# CHAPTER I

INTRODUCTION

Organic molecules may exist as several geometric isomers displaying distinct physical properties and chemical reactivities. A molecule containing two atoms of carbon attached together by a double bond with substituents may be found as two isomeric forms. According to the recent nomenclature based on the Cahn-Ingold-Prelog system, when two substituents on each carbon of the C-C double bond are similar, *trans*-isomer and *cis*-isomer are called. When there is no similarity between two substitutents on different carbon of C=C bond, one isomer is *E*-isomer and another one is *Z*-isomer. Trans and cis isomerism can also exist around a single bond in overcrowded molecules, in particular, in compounds that contain bulky substituents. This is reflected by differences in physical and chemical properties. As long as the energy barrier difference of interconversion between two isomers is not too large, both will easily interconverted.[1]

In general, cis and trans olefins interconvert neither spontaneously at room temperature nor in daylight in the absence of radical generator. Mechanisms for photoisomerization are classified as singlet or triplet according to the multiplicity of the excited state in which twisting occurs. Following excitation, the bond order of the olefinic C,C bond is substantially reduced and the excited olefin relaxes by twisting to a perpendicular excited state, P*. Radiationless decay from P* gives ground state *cis* and *trans* isomers. The rate of twisting varies from olefin to olefin since substitution of H with groups which extend the π system directly affects details of potential energy curves and tends to stabilize transoid, t*, and cisoid, c*, geometries of relevant excited state.[2] An example of a singlet mechanism is shown in scheme 1.1. This explains why the most stable isomer can transform into the less stable isomer upon photoisomerization.

The photoisomerization study has extensively been studied with a large number of olefins. Stilbene (**1**) is one of the most popular models for studying cis-trans photoisomerization of arylenes, and has been the subject of numerous inverstigtion.[3-4] Solvent, pressure and temperature as well as the nature and substituents position strongly influence both the cis-trans ratio and the isomerization kinetics.[5]
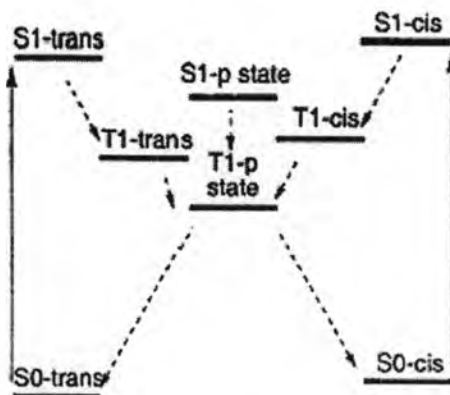
Scheme 1.1 Mechanism for olefin photoisomerization

Another interesting arylene system is cinnamate (**2**) which is widely used as a sunscreen and a negative photoresist polymer in a liquid crystal display technology.[6] Trans-cis photoisomerization of cinnamate and their derivatives has been the subject of numerous investigations. However, it is very surprising that there is a limited information on physical properties and mechanisms of photoisomerization of cinnamates found in scientific literature. In this work, therefore, characterization of the excited states of various methoxy substituted cinnamates has been carried out, mainly through fluorescence spectroscopy. Both steady-state and time-resolved fluorescence spectroscopy were used. In the steady-state experiment, with constant illumination, fluorescence quantum yield in various solvents and temperatures was determined. This quantum yield information is essential in order to understand the relaxation pathways. Through the time-resolved measurement, fluorescence intensity decay was observed and excited state lifetime could be estimated.

Literature review

It has been well accepted on the adverse affects of UV radiation which include direct cellular damage and immunosuppression. Consequences of a long term UV exposure include photoaging, mutations, and photocarcinogenesis.[7-9] Studies have demonstrated that the UVB radiation (280-320 nm) can act on DNA through direct excitation of the DNA bases resulting in the formation of cyclobutane dipyrimidine dimmer (CPDs) via a direct excitation pathway which results in gene mutation.[10,11] Although most human biological molecules cannot directly absorb the UVA radiation (320-400 nm), the damaging affects of UVA are, however, well recognized.

Evidences have been pointed out that this radiation is involved in immunosuppression[12], photoaging[13] and DNA damages[14]. Because UVA radiation is not directly absorbed by DNA, it had been considered to produce less harm than UVB. Recently, data have been indicating that in human skin, UVA produces not only the oxidative DNA damage through 8-oxo-7,8-dihydro-2'-deoxyguanosine, but the radiation also induces CPDs formation probably via a triplet energy transfer photosensitization mechanism. Interestingly, UVA also produces thymine cyclobutane dimmers which are less efficiently repaired than other CPDs produced upon UVB radiation.

Sunscreens are, therefore, widely used to minimize all those damaging effects and various photosensitivity and phototoxicity. Esters of *p*-methoxycinnamic acid have been used as UVB screening compounds in various cosmetic formulations. The most widely used cinnamate is the 2-ethylhexyl-*p*-methoxycinnamate (OMC; **1**).
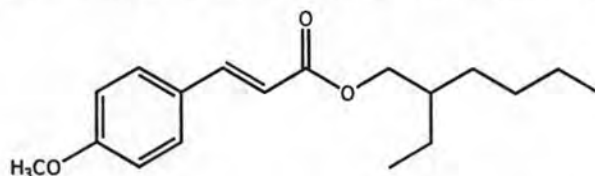

Figure 1.1 Chemical structure of 2-ethylhexyl-*p*-methoxycinnamate (OMC; **1**)

Although this UVB absorber possesses high molar absorption coefficient (about 22000-24000 $M^{-1}cm^{-1}$ depending on the solvent) and very few allergic reaction to human skin[12], the compound, however, undergoes photoisomerization from *trans* configuration to *cis* configuration which leads to the decrease in UV absorption efficiency due to the lower molar extinction coefficient of *cis*-OMC.[16-17] In contrast to the organic UVB filters, choices of organic UVA filters are quite limited. Popular UVA screening compounds include benzophenone and dibenzoylmethanes, however, benzophenones are broad-spectrum filters with solvent dependent absorption bands, low absorbing potential in UVA region and high transdermal absorption.[15] Dibenzoylmethanes have a disadvantage of photostability caused by their reactive chemical structures.[16] Other organic UVA filters include terephthalydenedicamphor sulfonic acid (Mexoryl® SX) (**2**)[19], 2,4-bis{[4-(2-ethylhexyloxy)-2-hydroxyl]-phrnyl}-6-(4-methoxyphenyl)-(1,3,5)-triazine (Tinosorb S)[20], a triazine derivative and bis-[6-(2H-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)]-phenol (Tinosorb-M) (Luther et al 1996), a benzotriazole derivative.[21]

This draw back of OMC together with our desire to develop better UV absorbers have lead us to the syntheses of many cinnamate derivatives. The new cinnamate, 2-ethylhexyl-2,4,5-trimethoxycinnamate shows very good UVA and UVB absorption with excellent photostability whereas 2-ethylhexyl-2,4,6-trimethoxycinnamate is the least photostable derivative with only UVB absorption property.[22] Dermatology tests on the new cinnamate derivatives gave promising results to further the effort on developing the compounds into UV absorber for cosmetic application.

This means more toxicological test and further experiments on photochemical and photophysical properties of the molecules will be required. Normally, the ideal sunscreens should have strong broad absorption band in the UV region and upon UV absorption it should relax quickly to its ground state without producing any harmful intermediates. The compound should be nontoxic, nonphoto-toxic and photostable over long exposure time. It is, therefore, a prudential act to carry out photochemical and photophysical studies on these novel UV absorbers. Hopefully, information on their excited state lifetimes and their relaxation pathways could help ensure the photo-inertness of the molecules.

Relatively little information is available concerning the fluorescence of cinnamic acid and its derivatives.[23-32] Cinnamic acid (3b) is reported to be non-fluorescence in solution. Most photochemical and photophysical studies of olefins were done on stilbenes (4). Although sunscreens are used under the sun, only few sunscreen chemicals have been well characterized for their photophysical properties. Photophysical studies of other sunscreens include studies on urocanic acid and methyl anthanilate. Kerry B. L. studied primary processes of the electronic excited states of *trans*-urocanic acid (5), a UVA/B absorptive metabolizing product of histidine present in epidermis, by ultrafast transient absorption spectroscopy.[24] It was found that two different closely spaced electronic states were observed. Excitation at 266 nm populates a $\pi\pi^*$ state that is localized on the imidazole ring. Steady-state excitation spectra suggest that a proton transfer process from *trans*-urocanic acid to the solvent occurs following the excitation at 266 nm at pH 5.6 which generates and electronically excited state of the deprotonated molecule. The population in this singlet state decays by intersystem crossing with a rate constant of 1.4×10^{11} s^{-1}. Isomerization is unlikely to occur from this triplet state. Excitation of *trans*-urocanic

acid at 306 nm populates an entirely different state which leads to isomerization. Beeby A. and Jones A. E studied the photophysical properties of methyl anthranilate (6), an UVA filter, in various solvents.[25] Luminescence studies indicated that indicated this compound was highly fluorescent (ϕ_f = 0.64 in ethanol). Phosphorescence was also been detected at low temperature with a lifetime of 2.5 seconds. Kinetic UV absorption measurements revealed a transient species with absorption maxima at 480 nm and solvent dependent lifetimes of 26-200 μs, attributed to the triplet state.

Cantrell et al studied the UVA sunscreen, Mexoryl® SX, in various solvent environments using a nanosecond laser flash photolysis.[23] The transient absorption was detected around 470-500 nm and a solvent dependent lifetime of 50-120 ns by nanosecond 355 nm laser excitation. This is attributed to the triplet state of Mexoryl® SX on the basis that it is quenched by molecular oxygen leading to the formation of singlet oxygen in acetonitrile. The singlet oxygen quantum yield is estimated as 0.09 ± 0.03 in acetonitrile. In contrast, in the commercial sunscreen formulation there was no observable difference in the measured triplet lifetime between sample exposed to oxygen or argon, suggesting that the singlet oxygen quantum yield in such environments is likely to be orders of magnitude lower than that measure in acetonitrile.

Shindo Y. studied the photoisomerization of ethylcinnamate (3d) in dilute solution with direct irradiation and irradiation sensitized with Michler's ketone.[26] It was found that the quantum yield of isomerization for *trans* to *cis* and *cis* to *trans* in ethanol were 0.26 and 0.29 respectively. Nearly half of the excited singlet state of each isomer is directly deactivated to the ground state of the same isomer, while the remainder is converted to both twisted singlet and twisted triplet states. Ishigami T. reported that direct *trans* to *cis* isomerization of a series of methyl cinnamates having the electron withdrawing substituents such as nitro, acetyl, cyano group on their para-substitution take place *via* the triplet excited state, where as the *cis/trans* isomerization occurs *via* the singlet excited state.[27] On the other hand, for unsubstituted methyl cinnamate and methyl cinnamate with the electron donating group such as methyl, isopropyl, methoxy group as its para substituent together with *p*-chloro and *p*-dimethylamino cinnamate, *trans/cis* and *cis/trans* isomerizations seem to occur *via* the excited singlet state. Lewis F. D *et al* studied the fluorescence

lifetime of methyl cinnamate using picosecond laser spectroscopy[28] and reported that methyl cinnamate fluorescence could not be resolved from the laser decay profile thus indicating a lifetime of shorter than 3 ps. The short lifetime is tentatively attributed to the competition between fluorescence from the originally populated π, π^* singlet state and its internal conversion to a lowest n, π^* singlet state. Furthermore, the efficiency of isomerization is independent of solvent, but dependent upon temperature and excitation wavelength. For *trans* to *cis* and *cis* to *trans* methyl cinnamate, isomerization quantum yields were 0.30 and 0.29 in both dichloromethane and benzene solution.
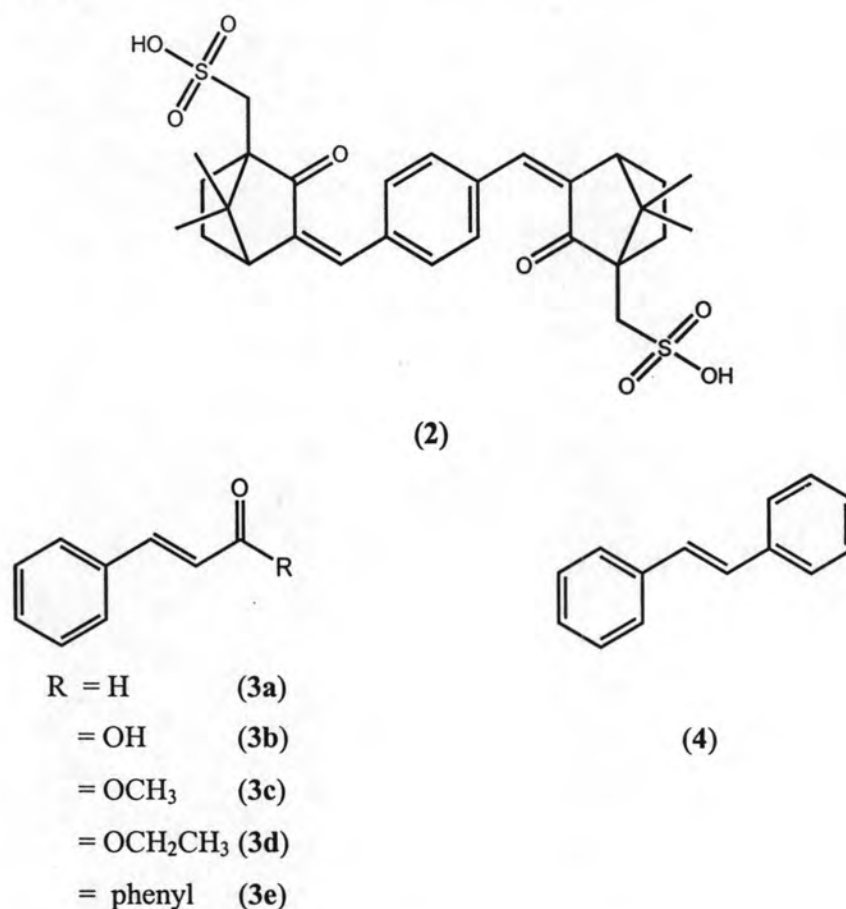

(2)

R = H   (3a)

   = OH   (3b)

   = OCH$_3$ (3c)

   = OCH$_2$CH$_3$ (3d)

   = phenyl   (3e)

(4)

Figure 1.2 Chemical structures of terephthalydenedicamphor sulfonic acid (Mexoryl® SX) (2), cinnamate derivatives (3), stilbene (4), *trans*-urocanic acid (5) and methyl anthranilate (6).
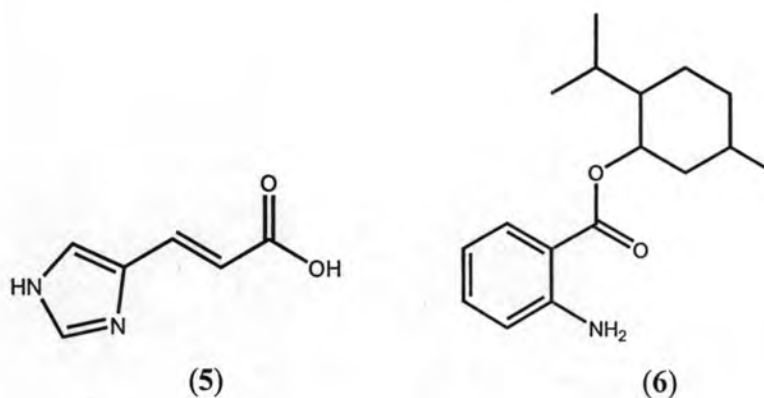
Figure 1.2 (continue) Chemical structures of terephthalydenedicamphor sulfonic acid (Mexoryl® SX) (2), cinnamate derivatives (3), stilbene (4), *trans*-urocanic acid (5) and methyl anthranilate (6)

Although 2-ethylhexyl-*p*-methoxycinnamate (OMC; 1) is one of the most widely used UV absorber on the market, its photophysical and photochemical properties are not very well characterized. One of only a few studies found in scientific literature was the steady state and laser flash photolysis of OMC done by Morliere P. *et al.* This study suggested that the *trans/cis* photoisomerizations occured in less than 50 ns, without any detectable intermediate.[29] The photochemical process, therefore, should take place *via* a singlet excited state or a very short live excited triplet state. The study also showed that cinnamates (1) were not photodynamic sensitizers but are able to quench the 8-methoxypsoralen and 5-methoxypsoralen triplet producing *trans/cis* isomerization. The other study was done by Gonzenbach H. et al[30] in which the triplet energy level of OMC was determined *via* its quenching of donor phosphorescence and more precisely by oxygen perturbation. It was found that the triplet energy level of OMC was at 57 kcal mol^{-1}. It was therefore concluded that OMC was unable to sensitize the formation of thymine triplets (75 kcal mol^{-1}). Smith and Miller[31] reported the effect of environment on the photochemistry of *p*-methoxycinnamic acid and OMC. It was found that the fluorescence quantum yields of solutions of these cinnamoyl compounds were low, $\leq 1.6 \times 10^{-3}$, indicating that these molecules should have very efficient non-radiative pathway for the excited singlet state relaxation. The photoinduced dynamics study of *trans*-cinnamaldehyde (**3a**), *trans*-cinnamic acid (**3b**), methyl-*trans*-cinnamate (**3c**) and phenyl-trans-3-phynyl-2-enoate (**3e**) in hexane and acetonitrile using a pump-supercontinuum-probe technique

have been reported by Lustres et al.[32] The proposed mechanism is given in scheme 1.2. The early sub-picosecond evolution (0.1-0.5 ps) is assigned to $S_3 \rightarrow S_1$ excited state relaxation and followed by a 3 ps decay of excited state absorption due to a structural intramolecular rearrangement which includes rotation around C=C bond and twist of the phenyl ring.

R= H, OH, CH$_3$ or phynyl
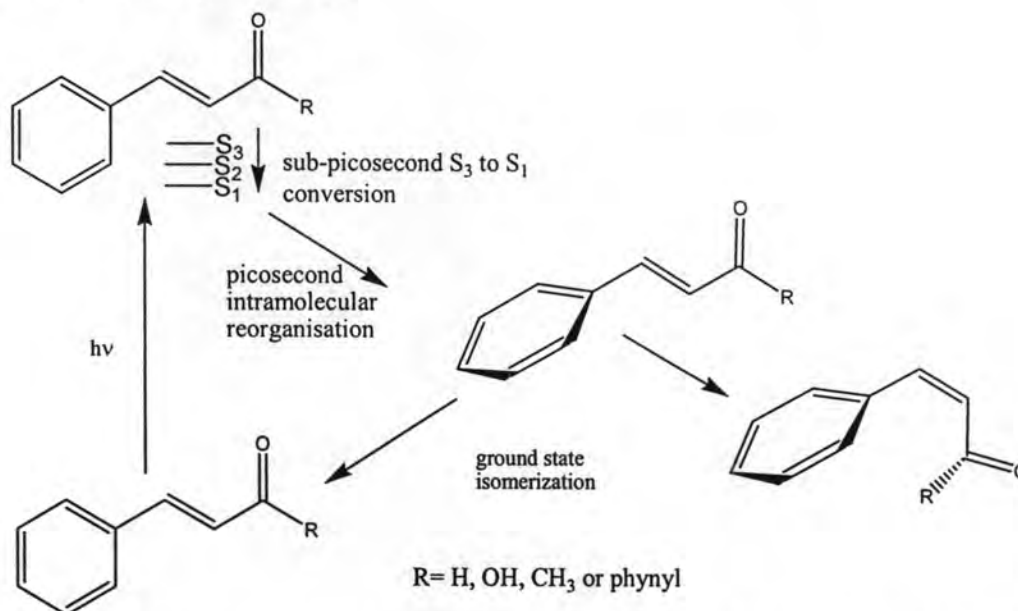
Scheme 1.2 Proposed mechanism for the photophysical behaviour exhibited by cinnamoyl compounds reported by Lustres et al.[32]

In this work, characterization of the excited states of various methoxy substituted cinnamates have been done, mainly through fluorescence spectroscopy. Both steady-state and time-resolved fluorescence spectroscopy have been carried out. In the steady-state experiment, with constant illumination, fluorescence quantum yield in various solvents and temperatures were determined. This quantum yield information is essential in order to understand the relaxation pathways. Through the time-resolved measurement, fluorescence intensity decay will be observed and excited state lifetime was estimated.

Although results from the above proposed works by themselves are enough to speculate photo-reactivity of the tested novel UV filter molecules, analyzing the relationship between structure of cinnamate derivatives and their photochemical/photophysical properties was also carried out. The result should benefit further development of other cinnamate derivatives for various photo-reaction applications.