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Short communication

Photoisomerization of octyl methoxycinnamate

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Abstract

The octyl-*p*-methoxy-*trans*-cinnamate (*E*-OMC) was exposed to sunlight to induce the *E* to *Z* transformation. Octyl-*p*-methoxy-*cis*-cinnamate (*Z*-OMC) was then purified from the mixture of the *E*- and the *Z*-OMC using C-18-semi-preparative HPLC. The UV absorption of the *Z* configuration at various concentrations in various solvents was measured. Molar absorption coefficient of the compound was then calculated. By using the obtained molar absorption coefficient of *Z*-OMC and of *E*-OMC, *E* to *Z* photoisomerization of octyl methoxycinnamate (OMC) in various solvents at various concentrations could be monitored by C-18 HPLC using UV detector. The result indicates that equilibrium of photoisomerization depends upon concentration and polarity of the solvent used.
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1. Introduction

Octyl methoxycinnamate (OMC, Fig. 1) is a widely used UV-B filter in various cosmetic formulations. A study of photoisomerization of this sunscreen has been done using steady state and laser flash photolysis [1]. Only few photosensitization and/or photoallergic reactions induced by this compound have been reported [2–6]. Previous studies have shown that when exposed to sunlight, this UV-B filter will change from octyl-*p*-methoxy-*trans*-cinnamate (*E*-OMC) to octyl-*p*-methoxy-*cis*-cinnamate (*Z*-OMC) [7,8]. The UV absorption spectrum of this UV-filter was also shown to be affected by solvents. The study showed a bathochromic shift of the λ_{max} in the UVB region (290–320 nm) from a non-polar solvent to a polar solvent [9]. Although no other degradation product was detected when *E*-OMC was exposed to sunlight except the configurational isomer *Z*-OMC (7), the UV-B filtering efficiency was shown to be decreased [7,10–12].

In this paper, the UV absorption spectrum of the configurational isomer, *Z*-OMC, was deduced. The experiments were carried to obtain the molar absorption coefficients of the compound in methanol, ethanol and hexane. By using natural sunlight as a light source, the studies of *E* to *Z* configurational change of octyl methoxycinnamate in various solvents were also undertaken. Attention was paid to the effects of solvent and concentration on photostationary equilibrium of the process. The kinetics picture of the decay of the excited molecules at photostationary equilibrium was then proposed.

2. Experimental

2.1. Materials

Standard OMC was obtained from Merck Co. Ltd. (Bangkok, Thailand), and was kept in a lightproof container at 0 °C until use to insure no photoisomerization. Cosmetic grade silicone oil (decamethylcyclopentasiloxane) was obtained from Dow Corning Company (Bangkok, Thailand). All other solvents used were analytical grade. Mineral oil, methanol and ethanol were purchased from Merck KgaA (Darmstadt, Germany). Ethyl acetate was purchased from Mallinckrodt Chemical (Paris, France). Hexane was purchased from Lab Scan Analysis Science (Bangkok, Thailand). Propylene glycol was obtained from Central Science company (USA).

2.2. Preparation of Z-OMC

The solution of 3.0×10^{-3} M *E*-OMC in methanol was exposed to sunlight until it turned very yellow. The light exposed solution was then concentrated by rotary evaporation at 40 °C to the final concentration of about 3×10^{-2} M. This

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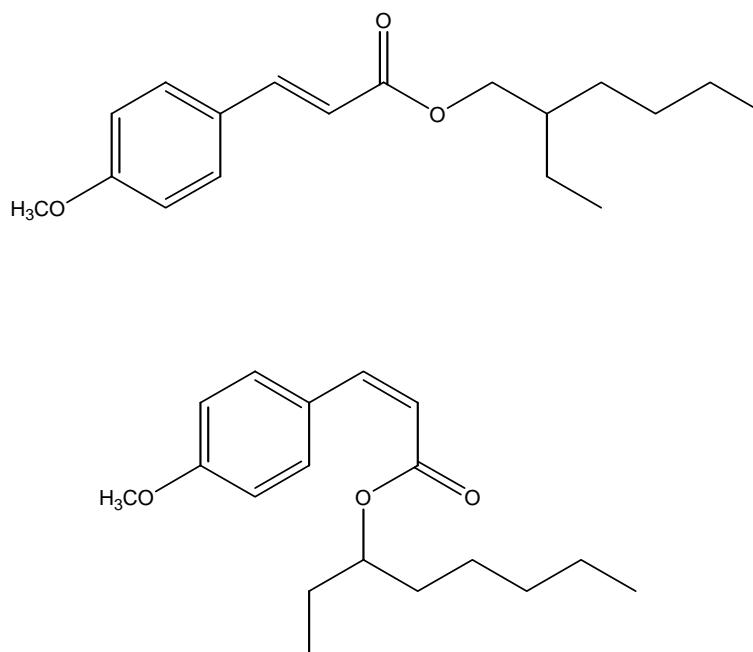*E-mail address:* psupason@chula.ac.th (S. Pattanaargson).

Fig. 1. Structure of octyl-*p*-methoxy-*trans*-cinnamate (*E*-OMC) (top) and octyl-*p*-methoxy-*cis*-cinnamate (*Z*-OMC) (bottom).

solution was then subjected to HPLC fractionation to isolate the *Z*-OMC out from the mixture of *E*-OMC and *Z*-OMC.

2.3. High performance liquid chromatography for separation of Z-OMC

The HPLC system consisted of a Model 662 pump (Waters Corp., Milford, USA), a manual injector (Rheodyne, Cotatica, USA), a Model 486MS variable-wavelength UV detector (Waters Corp., Milford, USA) and a Model 600 S controller (Waters Corp., Milford, USA). Chromatograms and peak area were processed using Millenium 2010 Chromatography Manager software. Isolation of *Z*-OMC was done at 25 °C using a Thermo Hypersil C18 column (particle size 12 µm, 250 mm × 10 mm i.d.; Thermo Hypersil-Keystone, Thermo Electron Corp., UK). The mobile phase used was methanol:water (90:10 (v/v)) at a flowrate of 1.0 ml/min. The UV detector was set at 309 nm. Fifty microlitres of the concentrated sample (light exposed OMC solution from 2.2; mixture of *E*-OMC and *Z*-OMC at the total concentration of 3×10^{-2} M) were injected and fractions at retention time of 96.5 min and 105.0 min were separately collected into the lightproof glass containers. The process was repeated many times and each collected fraction was immediately dried by rotary evaporation at 40 °C. Both 96.5 min and 105.0 min fractions were then subjected to NMR analyses to confirm that they were *Z*-OMC and *E*-OMC, respectively.

2.4. Determination of molar extinction coefficient

The 3.44×10^{-5}, 6.89×10^{-5} and 1.38×10^{-4} M Z-OMC solutions were prepared in methanol, ethanol and hexane us-

ing the isolated *Z*-OMC prepared as described earlier (the 96.5 min HPLC fraction). The solutions were immediately subjected to UV-visible absorption measurement (Hewlett Packard 8453 UV-Visible Spectroscopy System, Hewlett-Packard GmbH, Waldbronn, Germany) using 1 cm path-length, 1 ml quartz cuvettes. The same procedure was done with standard E-OMC. Absorbance at λ_{max} of each solution was recorded. The plots between absorbance and molarity of the solution were then constructed in order to obtain the molar absorption coefficients of the compound in each solvent.

2.5. Study of E to Z configurational change

All freshly prepared standard *E*-OMC solutions were immediately withdrawn and subjected to UV absorption measurement and HPLC analyses before they were placed under sunlight in the closed quartz cuvettes of 1 cm path-length at a temperature of around 32 °C. After appropriated sun exposure time (as indicated in the results), each solution was withdrawn for UV absorption measurement and HPLC analysis.

2.6. High performance liquid chromatography for configurational change monitoring

The HPLC system consisted of a Model 600 pump (Waters Corp., Milford, USA), Waters[TM] 717 plus Autosampler, Waters[TM] 996 Photodiode Array Detector, and a Waters[TM] 600 Controller. Chromatograms and peak area were processed using Millenium 2010 Chromatography Manager software. Analysis of *E*- and *Z*-OMC was done as described previously (7) using a LiChrosorb RP 18 column (particle size 5 µm, 125 mm × 8.0 mm i.d.; VDS optilap, Berlin,

Germany) at 25 °C. The mobile phase used was 90:10 (v/v) methanol:water at a flowrate of 0.5 ml/min. The UV detector was set at λ_{max} of each isomer. Injection volume was 2.5 μl. Withdrawn samples were diluted to 3.0×10^{-4} M using the corresponding solvents just prior to injection.

2.7. Calculation of isomer concentrations

The calculation for concentrations of *E*-OMC and *Z*-OMC at various light exposure times is based on the chromatographic peak area of each isomer detected by UV absorption. The molar absorption coefficients of *E*-OMC and of *Z*-OMC obtained earlier were used.

$$\frac{[E]}{[Z]} = \frac{\varepsilon_Z A_E}{\varepsilon_E A_Z} \tag{1}$$

$$[E] + [Z] = [OMC] \tag{2}$$

where [OMC] is the concentration of the prepared *E*-OMC solution (starting [*E*-OMC] before exposed to sunlight); ε_Z the molar absorption coefficient of *Z*-OMC; ε_E the molar absorption coefficient of *E*-OMC, A_E the peak area of the *E*-OMC peak in the chromatogram and A_Z the peak area of the *Z*-OMC peak in the chromatogram

The calculation is based on an assumption that the sunlight produces no side reactions other than the photoisomerization from *E*-OMC to *Z*-OMC as stated in Eq. (2) [7]. Solutions is, therefore, for two unknowns, [E] and [Z], in two equations, Eqs. (1) and (2).

Calculation was also done using UV absorption result as follows:

$$A = \varepsilon_E[E] + \varepsilon_Z[Z]$$

$$[E] + [Z] = [OMC]$$

where *A* is the absorbance of the solution.

3. Results and discussion

3.1. Molar absorption coefficient of Z-OMC

Chromatogram of the sun exposed standard OMC revealed an accumulation of the degradation product by an appearance of a new peak at retention time of 96.5 min. Collection of *E*-OMC (peak at retention time 105.0 min) and

Z-OMC (peak at retention time 96.5 min) were done and NMR spectrum for each fraction was obtained. The NMR results confirmed that a peak at retention time 96.5 min was *Z*-OMC whereas a peak at 105.0 min was *E*-OMC (7). ^{1}H NMR (CDCl$_3$) *E*-OMC: δ 7.61 (d, *J* = 16 Hz), 7.40 (d, *J* = 7 Hz), 6.87 (d, *J* = 7 Hz), 6.29 (d, *J* = 16 Hz), 4.10 (d, *J* = 6 Hz), 3.84 (s), 1.63 (br m), 1.34 (br m), 0.91 (t), 1.36 (m), 1.41 (m), 1.34 (br m), 0.94 (t); *Z*-OMC: δ 7.66 (d, *J* = 7 Hz), 6.80 (d, *J* = 7 Hz), 6.80 (d, *J* = 12 Hz), 5.82 (d, *J* = 12 Hz), 4.05 (d, *J* = 6 Hz), 3.83 (s), 1.63 (br m), 1.34 (br m), 0.91 (t), 1.36 (m), 1.41 (m), 1.34 (br m), 0.94 (t).

The shapes of the obtained UV absorption profiles of *Z*-OMC were quite similar to those of *E*-OMC. The plots between UV absorbance at maximum wavelength and the concentrations of Z-OMC in various solvents were constructed. All the graphs gave straight line with r^2 fit of more than 0.996. Those molar absorption coefficients obtained from the slopes of the graphs and λ_{max} were summarized in Table 1. To validate the numbers obtained by our procedure with the instrument used, molar absorption coefficient of the *E*-OMC was also measured in ethanol and hexane. The numbers obtained (Table 1) were very close to those previously reported [9]. It should be mentioned here that the molar absorption coefficient of *Z*-OMC is quite close to that of methyl-*p*-methoxy-*cis*-cinnamate, which was reported in acetonitrile to be 13,300 [10].

The above result explains very well the reduction of UV absorbance when OMC was exposed to UV light [1,13–17]. And this is the answer to why the UV-B filtering efficiency of OMC sunscreen decrease after sunlight exposure. With this first time reported ε of *Z*-OMC together with the previously known ε of *E*-OMC, one can now easily predict the ratio between the two configurations using HPLC with UV-absorption spectroscopy. Moreover, in the condition where *E*- and *Z*-configuration cannot be easily separated, e.g. when the chromophore is grafted on polymer, reduction of UV absorbance together with ε_Z and ε_E would be enough to estimate the *E* to *Z* configurational change.

3.2. E to Z transformation

To monitor the configurational change of *E*- to *Z*-OMC, chromatographic condition that take only 4 min to completely separating the two configurations was used [7]. Both condition and column were different from those used for

Table 1
Molar absorption coefficients of *Z*-OMC and *E*-OMC in various solvents

Solvent	Z-OMC		E-OMC	
	λ_{max} (nm)	ε (M^{-1} cm^{-1})	λ_{max} (nm)	ε (M^{-1} cm^{-1})
90:10 (v/v) methanol:water	301	12600	310	24000
Methanol	301	12600	310	24000
Ethanol	301	11900	310	24000 (23300)[a]
Hexane	291	11700	290	23600 (22900)[a]

[a] Previously reported value [9].

collecting *Z*-OMC from the mixture of *E*- and *Z*-OMC. In this latter experiment, only integrations of *E*- and *Z*-OMC peaks were needed while in the previous experiment there was a need for a big gap between *Z*- and *E*-OMC elution to avoid contamination. To follow the degradation of the light exposed OMC, the standard *E*-OMC solutions were put under the sunlight and withdrawn for HPLC analyses at appropriate time.

From the chromatograms taking at various light exposure times of *E*-OMC solutions, integration of *Z*-OMC peak and *E*-OMC peak was done, molarity of each isomer could be obtained as described in Section 2. Since 90:10 (v/v) methanol:water was used as mobile phase, ε_Z and ε_E of 12,600 and 24,000 (Table 1) were used.

Fig. 2 shows the decrease in [*E*-OMC] together with the increase in [*Z*-OMC] as the *E*-OMC solution was left under sunlight. It can be seen clearly that the photostationary equilibrium between the two configurations depends upon polarity of the solvent used. The equilibrium shifted to more *E*-OMC when less polar solvent was used. Explanation on this may partly due to the fact that *E*-OMC is more hydrophobic than *Z*-OMC.

From the data on *E*/*Z* ratio at equilibrium of the 3.44×10^{-4} M OMC solutions together with ε_E and ε_Z, kinetics picture of the photoisomerization could be deduced as follows:

$$E\text{-OMC} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \text{OMC}^* \underset{k_4}{\overset{k_3}{\rightleftharpoons}} Z\text{-OMC}$$
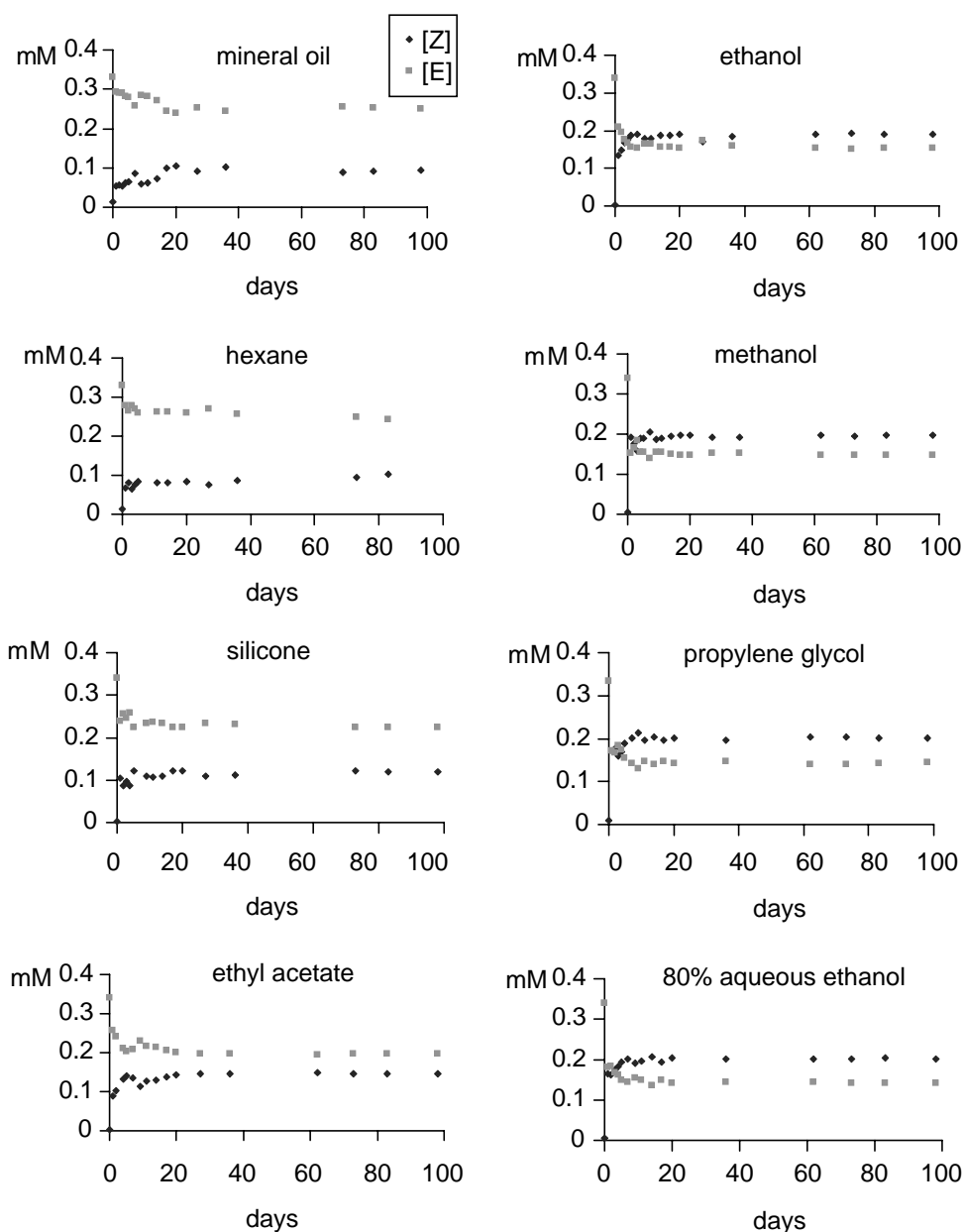

Fig. 2. Graphs between concentration of each OMC isomer and the sun exposure time of 3.44×10^{-4} M *E*-OMC solution in various solvents.

At photostationary state both [E] and [Z] are constant, therefore,

$$k_2[OMC^*] = k_1[E] \qquad (3)$$

$$k_3[OMC^*] = k_4[Z] \qquad (4)$$

Since ε_E is about two times ε_Z, therefore,

$$k_1 \approx 2k_4 \qquad (5)$$

Substitute (5) into (3),

$$k_2[OMC^*] = 2k_4[E] \qquad (6)$$

In non-polar solvent, such as mineral oil, $[E] \approx 2[Z]$ (see Fig. 2), therefore

$$k_2[OMC^*] = 4k_4[Z] \qquad (7)$$

From (4) and (7) one can get the relationship between k_2 and k_3 as

$$k_2 = 4k_3$$

Therefore, in mineral oil, k_2 is approximately four times k_3. This implies that at 3.44×10^{-4} M in non-polar solvent, upon the release of energy, the excited complex proceeds to the E-configuration four times faster than to the Z-configuration.

In ethyl acetate, a moderately polar solvent, at photostationary state, $[E] \approx [Z]$ (see Fig. 2). Therefore, with similar derivation as shown earlier, one can obtain $k_2 \approx 2k_3$. This means that at 3.44×10^{-4} M in medium polarity, the excited complex will decay to the E-configuration two times faster than to the Z-configuration.

In polar solvent, such as 80% aqueous ethanol, $[Z] \approx 2[E]$ (see Fig. 2). Using similar assumption ($k_1 \approx 2k_4$) as shown in the above derivation, one can obtain $k_2 \approx k_3$. It, therefore, can be concluded that, at 3.44×10^{-4} M in polar solvent, the excited complex would proceed to both the E- and Z-configuration at the same rate.

The above kinetics picture at photostationary state was based on the experiment with 3.44×10^{-4} M OMC solutions. The use of quartz cuvette with only 1 cm path length and low concentration (3.44×10^{-4} M) should minimize the filtering effect. The E/Z ratio at photostationary state also depends on concentration. In methanol, the E/Z ratio of 0.0344, 0.344 and 3.44 mM OMC solutions were 0.47, 0.75 and 1.1, respectively. Using the same derivation as shown earlier, these correspond to the ratio between $k_2:k_3$ of 1:1, 1:1.5 and 1:2.2, for the 0.0344, 0.344 and 3.44 mM solution, respectively. Since OMC itself is a less polar molecule, higher concentration of OMC, therefore, should help stabilizing the less polar excited complex. Higher concentration of OMC, therefore, shifts the photostationary equilibrium towards more E-configuration. The differences in k_2/k_3 ratios were probably governed by the structure of the excited molecules. In less polar solvent, the structure of the excited molecule is probably closer to the E configuration. As a result, upon energy release, the excited molecules more easily fall to the E configurations than to the Z configurations, making higher k_2/k_3.

It should be noted here that the ratio of k_2/k_3 provides at least some quantitative measures of how the excited molecules proceed regarding the two configurational pathways. And this ratio, as demonstrated in this paper, can be easily obtained by monitoring the two configurations at photostationary state. In facts, concentration of each isomer at photostationary equilibrium can also be calculated from the reduction in UV absorbance using information of molar absorption coefficient of each isomer if the following criteria can be met : (1) the interest isomer is the only product in the system, and (2) the λ_{max} of the isomerized product is closed to that of the starting molecule, i.e. absorption profiles of both isomers should be overlapped at the maximum absorption. It should also be mentioned here that there may be factors other than concentration and polarity of the solvent which affect photostationary equilibrium of the photoisomerization of OMC, the method proposed in this paper can then be used to investigate of how those factors affect the kinetics at the photostationary state.

Sunlight was used as the light source in this experiment because it is the light source in which sunscreen will be exposed. Although one may argue that the experiment may not be repeateable because of this uncontrollable light source. However, from our experience, the photostationary state was not affected much among different batch of experiments performing at different days. More importantly, the purpose of this paper was to report the value of molar absorption coefficient of the Z configuration of the OMC sunscreen and to demonstrate the use of this value to obtain the E/Z ratio together with structural picture of the excited complex in various solvents. If one change the experimental condition and want to find out the E/Z ratio in the new condition, the method from this paper can be used. Moreover, if one want to speculate the structure of the excited complexes at different conditions, one can also perform the kinetic derivation as demonstrated in this paper.

The structural differences of excited complexes in various solvents could also be interpreted from λ_{max} in Table 1. It is obvious that the energy gap between the ground state and the excited state in less polar solvent (290 nm) is wider than in more polar solvent (320 nm). The difference is about 6.3 kcal/mole. The structure of the lower energy excited molecule (exist in more polar solvent) probably is more resemble to the Z configuration. Therefore, this complex proceeds to more Z configuration upon the energy release.

The results above give us some quantitative detail of how much the E-OMC would change into the Z-OMC under various solvent and concentration conditions. From the ratio of the two configurations at photostationary state, kinetics picture of the decay of the excited complex can be interpreted.

Acknowledgements

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