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Stability of octyl methoxycinnamate and identification of its photo-degradation product

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Synopsis

A stability study of octyl methoxycinnamate (OMC) using C-18 HPLC indicated that OMC degraded into a new product when exposed to sunlight. When kept in the dark at 4, 20, 32 and 60 °C for one month, no degradation of OMC was detected. Online HPLC-APCI-MS revealed similar APCI mass spectra for OMC and its degradation product. Isolation of the photo-degradation product was done using semi-preparative HPLC. NMR spectra of OMC and the isolated photo-degradation product indicated the change from an *E*-octyl-*p*-methoxycinnamate into a Z-octyl-*p*-methoxycinnamate. NMR spectra of the unfractionated-light-exposed-OMC showed that the Z-OMC was the only product generated.

Résumé

Une étude de stabilité de l'octyl-méthoxycinnamate (OMC) utilisant l'HPLC en C-18 indique que l'OMC se dégrade en un nouveau produit lorsqu'il est exposé à la lumière du soleil. Lorsqu'il est maintenu dans le noir à 4, 20, 32 et 60 °C durant un mois, aucune dégradation de l'OMC n'est observée. La technique HPLC-APCI-MS enchaînée révèle des spectres de masse en APCI similaires pour l'OMC et son produit de dégradation. L'isolement du produit de photodégradation est effectué en utilisant l'HPLC semi-préparative. Les spectres RMN de l'OMC et du produit de photodégradation isolé indique la transformation du E-octyl-p-méthoxycinnamate en Z-octyl-p-méthoxycinnamate. Les spectres de RMN de l'OMC non fractionné exposé à la lumière montrent que le Z-OMC est le seul produit généré.

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Introduction

Octyl methoxycinnamate (OMC, Fig. 1) is a widely used sunscreen in various cosmetic formulations because of its large extinction coefficient in various solvents in the UV-B region. Only few photosensitization and/or photoallergic reactions induced by this compound have been reported [1, 2]. Qualitative and quantitative analyses of OMC can be done using reverse phase high performance liquid chromatography (HPLC) [3–5]. This UV filter has been shown to be light sensitive with a decrease in UV absorption efficiency upon light exposure [6]. Analysis of this compound after light exposure by reverse phase HPLC revealed a new peak and therefore indicated an accumulation of a new product [4]. It has been speculated that a *E* to Z configuration change occurs upon light exposure [4, 6]. This speculation was probably based on the report of a *E* to Z photo-isomerization of cinnamic acids and cinnamic acid esters [7, 8]. A study of photo-isomerization of OMC has been done using steady state and laser flash photolysis [9]. This paper presents the HPLC-isolation of the OMC's photo-degradation product generated by exposing the OMC to the sunlight. Identification of the structure of this photo-degradation product was done by NMR and HPLC-APCI-MS.

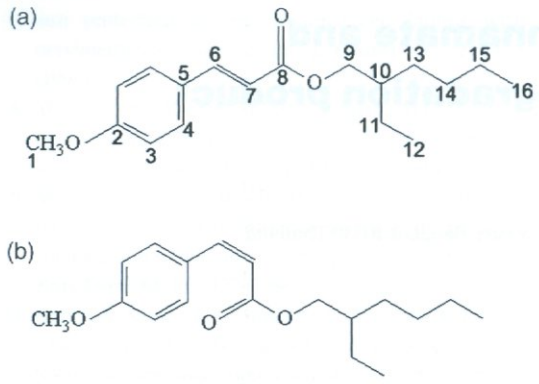

Figure 1 Structure of *E*-octyl-*p*-methoxycinnamate (original OMC) (a) and Z-octyl-*p*-methoxycinnamate (photo-degradation product of OMC) (b).

Materials and methods

Materials

Standard OMC was obtained from Merck Co. Ltd (Bangkok, Thailand), and was kept in a lightproof container at 0 °C.

OMC degradation study

Stock OMC solution of 1000 p.p.m. was prepared in methanol and this solution was kept away from light at 4 °C. The stock solution was divided into two parts; one kept in a closed glass container under sunlight at a temperature of around 32 °C, the other was kept in a lightproof container at 32 °C. Each solution was withdrawn for HPLC analysis at the appropriate time.

High performance liquid chromatography

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.) and a Model 600 S controller (Waters Corp.). Chromatograms and peak area were processed using PC 800, Version 2.0 software.

Following the degradation of OMC by HPLC. Analysis during the OMC degradation study was done using a Nucleosil 100C analytical column (particle size 5 μm, 125 × 4.0 mm I.D.; VDS optilap, Berlin, Germany) at 25 °C. The mobile phase used was pure methanol at a flowrate of 0.5 mL min^{-1}. The UV detector was set at 325 nm. The withdrawn sample was diluted 100 times with methanol before injection. Twenty-five μL of the diluted sample was injected for each analysis. All experiments were done in duplicate.

Isolation of photo-degradation product using semi-preparative HPLC. Collection of OMC and its degradation product was done at 25 °C using a Lichrosorb RP 18 column (particle size 5 μm, 125 × 8.0 mm I.D.; VDS optilap, Berlin, Germany). The mobile phase

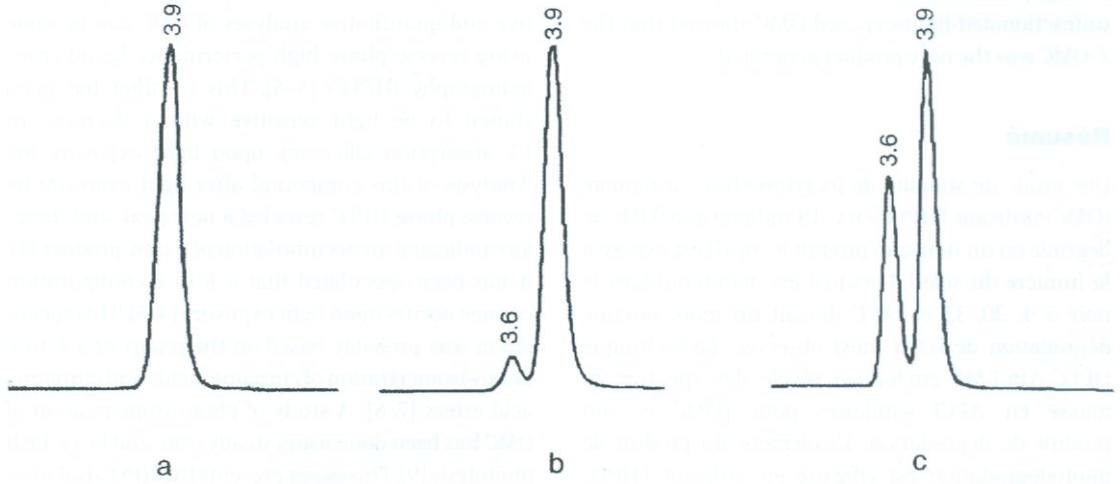

Figure 2 Chromatograms of standard OMC before (a) and after (b) and (c) light exposure. The HPLC was done using a Nucleosil 100C analytical column at 25 °C. The mobile phase used was pure methanol at the flowrate of 0.5 mL min^{-1}. The UV detector was set at 325 nm. The 1000 p.p.m. OMC stock solution was diluted 100 times with methanol before injection. Twenty-five μL of the diluted sample was injected for each analysis.

used was methanol:water (90 : 10 v/v) at a flowrate of 0.5 ml/min. The UV detector was set at 325 nm. The sample injection volume was 50 µl. Care was taken to prevent the collected fractions from being exposed to light.

Nuclear magnetic resonance (NMR) spectroscopy of the OMC and the photo-degradation product

^{1}H NMR was done on Cryomagnet NMR Spectroscopy BZH 200/52 (Spectrospin, Oxford Instruments; Bruker, Germany).

HMQC NMR was done on FT-NMR, JNM-A500 (JEOL, Japan).

The isolated OMC and the isolated photo-degradation product obtained from semi-preparative HPLC were dried under vacuum without exposure to light. The two dried fractions were dissolved in $CDCl_3$ and subjected to NMR spectroscopy.

The unfractionated 1000 p.p.m. OMC stock solution that had been exposed to sunlight for 15 days was also dried and dissolved in $CDCl_3$ before subjected to NMR spectroscopy.

Standard OMC (kept in the dark at 4 °C) was dissolved in $CDCl_3$ and subjected to NMR spectroscopy.

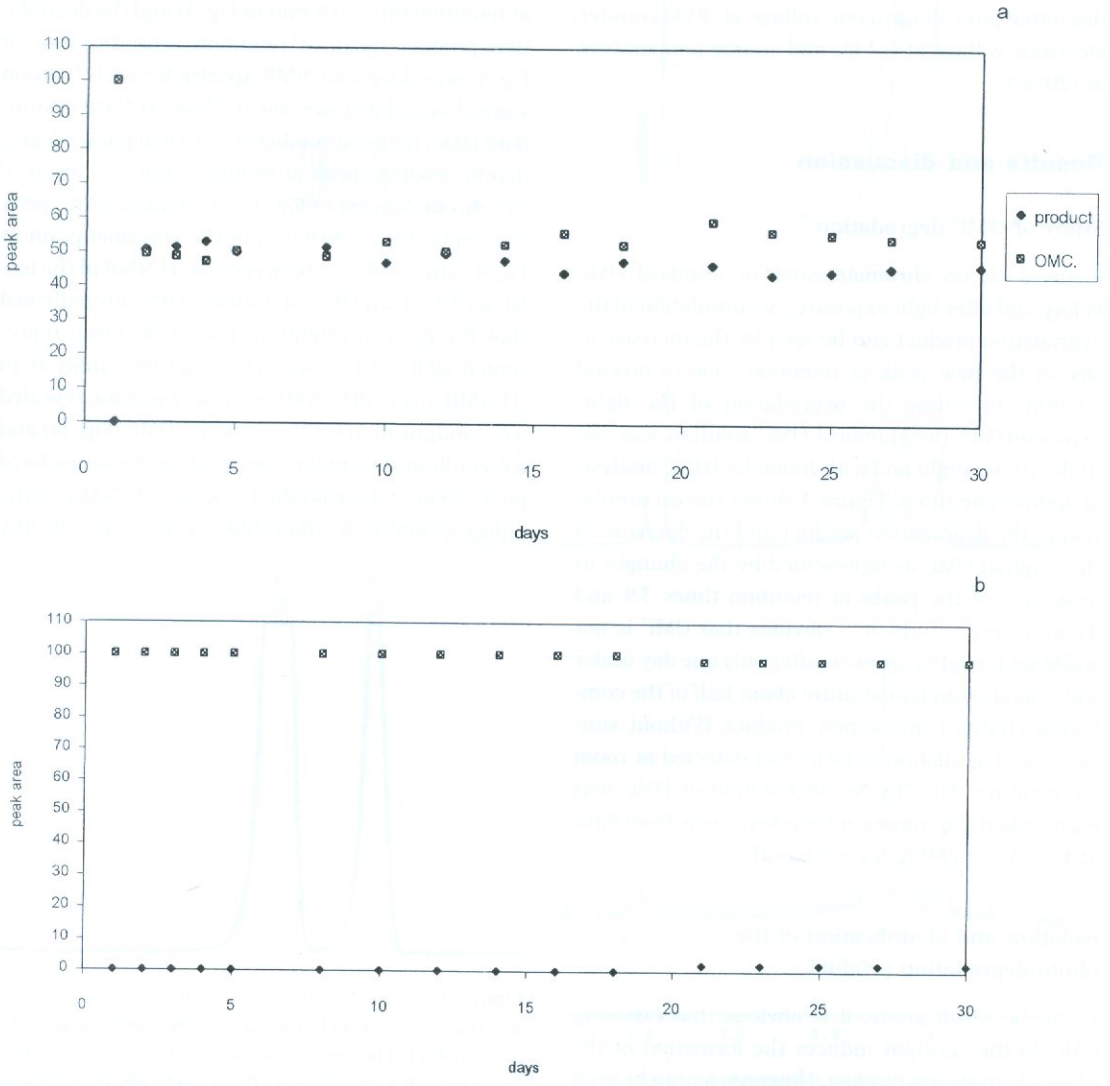

Figure 3 Degradation of OMC with (a) and without (b) light exposure. The accumulation of the degradation product and the decrease of the original OMC was represented by the changes in peak area of the peaks at retention times 3.9 and 3.6 min in the chromatograms (Fig. 2), respectively.

HPLC-atmospheric pressure chemical ionization mass spectrometry

The HPLC-APCI-MS instrument consisted of Model 662 pump (Waters Corp.), a manual injector with a 25-μL sample loop (Rheodyne, Cotatica, USA), a Model 486MS variable-wavelength UV detector (Waters Corp.), a Model 600 S controller (Waters Corp.), Lichrosorb RP 18 column (particle size 5 μm, 125 × 8.0 mm I.D.; VDS optilap) and a VG TRIO 2000 (Fisons Instruments, Altrincham, UK) quadruple mass spectrometer equipped with APCI ionization source. The mobile phase was methanol : water (90 : 10 v/v) at a flowrate of 0.5 mL min^{-1}. Positive-ion mass spectra were recorded at 3.5 kV corona discharge pin voltage (cone voltage at 30 V, counter electrode voltage at 0.2 kV, and source temperature at 120 °C).

Results and discussion

Study of OMC degradation

Figure 2 shows chromatograms of standard OMC before and after light exposure. Accumulation of the degradation product can be seen by the increase in size of the new peak at retention time of around 3.6 min. To follow the degradation of the light-exposed-OMC, the standard OMC solution was put under the sunlight and withdrawn for HPLC analysis at appropriate times. Figure 3 shows the accumulation of the degradation product and the decrease of the original OMC as represented by the changes in peak area of the peaks at retention times 3.9 and 3.6 min, respectively. It is obvious that OMC is not stable under light exposure; after only one day under sunlight at room temperature about half of the compound changed into a new product. Without sunlight, no degradation of OMC was detected at room temperature (Fig. 3b). No degradation of OMC was found when the compound was kept away from light at 4, 25, 32 and 60 °C for one month.

Isolation and identification of the photo-degradation product

From the result above, it is obvious that exposing OMC to the sunlight induces the formation of the photo-degradation product. However, as can be seen in Fig. 3(a), under the conditions used, not all OMC could be changed into the degradation product. Therefore, to separate the two compounds, the light-exposed OMC solution that contained both the original OMC and the degradation product was subjected to semi-preparative HPLC using the conditions stated in the experimental section. The result is shown in Fig. 4. It should be mentioned here that the change of mobile phase from pure methanol to methanol : water at 90 : 10 (V/V) was done in order to increase the resolution between the two peaks. This was to make sure that during the fraction collection of the two peaks there would be no contamination between the two compounds. Moreover, this good separation of the two peaks would prevent the cross-over effect when performing the online HPLC-APCI-MS, therefore yielding clean APCI-mass spectra of the two compounds. Collection of OMC (peak at retention time 30.9 min in Fig. 4) and the degradation product (peak at retention time 25.3 min in Fig. 4) was done and NMR spectra for each fraction were obtained. Figures 5(a–d) show ^{1}H NMR of standard OMC, light-exposed-OMC, isolated photo-degradation product (peak at retention time 25.3 min of the chromatogram in Fig. 4) and isolated OMC (peak at retention time 30.9 min of the chromatogram in Fig. 4). The similarity between the ^{1}H NMR of the isolated OMC (d) and that of standard OMC (a) confirmed that the peak at retention time of 30.9 min represented OMC of the original structure. Analysis of ^{1}H NMR and HMQC NMR (not shown) data, revealed a *E*-configuration for the standard OMC (Fig. 1a) and a Z-configuration at the same position for the isolated photo-degradation product (Fig. 1b). ^{1}H NMR of the light-exposed-OMC indicated the presence of only

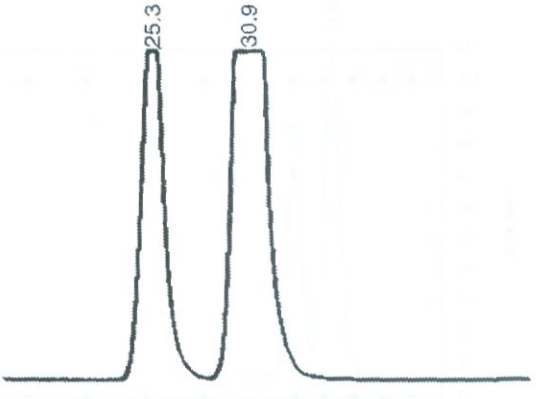

Figure 4 Chromatogram of the light-exposed-OMC solution that contained both the original OMC and the degradation product. The separation was done at 25 °C using a Lichrosorb RP 18 column. The mobile phase used was methanol : water (90 : 10 v/v) at the flowrate of 0.5 mL min^{-1}. The UV detector was set at 325 nm. The sample injection volume was 50 μL.

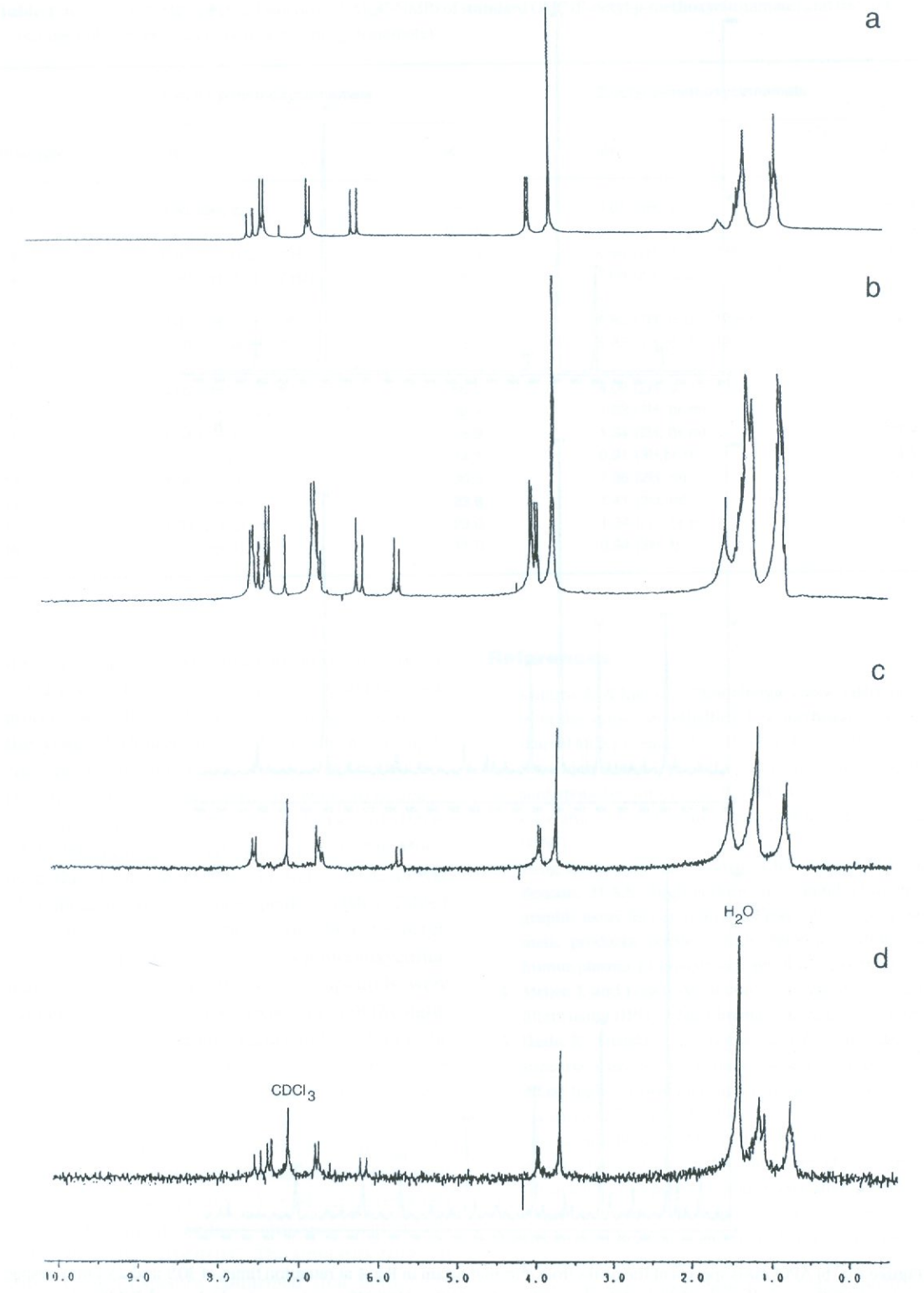

Figure 5 (a)–(d) show ^{1}H NMR of (a) standard OMC, (b) light exposed OMC, (c) isolated photo-degradation product (peak at retention time 49 min in Fig. 4) and (d) isolated OMC (peak at retention time 57 min in Fig. 5). All these ^{1}H NMR spectra were obtained from Cryomagnet NMR Spectroscopy BZH 200/52 (Spectrospin, Oxford Instruments; Bruker, Germany).

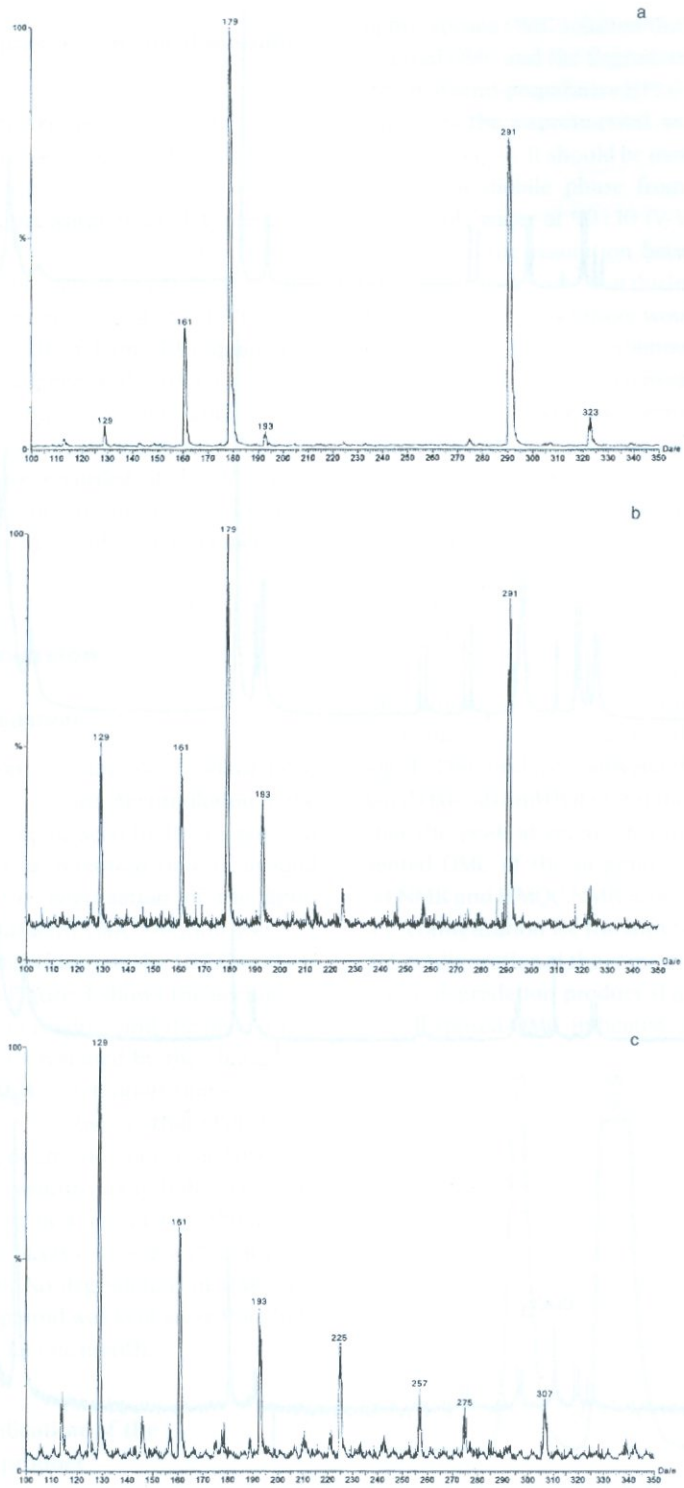

Figure 6(a, b) APCI mass spectra of the peaks from chromatogram in Fig. 4 at retention times of 30.9 and 25.3 min, respectively. (c) APCI mass spectrum of the mobile phase. The online HPLC-APCI-MS was done using Lichrosorb RP 18 column connected to the quadruple mass spectrometer equipped with APCI ionization source. Injection volume was 25 µL. The mobile phase was methanol:water (90 : 10 v/v) at a flowrate of 0.5 mL min^{-1}. Positive-ion mass spectra were recorded at 3.5 kV corona discharge pin voltage (cone voltage at 30 V, counter electrode voltage at 0.2 kV, and source temperature at 120 °C).

Table I ^{1}H- and ^{13}C-NMR Spectral Data (from HMQC-NMR) of standard OMC (*E*-octyl-*p*-methoxycinnamate) and the isolated photo-degradation product (Z-octyl-*p*-methoxycinnamate)

	E-octyl-*p*-methoxycinnamate		*Z*-octyl-*p*-methoxycinnamate	
Position	δH	δC	δH	δC
1	3.81 (3H, s)	55.3	3.81 (3H, s)	55.3
2	–	162.1	–	161.0
3	6.87 (2H, d, J = 7 Hz)	114.3	6.80 (2H, d, J = 7 Hz)	113.3
4	7.40 (2H, d, J = 7 Hz)	129.7	7.66 (2H, d, J = 7 Hz)	132.0
5	–	127.2	–	127.2
6	7.61 (1H, d, J = 16 Hz)	143.1	6.80 (1H, d, J = 12 Hz)	144.2
7	6.29 (1H, d, J = 16 Hz)	115.8	5.82 (1H, d, J = 12 Hz)	117.5
8	–	167.5	–	167.5
9	4.09 (2H, d, J = 6 Hz)	66.8	4.09 (2H, d, J = 6 Hz)	66.7
10	1.63 (1H, br m)	38.9	1.63 (1H, br m)	38.8
11	1.34 (2H, br m)	28.9	1.34 (2H, br m)	28.9
12	0.91 (3H,br t)	14.1	0.91 (3H,br t)	14.1
13	1.36 (2H, m)	30.5	1.36 (2H, m)	30.5
14	1.41 (2H, m)	23.8	1.41 (2H, m)	23.7
15	1.34 (2H, br m)	23.0	1.34 (2H, br m)	23.0
16	0.94 (3H, t)	11.0	0.94 (3H, t)	11.0

the *E*-octyl-*p*-methoxycinnamate and the Z-octyl-*p*-methoxycinnamate; no other photo-degradation product was detected during the light exposure of the OMC. Although it has been known that Z-cinnamates can dimerize to truxillic acid derivatives [10, 11], no other peak than those belong to *E- and* Z-cinnamates were seen in both ^{1}H-NMR and HMQC NMR of the unfractionated-light-exposed-OMC. Moreover, the chromatogram of the light-exposed-OMC also showed only one new peak (Z-OMC). Table I shows the interpreted NMR spectral data of *E*-octyl-*p*-methoxycinnamate and Z-octyl-*p*-methoxycinnamate. To confirm that the two compounds were isomers, an HPLC-APCI-MS experiment of the light-exposed-OMC was done. Figure 6(a,b) shows the APCI mass spectra of peaks at retention time of 30.9 and 25.3 min (see chromatogram in Fig. 4), respectively. Both spectra gave a protonated molecular peak $[CH_3O\ C_6H_4\ CH = CH\ C\ (O)\ C_8H_{18}]H^+$ at m/z of 291. Fragmentation at the ester bond in the ionization source gave the peak at m/z of 179, which corresponds to the protonated methoxy cinnamic acid $[CH_3O\ C_6H_4\ CH = CH\ C\ (O)OH]H^+$. The similarity between the two APCI-spectra confirmed that both compounds were configurational isomer. It should be mentioned here that all other peaks in the spectra correspond to the cluster ions of the mobile phase (see spectrum of the mobile phase in Fig. 6c).

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