe and environmentally friendly conditions (ambient temperature, in the presence of weak base, and halogen-free). It also represents the first example in which a carbon nucleophile, other than cyanide anion, is used in PPA process.

## 1.4. Experimental Section

### 1.4.1. General

Melting points were taken on YANACO MP-500 apparatus and uncorrected. NMR spectra were recorded on Varian Mercury 300 spectrometer (300 and 75 MHz for  $^1\text{H}$  and  $^{13}\text{C}$ , respectively) using tetramethylsilane as an internal standard. MS ( $\text{EI}^+$ ) were measured by Shimadzu QP-5050 mass spectrometer with Shimadzu GC-17A gas chromatograph. MS ( $\text{FAB}^+$ ) and HRMS ( $\text{EI}^+$  and  $\text{FAB}^+$ ) were measured by JEOL JMS-700 mass spectrometer. IR spectra were obtained from JASCO FT/IR-230 spectrophotometer. Elemental analyses were carried out on YANACO MT-6 or J-SCIENCE LAB JM-10 elemental analyzer. Single crystal X-ray crystallographic analyses were performed on Rigaku RAXIS-RAPID diffractometer. UV-vis absorption spectra were measured by JASCO HMC-358 spectrophotometer. Fluorescence spectra were obtained from JASCO FP-6300 spectrofluorometer. Cyclic voltammograms were recorded on CH Instruments ALS600C analyzer. Chiral gas-liquid chromatographic analyses (chiral GC) were performed on Shimadzu GC-2014 gas chromatograph with SPELCO GAMMA DEX 225 column, and recorded on Shimadzu C-R8A data processor. Preparative HPLCs (GPC) were performed by use of JASCO Megapak GEL 201C column, JASCO PU-986 pump, and Shodex RI-72 detector. Photoreactions were conducted under irradiation of Eikohsha EHB-W-300 high-pressure mercury lamp (300 W) through a Pyrex filter. Quantum chemical calculations were performed on the software *Spartan '04*<sup>29</sup> (for geometry optimizations) and *Gaussian 98*<sup>30</sup> (for vibrational and TD-DFT calculations) on Microsoft Windows XP Home Edition.

### 1.4.2. Materials

Acetonitrile was distilled over calcium hydride and then phosphorus(V) oxide before use. Water was deionized by ion-exchange resin. Benzene was distilled over

calcium hydride and then over sodium wire. 9-Cyanophenanthrene (9-CP) and di-*l*-menthyl naphthalene-1,4-dicarboxylate (**4**) was synthesized as follows. The other materials were purchased and used without further purification.

#### 9-Cyanophenanthrene (9-CP)

To a 200-mL round-bottomed flask equipped with a Dimroth condenser and a magnetic stirring bar were added 9-bromophenanthrene (5.0 g, 19 mmol), copper(I) cyanide (5.2 g, 58 mmol), and *N*-methyl-2-pyrrolidone (NMP, 40 mL). The mixture was refluxed under Ar atmosphere with stirring for 15 min by dipping into preheated oil bath (180–200 °C). After cooling, the crude mixture was added a large excess of aqueous ammonia, and extracted with toluene–diethyl ether. The organic extract was dried over anhydrous sodium sulfate and concentrated under reduced pressure, and then a vacuum distillation was performed to remove NMP. Purification of the residue by silica gel column chromatography and following recrystallization afforded 9-CP as white powder (2.5 g, 64%):  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  = 7.60–7.86 (m, 4H), 7.93–7.99 (m, 1H), 8.27–8.36 (m, 2H), 8.69–8.76 (m, 2H) ppm; MS ( $\text{EI}^+$ )  $m/z$  = 203 (100,  $\text{M}^+$ ), 175 (10), 102 (13), 88 (22), 75 (12); UV (MeCN)  $\lambda_{\text{max}}$  (log  $\epsilon$ ) = 299 (4.10), 311 (4.11), 339 (2.99), 356 (2.95) nm; fluorescence (MeCN,  $\lambda_{\text{ex}}$  = 311 nm)  $\lambda_{\text{max}}$  = 362, 378 nm; reduction potential (MeCN,  $n\text{-Et}_4\text{N}^+\text{ClO}_4^-$ )  $E_{1/2}^{\text{red}}$  = –1.08 V (vs  $\text{Ag}/\text{Ag}^+$ ) = –1.25 V (vs  $\text{Fc}/\text{Fc}^+$ ) = –0.87 V (vs SCE).

#### Di-*l*-menthyl naphthalene-1,4-dicarboxylate (**4**)<sup>20</sup>

The chiral photosensitizer **4** was synthesized from the condensation reaction between naphthalene-1,4-dicarboxylic acid and (–)-*l*-menthol in refluxed thionyl chloride.

White powder;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  = 0.85 (d,  $J$  = 7 Hz, 6H), 0.93 (d,  $J$  = 7 Hz, 6H), 0.97 (d,  $J$  = 7 Hz, 6H), 1.07–1.27 (m, 4H), 1.50–1.69 (m, 4H), 1.69–1.81 (m, 4H), 2.02 (qqd,  $J$  = 7, 7, 2 Hz, 2H), 2.25 (dm,  $J$  = 11 Hz, 2H), 5.35 (ddd,  $J$  = 11, 11, 4

Hz, 2H), 7.61–7.68 (m, 2H), 8.06 (s, 2H), 8.78–8.86 (m, 2H) ppm; MS (EI<sup>+</sup>)  $m/z$  = 492 (M<sup>+</sup>, 3), 337 (6), 216 (14), 199 (35), 138 (100, menthene (C<sub>10</sub>H<sub>18</sub>)).

#### 1.4.3. Determination of the Solubility of Lithium Carbonate in Acetonitrile

50 mL of saturated solution of lithium carbonate in acetonitrile at 18 °C was evaporated in vacuo, and to the residue was added deionized water to give 5 mL of the aqueous solution. An ICP–AES analysis was performed on the sample solution using  $4.94 \times 10^{-5}$  and  $4.94 \times 10^{-6}$  M aqueous solutions of lithium carbonate as external standards (correlation coefficient: 0.9999) to determine the concentration of lithium ion as  $1.05 \times 10^{-4}$  M, hence the solubility in acetonitrile was elucidated as  $5.25 \times 10^{-6}$  M.

#### 1.4.4. Photochemical Reactions

##### Typical Procedure for the Photoreactions (Table 1, entry 1)

To a Pyrex-made glass tube (1 cmϕ) was added an acetonitrile (4 mL)–water (1 mL) solution containing **1a** (165 mg, 2.5 mmol), **2a** (13.5 mg, 75 μmol), 9-CP (5.1 mg, 25 μmol), and lithium carbonate (92.4 mg, 1.25 mmol). Argon gas was bubbled through the solution for 5 min in order to reduce molecular oxygen dissolved in, and then the tube was sealed with a rubber septum. After 20-h irradiation by 300-W high-pressure mercury lamp, the reaction mixture was neutralized by dilute hydrochloric acid and extracted with diethyl ether. The organic extract was concentrated in vacuo giving a crude mixture, for which a <sup>1</sup>H-NMR analysis was performed using dibromomethane as an internal standard to determine the yields of **3aa** as 91%. Purification by silica gel chromatography (ethyl acetate after toluene) then HPLC (GPC column, chloroform) gave pure **3aa** as colorless blocks (mp 92–94 °C).

##### 2-(2,2-Diphenylethyl)propanedinitrile (**3aa**)<sup>31</sup>

Colorless blocks, mp 92–94 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  = 2.76 (dd,  $J$  = 8.1, 8.1 Hz, 2H, -CH<sub>2</sub>-), 3.44 (t,  $J$  = 8.1 Hz, 1H, -CH(CN)<sub>2</sub>), 4.22 (t,  $J$  = 8.1 Hz, 1H, -CHPh<sub>2</sub>), 7.22–7.43 (m, 10H, aromatic) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz)  $\delta$  = 21.8,

37.0, 48.4, 112.5 (2C, -CN), 127.7 (4C), 127.8 (2C), 129.4 (4C), 140.7 (2C, *ipso*) ppm; MS (EI<sup>+</sup>)  $m/z$  = 246 (18, M<sup>+</sup>), 168 (15), 167 (100, Ph<sub>2</sub>CH<sup>+</sup>), 165 (10); HRMS (EI<sup>+</sup>) calcd for C<sub>17</sub>H<sub>14</sub>N<sub>2</sub> 246.1157, found 246.1165; IR (NaCl)  $\nu$  = 703, 1451, 1496, 2255 (m, -CN), 2900, 3029 cm<sup>-1</sup>.

Crystallographic data: monoclinic,  $P2_1/c$  (#14),  $Z = 4$ ,  $R = 0.0669$ ,  $R_w = 0.1569$ ,  $a = 6.8830(8)$ ,  $b = 23.231(3)$ ,  $c = 9.5793(13)$  Å,  $\beta = 112.639(3)^\circ$ ,  $V = 1413.7(3)$  Å<sup>3</sup>,  $D_{\text{calcd}} = 1.157$  g/cm<sup>3</sup>.

### 2-(1-Methyl-2,2-diphenylethyl)propanedinitrile (**3ab**)

Pale yellow oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  = 1.30 (d,  $J$  = 6.7 Hz, 3H), 2.97–3.04 (m, 1H), 3.64 (d,  $J$  = 3.4 Hz, 1H), 3.80 (d,  $J$  = 11.8 Hz, 1H), 7.21–7.37 (m, 10H) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz)  $\delta$  = 16.1, 28.5, 40.4, 56.4, 111.0 (-CN), 113.0 (-CN), 127.5 (2C+1C), 127.8 (2C), 128.1, 129.2 (2C), 129.8 (2C), 140.7, 140.8 ppm; MS (EI<sup>+</sup>)  $m/z$  = 260 (4, M<sup>+</sup>), 167 (100, Ph<sub>2</sub>CH<sup>+</sup>); HRMS (EI<sup>+</sup>) calcd for C<sub>18</sub>H<sub>16</sub>N<sub>2</sub> 260.1313, found 260.1290; IR (NaCl)  $\nu$  = 2253 (C≡N) cm<sup>-1</sup>.

### 2-(1-Ethyl-2,2-diphenylethyl)propanedinitrile (**3ac**)

MS (EI<sup>+</sup>)  $m/z$  = 274 (3, M<sup>+</sup>), 167 (100, Ph<sub>2</sub>CH<sup>+</sup>), 165 (18), 152 (12).

### 2-[2,2-Bis(4-methoxyphenyl)ethyl]propanedinitrile (**3ae**)

Pale yellow oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  = 2.67 (dd,  $J$  = 8.3, 8.0 Hz, 2H), 3.44 (t,  $J$  = 8.0 Hz, 1H), 3.77 (s, 6H), 4.11 (d,  $J$  = 8.3 Hz, 1H), 6.86 (AA'XX',  $J$  = 8.8 Hz, 4H), 7.13 (AA'XX',  $J$  = 8.8 Hz, 4H) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz)  $\delta$  = 21.8, 37.4, 46.9, 55.7 (2C), 112.7 (2C, -CN), 114.8 (4C), 128.6 (4C), 133.2 (2C), 158.9 (2C) ppm; MS (EI<sup>+</sup>)  $m/z$  = 306 (17, M<sup>+</sup>), 240 (1, M<sup>+</sup> – CH<sub>2</sub>(CN)<sub>2</sub>), 228 (18), 227 (100, (MeOC<sub>6</sub>H<sub>4</sub>)<sub>2</sub>CH<sup>+</sup>); HRMS (EI<sup>+</sup>) calcd for C<sub>19</sub>H<sub>18</sub>N<sub>2</sub>O<sub>2</sub> 306.1368, found 306.1378; IR (NaCl)  $\nu$  = 579, 833, 1033, 1179, 1249 (C-O-C), 1509, 1609, 2255 (m, C≡N), 2838, 2905 cm<sup>-1</sup>.

### 2-(2-Phenylethyl)propanedinitrile (**3af**)<sup>32</sup>

Pale yellow powder, mp 42–43 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  = 2.35 (dt,  $J$  = 7.3, 7.3 Hz, 2H), 2.94 (t,  $J$  = 7.3 Hz, 2H), 3.57 (t,  $J$  = 7.3 Hz, 1H), 7.18–7.38 (m, 5H) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz)  $\delta$  = 22.1, 32.7, 33.0, 112.6 (2C, -CN), 127.5, 128.6 (2C), 129.3 (2C), 137.4 ppm; MS (EI<sup>+</sup>)  $m/z$  = 170 (36, M<sup>+</sup>), 91 (100, PhCH<sub>2</sub><sup>+</sup>); IR (NaCl)  $\nu$  = 2257 (C $\equiv$ N) cm<sup>-1</sup>.

### 2-(2-Phenylpropyl)propanedinitrile (**3ag**)

Colorless oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  = 1.38 (d,  $J$  = 6.9 Hz, 3H), 2.15–2.42 (m, 2H), 3.00–3.05 (m, 1H), 3.20–3.33 (m, 1H), 7.19–7.39 (m, 10H) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz)  $\delta$  = 21.6, 22.4, 38.0, 39.4, 112.5 (2C, -CN), 127.0 (2C), 127.9, 129.5 (2C), 142.2 ppm; MS (EI<sup>+</sup>)  $m/z$  = 184 (27, M<sup>+</sup>), 118 (11), 105 (100, Ph(Me)CH<sup>+</sup>); HRMS (EI<sup>+</sup>) calcd for C<sub>12</sub>H<sub>12</sub>N<sub>2</sub> 184.1000, found 184.0974; IR (NaCl)  $\nu$  = 2255 (C $\equiv$ N) cm<sup>-1</sup>.

### 2-{2-[4-(1,1-Dimethylethyl)phenyl]ethyl}propanedinitrile (**3ah**)

Pale yellow oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  = 1.36 (s, 9H), 2.34 (dt,  $J$  = 7.3, 7.3 Hz, 2H), 2.90 (t,  $J$  = 7.3 Hz, 2H), 3.56 (t,  $J$  = 7.3 Hz, 1H), 7.12 (AA'XX',  $J$  = 8.5 Hz, 2H), 7.36 (AA'XX',  $J$  = 8.5 Hz, 2H) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz)  $\delta$  = 22.0, 31.8 (3C), 32.1, 33.0, 35.0, 112.7 (2C, -CN), 126.2 (2C), 128.3 (2C), 134.2, 150.5 ppm; MS (EI<sup>+</sup>)  $m/z$  = 226 (10, M<sup>+</sup>), 211 (100, M<sup>+</sup> – Me); HRMS (EI<sup>+</sup>) calcd for C<sub>15</sub>H<sub>18</sub>N<sub>2</sub> 226.1470, found 226.1448; IR (NaCl)  $\nu$  = 2218 (C $\equiv$ N) cm<sup>-1</sup>.

### Dimethyl 2-(2,2-diphenylethyl)malonate (**3ba**)

Pale yellow oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  = 2.67 (dd,  $J$  = 8.1, 7.4 Hz, 2H, -CH<sub>2</sub>-), 3.28 (t,  $J$  = 7.4 Hz, 1H, -CH(CO<sub>2</sub>Me)<sub>2</sub>), 3.94 (t,  $J$  = 8.1 Hz, 1H, -CHPh<sub>2</sub>), 7.15–7.31 (m, 10H, aromatic) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz)  $\delta$  = 34.7, 48.9, 50.2, 52.8 (2C, -CO<sub>2</sub>Me), 126.5 (2C), 127.8 (4C), 128.6 (4C), 143.0 (2C), 169.5 (2C, C=O) ppm; MS (EI<sup>+</sup>)  $m/z$  = 312 (2, M<sup>+</sup>), 180 (100), 167 (23, Ph<sub>2</sub>CH<sup>+</sup>); IR (NaCl)  $\nu$  = 1736



(C=O)  $\text{cm}^{-1}$ .

Dimethyl 2-(2-phenylethyl)malonate (**3bf**)<sup>33</sup>

Colorless oil;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  = 2.23 (td,  $J$  = 7.7, 7.5 Hz, 2H,  $-\text{CH}_2-$ ), 2.65 (t,  $J$  = 7.7 Hz, 2H,  $-\text{CH}_2\text{Ph}$ ), 3.38 (t,  $J$  = 7.5 Hz, 1H,  $-\text{CH}(\text{CO}_2\text{Me})_2$ ), 3.73 (s, 6H,  $-\text{CO}_2\text{Me}$ ), 7.14–7.23 (m, 3H, aromatic), 7.23–7.32 (m, 2H, aromatic) ppm;  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  = 30.9 ( $2^\circ$ ), 33.8 ( $-\text{CHPh}_2$ ), 51.3 ( $-\text{CH}(\text{CO}_2\text{Me})_2$ ), 53.0 (2C,  $-\text{CO}_2\text{Me}$ ), 126.4, 128.6 (2C), 128.7 (2C), 140.6 (*ipso*), 169.8 (2C, C=O) ppm.

Dimethyl 2-(2-phenylpropyl)malonate (**3bg**)<sup>34</sup>

Pale yellow oil;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  = 1.28 (dd,  $J$  = 7.0, 0.4 Hz, 3H,  $-\text{CHMePh}$ ), 2.10–2.30 (m, 2H,  $-\text{CH}_2-$ ), 2.64–2.78 (m, 1H,  $-\text{CHMePh}$ ), 3.21 (dd,  $J$  = 8.9, 6.2 Hz, 1H,  $-\text{CH}(\text{CO}_2\text{Me})_2$ ), 3.63 (s, 3H,  $-\text{CO}_2\text{Me}$ ), 3.74 (s, 3H,  $-\text{CO}_2\text{Me}$ ), 7.13–7.23 (m, 3H, aromatic), 7.25–7.33 (m, 2H, aromatic) ppm;  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  = 23.0 ( $-\text{CHMePh}$ ), 37.5 ( $-\text{CH}_2-$ ), 38.4 ( $-\text{CHMePh}$ ), 50.5 ( $-\text{CH}(\text{CO}_2\text{Me})_2$ ), 52.8 (2C,  $-\text{CO}_2\text{Me}$ ), 126.6, 127.2 (2C), 128.7 (2C), 145.3 (*ipso*), 169.77 ( $-\text{CO}_2\text{Me}$ ), 169.85 ( $-\text{CO}_2\text{Me}$ ) ppm; MS ( $\text{EI}^+$ )  $m/z$  = 250 (3,  $\text{M}^+$ ), 132 (91,  $\text{CH}_2(\text{CO}_2\text{Me})_2^+$ ), 118 (100,  $\text{PhCHMe}=\text{CH}_2^+$ ), 105 (51,  $\text{PhC}^+\text{HMe}$ ); IR (NaCl)  $\nu$  = 702, 1154, 1237, 1436, 1739 (C=O), 2956  $\text{cm}^{-1}$ .

Ethyl 2-(2,2-diphenylethyl)-3-oxobutyrates (**3ca**)

Colorless oil;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  = 1.26 (t,  $J$  = 7.1 Hz, 3H,  $-\text{OCH}_2\text{Me}$ ), 2.15 (s, 3H,  $-\text{Ac}$ ), 2.55–2.71 (m, 2H,  $-\text{CH}_2-$ ), 3.36 (dd,  $J$  = 7.1, 7.1 Hz, 1H,  $-\text{CH}(\text{Ac})\text{CO}_2\text{Et}$ ), 3.94 (dd,  $J$  = 8.1, 8.1 Hz, 1H,  $-\text{CHPh}_2$ ), 4.17 (q,  $J$  = 7.1 Hz, 2H,  $-\text{OCH}_2\text{Me}$ ), 7.15–7.38 (m, 10H) ppm;  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  = 14.7 ( $-\text{OCH}_2\text{Me}$ ), 29.8 ( $-\text{C}(=\text{O})\text{Me}$ ), 34.1 ( $-\text{CH}_2-$ ), 49.2 ( $-\text{CHPh}_2$ ), 58.2 ( $-\text{CH}(\text{Ac})\text{CO}_2\text{Et}$ ), 61.9 ( $-\text{OCH}_2\text{Me}$ ), 126.7, 126.8, 128.0 (2C), 128.1 (2C), 128.7 (2C), 128.8 (2C), 143.56 (*ipso*), 143.62 (*ipso*), 169.6 ( $-\text{CO}_2\text{Et}$ ), 202.7 ( $-\text{C}(=\text{O})\text{Me}$ ) ppm; MS ( $\text{EI}^+$ )  $m/z$  = 292 (1), 265 (1,  $\text{M}^+ - \text{OEt}$ ), 180 (100,  $\text{Ph}_2\text{C}=\text{CH}_2^+$ ), 167 (16,  $\text{Ph}_2\text{CH}^+$ ), 165 (38); IR (NaCl)  $\nu$  = 702, 1718 (C=O), 1736 (C=O), 2981 ( $\text{C}\equiv\text{N}$ )  $\text{cm}^{-1}$ .

### Ethyl 2-cyano-4,4-diphenylbutyrate (**3da**)

Pale yellow oil;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  = 1.28 (t,  $J$  = 7.1 Hz, 3H,  $-\text{OCH}_2\text{Me}$ ), 2.53–2.62 (m, 1H,  $-\text{CH}_2-$ ), 2.72–2.81 (m, 1H,  $-\text{CH}_2-$ ), 3.29 (dd,  $J$  = 10.0, 5.5 Hz, 1H,  $-\text{CH}(\text{CN})\text{CO}_2\text{Et}$ ), 4.19 (q, 2H,  $J$  = 7.1 Hz,  $-\text{OCH}_2\text{Me}$ ), 4.19–4.25 (m, 1H,  $-\text{CHPh}_2$ ), 7.18–7.35 (m, 10H, aromatic) ppm;  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  = 14.1, 35.4, 36.3, 48.4, 62.9 ( $-\text{OCH}_2\text{Me}$ ), 116.1, 126.7, 127.0, 127.3 (2C), 127.6 (2C), 128.5 (2C), 128.8 (2C), 141.2, 142.3, 165.5 (C=O) ppm; MS ( $\text{EI}^+$ )  $m/z$  = 293 (6,  $\text{M}^+$ ), 180 (100,  $\text{Ph}_2\text{C}=\text{CH}_2^+$ ), 167 (29,  $\text{Ph}_2\text{CH}^+$ ); IR (NaCl)  $\nu$  = 2249 ( $\text{C}\equiv\text{N}$ )  $\text{cm}^{-1}$ .

### Ethyl 2-cyano-3-methyl-4,4-diphenylbutyrate (**3db**)

Mixture (86:14) of diastereomers, pale yellow oil;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  = 1.03 (d,  $J$  = 6.6 Hz, 3H,  $-\text{CHMe}$ -, major isomer), 1.12 (d,  $J$  = 6.7 Hz, 3H,  $-\text{CHMe}$ -, minor isomer), 1.31 (t,  $J$  = 7.1 Hz, 3H,  $-\text{CH}_2\text{Me}$ ), 3.10–3.24 (m, 1H,  $-\text{CHMe}$ -, major isomer), 3.49 (d,  $J$  = 3.0 Hz, 1H,  $-\text{CH}(\text{CN})\text{CO}_2\text{Et}$ , major isomer), 3.54 (d,  $J$  = 3 Hz, 1H,  $-\text{CH}(\text{CN})\text{CO}_2\text{Et}$ , minor isomer), 3.83 (d,  $J$  = 12.1 Hz, 1H,  $-\text{CHPh}_2$ ), major isomer), 4.08 (d,  $J$  = 12 Hz, 1H,  $-\text{CHPh}_2$ ), minor isomer), 4.26 (q,  $J$  = 7.1 Hz, 2H,  $-\text{CO}_2\text{CH}_2\text{Me}$ ), 7.12–7.42 (m, 10H) ppm; MS ( $\text{EI}^+$ )  $m/z$  = 307 (0.4,  $\text{M}^+$ ), 194 (65,  $\text{Ph}_2\text{C}=\text{CHMe}^+$ ), 167 (100,  $\text{Ph}_2\text{CH}^+$ ). HRMS ( $\text{FAB}^+$ ) calcd for  $\text{C}_{20}\text{H}_{22}\text{NO}_2$  ( $[\text{M}+\text{H}]^+$ ) 308.1651, found 308.1616.

### 2-(2,2-Diphenylethyl)-2-methylpropanedinitrile (**3ha**)

Pale yellow powder, mp 96–97 °C;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  = 1.67 (s, 3H,  $-\text{Me}$ ), 2.64 (d,  $J$  = 7.5 Hz, 2H,  $-\text{CH}_2-$ ), 4.28 (t,  $J$  = 7.5 Hz, 1H,  $-\text{CHPh}_2$ ), 7.16–7.29 (m, 10H, aromatic) ppm;  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  = 26.7 ( $-\text{Me}$ ), 31.2 ( $-\text{CMe}(\text{CN})_2$ ), 44.3 ( $-\text{CH}_2-$ ), 48.9 ( $-\text{CHPh}_2$ ), 115.5 (2C,  $-\text{CN}$ ), 127.4, 127.7, 128.9, 141.7 ppm; MS ( $\text{EI}^+$ )  $m/z$  = 260 (14,  $\text{M}^+$ ), 167 (100,  $\text{Ph}_2\text{CH}^+$ ); IR (NaCl)  $\nu$  = 2248 ( $\text{C}\equiv\text{N}$ )  $\text{cm}^{-1}$ .

### 2,2-Diphenylethanol (**5a**)<sup>35</sup>

Pale yellow oil;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  = 1.6 (brs, 1H,  $-\text{OH}$ ), 4.10–4.24 (m, 3H), 7.16–7.36 (m, 10H) ppm;  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  = 54.1, 66.5, 127.0 (2C),

128.5 (4C), 128.8 (4C), 141.5 (2C, *ipso*) ppm.

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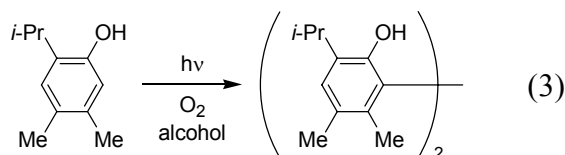
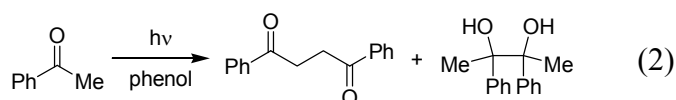
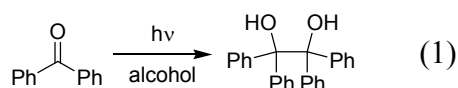
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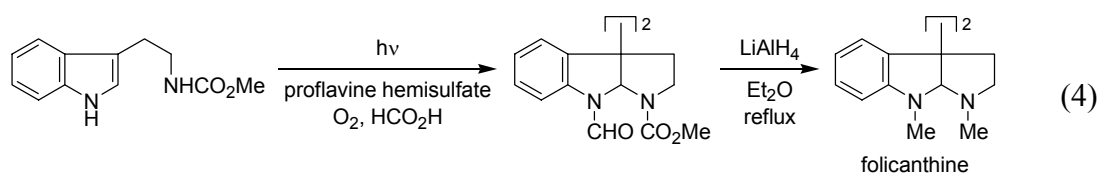
## CHAPTER 2. Synthesis of Active Methylene Compound-Incorporated Dimers by Use of Oxidative Photodimerization

### 2.1. Introduction

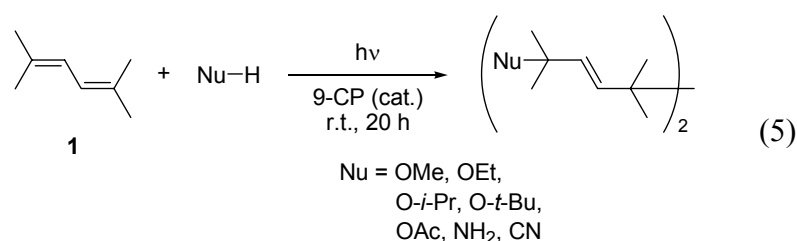
Oxidative and reductive photodimerization reactions have been a subject of diverse studies among organic chemists not only from mechanistic interests but also from their potentiality to form complicated skeletons, in particular that of natural compounds, from rather simple moieties. For example, pinacol coupling<sup>1</sup> is one of the most well-known reductive photodimerization reactions (eq. 1). Becker has reported the case of acetophenones, which both oxidative and reductive dimerizations occur concomitantly to produce 1,2-dibenzoyl ethanes and acetophenone pinacols, respectively (eq. 2).<sup>2</sup> Johnson and coworker have revealed oxidative photocoupling of phenols at *ortho*- and *para*-positions (eq. 3).<sup>3</sup> In terms of natural compounds, Hino and coworkers have succeeded in synthesizing folicanthine, chimonanthine, calycanthine, and ditryptophenaline using ring closing photodimerization reactions of indoles for their key steps (eq. 4).<sup>4</sup>



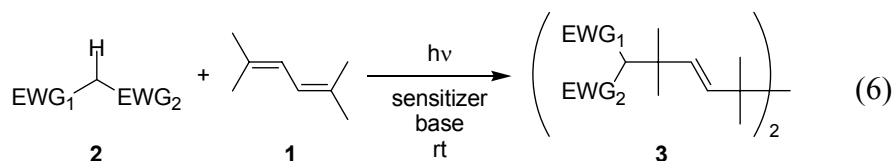




Mizuno and coworkers have also reported a kind of oxidative photodimerization reaction: photoirradiation of a methanol solution of 2,5-dimethylhexa-2,4-diene (**1**) in the presence of 9-cyanophenanthrene (9-CP) gives dimethoxy-substituted dimer of the diene (2,9-dimethoxy-2,5,5,6,6,9-hexamethyl-3,7-decadiene) and 9-cyano-9,10-dihydrophenanthrene (dihydro-9-CP).<sup>5</sup> Recently, the author has found out and reported in his master's thesis<sup>6</sup> that 9-CP performs as a catalyst for the formation of the dimer and that various nucleophiles such as alcohols, acetate,<sup>7</sup> ammonia,<sup>8</sup> and cyanide<sup>9</sup> can be introduced to **1** (eq. 5).



In this chapter, the author describes that the anions of active methylene compounds can take part in the above-mentioned photoreaction to form the dimers of the corresponding  $\alpha$ -monoalkylated active methylene compounds **3** (eq. 6).



## 2.2. Results and Discussion

### 2.2.1. Photochemical Reactions

Photoirradiation of an aqueous acetonitrile solution containing propanedinitrile (**2a**, malononitrile), **1**, lithium carbonate and a catalytic amount of 9-CP afforded the oxidative dimer of  $\alpha$ -monoalkylated propanedinitrile (**3a**) in 52% yield (Table 1, entry 1). Since the  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR spectra of **3a** are very simple and no molecular ion peak (but a signal corresponds to  $M^+/2$ ) is observed in the mass spectrum of **3a**, its structure was assigned by analogy with the dimethoxy-incorporated dimer<sup>6,9</sup> and

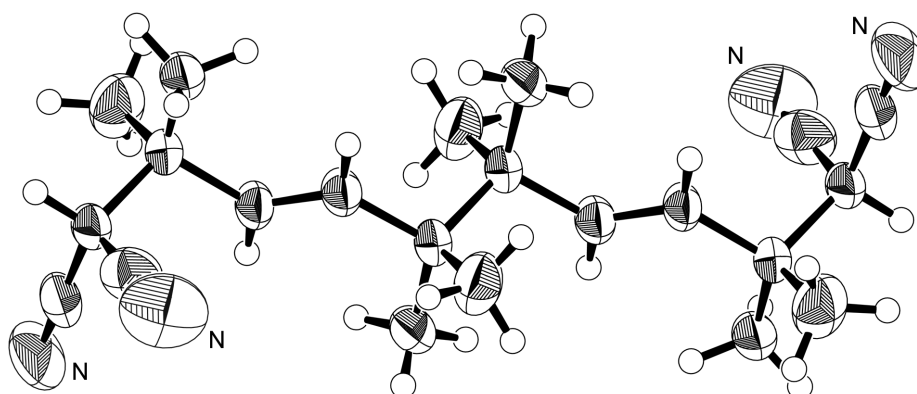
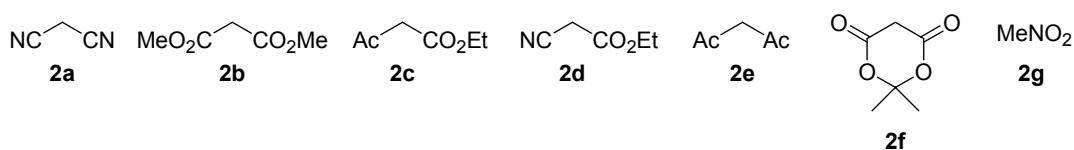
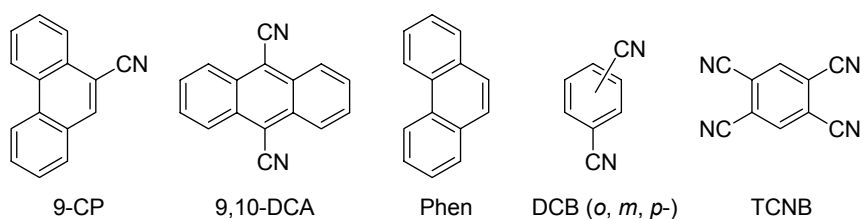


Figure 1. ORTEP diagram for **3a**.

#### Chart 1. Active Methylene Compounds (**2a–2g**)



#### Chart 2. Photosensitizers



**Table 1.** Oxidative Photodimerization of **1** with **2**

$\text{EWG}_1\text{CH}_2\text{EWG}_2 + \text{1} \xrightarrow[\text{conditions}^a]{h\nu} \text{3a-3g}$

entry	active methylene compound	sensitizer(s)	base	product	yield <sup>b</sup> / %
1	<b>2a</b>	9-CP	Li <sub>2</sub> CO <sub>3</sub>	<b>3a</b>	52
2			Na <sub>2</sub> CO <sub>3</sub>		50
3			K <sub>2</sub> CO <sub>3</sub>		46
4			Cs <sub>2</sub> CO <sub>3</sub>		46
5			none		0
6 <sup>c</sup>					31
7		9,10-DCA	Na <sub>2</sub> CO <sub>3</sub>		43
8		<i>m</i> -DCB, Phen			47
9		<i>o</i> -DCB, Phen			37
10		<i>p</i> -DCB, Phen			25
11		TCNB, Phen			22
12	<b>2b</b>	9-CP	Na <sub>2</sub> CO <sub>3</sub>	<b>3b</b>	0
13			NaOH		0
14 <sup>d</sup>			KO- <i>t</i> -Bu		57
15	<b>2c</b>	9-CP	NaOH	<b>3c</b>	41
16 <sup>d</sup>	<b>2d</b>	9-CP	KO- <i>t</i> -Bu	<b>3d</b>	41
17	<b>2e</b>	9-CP	NaOH	<b>3e</b>	45
18	Mg(acac) <sub>2</sub>		none	<b>3e</b>	11
19 <sup>d</sup>	<b>2f</b>	9-CP	KO- <i>t</i> -Bu	<b>3f</b>	(18) <sup>e</sup>
20 <sup>d</sup>	<b>2g</b>	9-CP	KO- <i>t</i> -Bu	<b>3g</b>	complex

<sup>a</sup> Conditions: 300-W high-pressure mercury lamp, Pyrex filter, active methylene compound (2.5 mmol), **1** (75 μmol), sensitizer(s) (25 μmol each), base (1.25 mmol), in MeCN (4 mL)–H<sub>2</sub>O (1 mL), under Ar, rt, 20 h. <sup>b</sup> Determined by <sup>1</sup>H NMR based on the amount of **1** used. <sup>c</sup> In dry DMSO (5 mL) with MS4A (250 mg). <sup>d</sup> In dry MeCN (5 mL). <sup>e</sup> Isolated yield (<sup>1</sup>H-NMR spectrum of the crude mixture was too complex to determine the yield).

by a single-crystal X-ray crystallographic analysis (Figure 1).

The above-mentioned photoreaction proceeds under mild conditions such as at ambient temperature, in the presence of weak base, and halogen free. Thus, the author

believes that it might be a useful synthetic method to extend carbon chains and to link two building blocks.

The strength of the base used in this process affects the yield of **3a**. Accordingly, reactions with heavier alkali metal carbonates result in slightly lower yields of **3a** (entries 2–4). The reaction does not proceed in the absence of base (entry 5) unless dry dimethyl sulfoxide (DMSO) is used as a solvent (entry 6).<sup>10</sup> Lastly, photosensitizers other than 9-CP can be used to promote the reaction albeit with lower yields (entries 7–11).

Other active methylene compounds undergo monoalkylation as well. Stronger bases, such as potassium *tert*-butoxide, promote alkylation of **2b** with diene **1** (entries 12–14) and similar reactions take place with **2c–2f** to form **3c–3f** (entries 15–17, and 19). Instead of the acetylacetone (**2e**)–sodium hydroxide pair (entry 17), magnesium acetylacetonate serves as a participant in this reaction in the absence of base (entry 18). A use of active “methyl” compound, nitromethane (**2g**), afforded complex mixture of photolysates (entry 20).

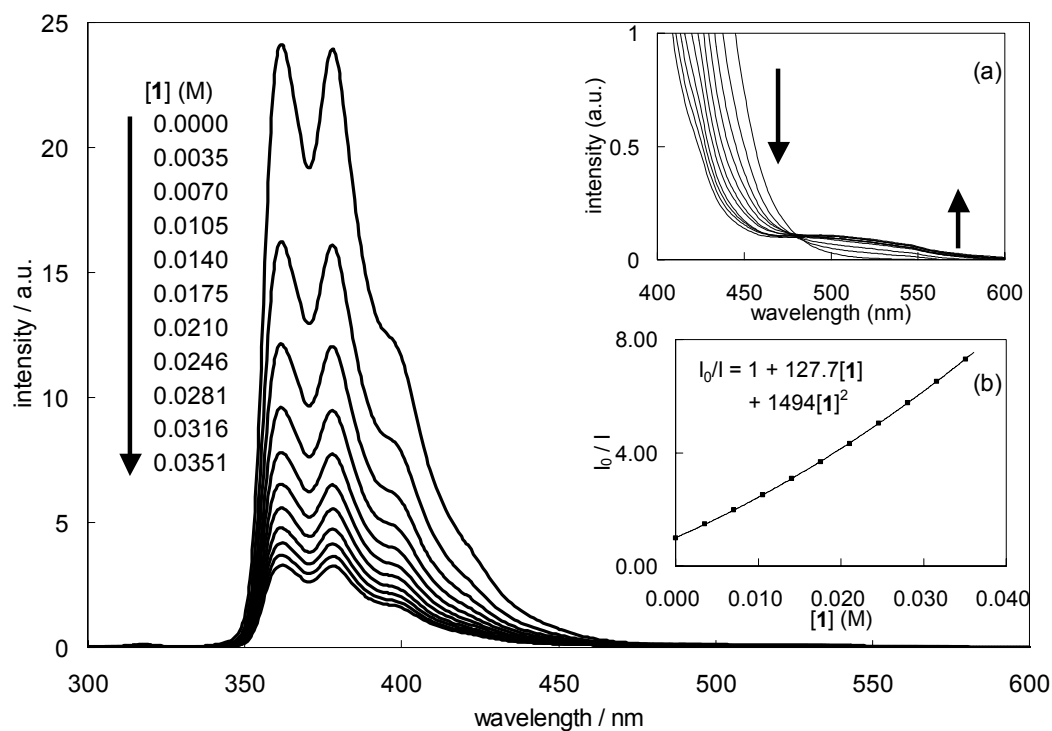
### 2.2.2. Fluorescence Quenching of 9-Cyanophenanthrene (9-CP) by 2,5-Dimethylhexa-2,4-diene (**1**)

Efficient quenching of the fluorescence of 9-CP and a rise of a very weak exciplex emission with an isoemissive point of 480 nm was observed along with the addition of diene **1** (Figure 2). A Stern–Volmer plot at 362 nm exhibited a second-order correlation of the reciprocal of relative fluorescence intensity ( $I_0/I$ ) with the concentration of **1** (Figure 2b, and eq. 7), from which the first-order quenching rate constant ( $k_q$ ) was determined as  $5.3 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ .<sup>11</sup> This second-order correlation indicates that not only one-to-one but also one-to-two quenching of the excited singlet state of 9-CP ( $^1\text{9-CP}^*$ ) with **1** is involved in the system.

$$\frac{I_0}{I} = 1 + 1.28 \times 10^2 [\mathbf{1}] + 1.49 \times 10^3 [\mathbf{1}]^2 \quad (7)$$

An electrochemical analysis was also performed to demonstrate that the photoinduced electron transfer (PET) from **1** to  $^1\text{9-CP}^*$  occurs highly exergonic manner ( $\Delta G_{\text{PET}} = -1.37 \text{ eV}$ ).<sup>12</sup>

These results indicate that PET occurs from **1** to  $^1\text{9-CP}^*$  at the initial stage of the photoreaction.



**Figure 2.** Fluorescence spectral change of 9-CP ( $1.02 \times 10^{-4}$  M,  $\lambda_{\text{ex}} = 311 \pm 2.5$  nm) in MeCN by the addition of **1**. The insets are (a) a magnification of the spectra around the isoemissive point of 480 nm and (b) a Stern–Volmer plot at 362 nm.

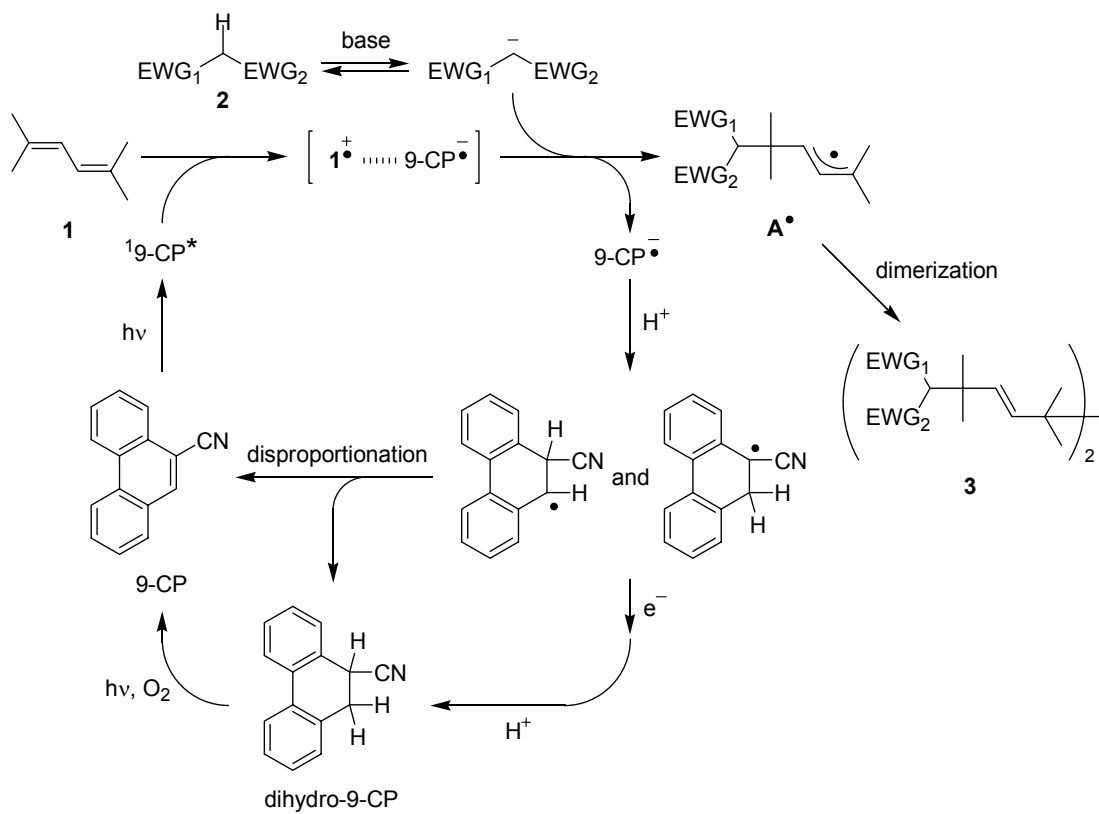
### 2.2.3. Plausible Mechanism

The author proposes the reaction mechanism as follows (Scheme 1). PET from **1** to excited singlet state of 9-CP ( $^19\text{-CP}^*$ ) affords radical ion pair ( $\mathbf{1}^{+\cdot}$  and  $9\text{-CP}^{\cdot-}$ ).<sup>13</sup> The radical cation of **1** reacts with the anion of active methylene compounds and the resulting allylic radical  $\mathbf{A}^{\cdot}$  dimerizes regioselectively at its terminal position to produce to give **3**, a result that correlates with the relative stabilities of the three possible dimers. Another possible pathway for the consumption of  $\mathbf{A}^{\cdot}$  is BET from  $\text{DCB}^{\cdot-}$ , but the resulting anion  $\mathbf{A}^-$  dissociates spontaneously ( $\Delta G^\ddagger \sim 2$  kcal/mol by HF/3-21G) to form the starting materials (i.e., **1** and the anion of **2**).

The radical anion of 9-CP is protonated on 9- or 10-position, and the resulting radicals undergo disproportionation or further reduction and subsequent protonation to produce dihydro-9-CP.<sup>14</sup> Dihydro-9-CP is stable enough to isolate under dark conditions but reacts rapidly under irradiation conditions with small amount of molecular oxygen remaining in the system to reproduce 9-CP, hence 9-CP has the catalytic ability for the formation of **3**.<sup>15</sup>

Similar mechanisms are estimated for the photosensitizers other than 9-CP, although their reproduction pathways are yet unknown.

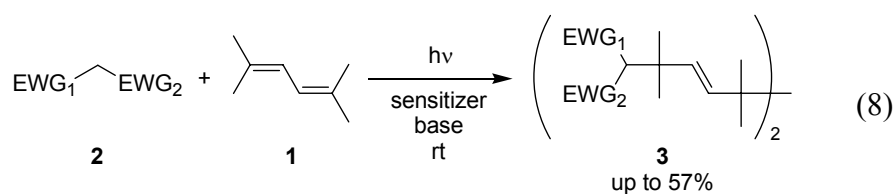
**Scheme 1.** Plausible Mechanism for the Formation of **3**





### 2.3. Conclusion

Photochemical synthetic method for oxidative dimers of diene **1** incorporating active methylene compounds was developed, by use of oxidative photodimerization (eq. 8). The reaction, which proceeds under mild conditions in up to 57% yield, might be a useful synthetic method.



## 2.4. Experimental Section

### 2.4.1. General

Experimental instruments are described in Chapter 1.

### 2.4.2. Materials

2,5-Dimethylhexa-2,4-diene (**1**) was distilled under reduced pressure before use. Preparations and pretreatments of other materials are described in Chapter 1.

### 2.4.3. Photochemical Reactions

#### Typical Procedure for the Photoreactions (Table 1, entry 1)

To a Pyrex-made glass tube (1 cm $\phi$ ) was added an acetonitrile (4 mL)–water (1 mL) solution containing **2a** (165 mg, 2.5 mmol), **1** (8.3 mg, 75  $\mu$ mol), lithium carbonate (92.4 mg, 1.25 mmol), and 9-CP (5.1 mg, 25  $\mu$ mol). Argon gas was bubbled through the solution for 5 min in order to reduce molecular oxygen dissolved in, and then the tube was sealed with a rubber septum. After 20-h irradiation by 300-W high-pressure mercury lamp, the reaction mixture was neutralized by addition of dilute hydrochloric acid and extracted with toluene–diethyl ether. The organic extracts were concentrated in vacuo giving a residue (52% yield, determined by  $^1\text{H}$ -NMR analysis using dibromomethane as an internal standard), which was chromatographed on silica gel (ethyl acetate after toluene) to give a crude product mixture. Further purification by HPLC (GPC column, chloroform) gave pure *trans,trans*-2,11-dicyano-3,3,6,6,7,7,10,10-octamethyldodeca-4,8-dienedinitrile (**3a**) as colorless blocks (mp 111–112  $^{\circ}\text{C}$ ).

#### *trans,trans*-2,11-Dicyano-3,3,6,6,7,7,10,10-octamethyldodeca-4,8-dienedinitrile (**3a**)

Colorless blocks, mp 111–112  $^{\circ}\text{C}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  = 1.00 (s, 12H), 1.36 (s, 12H), 3.61 (s, 2H), 5.36 (d,  $J$  = 15.8 Hz, 2H, olefin), 5.80 (d,  $J$  = 15.8 Hz, 2H, olefin) ppm;  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  = 23.4 (4C), 25.9 (4C), 35.9 (2C), 40.8 (2C), 41.5 (2C), 112.3 (4C, -CN), 129.8 (2C, olefin), 140.1 (2C, olefin) ppm; MS ( $\text{EI}^+$ )  $m/z$  =

175 (39,  $M^+/2$ ), 110 (100,  $M^+/2 - CH(CN)_2$ ), 109 (35,  $M^+/2 - CH_2(CN)_2$ ), 95 (30,  $M^+/2 - MeCH(CN)_2$ ); MS ( $Cl^+$ )  $m/z$  = 351 (5,  $[M+H]^+$ ), 203 (5), 175 (100,  $M^+/2$ ), 137 (11), 111 (12), 110 (30,  $M^+/2 - CH(CN)_2$ ), 109 (8,  $M^+/2 - CH_2(CN)_2$ ), 83 (6); HRMS ( $Cl^+$ ) calcd for  $C_{22}H_{31}N_4$  ( $[M+H]^+$ ) 351.2549, found 351.2555; IR (NaCl)  $\nu$  = 800, 1019, 1093, 1261, 1459, 2238 (w,  $C\equiv N$ ), 2252 (w,  $C\equiv N$ ), 2928, 2968  $cm^{-1}$ ; Anal. calcd for  $C_{22}H_{30}N_4$  C 75.39, H 8.63, N 15.98, found C 75.15, H 8.47, N 15.86.

Crystallographic data: monoclinic,  $P2_1/n$  (#14),  $Z = 2$ ,  $R = 0.0905$ ,  $R_w = 0.1121$ ,  $a = 6.305(3)$ ,  $b = 26.491(18)$ ,  $c = 6.608(4)$  Å,  $\beta = 99.89(3)^\circ$ ,  $V = 1087.4(10)$  Å<sup>3</sup>,  $D_{calcd} = 1.070$  g/cm<sup>3</sup>.

**Dimethyl *trans,trans*-2,11-bis(methoxycarbonyl)-3,3,6,6,7,7,10,10-octamethyldodeca-4,8-dienedioate (3b)**

Pale brown oil; <sup>1</sup>H NMR (300 MHz,  $CDCl_3$ )  $\delta$  = 0.89 (s, 12H), 1.23 (s, 12H), 3.36 (s, 2H,  $-CH(CO_2Me)_2$ ), 3.68 (s, 12H,  $-CO_2Me$ ), 5.45 (d,  $J = 16.1$  Hz, 2H, olefin), 5.49 (d,  $J = 16.1$  Hz, 2H, olefin) ppm; <sup>13</sup>C NMR (75 MHz,  $CDCl_3$ )  $\delta$  = 23.5 (4C, 1°), 26.3 (4C, 1°), 38.9 (2C, 4°), 40.9 (2C, 4°), 52.4 (4C,  $-CO_2Me$ ), 61.4 (2C,  $-CH(CO_2Me)_2$ ), 133.8 (2C, olefin), 135.8 (2C, olefin), 168.4 (4C, C=O) ppm; MS ( $Et^+$ )  $m/z$  = 241 (41,  $M^+/2$ ), 209 (10,  $M^+/2 - MeOH$ ), 183 (17), 177 (26), 149 (13), 121 (28), 110 (19,  $M^+/2 - CH(CO_2Me)_2$ ), 109 (100,  $M^+/2 - CH_2(CO_2Me)_2$ ), 101 (10), 95 (12,  $M^+/2 - MeCH(CO_2Me)_2$ ); HRMS ( $Et^+$ ) calcd for  $C_{13}H_{21}O_4$  ( $M^+/2$ ) 241.1440, found 241.1435; IR (NaCl)  $\nu$  = 1142 (C–O), 1243, 1736 (C=O), 1758 (C=O), 2967  $cm^{-1}$ .

**Diethyl *trans,trans*-2,11-diacetyl-3,3,6,6,7,7,10,10-octamethyldodeca-4,8-dienedioate (3c)**

Light yellow oil; <sup>1</sup>H NMR ( $CDCl_3$ , 300 MHz)  $\delta$  = 0.91 (s, 12H), 1.19 (s, 6H), 1.20 (s, 6H), 1.26 (t,  $J = 7.1$  Hz, 6H,  $-CO_2CH_2Me$ ), 2.19 (d,  $J = 0.3$  Hz, 6H,  $-Ac$ ), 3.41 (brs, 2H,  $-CH(Ac)CO_2Et$ ), 4.15 (q,  $J = 7.1$  Hz, 4H,  $-CO_2CH_2Me$ ), 5.46 (d,  $J = 17$  Hz, olefin), 5.52 (d,  $J = 17$  Hz, olefin) ppm; <sup>13</sup>C NMR ( $CDCl_3$ , 75 MHz)  $\delta$  = 14.7 (2C,

-CO<sub>2</sub>CH<sub>2</sub>Me), 23.4 (2C), 23.6 (2C), 26.5 (4C), 32.0 (2C), 39.3 (2C), 41.0 (2C), 61.3 (2C), 68.9 (2C), 133.9 (2C, olefin), 135.6 (2C, olefin), 168.8 (2C, -C=O), 202.9 (2C, -C(=O)Me) ppm; MS (EI<sup>+</sup>)  $m/z$  = 239 (42, M<sup>+</sup>/2), 121 (47), 110 (67, M<sup>+</sup>/2 - CH(Ac)CO<sub>2</sub>Et), 109 (100, M<sup>+</sup>/2 - CH<sub>2</sub>(Ac)CO<sub>2</sub>Et), 95 (77, M<sup>+</sup>/2 - MeCH(Ac)CO<sub>2</sub>Et), 67 (99); HRMS (EI<sup>+</sup>) calcd for C<sub>14</sub>H<sub>23</sub>O<sub>3</sub> (M<sup>+</sup>/2) 239.1647, found 239.1649; IR (NaCl)  $\nu$  = 1142, 1366, 1718 (C=O), 1734 (C=O), 2973 cm<sup>-1</sup>.

**Diethyl *trans,trans*-2,11-dicyano-3,3,6,6,7,7,10,10-octamethyldodeca-4,8-dienedioate (**3d**)**

Mixture (1:1) of *dl*- and *meso*-isomers, brown oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  = 0.95 (s, 12H), 1.27 (s, 6H), 1.28 (s, 6H), 1.31 (dd,  $J$  = 7.1, 7.1 Hz, 6H, -OCH<sub>2</sub>Me), 3.367 (s, 2H, -CH(CN)CO<sub>2</sub>Et, one of the isomers), 3.373 (s, 2H, -CH(CN)CO<sub>2</sub>Et, the other isomer), 4.20 (dq,  $J$  = 10.9, 7.1 Hz, 2H, -OCH<sub>2</sub>Me, one of the isomers), 4.23 (dq,  $J$  = 10.9, 7.1 Hz, 2H, -OCH<sub>2</sub>Me, the other isomer), 5.37 (d,  $J$  = 16.1 Hz, 2H, olefin), 5.64 (d,  $J$  = 16.1 Hz, 2H, olefin) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz)  $\delta$  = 14.6 (2C, -OCH<sub>2</sub>Me), 23.41 (2C, 1°, isomer A), 23.46 (2C, 1°, isomers A and B), 23.50 (2C, 1°, isomer B), 26.2 (2C, 1°), 26.4 (2C, 1°), 39.9 (2C, 4°), 41.2 (2C, 4°), 49.6 (2C, -CH(CN)CO<sub>2</sub>Et), 62.7 (2C, -OCH<sub>2</sub>Me), 116.1 (2C, -CN), 131.7 (2C, olefin), 137.7 (2C, olefin), 165.0 (2C, C=O) ppm; MS (EI<sup>+</sup>)  $m/z$  = 222 (45, M<sup>+</sup>), 176 (12, M<sup>+</sup> - EtOH), 148 (11), 110 (29, M<sup>+</sup> - CH(CN)CO<sub>2</sub>Et), 109 (100, M<sup>+</sup> - CH<sub>2</sub>(CN)CO<sub>2</sub>Et), 95 (13, M<sup>+</sup> - MeCH(CN)CO<sub>2</sub>Et); HRMS (EI<sup>+</sup>) calcd for C<sub>13</sub>H<sub>20</sub>O<sub>2</sub>N (M<sup>+</sup>/2) 222.1494, found 222.1472; IR (NaCl)  $\nu$  = 1037, 1189 (C-O), 1250 (C-O), 1370, 1467, 1742 (C=O), 2247 (w, C≡N), 2973 cm<sup>-1</sup>.

***trans,trans*-3,12-Diacetyl-4,4,7,7,8,8,11,11-octamethyltetradeca-5,9-diene-2,13-dione (**3e**)**

Colorless oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  = 0.92 (s, 12H), 1.16 (s, 12H), 2.18 (d,  $J$  = 0.4 Hz, 12H, -Ac), 3.72 (brs, 2H, -CHAc<sub>2</sub>), 5.45 (d,  $J$  = 16.2 Hz, 2H, olefin), 5.52 (d,  $J$  = 16.2 Hz, 2H, olefin) ppm; <sup>13</sup>C NMR (C<sub>6</sub>D<sub>6</sub>, 75 MHz)  $\delta$  = 23.2 (4C), 26.2 (4C), 31.8

(4C, -C(=O)Me), 39.4 (2C, 4°), 40.7 (2C, 4°), 75.9 (2C, -CHAc<sub>2</sub>), 134.0 (2C, olefin), 135.0 (2C, olefin), 202.0 (4C, C=O) ppm; MS (EI<sup>+</sup>)  $m/z$  = 209 (69, M<sup>+</sup>/2), 149 (46, M<sup>+</sup>/2 – AcOH), 110 (24, M<sup>+</sup>/2 – Ac<sub>2</sub>CH), 109 (100, M<sup>+</sup>/2 – Ac<sub>2</sub>CH<sub>2</sub>), 85 (27); HRMS (EI<sup>+</sup>) calcd for C<sub>13</sub>H<sub>21</sub>O<sub>2</sub> (M<sup>+</sup>/2) 209.1541, found 209.1527; IR (NaCl)  $\nu$  = 665, 986, 1143, 1355, 1696 (C=O), 1719, 2967 cm<sup>-1</sup>.

**2,9-Bis(4,4-dimethyl-3,5-dioxacyclohexa-2,6-dionyl)-2,5,5,6,6,9-hexamethyldeca-3,7-diene (3f)**

White powder, mp 133–135 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  = 0.93 (s, 12H), 1.31 (s, 12H), 1.69 (s, 6H, -O-CMe<sub>2</sub>-O-), 1.72 (s, 6H, -O-CMe<sub>2</sub>-O-), 3.25 (s, 2H, 3°), 5.41 (d,  $J$  = 16.1 Hz, 2H), 5.54 (d,  $J$  = 16.1 Hz, 2H) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz)  $\delta$  = 23.4 (4C), 27.3 (4C), 28.4 (2C, 4°), 29.6 (2C, 4°), 41.2 (2C, -O-CMe<sub>2</sub>-O-), 41.3 (2C, -O-CMe<sub>2</sub>-O-), 105.0 (2C, -O-CMe<sub>2</sub>-O-), 132.6 (2C, olefin), 136.6 (2C, olefin), 164.6 (4C, C=O) ppm; MS (EI<sup>+</sup>)  $m/z$  = 110 (100, (Me<sub>2</sub>C=CH-)<sub>2</sub><sup>+</sup>), 109 (4), 95; IR (NaCl)  $\nu$  = 1277, 1752, 2972 cm<sup>-1</sup>.

## 2.5. References and Notes

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11. Fluorescence lifetime of 9-CP is reported as 24 ns: Tsujimoto, Y.; Hayashi, M.;

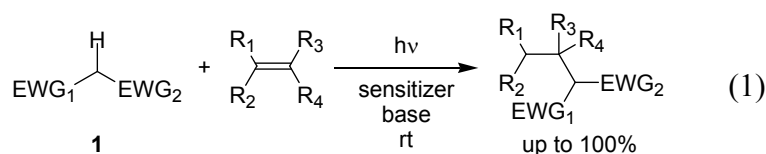
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13. The one-to-one quenching of  $^19\text{-CP}^*$  with **1** is dominant under the reaction conditions.
14. The radical anion of 9-CP might be responsible for the reduction of the radical intermediates.
15. This catalytic reaction can be considered as a redox-photosensitized reaction in a wide sense, but quite different in the respect that the catalytic intermediate dihydro-9-CP can be isolated; *Cf.* Majima, T.; Pac, C.; Nakasone, A.; Sakurai, H. *J. Am. Chem. Soc.* **1981**, 103, 4499–4508.

## CHAPTER 3. Synthesis of Tandem $\alpha$ -Monoalkylated Active Methylene Compounds by Use of Photochemical Three-Component Coupling Reaction

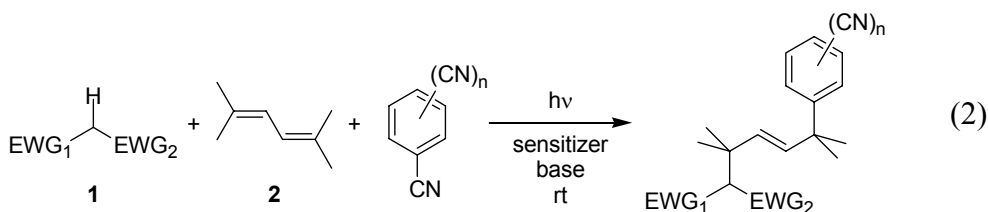
### 3.1. Introduction

The linkage chains to tether two building blocks into intramolecular dyads are important for the development of highly functionalized molecules. One of the most commonly-used tools for this purpose is sequential  $S_N2$  reactions of the anion of active methylene compounds (**1**),<sup>1-4</sup> arising from the reactivity and commercial availability of the compounds. However, these reactions often resulted in low yield due to overreaction to give symmetrically-disubstituted products,<sup>2</sup> and due to oligomerization of the anion intermediates.<sup>1</sup>

To circumvent this difficulty, the author has chosen a photochemical method<sup>5</sup> instead of uses of strong bases and, as described in Chapter 1 of this dissertation, has succeeded to develop a novel method for  $\alpha$ -monoalkylation of **1**, which proceeds selectively under mild conditions (eq 1).



In this study, the author expanded this strategy to develop three-component coupling reaction,<sup>6</sup> so-called photo-NOCAS (Nucleophile–Olefin Combination, Aromatic Substitution) reaction,<sup>7</sup> to obtain tandem  $\alpha$ -monoalkylation products of **1** in high yields (eq. 2).





## 3.2. Results and Discussion

### 3.2.1. Three-Component Coupling Reaction of Dicyanobenzenes

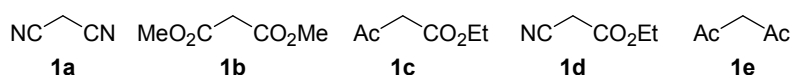
#### 3.2.1.1. Photochemical Reactions

Photoirradiation of an aqueous acetonitrile solution containing **1a**, 2,5-dimethylhexa-2,4-diene (**2**), *p*-dicyanobenzene (*p*-DCB), and lithium carbonate in the presence of phenanthrene (Phen)<sup>8</sup> gives tandem  $\alpha$ -monoalkylated propanedinitrile *p*-**3a** in high yield of 84% together with **4a** in 23% yield (Table 1, entry 1). The structure of the photoproduct was determined by its spectral data of <sup>1</sup>H and <sup>13</sup>C NMR, MS, HRMS, and IR. Much higher yields (up to 96%) are obtained when heavier alkali metal carbonates are used in this process (entries 2 and 3). A similar reaction with *o*-DCB affords *o*-**3a** in modest yield (entry 5), but the *meta* analogue *m*-DCB does not undergo this NOCAS type reaction to produce *m*-**3a** (entry 7). It should be noted that these reactions occur in the absence of the mediator Phen but the yield of *o*-**3a** is lower in this case (entries 4, 6, and 8).

When **1b** and potassium *tert*-butoxide is employed as the substrate and base, respectively, not only are adducts *o*- and *p*-**3b** formed from reactions of the corresponding dicyanobenzenes but *m*-DCB also reacts to form *m*-**3b** (entries 9–11). The use of strong bases also enhances the yields of tandem alkylation reactions of **1c–1e** (entries 12–14).

This tandem three-component reaction not only broadens the synthetic usability of the photochemical  $\alpha$ -monoalkylation method of **1** described in Chapter 1, but enables to accomplish photoinduced cross coupling under mild and safe conditions such as ambient temperature and in the presence of water and weak base, employing cyano

**Chart 1.** Active Methylene Compounds (**1a–1e**)



**Table 1.** Three-Component Photoreaction of **1**, **2**, and DCBs

Reaction scheme:  $\text{EWG}_1\text{CH}_2\text{EWG}_2 + \text{2} + \text{DCB (o, m, p-)} \xrightarrow[\text{conditions}^a]{h\nu} \text{3a-3e (o, m, p-)} + \text{4a-4e}$

entry	active methylene compound	dicyanobenzene	sensitizer	carbonate	products (yields <sup>b</sup> / %)	
1	<b>1a</b>	<i>p</i> -DCB	Phen	Li <sub>2</sub> CO <sub>3</sub>	<i>p</i> - <b>3a</b> (84)	<b>4a</b> (23)
2				Na <sub>2</sub> CO <sub>3</sub>	(87)	(25)
3				K <sub>2</sub> CO <sub>3</sub>	(96)	(25)
4				Na <sub>2</sub> CO <sub>3</sub>	(87)	(26)
5		<i>o</i> -DCB	Phen		<i>o</i> - <b>3a</b> (52)	(37)
6			none		(38)	(45)
7		<i>m</i> -DCB	Phen		<i>m</i> - <b>3a</b> (0)	(47)
8			none		(0)	(46)
9 <sup>c</sup>	<b>1b</b>	<i>p</i> -DCB	Phen	KO- <i>t</i> -Bu	<i>p</i> - <b>3b</b> (76)	<b>4b</b> (35)
10 <sup>c</sup>		<i>o</i> -DCB			<i>o</i> - <b>3b</b> (47)	(38)
11 <sup>c</sup>		<i>m</i> -DCB			<i>m</i> - <b>3b</b> (13)	(30)
12	<b>1c</b>	<i>p</i> -DCB	Phen	NaOH	<i>p</i> - <b>3c</b> (97)	<b>4c</b> (32)
13 <sup>c</sup>	<b>1d</b>	<i>p</i> -DCB	Phen	KO- <i>t</i> -Bu	<i>p</i> - <b>3d</b> (73)	<b>4d</b> (31)
14	<b>1e</b>	<i>p</i> -DCB	Phen	NaOH	<i>p</i> - <b>3e</b> (76)	<b>4e</b> (22)

<sup>a</sup> Conditions: 300-W high-pressure mercury lamp, Pyrex filter, **1** (2.5 mmol), **2** (75 μmol), dicyanobenzene (25 μmol), sensitizer (25 μmol), base (1.25 mmol), in MeCN (4 mL)–H<sub>2</sub>O (1 mL), under Ar, rt, 20 h. <sup>b</sup> Determined by <sup>1</sup>H NMR based on the amount of dicyanobenzene (for **3**) and **2** (for **4**) used. <sup>c</sup> In dry MeCN (5 mL).

group as a leaving group. While cleavage of carbon–cyano bond is highlighted during recent years but still a challenging task,<sup>7,9,10</sup> this noble metal-free photoreaction offers a novel methodology of activating aryl–cyano bonds. Besides, this is a rare example of introducing carbon nucleophile in photoinduced electron transfer (PET) reaction, except that of cyanide ion.<sup>6,11</sup>

### 3.2.1.2. Plausible Mechanism

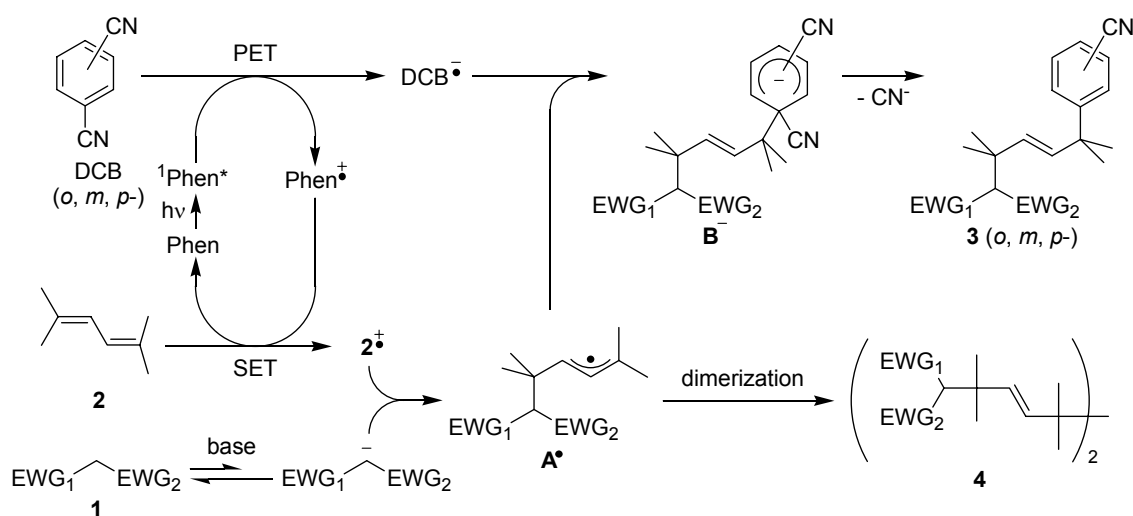
The author proposes that the reaction is promoted by single electron transfer (SET)

from the excited singlet state of Phen ( $^1\text{Phen}^*$ ) to DCB, followed by secondary SET from **2** to  $\text{Phen}^{++}$  (Scheme 1).<sup>8</sup> SET from Phen or **2** to  $^1\text{DCB}^*$  can also take place. These processes afford  $\mathbf{2}^{++}$ , which is trapped by the anion of **1** to form an allylic radical intermediate  $\mathbf{A}^\cdot$ . A competitive pathway can involve SET from the anion of **1** to  $\text{Phen}^{++}$ , which is followed by a coupling of the resulting radical with **2** to form  $\mathbf{A}^\cdot$ , as described in Chapter 1 of this dissertation.

Radical coupling between  $\mathbf{A}^\cdot$  and  $\text{DCB}^-$  takes place to give an anion intermediate  $\mathbf{B}^-$ . Stabilization of the anion charge of  $\mathbf{B}^-$  by a cyano group on *ortho*- or *para*-position of the former benzene ring is crucial for the smooth progression of the radical coupling. Elimination of cyanide ion from *ipso*-position of  $\mathbf{B}^-$  regenerates the aromaticity of the benzene ring to afford three-component coupling product **3**.<sup>7</sup> If  $\mathbf{A}^\cdot$  diffuses out of solvent cage, it dimerizes regioselectively at its terminal position to produce **4**.

The third competitive pathway for the consumption of  $\mathbf{A}^\cdot$  is the BET from  $\text{DCB}^-$ , but the resulting anion  $\mathbf{A}^-$  dissociates spontaneously ( $\Delta G^\ddagger \sim 2$  kcal/mol by HF/3-21G) to form the starting materials (i.e., anion of **1** and **2**).

**Scheme 1.** Plausible Mechanism for the Formation of **3** and **4**



### 3.2.2. Three-Component Coupling Reaction of 1,2,4,5-Tetracyanobenzene

#### 3.2.2.1. Photochemical Reactions

Not a monosubstituted product **5a** but a 1,3-disubstituted one **6a** is obtained in 18% yield when 1,2,4,5-tetracyanobenzene (TCNB) is employed instead of DCB in the photoreaction in the presence of lithium carbonate (Table 2, entry 1). This fact means that TCNB undergoes the three-component coupling twice; that is, the first coupling among **1a**, **2**, and TCNB leads to the primary product **5a**, which is rapidly consumed by the second regioselective coupling reaction with **1a** and **2** to form **6a**. The yield of **6a** increases (up to 56%) by uses of heavier alkali metal carbonates (entries 2 and 3).

**Table 2.** Three-Component Photoreaction of **1a**, **2**, and TCNB

**1a** + **2** +  $\xrightarrow[\text{conditions}^a]{h\nu}$  **5a** + **6a** + **4a**

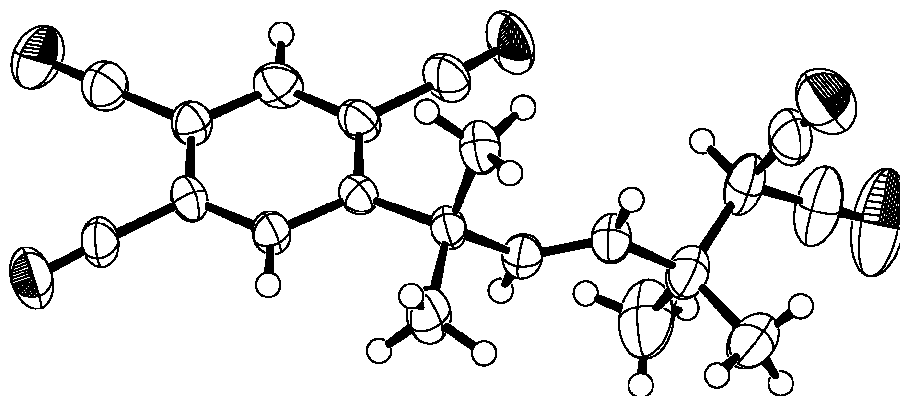
entry	sensitizer	carbonate	yields <sup>b</sup> / %		
			<b>5a</b>	<b>6a</b>	<b>4a</b>
1	Phen	Li <sub>2</sub> CO <sub>3</sub>	0	18	36
2		Na <sub>2</sub> CO <sub>3</sub>	0	46	27
3		K <sub>2</sub> CO <sub>3</sub>	0	56	25
4	none	K <sub>2</sub> CO <sub>3</sub>	84	0	15

<sup>a</sup> Conditions: 300-W high-pressure mercury lamp, Pyrex filter, **1a** (2.5 mmol), **2** (75 μmol), TCNB (25 μmol), sensitizer (25 μmol), carbonate (1.25 mmol), in MeCN (4 mL)–H<sub>2</sub>O (1 mL), under Ar, rt, 20 h.

<sup>b</sup> Determined by <sup>1</sup>H NMR based on the amount of TCNB (for **5a** and **6a**) and **2** (for **4a**) used.

The primary photoproduct **5a** can be obtained (84%) along with **4a** (15%) in the absence of Phen. This result and that of *o*-**3a** described above (Table 1, entries 5 and 6) indicate that Phen acts as a reaction accelerator by mediating the electron transfer (acting as a redox photosensitizer or a co-sensitizer)<sup>8</sup> to suppress back electron transfer (BET) deactivation process.

The structures of all the photoproducts were determined by using their spectral data. An X-ray crystallographic analysis was also performed for a single crystal of **5a** to confirm its structure (Figure 1). The disubstituted product **6a** was determined as 1,3-disubstituted regioisomer since two resonances appeared in the aromatic region of its <sup>1</sup>H-NMR spectrum, while only one identical proton is expected for each of other possible regioisomers (i.e., 1,2- and 1,4-products).



**Figure 1.** ORTEP diagram for **5a**

#### 3.2.2.2. Plausible Mechanism

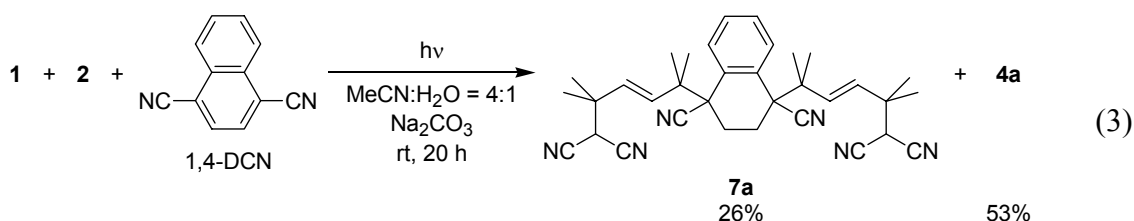
From the above-mentioned results, it is estimated that both primary and secondary photoreaction for TCNB proceeds in a similar manner as that for DCB (Scheme 1). The regioselectivity for the second substitution can be explained by the existence of charge-stabilizing cyano group on *para*-position of the reaction site, and the steric hindrance around the reaction center.

### 3.2.3. Three-Component Coupling Reaction of Polycyclic Cyanoarenes

#### 3.2.3.1. Photochemical Reactions

The author has also tested the coupling reaction for some  $\pi$ -expanded polycyclic cyanoarenes.

1,4-Dicyanonaphthalene (1,4-DCN) does not undergo substitution reaction but partially loses its aromaticity upon photoirradiation to afford a tetralin derivative **7a** in 26% yield (eq. 3). Only dual adduct **7a** is obtained in the reaction. In this case, in contrary to the observation for the reaction of TCNB, monoadduct is never obtained even in the absence of Phen. This can be attributed to the highly reactive nature of  $\alpha$ -cyanostyrene moiety of the monoadduct.<sup>12</sup>



On the other hand, neither substitution nor addition is observed for the photoreaction of 9,10-dicyanoanthracene (9,10-DCA) and 9-cyanophenanthrene, as in the case of *m*-DCB. The former is probably due to the steric hindrance among peri-hydrogens, while the latter might owe to insufficient stability of the corresponding anion intermediate.

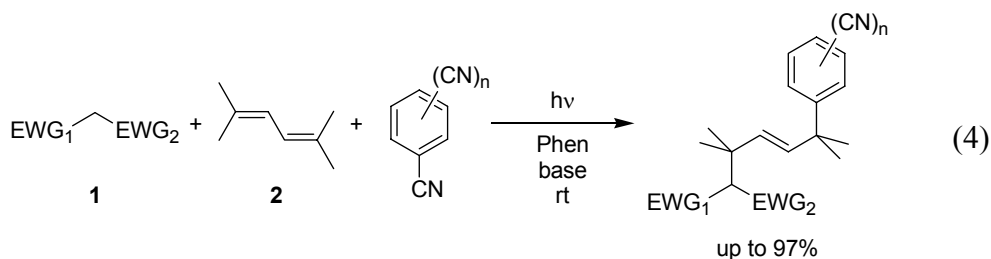
#### 3.2.3.2. Plausible Mechanism

The author estimated that the reaction for 1,4-DCN proceeds in a similar mechanism to that of DCB (Scheme 1), except that the protonation instead of cyanide elimination occurs on the anion intermediate that corresponds to **B**<sup>−</sup>, due to the lower rearomatization energy of the 1,2-dihydronaphthalene ring.

### 3.3. Conclusion

A three-component coupling reaction between **1**, **2**, and polycyanoarenes leading to selective and high-yielding tandem  $\alpha$ -monoalkylation of **1** is developed (eq. 4). The reaction proceeds via photo-NOCAS type mechanism under mild, safe, and environmentally friendly conditions such as ambient temperature, absence of noble metals and halogens, and using a weak base. The author believes that the photoreaction will serve to broaden the synthetic usefulness of the photochemical  $\alpha$ -monoalkylation method of **1**, which is described in Chapter 1 of this thesis.

The reaction also represents a new type of cross-coupling reaction that leads to aryl–cyano bond cleavage in the absence of noble metals. In addition, the reaction is a rare example of introducing carbon nucleophile in PET reaction, except that of cyanide ion.



### 3.4. Experimental Section

#### 3.4.1. General

Experimental instruments are described in Chapter 1.

#### 3.4.2. Materials

2,5-Dimethylhexa-2,4-diene (**2**) was distilled under reduced pressure before use. Preparations and pretreatments of other materials are described in Chapter 1.

#### 3.4.3. Photochemical Reactions

##### Typical Procedure for the Photoreactions (Table 1, entry 3)

To a Pyrex-made glass tube (1 cm $\phi$ ) was added an acetonitrile (4 mL)–water (1 mL) solution containing **1a** (165 mg, 2.5 mmol), **2** (10.7  $\mu$ L, 75  $\mu$ mol), *p*-DCB (3.2 mg, 25  $\mu$ mol), Phen (4.5 mg, 25  $\mu$ mol), and potassium carbonate (132 mg, 1.25 mmol). Argon gas was bubbled through the solution for 5 min in order to reduce molecular oxygen dissolved in, and then the tube was sealed with a rubber septum. After 20-h irradiation by 300-W high-pressure mercury lamp, the reaction mixture was neutralized by the addition of dilute hydrochloric acid and extracted with toluene–diethyl ether for twice. The organic extract was concentrated in vacuo giving a crude mixture, for which a <sup>1</sup>H-NMR analysis was performed using dibromomethane as an internal standard to determine the yields of *p*-**3a** and **4a** as 96 and 25%, respectively. Purification by silica gel chromatography (ethyl acetate after toluene) then HPLC (GPC column, chloroform) gave pure *p*-**3a** (colorless oil) and **4** (colorless blocks).

##### 2-[*trans*-4-(4-Cyanophenyl)-1,1,4-trimethylpent-2-enyl]propanedinitrile (*p*-**3a**)

Colorless oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$ =1.39 (s, 6H), 1.44 (s, 6H), 3.56 (s, 1H), 5.50 (d, *J* = 15.9 Hz, 1H), 5.87 (d, *J* = 15.9 Hz, 1H), 7.42 (AA'XX', *J* = 8.7 Hz, 2H), 7.60 (AA'XX', *J* = 8.7 Hz, 2H) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz)  $\delta$ = 25.6 (2C), 28.9 (2C), 36.1, 40.6, 41.6, 110.3, 111.9 (2C), 119.1, 127.2 (2C), 129.6, 132.3 (2C),



141.4, 153.3 ppm; MS ( $\text{EI}^+$ )  $m/z = 277$  (4,  $\text{M}^+$ ), 212 (18,  $\text{M}^+ - \text{CH}(\text{CN})_2$ ), 182 (14), 170 (100,  $\text{M}^+ - \text{CMe}_2\text{CH}(\text{CN})_2$ ), 156 (18); HRMS ( $\text{EI}^+$ ) calcd for  $\text{C}_{18}\text{H}_{19}\text{N}_3$  277.1579, found 277.1572; IR (NaCl) 840, 2228 ( $\text{C}\equiv\text{N}$ ), 2252 (w,  $\text{C}\equiv\text{N}$ ), 2972  $\text{cm}^{-1}$ .

**2-[*trans*-4-(2-Cyanophenyl)-1,1,4-trimethylpent-2-enyl]propanedinitrile  
(*o*-3a)**

Pale brown oil;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta = 1.40$  (s, 6H), 1.58 (s, 6H), 3.66 (s, 1H), 5.49 (d,  $J = 15.9$  Hz, 1H), 5.94 (d,  $J = 15.9$  Hz, 1H), 7.32 (ddd,  $J = 7, 7, 2$  Hz, 1H), 7.50–7.60 (m, 2H), 7.66 (dd,  $J = 7, 2$  Hz, 1H) ppm;  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta = 25.1$  (2C), 29.1 (2C), 35.8, 40.4, 41.6, 111.98, 112.01 (2C), 120.0, 126.8, 127.1, 131.3, 133.0, 135.7, 140.1, 150.9 ppm; MS ( $\text{EI}^+$ )  $m/z = 277$  (2,  $\text{M}^+$ ), 262 (10), 212 (58,  $\text{M}^+ - \text{CH}(\text{CN})_2$ ), 197 (20,  $\text{M}^+ - \text{MeCH}(\text{CN})_2$ ), 182 (19), 170 (100,  $\text{M}^+ - \text{CMe}_2\text{CH}(\text{CN})_2$ ); HRMS ( $\text{EI}^+$ ) calcd for  $\text{C}_{18}\text{H}_{19}\text{N}_3$  277.1579, found 277.1573; IR (NaCl) 766, 1467, 2221 ( $\text{C}\equiv\text{N}$ ), 2252 (w,  $\text{C}\equiv\text{N}$ ), 2972  $\text{cm}^{-1}$ .

**Dimethyl 2-[*trans*-4-(4-cyanophenyl)-1,1,4-trimethylpent-2-enyl]-  
malonate (*p*-3b)**

Colorless oil;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta = 1.25$  (s, 6H, -Me), 1.38 (s, 6H, -Me), 3.39 (s, 1H,  $-\underline{\text{CH}}(\text{CO}_2\text{Me})_2$ ), 3.69 (s, 6H,  $-\text{CO}_2\underline{\text{Me}}$ ), 5.57 (d,  $J = 15.9$  Hz, 1H, olefin), 5.70 (d,  $J = 15.9$  Hz, 1H, olefin), 7.43 (AA'XX',  $J = 8.2$  Hz, 2H, aromatic), 7.58 (AA'XX',  $J = 8.2$  Hz, 2H, aromatic) ppm;  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta = 26.3$  (2C, -Me), 29.1 (2C, -Me), 38.6 ( $4^\circ$ ), 41.2 ( $4^\circ$ ), 52.4 (2C,  $-\text{CO}_2\underline{\text{Me}}$ ), 61.3 ( $-\underline{\text{CH}}(\text{CO}_2\text{Me})_2$ ), 109.8 ( $4^\circ$ ), 119.2 (-CN), 127.2 (2C), 132.0 (2C), 134.1 (olefin), 136.4 (olefin), 154.8 (*ipso*), 168.2 (2C,  $-\underline{\text{CO}}_2\text{Me}$ ) ppm; MS ( $\text{EI}^+$ )  $m/z = 343$  (5,  $\text{M}^+$ ), 264 (24), 212 (40,  $\text{M}^+ - \text{CH}(\text{CO}_2\text{Me})_2$ ), 211 (34,  $\text{M}^+ - \text{CH}_2(\text{CO}_2\text{Me})_2$ ), 196 (69), 173 (49), 170 (100,  $\text{NC-C}_6\text{H}_4\text{-CMe}_2\text{CH=CH}^+$ ); HRMS ( $\text{EI}^+$ ) calcd for  $\text{C}_{20}\text{H}_{25}\text{NO}_4$  343.1784, found 343.1783; IR (NaCl)  $\nu = 1146, 1245, 1735$  ( $\text{C}=\text{O}$ ), 1756 ( $\text{C}=\text{O}$ ), 2227 ( $\text{C}\equiv\text{N}$ ), 2966  $\text{cm}^{-1}$ .

Dimethyl 2-[*trans*-4-(2-cyanophenyl)-1,1,4-trimethylpent-2-enyl]-  
malonate (***o*-3b**)

Colorless oil;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  = 1.27 (s, 6H, -Me), 1.53 (s, 6H, -Me), 3.38 (s, 1H, - $\underline{\text{CH}}(\text{CO}_2\text{Me})_2$ ), 3.66 (s, 6H, - $\text{CO}_2\text{Me}$ ), 5.58 (d,  $J$  = 16.1 Hz, 1H, olefin), 5.74 (d,  $J$  = 16.1 Hz, 1H, olefin), 7.25–7.32 (m, 1H, aromatic), 7.45–7.55 (m, 2H, aromatic), 7.61–7.67 (m, 2H, aromatic) ppm;  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  = 25.8 (2C, -Me), 29.2 (2C, -Me), 38.8 ( $4^\circ$ ), 41.2 ( $4^\circ$ ), 52.3 (2C, - $\text{CO}_2\text{Me}$ ), 61.2 (- $\underline{\text{CH}}(\text{CO}_2\text{Me})_2$ ), 112.1 ( $4^\circ$ ), 119.9 ( $4^\circ$ ), 126.5, 127.0, 132.6, 135.5, 135.8 (olefin), 136.2 (olefin), 152.4 (*ipso*), 168.3 (2C, - $\text{CO}_2\text{Me}$ ) ppm; MS ( $\text{EI}^+$ )  $m/z$  = 343 (12,  $\text{M}^+$ ), 328 (60), 284 (44), 212 (100,  $\text{M}^+ - \text{CH}(\text{CO}_2\text{Me})_2$ ), 196 (80), 170 (63,  $\text{NC-C}_6\text{H}_4\text{-CMe}_2\text{CH=CH}^+$ ); HRMS ( $\text{EI}^+$ ) calcd for  $\text{C}_{20}\text{H}_{25}\text{NO}_4$  343.1784, found 343.1785; IR (NaCl)  $\nu$  = 1146, 1244, 1437, 1735 (C=O), 1757 (C=O), 2221 (C $\equiv$ N), 2968  $\text{cm}^{-1}$ .

Dimethyl 2-[*trans*-4-(3-cyanophenyl)-1,1,4-trimethylpent-2-enyl]-  
malonate (***m*-3b**)

Pale yellow oil;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  = 1.25 (s, 6H, -Me), 1.38 (s, 6H, -Me), 3.38 (s, 1H, - $\underline{\text{CH}}(\text{CO}_2\text{Me})_2$ ), 3.70 (s, 6H, - $\text{CO}_2\text{Me}$ ), 5.56 (d,  $J$  = 16.0 Hz, 1H, olefin), 5.69 (d,  $J$  = 16.0 Hz, 1H, olefin), 7.39 (dd,  $J$  = 7.8, 7.7 Hz, 1H, 5-position), 7.47 (ddd,  $J$  = 7.7, 1.4, 1.4 Hz, 1H), 7.56 (ddd,  $J$  = 7.8, 1.4, 1.4 Hz, 1H), 7.61 (dd,  $J$  = 1.4, 1.4 Hz, 1H, 2-position) ppm;  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  = 26.3 (2C, -Me), 29.2 (2C, -Me), 38.6 ( $4^\circ$ ), 40.8 ( $4^\circ$ ), 52.4 (2C, - $\text{CO}_2\text{Me}$ ), 61.3 (- $\underline{\text{CH}}(\text{CO}_2\text{Me})_2$ ), 112.3 ( $4^\circ$ ), 119.4 (-CN), 129.0, 129.6, 130.2, 131.0, 134.2, 136.5, 150.7 (*ipso*), 168.2 (2C, - $\text{CO}_2\text{Me}$ ) ppm; MS ( $\text{EI}^+$ )  $m/z$  = 343 (8,  $\text{M}^+$ ), 212 (47,  $\text{M}^+ - \text{CH}(\text{CO}_2\text{Me})_2$ ), 196 (43), 173 (47), 170 (100,  $\text{NC-C}_6\text{H}_4\text{-CMe}_2\text{CH=CH}^+$ ), 141 (44); HRMS ( $\text{EI}^+$ ) calcd for  $\text{C}_{20}\text{H}_{25}\text{NO}_4$  343.1784, found 343.1781; IR (NaCl)  $\nu$  = 1145, 1243, 1735 (C=O), 2228 (C $\equiv$ N), 2964  $\text{cm}^{-1}$ .

Ethyl 2-acetyl-6-(4-cyanophenyl)-3,3,6-trimethylhept-4-enoate (***p*-3c**)

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  = 1.21 (s, 3H, -Me), 1.22 (s, 3H, -Me), 1.26 (t,  $J$  =

7.3 Hz, 3H, -CO<sub>2</sub>CH<sub>2</sub>Me), 1.39 (s, 6H, -Me), 2.19 (s, 3H, -Ac), 3.43 (s, 1H, -CH(Ac)CO<sub>2</sub>Et), 4.15 (q, *J* = 7.3 Hz, 2H, -CO<sub>2</sub>CH<sub>2</sub>Me), 5.55 (d, *J* = 16.1 Hz, 1H, olefin), 5.71 (d, *J* = 16.1 Hz, 1H, olefin), 7.43 (AA'XX', *J* = 8.2 Hz, 2H, aromatic), 7.58 (AA'XX', *J* = 8.2 Hz, 2H, aromatic) ppm; <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  = 14.7 (-CO<sub>2</sub>CH<sub>2</sub>Me), 26.4 (-Me), 26.6 (-Me), 29.0 (-Me), 29.1 (-Me), 31.8, 39.0, 41.2, 61.3 (-CO<sub>2</sub>CH<sub>2</sub>Me), 68.7 (-CH(Ac)CO<sub>2</sub>Et), 109.9 (4°), 119.2 (-CN), 127.2 (2C), 132.0 (2C), 132.0 (olefin), 134.4 (olefin), 136.2 (olefin), 154.7 (*ipso*), 168.6 (2C, -C=O), 202.2 (-C(=O)Me) ppm; MS (EI<sup>+</sup>) *m/z* = 341 (0.5, M<sup>+</sup>), 196 (14), 170 (20, NC-C<sub>6</sub>H<sub>4</sub>-CMe<sub>2</sub>CH=CH<sup>+</sup>), 129 (16, <sup>+</sup>CH(Ac)CO<sub>2</sub>Et), 116 (11), 43 (100, Ac<sup>+</sup>); IR (NaCl)  $\nu$  = 1145, 1365, 1717 (C=O), 2227 (C≡N), 2969 cm<sup>-1</sup>.

**Ethyl 2-cyano-6-(4-cyanophenyl)-3,3,6-trimethylhept-4-enoate (*p*-**3d**)**

Pale yellow oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  = 1.26–1.33 (m, 3H, -OCH<sub>2</sub>Me), 1.29 (s, 3H, -Me), 1.30 (s, 3H, -Me), 1.41 (s, 6H, -Me), 3.39 (s, 1H, -CH(CN)CO<sub>2</sub>Et), 4.15–4.29 (m, 2H, -OCH<sub>2</sub>Me), 5.55 (d, *J* = 16.0 Hz, 1H, olefin), 5.69 (d, *J* = 16.0 Hz, 1H, olefin), 7.44 (AA'XX', *J* = 8.8 Hz, 2H, aromatic), 7.59 (AA'XX', *J* = 8.8 Hz, 2H, aromatic) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz)  $\delta$  = 14.6 (-OCH<sub>2</sub>Me), 26.0 (-Me), 26.3 (-Me), 29.0 (2C, -Me), 39.8 (4°), 41.3 (4°), 49.7 (-CH(CN)CO<sub>2</sub>Et), 62.9 (-OCH<sub>2</sub>Me), 110.0 (4°), 115.9 (4°), 119.2 (4°), 127.2 (2C), 131.9 (olefin), 132.2 (2C), 138.5 (olefin), 154.0 (*ipso*), 164.8 (C=O) ppm; MS (EI<sup>+</sup>) *m/z* = 324 (7, M<sup>+</sup>), 212 (17, M<sup>+</sup> - CH(CN)CO<sub>2</sub>Et), 196 (16), 170 (100, M<sup>+</sup> - CMe<sub>2</sub>CH(CN)CO<sub>2</sub>Et), 156 (20), 116 (16); HRMS (EI<sup>+</sup>) calcd for C<sub>20</sub>H<sub>24</sub>N<sub>2</sub>O<sub>2</sub> 324.1838, found 324.1812; IR (NaCl)  $\nu$  = 1251, 1741 (C=O), 2227 (C≡N), 2972 cm<sup>-1</sup>.

***trans,trans*-2,11-Dicyano-3,3,6,6,7,7,10,10-octamethyldodeca-4,8-dienedinitrile (**4a**)**

Colorless blocks, mp 111–112 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  = 1.00 (s, 12H), 1.36 (s, 12H), 3.61 (s, 2H), 5.36 (d, *J* = 15.8 Hz, 2H, olefin), 5.80 (d, *J* = 15.8 Hz, 2H,

olefin) ppm;  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  = 23.4 (4C), 25.9 (4C), 35.9 (2C), 40.8 (2C), 41.5 (2C), 112.3 (4C, -CN), 129.8 (2C, olefin), 140.1 (2C, olefin) ppm; MS ( $\text{EI}^+$ )  $m/z$  = 175 (39,  $\text{M}^+/2$ ), 110 (100,  $\text{M}^+/2 - \text{CH}(\text{CN})_2$ ), 109 (35,  $\text{M}^+/2 - \text{CH}_2(\text{CN})_2$ ), 95 (30,  $\text{M}^+/2 - \text{MeCH}(\text{CN})_2$ ); MS ( $\text{CI}^+$ )  $m/z$  = 351 (5,  $[\text{M}+\text{H}]^+$ ), 203 (5), 175 (100,  $\text{M}^+/2$ ), 137 (11), 111 (12), 110 (30,  $\text{M}^+/2 - (\text{NC})_2\text{CH}$ ), 109 (8,  $\text{M}^+/2 - (\text{NC})_2\text{CH}_2$ ), 83 (6); HRMS ( $\text{CI}^+$ ) calcd for  $\text{C}_{22}\text{H}_{31}\text{N}_4$  ( $[\text{M}+\text{H}]^+$ ) 351.2549, found 351.2555; IR (NaCl)  $\nu$  = 800, 1019, 1093, 1261, 1459, 2238 (w,  $\text{C}\equiv\text{N}$ ), 2252 (w,  $\text{C}\equiv\text{N}$ ), 2928, 2968  $\text{cm}^{-1}$ ; Anal. calcd for  $\text{C}_{22}\text{H}_{30}\text{N}_4$ : C, 75.39; H, 8.63; N, 15.98. Found: C, 75.15; H, 8.47; N, 15.86.

Crystallographic data: monoclinic,  $P2_1/n$  (#14),  $Z = 2$ ,  $R = 0.0905$ ,  $R_w = 0.1121$ ,  $a = 6.305(3)$ ,  $b = 26.491(18)$ ,  $c = 6.608(4)$  Å,  $\beta = 99.89(3)^\circ$ ,  $V = 1087.4(10)$  Å<sup>3</sup>,  $D_{\text{calcd}} = 1.070$  g/cm<sup>3</sup>.

**Dimethyl *trans,trans*-2,11-bis(methoxycarbonyl)-3,3,6,6,7,7,10,10-octamethyldodeca-4,8-dienedioate (**4b**)**

Pale brown oil;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  = 0.89 (s, 12H), 1.23 (s, 12H), 3.36 (s, 2H,  $-\text{CH}(\text{CO}_2\text{Me})_2$ ), 3.68 (s, 12H,  $-\text{CO}_2\text{Me}$ ), 5.45 (d,  $J = 16.1$  Hz, 2H, olefin), 5.49 (d,  $J = 16.1$  Hz, 2H, olefin) ppm;  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  = 23.5 (4C,  $1^\circ$ ), 26.3 (4C,  $1^\circ$ ), 38.9 (2C,  $4^\circ$ ), 40.9 (2C,  $4^\circ$ ), 52.4 (4C,  $-\text{CO}_2\text{Me}$ ), 61.4 (2C,  $-\text{CH}(\text{CO}_2\text{Me})_2$ ), 133.8 (2C, olefin), 135.8 (2C, olefin), 168.4 (4C, C=O) ppm; MS ( $\text{EI}^+$ )  $m/z$  = 241 (41,  $\text{M}^+/2$ ), 209 (10,  $\text{M}^+/2 - \text{MeOH}$ ), 183 (17), 177 (26), 149 (13), 121 (28), 110 (19,  $\text{M}^+/2 - \text{CH}(\text{CO}_2\text{Me})_2$ ), 109 (100,  $\text{M}^+/2 - \text{CH}_2(\text{CO}_2\text{Me})_2$ ), 101 (10), 95 (12,  $\text{M}^+/2 - \text{MeCH}(\text{CO}_2\text{Me})_2$ ); HRMS ( $\text{EI}^+$ ) calcd for  $\text{C}_{13}\text{H}_{21}\text{O}_4$  ( $\text{M}^+/2$ ) 241.1440, found 241.1435; IR (NaCl)  $\nu$  = 1142 (C-O), 1243, 1736 (C=O), 1758 (C=O), 2967  $\text{cm}^{-1}$ .

**Diethyl *trans,trans*-2,11-diacetyl-3,3,6,6,7,7,10,10-octamethyldodeca-4,8-dienedioate (**4c**)**

Light yellow oil;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  = 0.91 (s, 12H), 1.19 (s, 6H), 1.20 (s, 6H), 1.26 (t,  $J = 7.1$  Hz, 6H,  $-\text{CO}_2\text{CH}_2\text{Me}$ ), 2.19 (d,  $J = 0.3$  Hz, 6H, -Ac), 3.41 (brs,

2H, -CH(Ac)CO<sub>2</sub>Et), 4.15 (q,  $J = 7.1$  Hz, 4H, -CO<sub>2</sub>CH<sub>2</sub>Me), 5.46 (d,  $J = 17$  Hz, olefin), 5.52 (d,  $J = 17$  Hz, olefin) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz)  $\delta = 14.7$  (2C, -CO<sub>2</sub>CH<sub>2</sub>Me), 23.4 (2C), 23.6 (2C), 26.5 (4C), 32.0 (2C), 39.3 (2C), 41.0 (2C), 61.3 (2C), 68.9 (2C), 133.9 (2C, olefin), 135.6 (2C, olefin), 168.8 (2C, -CO<sub>2</sub>Et), 202.9 (2C, -C(=O)Me) ppm; MS (EI<sup>+</sup>)  $m/z = 239$  (42, M<sup>+</sup>/2), 121 (47), 110 (67, M<sup>+</sup>/2 - CH(Ac)CO<sub>2</sub>Et), 109 (100, M<sup>+</sup>/2 - CH<sub>2</sub>(Ac)CO<sub>2</sub>Et), 95 (77, M<sup>+</sup>/2 - MeCH(Ac)CO<sub>2</sub>Et), 67 (99); HRMS (EI<sup>+</sup>) calcd for C<sub>14</sub>H<sub>23</sub>O<sub>3</sub> (M<sup>+</sup>/2) 239.1647, found 239.1649; IR (NaCl)  $\nu = 1142, 1366, 1718$  (C=O), 1734 (C=O), 2973 cm<sup>-1</sup>.

**Diethyl *trans,trans*-2,11-dicyano-3,3,6,6,7,7,10,10-octamethyldodeca-4,8-dienedioate (4d)**

Mixture (1:1) of *dl*- and *meso*-isomers, brown oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta = 0.95$  (s, 12H), 1.27 (s, 6H), 1.28 (s, 6H), 1.31 (dd,  $J = 7.1, 7.1$  Hz, 6H, -OCH<sub>2</sub>Me), 3.367 (s, 2H, -CH(CN)CO<sub>2</sub>Et, an isomer), 3.373 (s, 2H, -CH(CN)CO<sub>2</sub>Et, the other isomer), 4.20 (dq,  $J = 10.9, 7.1$  Hz, 2H, -OCH<sub>2</sub>Me, an isomer), 4.23 (dq,  $J = 10.9, 7.1$  Hz, 2H, -OCH<sub>2</sub>Me, the other isomer), 5.37 (d,  $J = 16.1$  Hz, 2H, olefin), 5.64 (d,  $J = 16.1$  Hz, 2H, olefin) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz)  $\delta = 14.6$  (2C, -OCH<sub>2</sub>Me), 23.41 (2C, 1°, isomer A), 23.46 (2C, 1°, isomers A and B), 23.50 (2C, 1°, isomer B), 26.2 (2C, 1°), 26.4 (2C, 1°), 39.9 (2C, 4°), 41.2 (2C, 4°), 49.6 (2C, -CH(CN)CO<sub>2</sub>Et), 62.7 (2C, -OCH<sub>2</sub>Me), 116.1 (2C, -CN), 131.7 (2C, olefin), 137.7 (2C, olefin), 165.0 (2C, C=O) ppm; MS (EI<sup>+</sup>)  $m/z = 222$  (45, M<sup>+</sup>), 176 (12, M<sup>+</sup> - EtOH), 148 (11), 110 (29, M<sup>+</sup> - CH(CN)CO<sub>2</sub>Et), 109 (100, M<sup>+</sup> - CH<sub>2</sub>(CN)CO<sub>2</sub>Et), 95 (13, M<sup>+</sup> - MeCH(CN)CO<sub>2</sub>Et); HRMS (EI<sup>+</sup>) calcd for C<sub>13</sub>H<sub>20</sub>O<sub>2</sub>N (M<sup>+</sup>/2) 222.1494, found 222.1472; IR (NaCl)  $\nu = 1037, 1189$  (C-O), 1250 (C-O), 1370, 1467, 1742 (C=O), 2247 (w, C≡N), 2973 cm<sup>-1</sup>.

***trans,trans*-3,12-Diacetyl-4,4,7,7,8,8,11,11-octamethyltetradeca-5,9-diene-2,13-dione (4e)**

Colorless oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta = 0.92$  (s, 12H), 1.16 (s, 12H), 2.18 (d,

$J = 0.4$  Hz, 12H, -Ac), 3.72 (brs, 2H, -CHAc<sub>2</sub>), 5.45 (d,  $J = 16.2$  Hz, 2H, olefin), 5.52 (d,  $J = 16.2$  Hz, 2H, olefin) ppm; <sup>13</sup>C NMR (C<sub>6</sub>D<sub>6</sub>, 75 MHz)  $\delta = 23.2$  (4C), 26.2 (4C), 31.8 (4C, -C(=O)Me), 39.4 (2C, 4°), 40.7 (2C, 4°), 75.9 (2C, -CHAc<sub>2</sub>), 134.0 (2C, olefin), 135.0 (2C, olefin), 202.0 (4C, C=O) ppm; MS (EI<sup>+</sup>)  $m/z = 209$  (69, M<sup>+</sup>/2), 149 (46, M<sup>+</sup>/2 - AcOH), 110 (24, M<sup>+</sup>/2 - Ac<sub>2</sub>CH), 109 (100, M<sup>+</sup>/2 - Ac<sub>2</sub>CH<sub>2</sub>), 85 (27); HRMS (EI<sup>+</sup>) calcd for C<sub>13</sub>H<sub>21</sub>O<sub>2</sub> (M<sup>+</sup>/2) 209.1541, found 209.1527; IR (NaCl)  $\nu = 665, 986, 1143, 1355, 1696$  (C=O), 1719, 2967 cm<sup>-1</sup>.

**2-[*trans*-4-(2,4,5-Tricyanophenyl)-1,1,4-trimethylpent-2-enyl]-propanedinitrile (**5a**)**

Colorless block, mp 145.5–146.5 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta = 1.40$  (s, 6H), 1.64 (s, 6H), 3.60 (s, 1H), 5.56 (d,  $J = 16.1$  Hz, 1H), 5.90 (d,  $J = 16.1$  Hz, 1H), 7.97 (s, 1H), 8.05 (s, 1H) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz)  $\delta = 24.5$  (2C), 28.0 (2C), 35.2, 40.0, 41.8, 111.1 (2C), 113.0, 113.8, 114.7, 115.8, 116.9, 119.2, 131.6, 132.9, 137.2, 138.7, 156.3 ppm; MS (EI<sup>+</sup>)  $m/z = 262$  (100, M<sup>+</sup> - CH(CN)<sub>2</sub>), 220 (37, M<sup>+</sup> - CMe<sub>2</sub>CH(CN)<sub>2</sub>); HRMS (EI<sup>+</sup>) calcd for C<sub>20</sub>H<sub>17</sub>N<sub>5</sub> 327.1484, found 327.1465; IR (NaCl) 734, 913, 1467, 2237 (C≡N), 2975 cm<sup>-1</sup>.

Crystallographic data: triclinic, *P*-1 (#2),  $Z = 2$ ,  $R = 0.1031$ ,  $R_w = 0.1023$ ,  $a = 7.923(6)$ ,  $b = 8.614(7)$ ,  $c = 13.850(15)$  Å,  $\alpha = 98.94(4)$ ,  $\beta = 100.46(4)$ ,  $\gamma = 94.32(3)^\circ$ ,  $V = 914.3(13)$  Å<sup>3</sup>,  $D_{\text{calcd}} = 1.189$  g/cm<sup>3</sup>.

**4,6-Bis(*trans*-5,5-dicyano-1,1,4,4-tetramethylpent-2-enyl)-isophthalonitrile (**6a**)**

Colorless solid, mp 151.0–152.5 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta = 1.41$  (s, 12H), 1.61 (s, 12H), 3.64 (s, 2H), 5.54 (d,  $J = 16.1$  Hz, 2H), 5.92 (d,  $J = 16.1$  Hz, 2H), 7.69 (s, 1H), 7.91 (s, 1H) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz)  $\delta = 24.5$  (4C), 28.1 (4C), 35.2 (2C), 39.9 (2C), 41.8 (2C), 110.8 (2C), 111.2 (4C), 117.1 (2C), 124.9, 131.8 (2C), 138.2 (2C), 140.9, 155.0 (2C) ppm; MS (EI<sup>+</sup>)  $m/z = 476$  (4, M<sup>+</sup>), 411 (91, M<sup>+</sup> - CH(CN)<sub>2</sub>), 369 (100,

$M^+ - CMe_2CH(CN)_2$  ; HRMS (FAB<sup>+</sup>) calcd for  $C_{30}H_{33}N_6$  ( $[M+H]^+$ ) 477.2767, found 47.2801; IR (NaCl) 757, 981, 1467, 1596, 2229 (-CN), 2252 (w,  $C\equiv N$ ), 2974  $cm^{-1}$ .

**1,4-Bis(*trans*-5,5-dicyano-1,1,4,4-tetramethylpent-2-enyl)-1,2,3,4-tetrahydronaphthalene-1,4-dicarbonitrile (**7a**)**

Mixture of *dl*- and *meso*-isomers, colorless oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  = 1.16 (s, 6H, minor isomer), 1.23 (s, 6H, major isomer), 1.31 (s, 6H, minor isomer), 1.37 (s, 6H, major isomer), 2.22–2.30 (m, 2H), 2.38–2.48 (m, 2H), 3.56 (s, 2H), 5.45 (d,  $J$  = 16.1 Hz, 2H), 5.69 (brd,  $J$  = 16.1 Hz, 2H), 7.34–7.42 (m, 2H), 7.68–7.74 (m, 2H) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz)  $\delta$  = 23.5 (2C), 25.1 (4C, major isomer), 25.2 (4C, minor isomer), 27.4 (4C, minor isomer), 28.0 (4C, major isomer), 35.7 (2C), 40.7 (2C), 45.1 (2C), 47.4 (2C), 111.7 (4C, minor isomer), 111.8 (4C, major isomer), 122.7 (2C), 128.3 (2C), 129.8 (2C), 131.2 (2C), 133.4 (2C), 138.6 (2C) ppm; MS (EI<sup>+</sup>, 20 eV)  $m/z$  = 530 (0.2,  $M^+$ ), 356 (9,  $M^+ - CMe_2CH=CHCMe_2CH(CN)_2$ ), 182 (18), 181 (11), 175 (39,  $C^+Me_2CH=CHCMe_2CH(CN)_2$ ), 110 (100,  $(Me_2C=CH-)_2^+$ ), 109 (30); HRMS (FAB<sup>+</sup>) calcd for  $C_{34}H_{39}N_6$  ( $[M+H]^+$ ) 531.3237, found 531.3198; IR (NaCl) 734, 914, 988, 1375, 1396, 1467, 2230 (w,  $C\equiv N$ ), 2254 (w,  $C\equiv N$ ), 2975  $cm^{-1}$ .

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## CHAPTER 4. Spectroscopic and Quantum Chemical Analyses on Enhancement Effect of Magnesium Salts on Photoinduced Electron Transfer Reaction

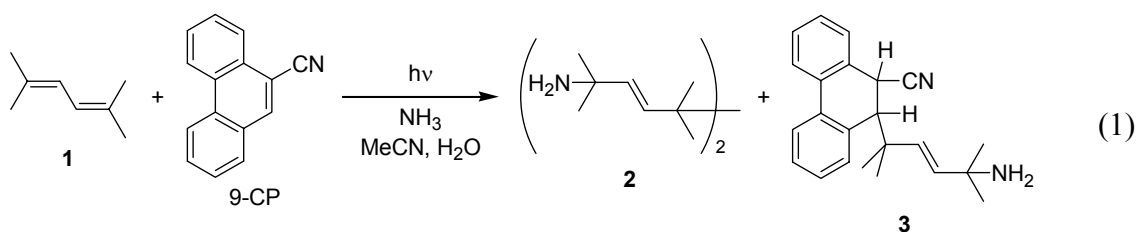
### 4.1. Introduction

Photochemical reactions proceed by way of high-energy intermediates such as electronically excited states, radical ions, and radicals. The highly reactive nature of these species enables some photochemical reactions to occur through thermally forbidden pathways that lead to the construction of highly strained structures. However, these processes are often attended by competitive and secondary reactions, which result in reactant degradation and formation of complex product mixtures.

Much effort has been given to finding ways to improve photoreaction selectivities, especially in the case of electron transfer photochemical reactions. One approach involves the use of additives. An example of this is found in the dramatic improvement seen in the efficiencies and the selectivities of photoinduced electron transfer (PET) reactions brought about by the addition of aromatic hydrocarbons (e.g., phenanthrene and biphenyl) that serve as redox photosensitizers.<sup>1</sup> Specific inorganic metal salts, such as  $\text{Mg}(\text{ClO}_4)_2$ , act as enhancers of charge separation<sup>2</sup> and lead to the improvement of yields and selectivities of various photoreactions.<sup>3</sup> The salts have advantages over organic additives in terms of synthetic applications since they can be easily removed after termination of photoirradiation by using simple extraction techniques. Thus far, charge separation effects of salts have only been investigated by using either spectroscopic approaches or product distribution analyses independently. Studies, in which both mechanistic explorations and product analyses were carried out simultaneously within a single photoreaction system in order to gain a comprehensive understanding of the salt effects, are rare.<sup>4</sup>

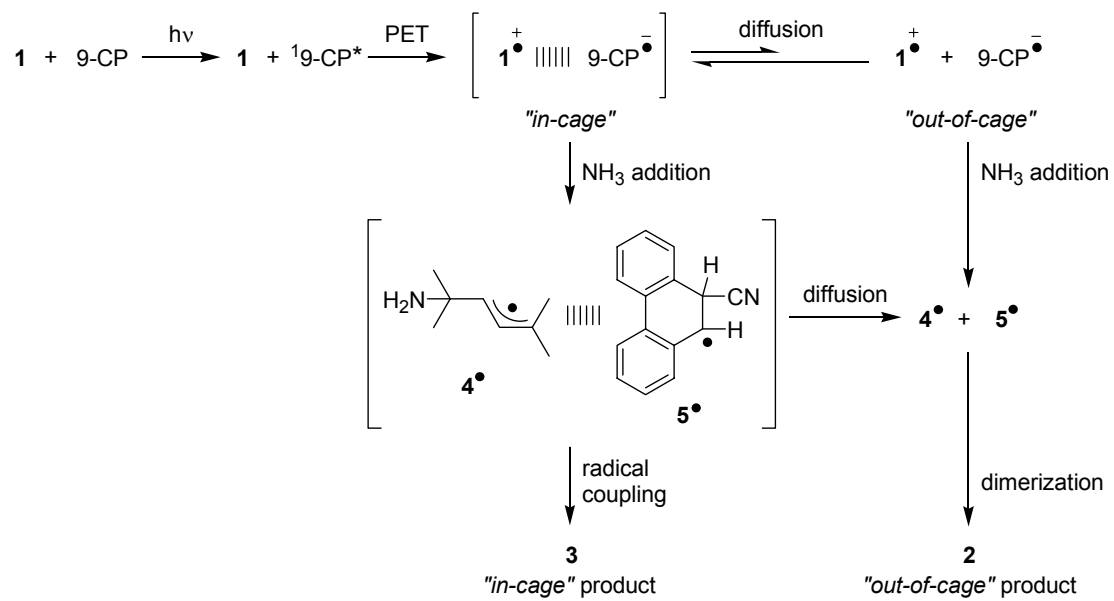
Previously, the author reported in his master's thesis<sup>5</sup> that the photoamination

reaction, promoted by irradiation of an acetonitrile–water solution of ammonia, 2,5-dimethylhexa-2,4-diene (**1**), and 9-cyanophenanthrene (9-CP), leads to formation of the ammonia-incorporated dimer **2**<sup>6</sup> and the three-component adduct **3**<sup>7</sup> (eq. 1). It was proposed that this reaction is initiated by single electron transfer (SET) from **1** to excited singlet state of 9-CP (<sup>1</sup>9-CP\*),<sup>8</sup> giving **1**<sup>•+</sup> which reacts with ammonia to form the allylic radical intermediate **4**<sup>•</sup> (Scheme 1). Diffusion (out-of-cage) and coupling of **4** affords **2**, while radical coupling between **4**<sup>•</sup> and **5**<sup>•</sup> (protonated 9-CP<sup>•-</sup>) within the solvent cage (in-cage) results in production of **3**.



Below, the results of a detailed examination of the effects of additives on the photoamination reaction of **1** are described. In particular, the effects of magnesium salts on the **2:3** product ratio, the fluorescence properties of 9-CP, and transients generated by using nanosecond laser flash photolysis (LFP) were evaluated.

**Scheme 1.** Proposed Mechanism for the Formation of **2** and **3**

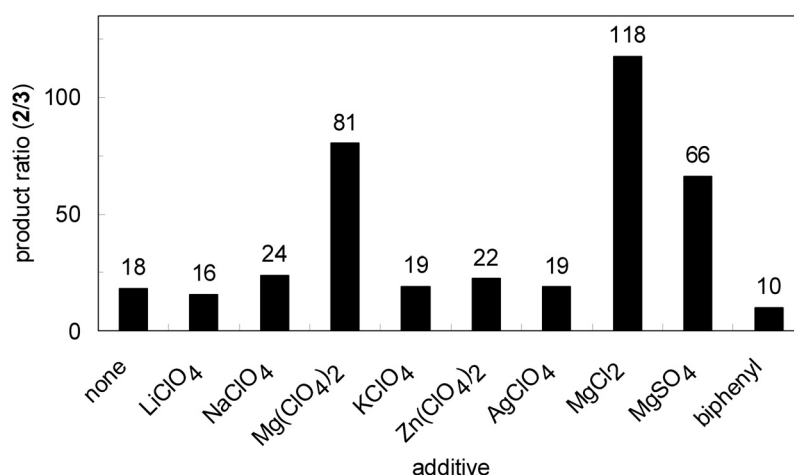


## 4.2. Results and Discussion

### 4.2.1. Improvement of Product Selectivity in the Photoamination Reaction of **1** Caused by $\text{Mg}^{2+}$

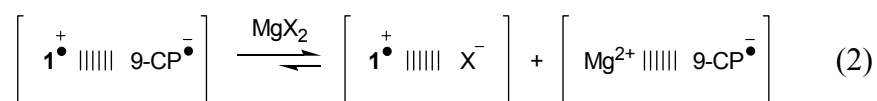
Photoirradiation of an acetonitrile–water (4:1, v/v) solution containing diene **1**, 9-CP and ammonia results in the formation of **2** and **3** in a **2:3** molar ratio of 18:1 (Figure 1).<sup>5</sup> A significant increase in product selectivity (**2:3** = 81:1) that is caused by the suppression of the formation of **3** occurs when  $\text{Mg}(\text{ClO}_4)_2$  is present in the reaction mixture. In contrast, other metal perchlorates ( $\text{LiClO}_4$ ,  $\text{NaClO}_4$ ,  $\text{KClO}_4$ ,  $\text{Zn}(\text{ClO}_4)_2$ , and  $\text{AgClO}_4$ ), do not bring about any notable effects on the **2:3** ratio (16–24:1). Enhancement of the selectivity of the process also takes place when  $\text{MgCl}_2$  and  $\text{MgSO}_4$  (**2:3** = 118:1 and 66:1, respectively) are present. In the case where biphenyl is employed as a redox photosensitizer,<sup>1</sup> a low selectivity of **2:3** = 10:1 is obtained.

The results summarized above indicate that no cation other than  $\text{Mg}^{2+}$  causes an enhancement in the **2:3** product selectivity and that the nature of the counter anion is



**Figure 1.** Effects of additives on photoamination of **1** with  $\text{NH}_3$ . Conditions: 300-W high-pressure mercury lamp, Pyrex filter, **1** (75  $\mu\text{mol}$ ), 9-CP (25  $\mu\text{mol}$ ),  $\text{NH}_3$  (2.5 mmol), additive (2.5  $\mu\text{mol}$ ), in MeCN (4 mL)– $\text{H}_2\text{O}$  (1 mL), under Ar, rt, 20 h. Product ratios were determined by  $^1\text{H}$ -NMR analyses.

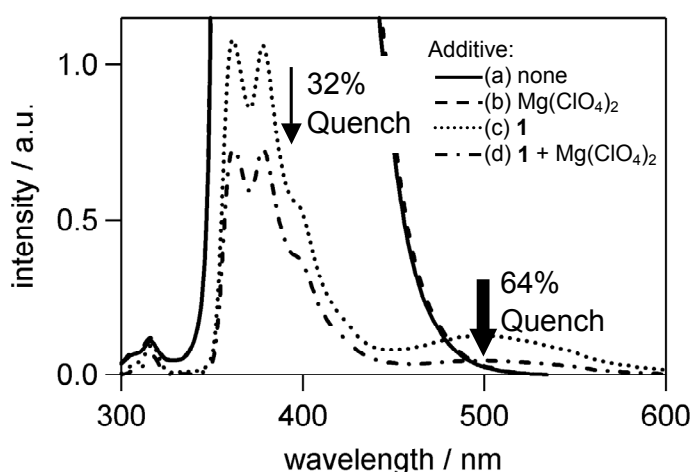
also relevant. In the mechanistic pathway for this process (*vide supra*),<sup>5</sup> coupling between the respective radical cation- and radical anion-derived intermediates **4**<sup>•</sup> and **5**<sup>•</sup> takes place within the solvent cage to produce the “in-cage” product **3**. Based on the observations made, it appears plausible that magnesium salts interfere with the radical coupling process by promoting separation of **1**<sup>•+</sup> and 9-CP<sup>•-</sup> (eq. 2).<sup>2</sup>



#### 4.2.2. Exciplex Quenching Promoted by $\text{Mg}(\text{ClO}_4)_2$

For the purpose of gaining insight into the mechanistic features associated with the effects of magnesium salts, spectroscopic investigations were conducted. Fluorescence spectra of 9-CP in acetonitrile were measured in the absence and presence of  $\text{Mg}(\text{ClO}_4)_2$  and/or **1**. In the absence of the additives, an acetonitrile solution of 9-CP solution contains a fluorescence band with  $\lambda_{\text{max}}$  at 361 and 377 nm (Figure 2a, solid line). No change in this spectrum was observed to occur when  $\text{Mg}(\text{ClO}_4)_2$  was added, indicating that  $\text{Mg}^{2+}$  does not alter the fluorescence properties of 9-CP (Figure 2b, dashed line).<sup>9</sup>

The fluorescence of 9-CP is quenched by diene **1** at a near diffusion controlled rate ( $k_q = 6.1 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ , from a Stern–Volmer analysis<sup>10,11</sup>) and a weak and broad emission ( $\lambda_{\text{max}} \sim 496 \text{ nm}$ ) with an isoemissive point of  $\sim 480 \text{ nm}$  appears simultaneously (Figure 2c, dotted line). The quenching is associated with the formation of an singlet exciplex ( $^1[\text{1}^{\delta+} \cdots 9\text{-CP}^{\delta-}]^*$ ), which decays via three pathways including emission at 496 nm, nonradiative deactivation, and single electron transfer to form a radical ion pair



**Figure 2.** Effects of additives on the fluorescence of 9-CP ( $1.01 \times 10^{-4} \text{ M}$ ) in MeCN ( $\lambda_{\text{ex}} = 311 \text{ nm}$ ). Additive (0.10 M each): (a) none (solid line), (b)  $\text{Mg}(\text{ClO}_4)_2$  (dashed line), (c) **1** (dotted line), (d) **1** and  $\text{Mg}(\text{ClO}_4)_2$  (chain line).

([**1**<sup>•+</sup> ... 9-CP<sup>•-</sup>]).

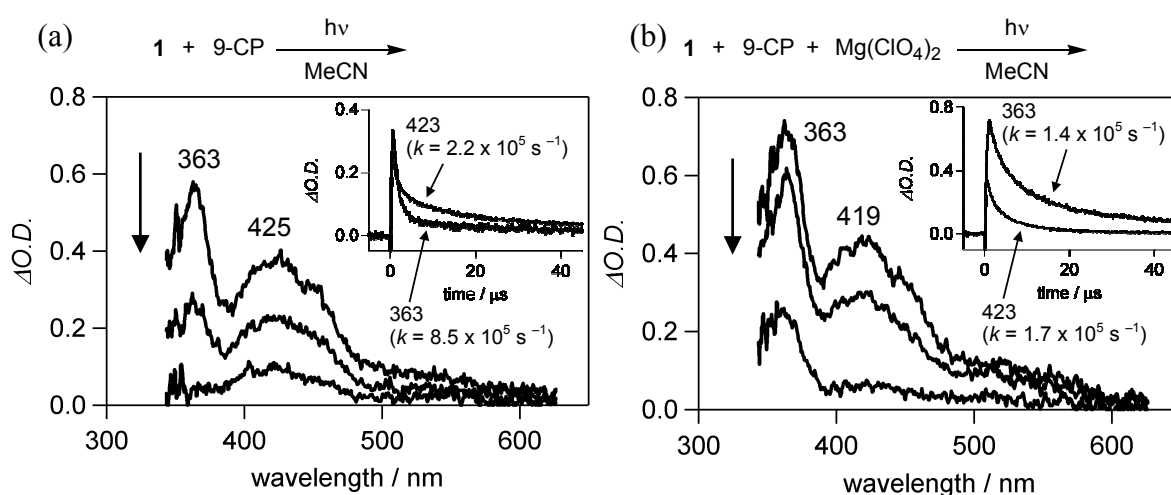
Both the monomer and exciplex emission of a mixture of **1** and 9-CP is diminished by the addition of Mg(ClO<sub>4</sub>)<sub>2</sub> (Figure 2d, chain line).<sup>12</sup> The exciplex emission is more effectively quenched (64% quenching) than the monomer emission (32% quenching). Thus, it appears that Mg<sup>2+</sup> selectively interacts with the exciplex bringing about its decay by enhancing SET. The simultaneous decrease of monomer emission could be due to a shift in the equilibrium from the excited monomer to the exciplex as a result of exciplex consumption.<sup>13</sup>



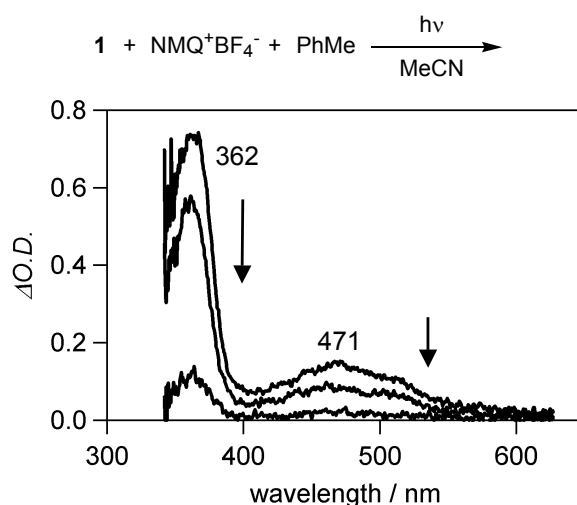
#### 4.2.3. Long-Lived Transient Radical Ion Formation in the Presence of $\text{Mg}(\text{ClO}_4)_2$

The results of LFP experiments show that irradiation of an acetonitrile solution of **1** and 9-CP results in the formation of transients with absorption maxima at 363 ( $k_{\text{decay}} = 8.5 \times 10^5 \text{ s}^{-1}$ ) and 425 ( $2.2 \times 10^5 \text{ s}^{-1}$ ) nm (Figure 3a). A substantial decrease in the rate constant for decay of the former species ( $k_{\text{decay}} = 1.4 \times 10^5 \text{ s}^{-1}$ ) occurs when  $\text{Mg}(\text{ClO}_4)_2$  is present in the solution (Figure 3b).<sup>4,14</sup> On the other hand, decay of the 425-nm band is only slightly changed ( $k_{\text{decay}} = 1.7 \times 10^5 \text{ s}^{-1}$ ) on addition of this salt. Thus,  $\text{Mg}^{2+}$  stabilizes the transient species with the 363-nm absorption maximum, but not the one associated with the 425-nm maximum.

The transient in Figure 3 absorbing at 425 nm might be  $9\text{-CP}^-$ . The 363-nm transient (Figure 3) is assigned to  $\mathbf{1}^{+}$  by using a control LFP experiment with *N*-methylquinolinium tetrafluoroborate ( $\text{NMQ}^+\text{BF}_4^-$ ) as an electron-accepting photosensitizer.<sup>15</sup> Pulsed irradiation of  $\text{NMQ}^+\text{BF}_4^-$  in a solution containing **1** and toluene as a cosensitizer brings about formation of an intense transient absorption band



**Figure 3.** Time-resolved UV-vis absorption spectra of degassed MeCN solutions containing **1** (20 mM) and 9-CP (2 mM) in the (a) absence and (b) presence (0.1 M) of  $\text{Mg}(\text{ClO}_4)_2$  at 0.1, 1.0, and 10.0  $\mu\text{s}$  after LFP ( $\lambda_{\text{ex}} = 355 \text{ nm}$ ). The insets are time profiles at 363 and 423 nm.

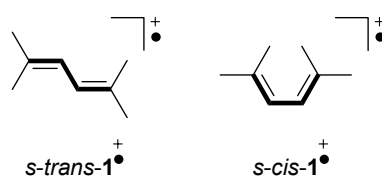


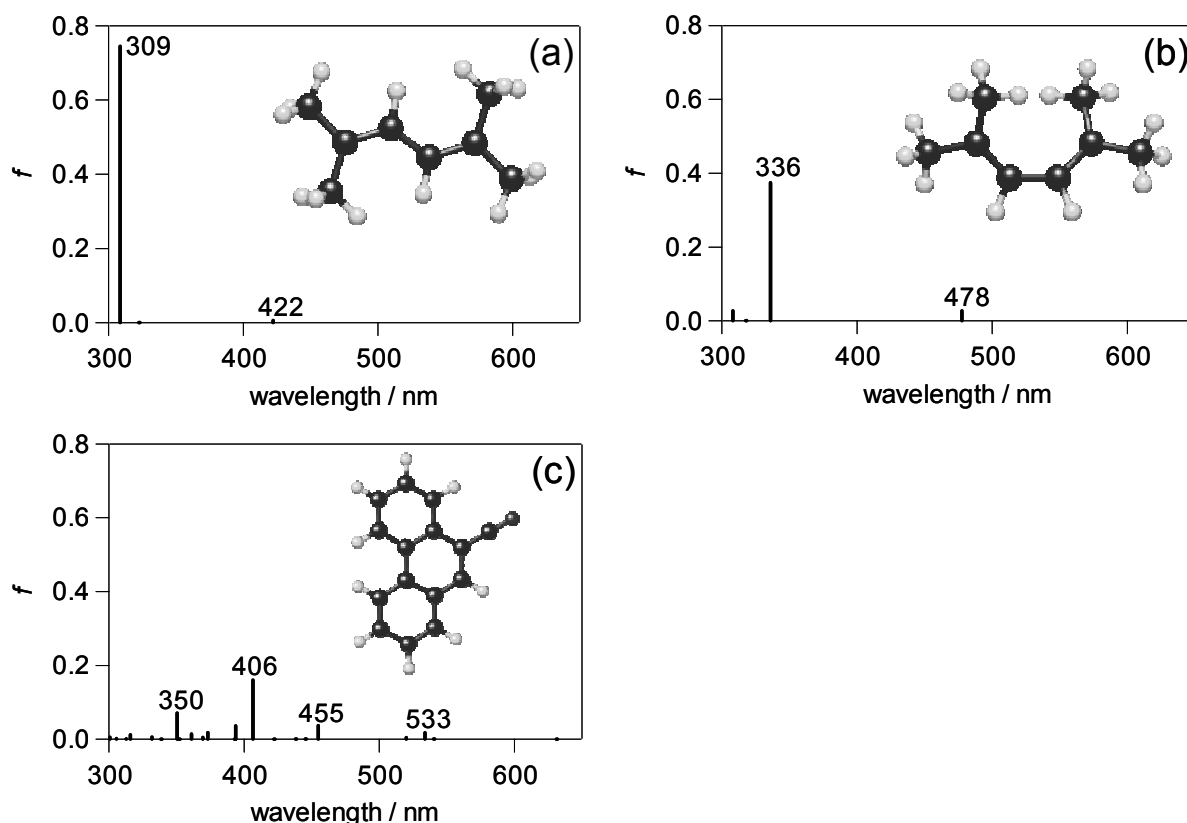
**Figure 4.** Time-resolved UV-vis absorption spectra of an aerated MeCN solution at 0.1, 1.0, and 10.0  $\mu\text{s}$  after LFP ( $\lambda_{\text{ex}} = 355 \text{ nm}$ ). **1** (20 mM),  $\text{NMQ}^+\text{BF}_4^-$  (10 mM), toluene (1 M).

with a maximum of 362 (lit. 365)<sup>16</sup> nm along with a weak and broad transient around 471 (lit. 470)<sup>16</sup> nm (Figure 4).

Support for the assignments of these transients was gained by using TD-DFT (time-dependent density functional theory) calculations (TD-UB3LYP/6-31+G\*). The results of the calculations reveal that electronic transitions should exist at 309 ( $f = 0.74$ ) and 422 (0.01) nm for the optimized structure of **1**<sup>+</sup>, which exists in a *s-trans* conformation (dihedral angle around the central C–C single bond: 179°) (Figure 5a). The calculated absorptions are at far shorter than the 362 and 471 nm transients observed in the LFP studies. A possible explanation for the differences between the experimentally observed and calculated spectra is that **1**<sup>+</sup> possesses a *s-cis*-like

**Chart 1.** Two Possible Conformations of **1**<sup>+</sup>





**Figure 5.** Electronic transition calculated with TD-DFT calculations (TD-UB3LYP/6-31+G\*) of (a) *s-trans*- $\mathbf{1}^{++}$ , (b) *s-cis*- $\mathbf{1}^{++}$ , and (c) 9-CP $^-$ .

conformation in the reaction system, which should have a longer wavelength maxima than *s-trans*- $\mathbf{1}^{++}$  owing to through-space electronic coupling.<sup>17</sup> The transitions for *s-cis*- $\mathbf{1}^{++}$  (dihedral angle: 32°) were calculated to take place at 336 ( $f = 0.37$ ) and 478 (0.03) nm (Figure 5b). The results of a calculation on 9-CP $^-$  reveal that its major electronic transition should correspond to an absorption band at 406 nm ( $f = 0.16$ ), which well supports the assignment made to the 425-nm transient (Figure 5c).

Based on these results, it can be concluded that the lifetime of  $\mathbf{1}^{++}$  is enhanced by the presence of Mg $^{2+}$ , which suppresses back electron transfer (BET) from 9-CP $^-$  to  $\mathbf{1}^{++}$ . The complex [Mg $^{2+} \cdots$  9-CP $^-$ ] formed by the interaction of 9-CP $^-$  with Mg $^{2+}$  possesses a positive charge and, consequently, it should repel  $\mathbf{1}^{++}$  slowing BET. The reason why

only a slight effect was observed for  $\text{Mg}^{2+}$  on  $9\text{-CP}^-$  is uncertain at this point but it may be a result of the fact that the complex  $[\text{Mg}^{2+} \cdots 9\text{-CP}^-]$  has different absorption properties than free  $9\text{-CP}^-$  or that  $\text{Mg}^{2+}$  influences other consumption pathways for  $9\text{-CP}^-$  such as protonation to form **5**.<sup>5</sup>

### 4.3. Conclusion

In this investigation, the author has successfully combined spectroscopic observations and product analysis in developing a comprehensive explanation for the effects of  $\text{Mg}^{2+}$  on the photoamination reaction of diene **1**. A dramatic improvement of the **2:3** product selectivity in this process was achieved by the addition of  $\text{Mg}^{2+}$  salts. Precise analyses of steady-state fluorescence and time-resolved absorption data show that the addition of  $\text{Mg}^{2+}$  causes an enhanced rate of decay of the exciplex  $^1[\mathbf{1}^{\delta+} \cdots 9\text{-CP}^{\delta-}]^*$ , and stabilization of the transient  $\mathbf{1}^{++}$ . A plausible explanation for these effects is that  $\text{Mg}^{2+}$  enhances SET within the exciplex  $^1[\mathbf{1}^{\delta+} \cdots 9\text{-CP}^{\delta-}]^*$  and promotes charge separation of the resulting radical ion pair  $[\mathbf{1}^{++} \cdots 9\text{-CP}^{\cdot-}]$  by interacting with  $9\text{-CP}^{\cdot-}$ . These phenomena lead to increased product selectivity by increasing the amount of the out-of-cage product **2** formed in the reaction.

This study represents one of only a few, in which both spectroscopic and product analyses are used to probe a single photoreaction system. In addition, the effort has provided a rare example where all of the common steps of a single PET reaction, including excited monomer, exciplex, solvent caged and free radical ion formation, are observed in either a direct or indirect manner.

## 4.4. Experimental Section

### 4.4.1. General

LFP experiments were conducted with Continuum Surelight-10 Nd-YAG LASER (the 3rd harmonic generation:  $\lambda_{\text{pulse}} = 355 \text{ nm}$ ) and Unisoku USP-600 detector. Other experimental instruments are described in Chapter 1.

### 4.4.2. Materials

2,5-Dimethylhexa-2,4-diene (**1**) was distilled under reduced pressure before use. Preparations and pretreatments of other materials are described in Chapter 1.

### 4.4.3. Photochemical Reactions

#### Procedure for the Photoirradiation

To a Pyrex glass tube (1 cm $\phi$ ) was added an acetonitrile (4 mL)–water (1 mL) solution containing **1** (8.3 mg, 75  $\mu\text{mol}$ ), 9-CP (5.1 mg, 25  $\mu\text{mol}$ ), ammonia (43 mg, 2.5 mmol), and an additive (metal salt or biphenyl, 25  $\mu\text{mol}$ ). The solution was purged with argon for 5 min and then the tube was sealed with a rubber septum. After irradiation for 20 h by using a 300-W high-pressure mercury lamp, the photolysate was extracted with toluene–diethyl ether. The organic extracts were combined and concentrated in vacuo giving a crude mixture, on which  $^1\text{H}$ -NMR analysis was performed using tetrahydrofuran as an internal standard to determine the yields of **2** and **3**. Purification by silica gel chromatography (ethyl acetate after toluene) followed by HPLC (GPC column, chloroform) gave **2** as brown oil.

#### *trans,trans*-2,5,5,6,6,9-Hexamethyldeca-3,7-diene-2,9-diamine (**2**)<sup>5</sup>

Brown oil;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  = 0.94 (s, 12H, -Me), 1.20 (s, 12H, -Me), 1.6br (s, 4H, -NH<sub>2</sub>), 5.42 (d,  $J$  = 16.1 Hz, 2H, olefin), 5.58 (d,  $J$  = 16.1 Hz, 2H, olefin) ppm;  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  = 23.5 (4C, -Me), 31.4 (4C, -Me), 40.4 (2C, 4), 50.9 (2C, 4), 133.2 (2C, olefin), 137.4 (2C, olefin) ppm; MS ( $\text{EI}^+$ )  $m/z$  = 126 (100,  $\text{M}^+/2$ ), 110 (67,  $\text{M}^+/2 - \text{NH}_2$ ), 109 (56,  $\text{M}^+/2 - \text{NH}_3$ ), 96 (26), 95 (19,  $\text{M}^+/2 - \text{MeNH}_2$ );

IR (NaCl)  $\nu$  = 982, 1590 (H–N–H), 2965, 3285 (N–H), 3355 (N–H)  $\text{cm}^{-1}$ .

10-(*trans*-4-Amino-1,1,4-trimethylpent-2-enyl)-9-cyano-9,10-dihydro-phenanthrene (**3**)<sup>5</sup>

MS ( $\text{EI}^+$ )  $m/z$  = 315 (3,  $\text{M}^+ - \text{Me}$ ), 204 (27,  $\text{M}^+ - \text{CMe}_2\text{CH}=\text{CHCMe}_2\text{NH}_2$ ), 203 (27, 9- $\text{CP}^+$ ), 177 (22), 126 (100,  $\text{H}_2\text{NCMe}_2\text{CH}=\text{CHCMe}_2^+$ ), 110 (24,  $(\text{Me}_2\text{C}=\text{CH-})_2^+$ ), 109 (54).

#### 4.4.4. Results of the Quantum Chemical Calculations ((TD-)UB3LYP/6-31+G\*)

##### *s-trans*-2,5-Dimethylhexa-2,4-diene radical cation (*s-trans*-1<sup>•+</sup>)

atomic symbol	coordinates / Å		
	<i>x</i>	<i>y</i>	<i>z</i>
C	1.900057	−0.010680	−0.005090
C	0.557076	−0.425280	−0.017090
C	−0.557110	0.425273	−0.017090
C	−1.900090	0.010681	−0.005100
C	2.979127	−1.041400	−0.009090
C	2.340072	1.414494	0.022908
C	−2.34010	−1.414490	0.022893
C	−2.97916	1.041401	−0.009110
H	0.390342	−1.499100	−0.020090
H	−0.390370	1.499103	−0.020090
H	2.603111	−2.058250	0.124910
H	3.726061	−0.822730	0.765912
H	3.523910	−0.995730	−0.966090
H	1.553494	2.141647	−0.180090
H	3.159315	1.571516	−0.690090
H	2.761984	1.637566	1.015904
H	−3.15934	−1.571510	−0.690110
H	−2.76202	−1.637570	1.015889
H	−1.55353	−2.141640	−0.180110
H	−3.52294	0.995734	−0.966110
H	−2.60314	2.058257	0.124893
H	−3.72610	0.822736	0.765889

There is no imaginary frequency.  $E = -312.813337$  hartree.  
 $\langle S^2 \rangle = 0.7592$ .  $\lambda_{\text{et}}(f) = 422.18$  (0.0062), 322.49 (0.0004),  
308.58 (0.7444), 289.08 (0.0000), 279.59 (0.0002), 263.39  
(0.0023), 250.20 (0.0022), 241.30 (0.0013), 240.89 (0.0541),  
232.00 (0.0000) nm.



*s-cis*-2,5-Dimethylhexa-2,4-diene radical cation (*s-cis*-1<sup>+</sup>)

atomic symbol	coordinates / Å		
	<i>x</i>	<i>y</i>	<i>z</i>
C	1.664624	−0.066520	−0.074130
C	0.700307	−1.070520	0.092420
C	−0.700310	−1.070510	−0.092420
C	−1.664630	−0.066520	0.074127
C	3.069396	−0.346520	0.348746
C	1.424973	1.233485	−0.767000
C	−1.424970	1.233486	0.767002
C	−3.069390	−0.346520	−0.348750
H	1.109592	−2.057520	0.315591
H	−1.109590	−2.057520	−0.315590
H	3.163707	−1.250520	0.955495
H	3.479107	0.506483	0.904932
H	3.710291	−0.454520	−0.540320
H	0.447623	1.307484	−1.242580
H	2.196940	1.377484	−1.535060
H	1.552551	2.071486	−0.065000
H	−2.196940	1.377487	1.535056
H	−1.552550	2.071486	0.064994
H	−0.447620	1.307486	1.242577
H	−3.710290	−0.454520	0.540325
H	−3.163710	−1.250520	−0.955490
H	−3.479110	0.506483	−0.904930

There is no imaginary frequency.  $E = -312.798080$  hartree.  
 $\langle S^2 \rangle = 0.7598$ .  $\lambda_{\text{et}}(f) = 477.56$  (0.0269), 335.95 (0.3743),  
317.64 (0.0006), 308.23 (0.0272), 288.19 (0.0017), 241.31  
(0.0004), 254.08 (0.0071), 247.63 (0.0064), 245.47 (0.0367),  
239.25 (0.0085) nm.

9-Cyanophenanthrene radical anion (9-CP<sup>-</sup>)

atomic symbol	coordinates / Å		
	<i>x</i>	<i>y</i>	<i>z</i>
C	3.563704	-1.458186	0.000000
C	2.315682	-2.050580	0.000000
C	2.519545	0.728834	0.000000
C	1.109701	-1.272610	0.000000
C	3.684348	-0.052777	0.000000
C	1.234716	0.169879	0.000000
C	-0.154991	-1.877816	0.000000
C	-1.352995	-1.108416	0.000000
C	-1.281660	0.332341	0.000000
C	-2.449785	1.140368	0.000000
C	0.000000	0.981664	0.000000
C	-2.381194	2.527483	0.000000
C	-1.133184	3.165944	0.000000
C	0.027639	2.389737	0.000000
C	-2.605129	-1.757138	0.000000
H	4.458090	-2.081153	0.000000
H	2.224010	-3.136046	0.000000
H	4.662474	0.422768	0.000000
H	0.985541	2.902600	0.000000
H	2.635776	1.809590	0.000000
H	-0.225184	-2.963040	0.000000
H	-3.419139	0.646848	0.000000
H	-3.299189	3.113103	0.000000
H	-1.062526	4.252048	0.000000
N	-3.648322	-2.302726	0.000000

There is no imaginary frequency.  $E = -631.644497$  hartree.  $\langle S^2 \rangle = 0.7623$ .  $\lambda_{\text{et}}(f) = 1524.49$  (0.0046), 788.41 (0.0001), 766.55 (0.0345), 707.47 (0.0007), 631.11 (0.0000), 540.21 (0.0003), 533.86 (0.0176), 520.04 (0.0042), 454.83 (0.0370), 445.26 (0.0003), 437.97 (0.0003), 422.13 (0.0000), 406.55 (0.1601), 393.85 (0.0362), 392.92 (0.0001), 373.19 (0.0178), 369.48 (0.0048), 361.14 (0.0144), 351.85 (0.0000), 350.44 (0.0708), 338.45 (0.0001), 331.74 (0.0057), 315.89 (0.0118), 312.77 (0.0009), 305.62 (0.0020), 300.60 (0.0051), 296.17 (0.0416), 293.62 (0.0651), 293.46 (0.0000), 279.22 (0.0001) nm.

#### 4.5. References and Notes

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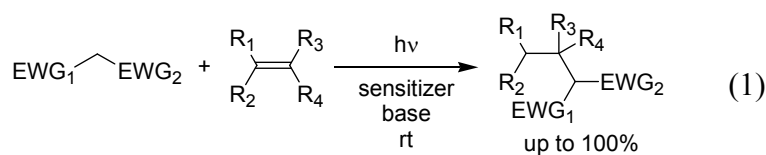
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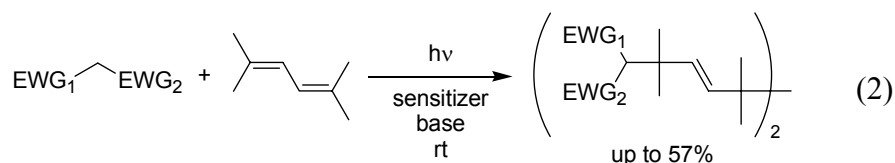
## CONCLUSION

This dissertation dealt with the studies on synthetically useful carbon–carbon bond forming reactions via photoinduced electron transfer. The result was successful: various active methylene compounds such as propanedinitrile (malononitrile), malonate, and cyanoacetate were revealed to react under green and safe photoirradiation conditions. In addition, the reactions developed in the studies are rare examples of introducing carbon nucleophiles in the photoinduced electron transfer reactions, except those of cyanide ion. The author believes that these reactions will serve as a facile synthetic method for the  $\alpha$ -monoalkylation of active methylene compounds. The following are the results obtained in each study.

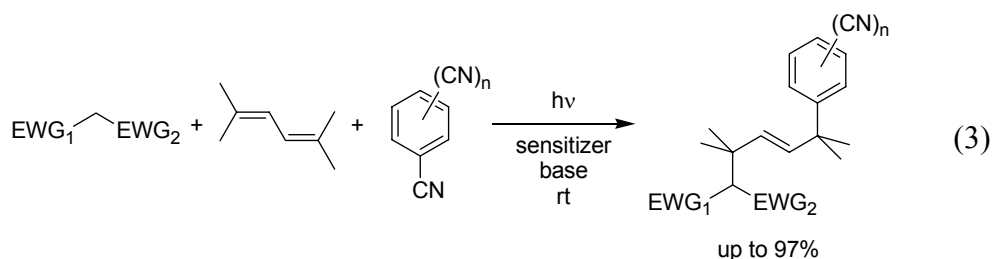
In Chapter 1, the development of a novel synthetic method for the direct  $\alpha$ -monoalkylation of active methylene compounds using photochemical polar addition was described (eq. 1). The enantiodifferentiating reaction was also accomplished by the use of a chiral photosensitizer. It might be synthetically important since it proceeds in safe and environmentally friendly conditions. It also represents the first example in which a carbon nucleophile, other than cyanide anion, is used in PPA process.



In Chapter 2, the use of oxidative photodimerization reaction to synthesize active methylene compounds-incorporated dimers was described (eq. 2). The reaction, which proceeds under mild and safe conditions, might be synthetically useful. It is the first example of introducing carbon nucleophiles, except that of cyanide ion, in oxidative photodimerization reaction.



In Chapter 3, the development of tandem  $\alpha$ -monoalkylation method for active methylene compounds by use of photo-NOCAS type three-component coupling reaction was described (eq. 3). The reaction also represents a new type of cross-coupling reaction that leads to aryl–cyano bond cleavage in the absence of noble metals.



In Chapter 4, the mechanism of the enhancement effects of magnesium salts on the photoinduced electron transfer reaction was described. The author estimated that the mechanism of the effects is that magnesium ion enhances the single electron transfer within the exciplex, and promotes diffusion of the resulted radical ion pair by interacting with the radical anion. This reaction also represents a rare example of observing all of the common steps of a single PET reaction system—excited monomer, exciplex, radical ion pair within the solvent cage, and diffused free radical ions—by some direct and indirect manners.

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## LIST OF PUBLICATIONS

1. "Catalytic Ability of 9-Cyanophenanthrene in Oxidative Photodimerization of 2,5-Dimethyl-2,4-hexadiene"  
Ohashi, M.; Maeda, H.; Mizuno, K. *Chem. Lett.* **2006**, 35, 482–483.
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3. "Photoinduced Tandem Three-Component Coupling of Propanedinitrile, 2,5-Dimethylhexa-2,4-diene, and Cyanoarenes"  
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4. "Selective Photochemical Monoalkylation of Active Methylene Compounds by Alkenes. A Green Pathway for Carbon–Carbon Bond Formation"  
Ohashi, M.; Nakatani, K.; Maeda, H.; Mizuno, K. *Eur. J. Org. Chem.*, submitted for publication.
5. "Effects of Magnesium Salts on Photoinduced Electron Transfer Reaction between Ammonia, 2,5-Dimethyl-2,4-hexadiene, and 9-Cyanophenanthrene"  
Ohashi, M.; Kano, Y.; Ikeda, H.; Mizuno, K. *Tetrahedron*, submitted for publication.