Communications

Intramolecular [2+2] Photocycloaddition and Cycloreversion of Ferulic Acid Derivatives

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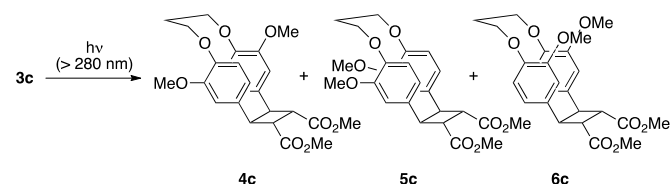
ABSTRACT: Intramolecular photocycloaddition of ferulic acid derivatives proceeded in high yields to give head-to-head intramolecular photodimers as three atropisomers. The photocycloaddition was sensitized by triplet sensitizers such as benzophenone, whereas photocycloreversion was promoted by 9,10-dicyanoanthracene (DCA) as an electron-transfer photocatalyst. On the other hand, intermolecular photocycloaddition afforded a head-to-tail photodimer.

Recently, much attention has been focused on the chemical and biological properties of ferulic acid derivatives including the anti-carcinogenesis and the anti-oxidation.[1] We have recently found a convenient method for the mass production of ferulic acid from the oily component of rice bran, which contribute to the eco chemistry.[2] Ferulic acid (**1**) and its derivatives are expected to be photochemically reactive, because the inter- and intra-molecular photocycloaddition of cinnamic acid and its derivatives have been widely investigated from the synthetic and mechanistic viewpoints. The topochemical intermolecular photocyclodimerization of cinnamic acid in solid states,[3–16] crystalline polymer,[17–19] clay,[20–21] and micells[22–24] are known to give truxllic acids depending on the orientations, but most of cinnamate derivatives in solution did not give or inefficiently afforded [2π+2π] photocycloadducts.[25–30] On the other hand, the intramolecular photocycloaddition of dicinnamates connected by spacers or polycinnamates have proceeded effectively in some cases.[31–38] However, the switching ability of the photocycloadducts including their fluorescence behavior is not clarified yet. We now report an intramolecular [2π+2π] photocycloaddition and an efficient photocycloreversion of the compounds which have two ferulate chromophores.

Compounds **3a-e** in which two ferulic acids were connected by methylene chains were prepared as shown in Scheme 1. Reaction of ferulic acid **1** with Me$_3$SiCl in MeOH gave methyl ferulate **2**, which was allowed to react with CH$_2$Cl$_2$ or Br(CH$_2$)$_n$Br to give substrates **3a-e** for intramolecular photoreaction. All the compounds **3a-e** were solids and purified by recrystallization from toluene or ethyl acetate before use.

Irradiation of a benzene solution containing **3c** (n=3; 5.0 mM) with a 300 W high-pressure Hg lamp through a Pyrex filter (>280 nm) under argon atmosphere for 15 h afforded three types of This photoreaction proceeded in various solvents and it was senstized by triplet sensitizers such as benzophenone. In the benzophenone-sensitized photoreaction in acetonitrile, total yields of **4c-6c** were ca. 80% (about 4 : 1 : 1 ratio) in less than a few hours.

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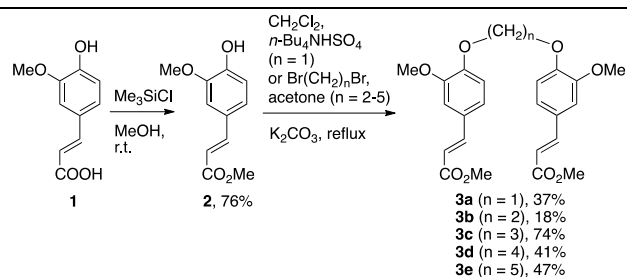
Scheme 1. Preparation of substrates for intramolecular photoreaction.

Scheme 2. Intramolecular photocycloaddition of **3c**.

Table 1. Effect of Solvents and Sensitizers in Intramolecular Photocycloaddition of **3c**.

Solvent	Sensitizer	Time (h)	Isolated Yield (%)			
			4c	**5c**	**6c**	Recovery of **3c**[a]
benzene	none	15	21	3	3	38
benzene	benzophenone	8	(2 : 1 : 1)[b]			0
acetonitrile	benzophenone	4	44	3	2	0
			(50-55 10-15 10-15)[b]			

[a] Mixture of *trans-trans*, *trans-cis*, and *cis-cis* isomers. [b] The ratio and yields were estimated from a mixture by use of ^{1}H NMR.

The photoproducts were isolated by column chromatography on silica gel. Product **4c** has a good crystallized habit but those of **5c** and **6c** are not good, so separation was difficult hence the isolated yields of **5c** and **6c** became relatively low.

The structures of photoproducts were assigned from their spectral properties (^{1}H NMR, ^{13}C NMR, IR, and mass) and elemental analyses. The ^{1}H NMR spectrum of **4c** showed the disappearance of olefinic protons of **3c** and the appearance of four methine protons at 4.1-4.5 ppm. The aromatic protons appeared at the higher field than those of **3c**, which suggested the formation of intramolecular cyclophane-type cycloadduct. Mass spectrum showed the m/z at 456 as an intramolecular cycloadduct. However, the stereochemistry of methoxy groups was not clarified in these analyses. Finally, we have decided the structures of all of these three photocycloadducts by use of X-ray crystallographic analyses. Figure 1 shows the ORTEP drawings of **4c**, **5c**, and **6c**, which clearly demonstrate the cyclophanes having sandwich type structure. For
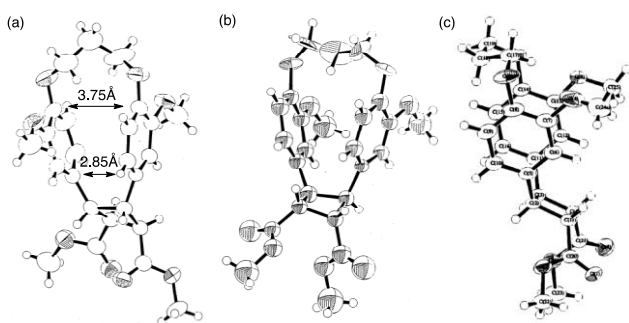
Figure 1. ORTEP drawings of (a) **4c**, (b) **5c**, and (c) **6c**.

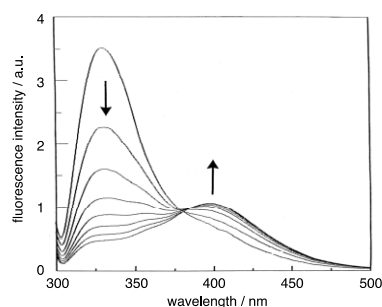**Figure 2.** Change of fluorescence spectrum of **4c** in benzene ($\lambda_{ex} = 290$ nm).

example, the two benzene rings of **4c** locates parallel whose distance of ipso carbons are 2.85 Å (cyclobutane side) and 3.75 Å (methylene side), respectively.

From the structure of **4c** which has sandwich-type overlapping of two benzene rings, appearance of intramolecular excimer emision is expected. However, fluorescence measurement of **4c** in benzene solution exhibited a broad emission spectrum whose maximum is 330 nm, without intramolecular excimer emision (Figure 2). Interestingly, when the fluorescence measurement repeated, intensity of emission at 330 nm decreased with increasing emission whose maximum is 400 nm, with isoemissive point at 380 nm. The emission at 400 nm is corresponded to the fluorescence spectrum of **3c**. The product by irradiation of **4c** was confirmed to be **3c** also by ^{1}H NMR analysis. These results indicate that cycloreversion from **4c** to give **3c** proceeds even by feeble light ($\lambda_{ex} = 290$ nm) emitted from fluorescence spectrophotometer.

Then, the conditions of photocycloreversion form **4c** to **3c** was investigated. As a result, benzophenone-sensitized photocycloreversion from **4c** in acetonitrile hardly proceeded, but 9,10-dicyanoanthracene (DCA)-sensitized photoreaction of **4c** in acetonitrile smoothly proceeded to give **3c**.

Photocycloaddition and cycloreversion can be summarized as shown in Scheme 3. Both photocycloaddition and photocycloreversion proceed efficiently under direct irradiation to benzene solutions containing **3c** or **4c** via excited singlet states. Benzophenone-sensitized photoreaction in acetonitrile proceeds via excited triplet states of **3c** and **4c**. Since triplet energy of **4c** is lower than that of **3c**, photocycloaddition of **3c** to give **4c** occurs faster than photocycloreversion from **4c**. On the other hand, DCA-sensitized photoreaction proceeds via electron-transfer mechanism shown in Scheme 4. Since oxidation potential of **4c** is lower than that of **3c**, the equilibrium between **3c** and **4c** shifts to ring-opening (**3c**), hence photocycloadduct **4c** is almost not obtained.

Next, we compared photoreactions of **3a-e** to examine effect of lengths of methylene chains. Similar irradiation of **3a** (n=1) and **3b** (n=2) in the absence or presence of benzophenone did not afford the corresponding intramolecular photocycloadducts in an appreciable
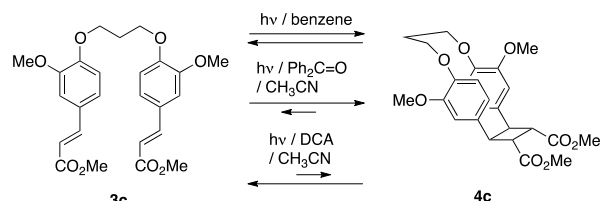

Scheme 3. Reversibility on the photoreaction between **3c** and **4c**.
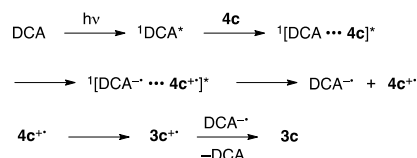

Scheme 4. DCA–sensitized photocycloreversion from **4c**.

amount. On the other hand, irradiation of **3d** (n=4) or **3e** (n=5) gave mixtures containing intramolecular photocycloadducts in comparable amounts with the reaction of **3c**.

Photoreaction of **7** derived from *myo*-inositol,[39] in the presence of benzophenone in benzene or acetonitrile gave the corresponding intramolecular [2π+2π] photocycloadduct **8** as a sole product. The calixarene derivative **9**[40,41] bearing two ferulate derivatives also afforded the intramolecular [2π+2π] photocycloadduct **10** in 43% yield.
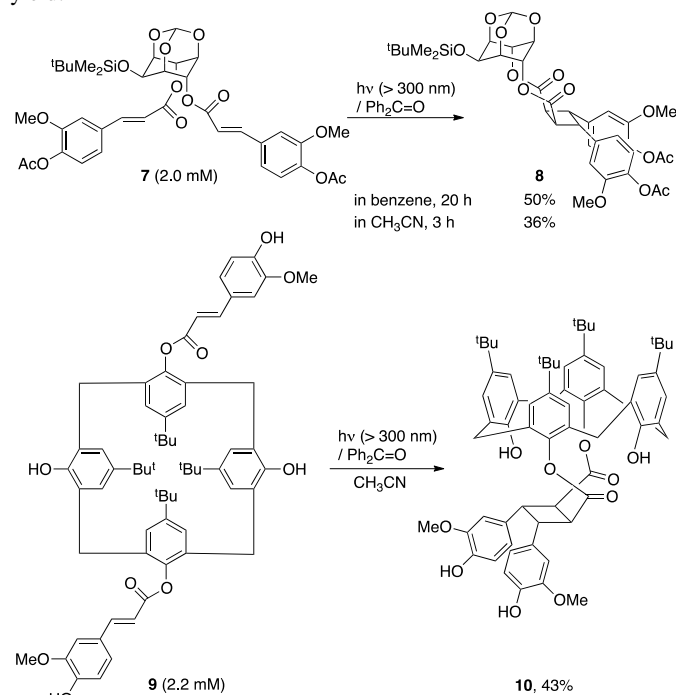

Scheme 5. Intramolecular photocycloaddition of ferulic acid derivatives **7** and **9**.

On the other hand, the intermolecular photocyclodimerization of ethoxy derivative **11**, derived from **2**, occurred to give head-to-tail cycloadduct **12** as a main product (Scheme 6), regardless of the presence or absence of benzophenone. The structure of **12** was characterized by X-ray analysis (Figure 3). In general, photoreaction of cinnamic acid esters in solution only causes *cis-trans* photoisomerization, and cyclobutane derivatives are not obtained.[31–38] The reason why photodimerization of **11** efficiently took place may be the presence of electron-donating substituents on phenyl group.[42]
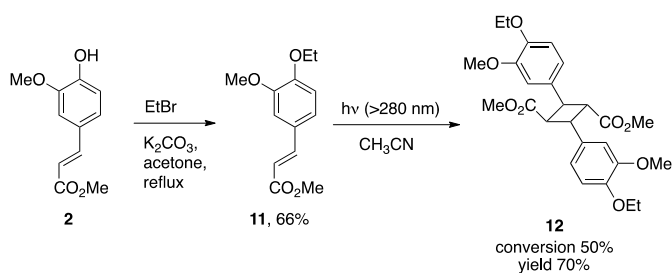
Scheme 6. Intermolecular photodimerization of **11**.
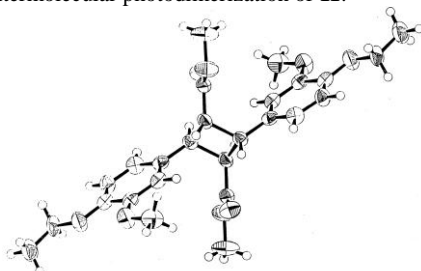
Figure 3. ORTEP drawing of **12**.
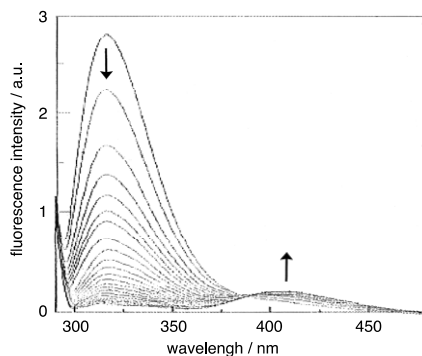
Figure 4. Change of fluorescence spectrum of **12** in acetonitrile (λ_{ex} = 282 nm).

Photocycloreversion from **12** also took place by feeble light from fluorescence spectrophotometer (Figure 4). During the measurement of fluorescence spectrum of **12** in acetonitrile, emission from **12** (λ_{em} = 320 nm) efficiently changed to the fluorescence of **11** (λ_{em} = 410 nm) by incident light (λ_{ex} = 282 nm) accompanied by isoemissive point at 385 nm. Formation of **11** by irradiation to acetonitrile solution of **12** was also confirmed by ^{1}H NMR.

In conclusion, intramolecular photocycloaddition of ferulic acid derivatives efficiently proceeded when length of methylene chains is n = 3–5 to give head-to-head three atropisomers based on orientation of the methoxy groups. On the other hand, intermolecular photodimerization took place to give a head-to-tail photodimer. Benzophenone-sensitized reaction gave photocycloadducts efficiently, whereas DCA-sensitized reaction promoted photocycloreversion. The reversibility depending on irradiation conditions might be useful for photoswitching devices.

REFERENCES AND NOTES
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