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Photoconversion of *o*-hydroxycinnamates to coumarins and its application to fluorescence imaging

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ABSTRACT

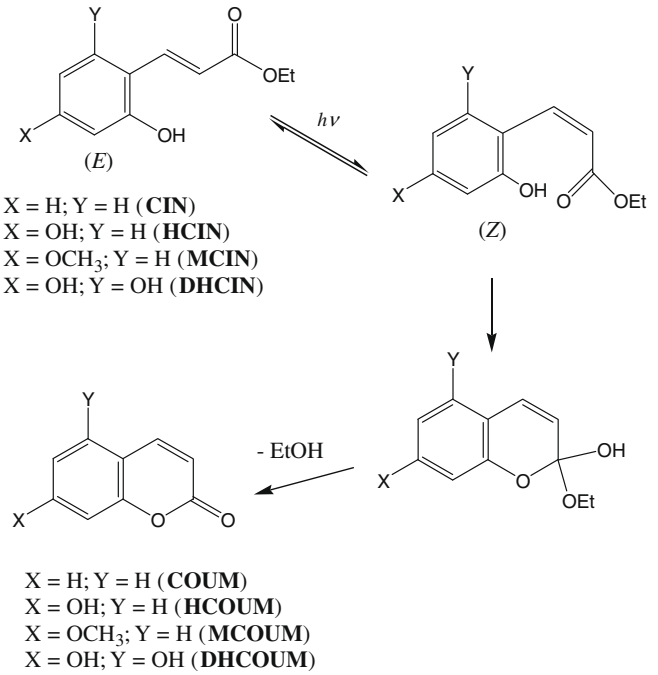
(*E*)-*o*-Hydroxycinnamates were synthesized and their photochemical behavior was investigated in liquid and solid states. It was confirmed by ^{1}H NMR spectroscopy that the (*E*)-*o*-hydroxycinnamates converted into the corresponding coumarins via (*Z*)-*o*-hydroxycinnamate intermediates. The photoconversion was greatly accelerated in the presence of *p*-toluenesulfonic acid. The optical properties of the cinnamates were compared with those of the corresponding coumarins. Fluorescence imaging was successfully accomplished by photoirradiation of PMMA films containing the cinnamates.

Recently the development of patterned fluorescent images in polymer films attracted considerable interest due to their possible application in the areas of displays, optical memory devices, and molecular switches, as well as in the sensor and imaging industries.[1] A typical method of the formation of fluorescent images employs photoirradiation through a photomask. In a conventional chemisorption approach, reactive functional groups are generated through photoacid-catalyzed deprotection, followed by a wet developing process in which fluorescent dye molecules are attached to the exposed areas through covalent bonding or intermolecular interactions.[2–4] A recently developed 'precursor approach' enables fluorescence imaging to be carried out without the need for wet developing process. This approach includes photoacid-catalyzed deprotection,[5–8] photoinduced protonation,[9–11] and photogeneration of conjugated structure.[12] The approach consists of two steps, (1) photochemical acid generation from a photoacid generator (PAG) and (2) post-exposure baking step for acid-induced reactions. Photochromism is an alternative imaging method that is based on a single photochemical step,[13–16] but it includes relatively complicated precursor synthesis.[1]

In this Letter we report a new method in which fluorescence imaging can be accomplished via photoconversion of (*E*)-*o*-hydroxycinnamate to coumarin. Our method does not need any additional process such as wet developing and post-exposure bake. In addition, our precursor compounds can be synthesized easily.

Four (*E*)-*o*-hydroxycinnamates (Scheme 1) have been prepared by reacting salicylaldehydes with (carbethoxymethylene)triphenylphosphorane.[17–19] DHCIN was newly synthesized, and obtained as pale yellow crystals in a yield of 97%. The chemical structures of the cinnamates were confirmed by ^{1}H and ^{13}C nuclear magnetic resonance (NMR), Fourier transform infrared (FT-IR) spectroscopy, and elemental analysis.

Photochemical behavior of the (*E*)-*o*-hydroxycinnamates was investigated in liquid and solid states. First, we carried out photol-



Scheme 1. Photoconversion of (*E*)-*o*-hydroxycinnamates to coumarins.

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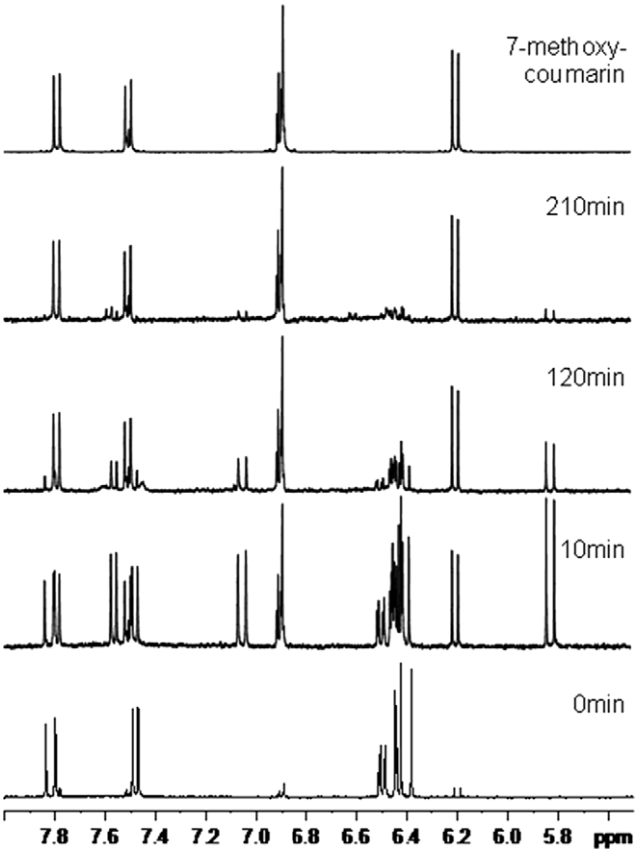

Figure 1. ^{1}H NMR spectra showing the transformation of MCIN into MCOUM (duration of photoirradiation in minutes: 0, 10, 120, and 210). A spectrum of an authentic MCOUM is presented at the top for reference.

ysis of the cinnamates in ethanol. Typically, 200 mg of a cinnamate was dissolved in 300 mL of ethanol and photolyzed with a photoreactor at a wavelength of 300 nm at room temperature. After photolysis, the photoproduct was obtained as white powders by evaporating the solvent. It was confirmed by ^{1}H NMR spectroscopy that each cinnamate quantitatively afforded its corresponding coumarin (Scheme 1). The photoconversion of CIN and HCIN into COUM and HCOUM, respectively, is in accordance with the previously reported results.[18,20] As far as we know, there has been no report on photochemical conversion of MCIN into MCOUM and DHCIN into DHCOUM.

The course of the photoconversion of cinnamates into coumarins in liquid state was monitored by ^{1}H NMR spectroscopy. MCIN was dissolved in CD_3CN, and irradiated in an NMR tube at the wavelength of 300 nm. The ^{1}H NMR spectral change of MCIN with increasing exposure time is shown in Figure 1. The starting MCIN showed vinylic proton peaks exhibiting a coupling constant of 16.0 Hz at 6.40 and 7.82 ppm. Upon irradiation for 10 min, new vinylic protons exhibiting a coupling constant of 12.8 Hz appeared at 5.82 and 7.05 ppm. This indicates that MCIN first converted into its (*Z*) isomer through photoisomerization. When irradiated for 10 min, new vinylic protons exhibiting a coupling constant of 9.6 Hz also appeared at 6.20 and 7.79 ppm, indicating the formation of a small amount of MCOUM. The generation of ethanol along with MCOUM formation was also observed in the NMR study (not shown in Fig. 1). With increasing exposure time, the amount of MCOUM increased while MCIN and its (*Z*) isomer gradually disappeared. The ^{1}H NMR spectrum for the final product was the same as that for an authentic MCOUM (Fig. 1). The other three cinnamates (CIN, HCIN, and DHCIN) showed photochemical behavior

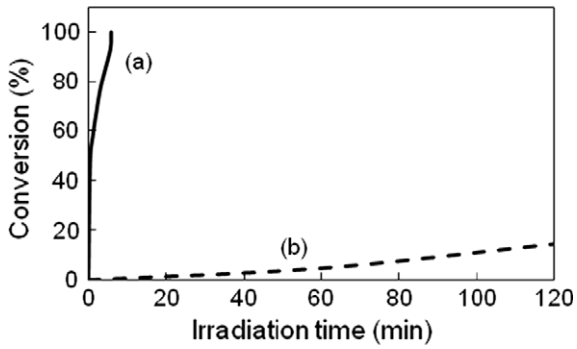

Figure 2. A plot of conversions of MCIN in PMMA films versus irradiation time: (a) in the presence of TSA (mole ratio of MCIN:TSA = 1:0.2), and (b) without TSA. The mass ratio of MCIN:PMMA was 1:2.33 and the films were prepared by casting.

similar to that of MCIN. It has been proposed that (*Z*) isomers of *o*-hydroxycinnamates undergo intramolecular cyclization through the nucleophilic addition of the *o*-hydroxy group onto the ethyl ester moiety to give benzopyran hemiacetals, which finally convert into coumarins (Scheme 1).[18,20]

We also studied the photoreaction of the cinnamates in the film state. A solution of a cinnamate and poly(methyl methacrylate) (PMMA) in tetrahydrofuran was cast and the solvent was removed in vacuo at room temperature. After irradiation for a given period of time at the wavelength of 300 nm, the film was dissolved in dimethyl sulfoxide-d_6. ^{1}H NMR spectral analysis showed that the cinnamates converted into their corresponding coumarins. However, only a trace amount of (*Z*) form was detected in the NMR spectroscopy during the photoreaction. It was thought that the intramolecular cyclization of (*Z*)-*o*-hydroxycinnamates to hemiacetal intermediates occurred faster in the film state than in the liquid state.

The degrees of conversion of MCIN to MCOUM (in the film state) are shown as a function of irradiation time in Figure 2b. In order to accelerate the lactonization of MCIN to MCOUM, we added a small amount of *p*-toluenesulfonic acid (TSA) to the photoreactive formulation, based on reports on acid-catalyzed lactonization of cinnamic acids.[21,22] As shown in Figure 2a, the photoconversion of MCIN was greatly accelerated, and completed by irradiation for 4.5 min. Quantum yields for the photoconversion of cinnamates into coumarins in the presence of TSA (20 mol % with respect to cinnamate) were measured in the film state. When irradiated at 328 m, CIN, HCIN, MCIN, and DHCIN showed quantum yields of 0.29, 0.51, 0.39, and 0.39, respectively.

We have determined the optical absorption and emission spectra of the cinnamates and coumarins in PMMA films. The absorption and fluorescence maxima are given in Table 1. The absorption spectrum of MCIN in a thin PMMA film is shown in Figure 3a, and three main absorption bands are observed in the range of 240–400 nm. The optical absorption of MCOUM is somewhat lower than that of MCIN (Fig. 3b). Emission spectra of the cinna-

Table 1
Optical absorption and fluorescence maxima wavelengths of cinnamates and coumarins in PMMA films

	Absorption (nm)	Fluorescence (nm)[a]
CIN	275, 325	398
HCIN	242, 294, 330	395
MCIN	240, 293, 328	397
DHCIN	320	395
COUM	274, 311	—
HCOUM	324	419
MCOUM	320	391
DHCIN	328	422

[a] Excitation wavelength was 330 nm.

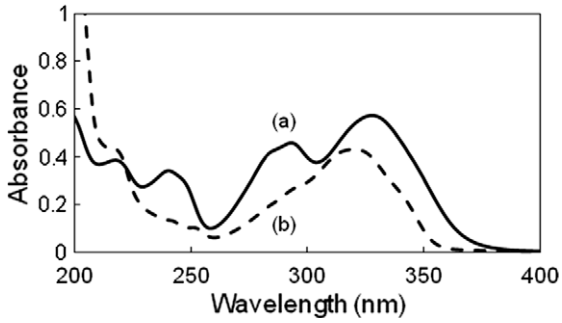

Figure 3. Optical absorption spectra of PMMA films containing (a) MCIN and (b) MCOUM. The films were prepared at a concentration of 9.10×10^{-5} mol of MCIN or MCOUM in 0.070 g of PMMA by spin coating (film thickness: (a) 0.51 μm; (b) 0.45 μm).

mates and coumarins in thin PMMA films are shown in Figure 4. Fluorescence intensity of coumarins (HCOUM, DHCOUM, and MCOUM) is much greater than that of the corresponding cinnamates (HCIN, DHCIN, and MCIN). In contrast, CIN showed much higher fluorescence intensity than COUM. It is known that coumarins with either no substituent or no electron-withdrawing groups in the 7-position are virtually non-emissive compared with those having electron-donating groups.[7,23] We expected that the usage of CIN in fluorescence imaging would afford a 'reverse' image, compared to the imaging with HCIN, DHCIN, and MCIN.

Preliminary fluorescent imaging was performed using the cinnamates. Thin PMMA films containing each cinnamate were prepared by spin coating. Irradiation of the films with light of λ >300 nm through a photomask resulted in a drastic change in the luminescent property of the exposed areas due to the photoconver-

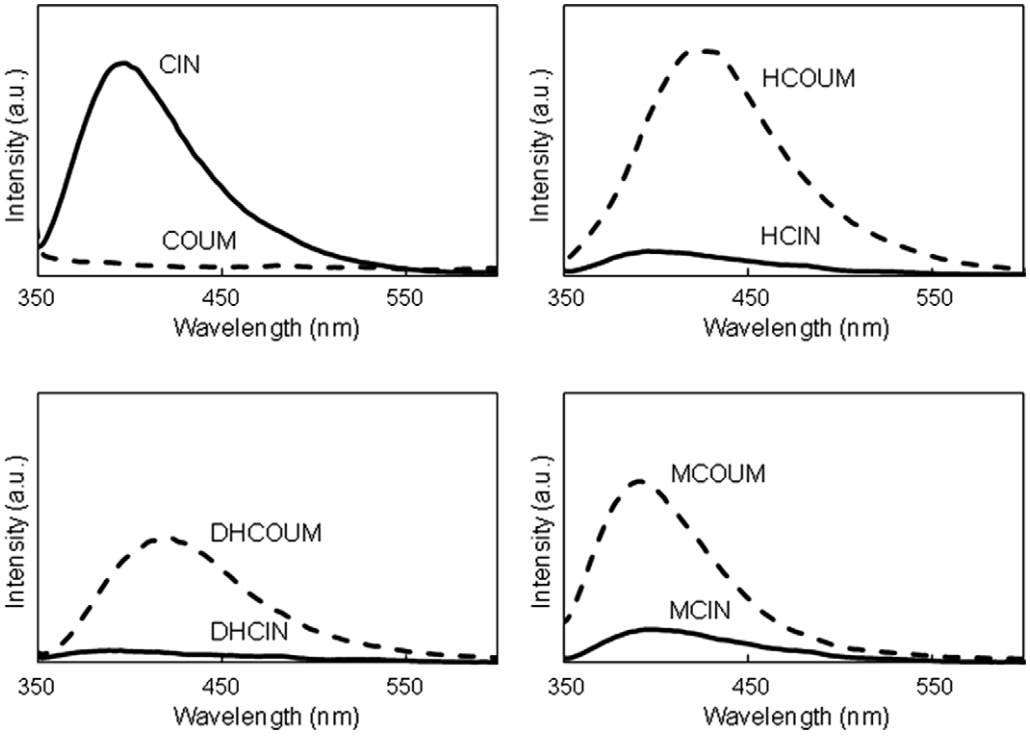

Figure 4. Emission spectra of cinnamates and coumarins. The films were prepared at a concentration of 9.10×10^{-5} mol of cinnamate (or coumarin) in 0.070 g of PMMA by spin coating (film thickness: 0.43–0.51 μm, excitation wavelength: 330 nm).

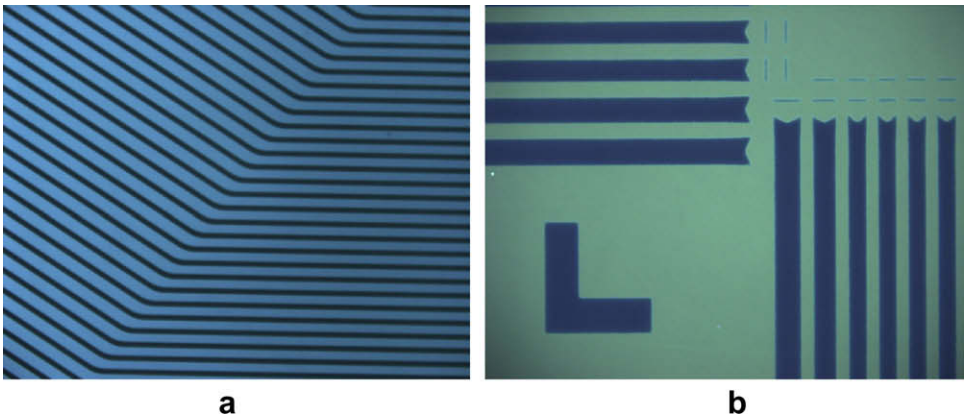

Figure 5. Fluorescent images obtained with 0.50-μm thick PMMA films containing (a) CIN and (b) MCIN (mass ratio of cinnamate:PMMA = 1:2.33 and mole ratio of cinnamate:TSA = 1.0.2). The actual colors may slightly differ because of computer image processing. Width of the long, dark lines in the images is 30 μm.

sion of cinnamate into coumarin. As shown in Figure 5 high-contrast fluorescent image patterns were successfully obtained. As expected, the exposed regions are dark ('turn off') in the case of CIN-based film (Fig. 5a), but brightly colored ('turn on') in the case of MCIN-based film (Fig. 5b). Thin PMMA films containing HCIN and DHCIN gave fluorescent images similar to those containing MCIN.

In summary, four (*E*)-*o*-hydroxycinnamates were readily synthesized from salicylaldehydes, and it was confirmed by ^{1}H NMR spectroscopy that the cinnamates photochemically converted into their corresponding coumarins via (*Z*)-*o*-hydroxycinnamate intermediates. Fluorescence imaging was accomplished for the first time through the photoconversion of (*E*)-*o*-hydroxycinnamate to coumarin. The photoconversion of (*E*)-*o*-hydroxycinnamates is promising for the application to fluorescence imaging because there is no necessity for any additional processes such as wet developing and post-exposure bake, coupled with the ease of synthesis of the precursors.

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Supplementary data

Supplementary data (materials and instruments, and synthesis of DHCIN) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.06.031.

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