

CHAPTER III

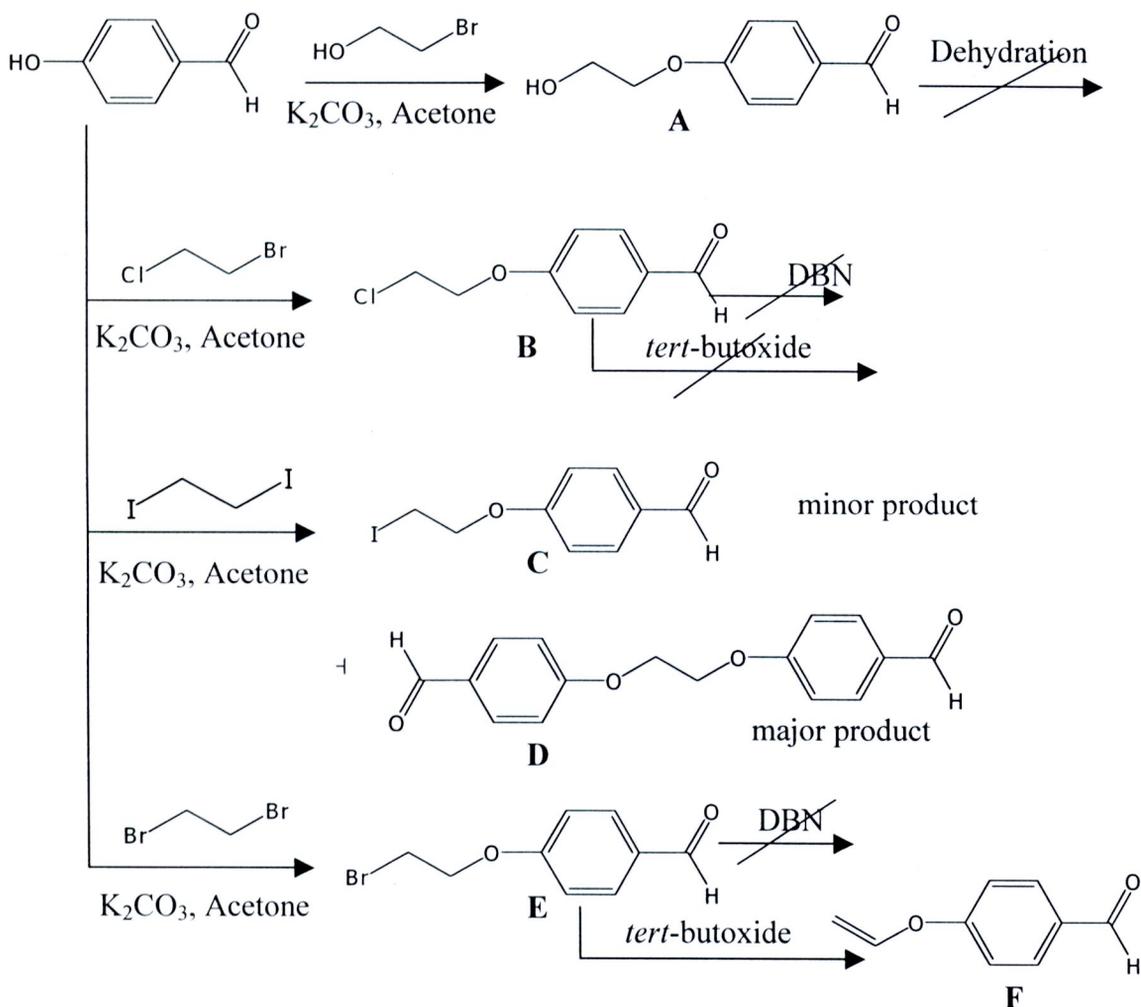
RESULT AND DISCUSSION



3.1 Synthesis of Poly(diethylbenzmalonate vinyl ether)

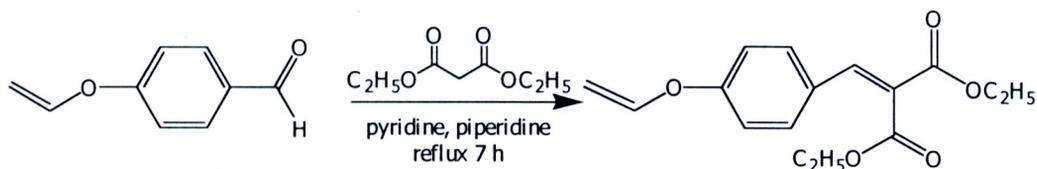
3.1.1 Synthesis of diethylbenzmalonate vinyl ether

To prepare 4-vinyloxybenzaldehyde (**F**) various processes were tried. The overall trial of **F** was depicted in Scheme 3.1. Successful preparation of **F** was done through the debromination of 4-((2-bromo)ethoxy)benzaldehyde (**E**) using *tert*-butoxide as a bulky non-nucleophilic base.



Scheme 3.1 Trials for the synthesis 4-vinyloxybenzaldehyde.

The synthesis of diethylbenzmalonate vinyl ether monomer was done through Knoevenagel-Doebner condensation between one mole equivalent of 4-vinyloxybenzaldehyde and one mole equivalent of diethylmalonate. The general equation is shown below:



The formation of diethylbenzmalonate vinyl ether monomer could be monitored by TLC. Column chromatography allowed the isolation of diethyl benzmalonate vinyl ether monomer in a purity. The product is pale yellowish oil, which was well soluble in both polar and non polar solvents including hexane, dichloromethane, ethyl acetate, chloroform, acetone, methanol and ethanol. The structure of this compound was elucidated on the basis of the ^1H , ^{13}C -NMR spectroscopy.

3.1.2 Synthesis of poly(diethylbenzmalonate vinyl ether)

After successful synthesis and characterization of the diethylbenzmalonate vinyl ether monomer which processes the functionality to permit free radical polymerization. Free radical polymerization of the compound at 80 °C in acetonitrile using dibenzoyl peroxide as the initiator gave poly(diethylbenzmalonate vinyl ether). The yellow oil product was characterized by ^1H -NMR and IR spectroscopy. From NMR data (see section 3.3) it can be concluded that the product was poly(diethylbenzmalonate vinyl ether). The decrease of vinylic proton resonances at 6.68 ppm (dd, 1H, $=\text{CHOAr}$, $J = 14.04, 6.24$ Hz), 4.90 (dd, 1H, $\text{CH}_{2a}=\text{CHO}$, $J = 14.04, 0-1$ Hz) and 4.58 (dd, 1H, $\text{CH}_{2b}=\text{CHO}$, $J = 6.24, 0-1$ Hz) indicated that the polymerization had been taking places. The weight average molecular weight (\overline{M}_w) of the product obtained by gel permeation chromatography technique (GPC, see section 3.3.3) was 1943, with the polydispersity of 1.30.

Experiment was done to obtain UV absorption property (λ_{\max} and ϵ) of this poly(diethylbenzmalonate vinyl ether). As show in Figure 3.1, the oligomer has absorption band with λ_{\max} of 308 nm ($\epsilon = 148,000 \text{ M}^{-1}\text{cm}^{-1}$) in ethanol, which corresponds to the UVB region. Since the weight average molecular weight (\bar{M}_w) of the oligomer was 1943, the average degree of polymerization was 6.7. Molar absorption coefficient calculated per mole of monomeric unit was, therefore, 22,000 $\text{M}^{-1}\text{cm}^{-1}$. Molar absorption coefficient (ϵ) of poly(diethylbenzmalonate vinyl ether), therefore, agree with the value of the octyl-*p*-methoxycinnamate (OMC) (λ_{\max} of 309 nm, $\epsilon = 18,900 \text{ M}^{-1}\text{cm}^{-1}$ in ethanol) (32).

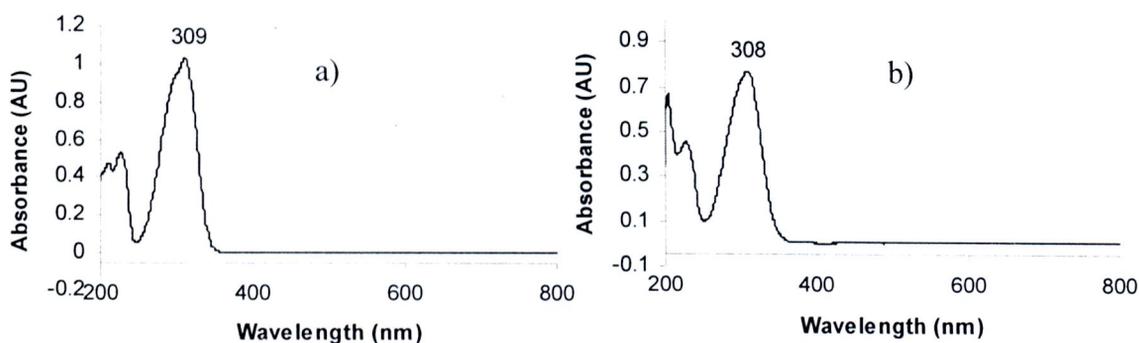


Figure 3.1 UV spectrum of a) $5.43 \times 10^{-5} \text{ M}$ octyl-*p*-methoxycinnamate (OMC) and b) $3.60 \times 10^{-5} \text{ mol}$ of chromophore/L of poly(diethylbenzmalonate vinyl ether) in ethanol.

As demonstrated here that poly(diethylbenzmalonate vinyl ether) could be synthesized through the simple free radical polymerization of diethylbenzmalonate vinyl ether, this opens up the possibility to prepare this particular oligomeric/polymeric UV-filter. Preliminary UVA/B photostability study also showed that the oligomeric material was quite stable upon being exposed to UVA and UVB radiation at 1.10 mw/cm^2 and 0.07 mw/cm^2 , respectively for 30 min. Figure 3.2 shows UV absorption spectra of the compound before and after UVA/B irradiation and Figure 3.3 shows photostability results of octyl-*p*-methoxycinnamate (OMC) and poly(diethylbenzmalonate vinyl ether). It should be noted here that the UVA and UVB irradiation in the sunlight around noon-time during summer in Bangkok are

2.00-3.00 mw/cm^2 and 0.05-0.08 mw/cm^2 , respectively. Therefore, this means that the prepared oligomeric material will be very stable upon sun exposure.

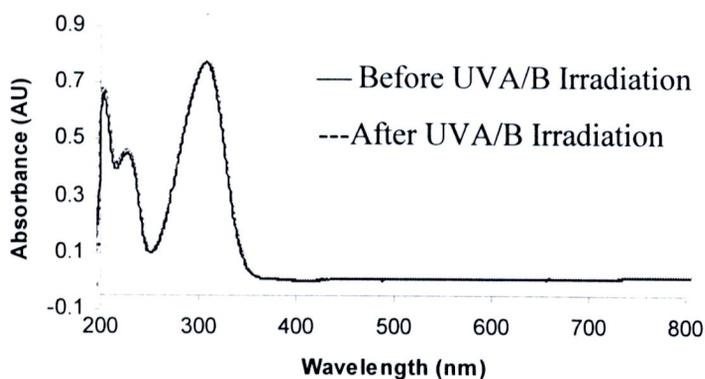


Figure 3.2 UV spectrum of 3.60×10^{-5} mol of chromophore/L of poly(diethyl benzalmonate vinyl ether) in ethanol; the irradiation was done for 30 min at 1.10 mw/cm^2 UVA and 0.07 mw/cm^2 UVB.

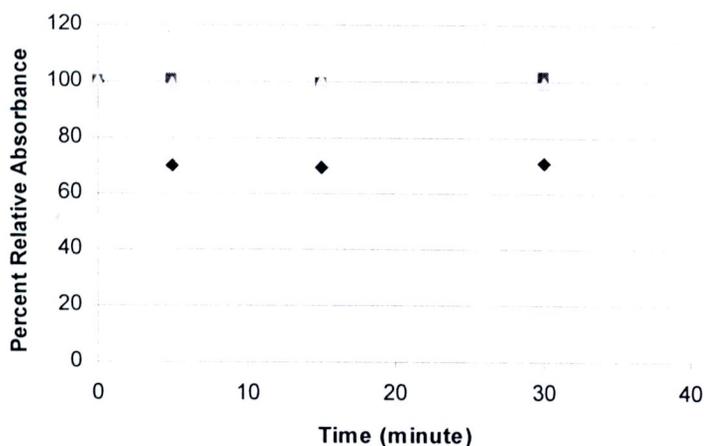


Figure 3.3 Photostability of octyl-*p*-methoxycinnamate (OMC) and poly(diethylbenzalmonate vinyl ether) in ethanol; the irradiation was done for 30 min at 1.10 mw/cm^2 UVA and 0.07 mw/cm^2 UVB.

- ◆ 5.43×10^{-5} M of octyl-*p*-methoxycinnamate (OMC)
- 1.80×10^{-5} mol of chromophore/L of poly(diethylbenzalmonate vinyl ether)
- ▲ 3.60×10^{-5} mol of chromophore/L of poly(diethylbenzalmonate vinyl ether)

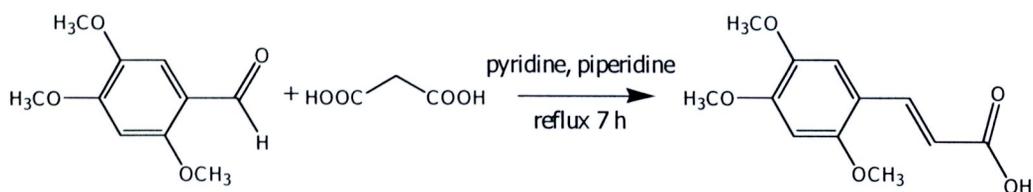
From Figure 3.3, it is obvious that the oligomeric material was more stable than the commonly used OMC. The result is encouraging for further developing of this oligomeric material for sunscreen application. Previous studies indicated that the reduction of absorption efficiency of OMC corresponded to the *trans* to *cis* photoisomerization of the compound. This is because the *cis*-configuration processes only half ϵ value comparing to that of *trans*-configuration (30). Therefore by changing from cinnamate into benzalmalonate, *trans/cis* photoisomerization can be avoided.

Since the oligomer was soluble in various solvents including hexane, dichloromethane, ethyl acetate, chloroform, acetone, methanol and ethanol, applications in cosmetic formation would be very possible. Further study on the correlation between physical properties and molecular weight of the compound should be done.

3.2 Grafting of *trans*-2,4,5-Trimethoxycinnamic Acid on Poly(Vinyl Alcohol)

3.2.1 Preparation of *trans*-2,4,5-trimethoxycinnamic acid

In this research *trans*-2,4,5-trimethoxycinnamic acid was used as a UVA/B absorbing chromophore to be grafted onto poly(vinyl alcohol). This compound is a novel UVA/B filter discovered earlier by Monhaphol and Wanichwecharungrueng (32). The synthesis of the compound was done through Knoevenagel-Doebner condensation between one mole equivalent of malonic acid and one mole equivalent of *trans*-2,4,5-trimethoxybenzaldehyde. The general equation is shown below:



The structure of the synthesized compound was characterized using various spectroscopic techniques including ^1H , ^{13}C -NMR, IR.

Experiment was done to obtain UV absorption property (λ_{max} and ϵ) of this *trans*-2,4,5-trimethoxycinnamic acid. As show in Figure 3.4, this compound has two absorption bands; λ_{max} of 286 nm ($\epsilon = 11,900 \text{ M}^{-1}\text{cm}^{-1}$) and 344 nm ($\epsilon = 13,300 \text{ M}^{-1}\text{cm}^{-1}$), covering both the UVA and UVB spectral regions.

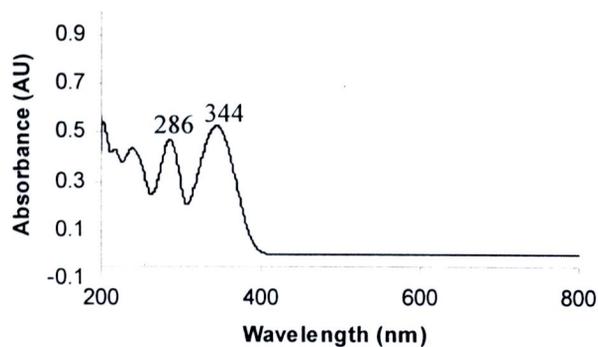
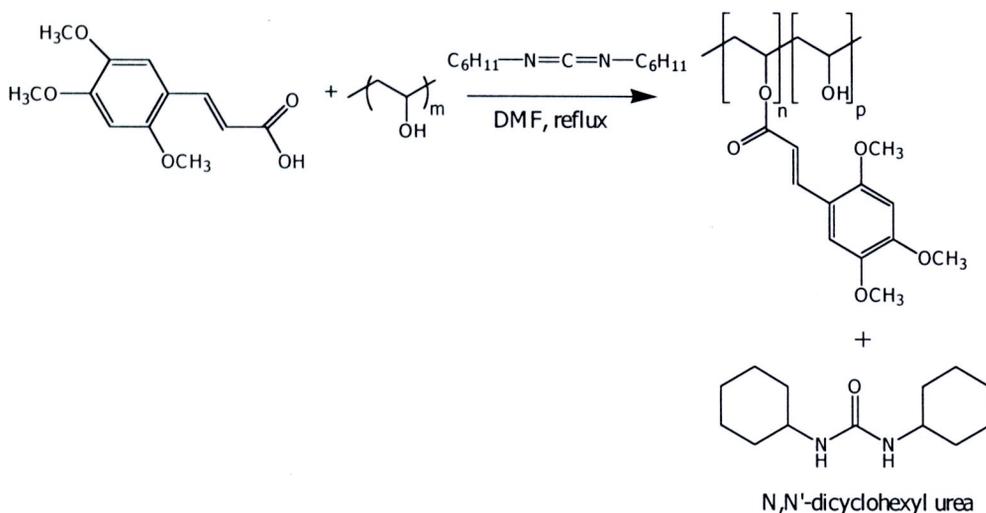


Figure 3.4 UV spectrum of 4.00×10^{-5} M *trans*-2,4,5-trimethoxycinnamic acid in ethanol.

3.2.2 Grafting of the UV filter chromophore; *trans*-2,4,5-trimethoxycinnamic acid onto poly(vinyl alcohol)

Grafting of the UV filter chromophore; *trans*-2,4,5-trimethoxycinnamic acid onto poly(vinyl alcohol) was done with the coupling agent; N,N'-dicyclohexyl carbodiimide (see Scheme 3.2). Experiments were carried out at 50°C, 70°C, 90°C, 120°C and 150°C to find out the best grafting temperature. After stirring for 60 hours, the mixture was placed without agitation to precipitate out N,N'-dicyclohexyl urea (DCU) and the solution was then filtered. The liquid part was then mixed with 300 mL of 15 % (v/v) cool hydrochloric acid solution under vigorous stirring. The precipitated product was separated by suction filtration, washed with cold water and recrystallized with hexane. The grafted product was further purified by dialysis technique.



Scheme 3.2 Grafting of the UV filter chromophore; *trans*-2,4,5-trimethoxy cinnamic acid onto poly(vinyl alcohol).

As mentioned in the experimental section, grafting could not be done at 120°C and 150°C because of thermal decomposition of poly(vinyl alcohol).

Solubility of the grafted products is described in Table 3.1. It can be concluded that solubility in organic solvent increases as the degree of substitution increases. The very interesting point is that the product obtain from 90°C reaction is very soluble in many organic solvent including ethanol. This permits the easy use of this grafted product in various cosmetic preparations. Therefore, the product obtain from 90°C reaction, which was the best grafting temperature, was chosen for further characterization of molecular weight using gel permeation chromatography technique (GPC). The GPC analysis of this compound (see section 3.3.3) gave weight average molecular weight (\bar{M}_w) of 31557 with the polydispersion value of 1.69. From the weight average molecular weight of the grafted product and the molecular weight of the starting material, degree of cinnamoyl substitution could be calculated (see Appendix B). The average degree of cinnamoyl substitution value was 43% by mole.

Table 3.1 Solubility of the poly(vinyl alcohol) and three grafted products

Solvent	Solubility* of PVA	Solubility* of the various temperatures of grafted products		
		50°C	70°C	90°C
hexane	--	--	--	--
dichloromethane	--	+/-+ ^a	+/-+ ^a	+/-+ ^a
diethyl ether	--	--	--	--
ethyl acetate	--	+/-+ ^a	+/-+ ^a	+/-+ ^a
chloroform	--	+/-++ ^a	+/-++ ^a	++
methanol	--	+/-++ ^a	+/-++ ^a	++
ethanol	--	+/-++ ^a	+/-++ ^a	++
pyridine	--	++	++	++
THF	--	+/-++ ^a	+/-++ ^a	++
DMF	--/+ ^a	++	++	++
DMSO	--/+ ^a	++	++	++
H ₂ O	--	--	--	--

^a Heating of solvent

Solubility* 10 mg sample was dissolved in 2 mL of a solvent

-- insoluble

+ - partial soluble

++ soluble

Experiments were done to obtain UV absorption property (λ_{\max} and ϵ) of the 90°C grafted product. As show in Figure 3.5, this compound show two absorption bands; λ_{\max} of 284 nm ($\epsilon = 1,180,000 \text{ M}^{-1}\text{cm}^{-1}$) and 342 nm ($\epsilon = 1,220,000 \text{ M}^{-1}\text{cm}^{-1}$), which correspond to the UVB and UVA region respectively. Since the weight average molecular weight (\bar{M}_w) of the polymer was 31557, the average degree of cinnamoyl substitution value was 43% by mole. Molar absorption coefficient calculated per mole of cinnamoyl unit were, therefore, $12,100 \text{ M}^{-1}\text{cm}^{-1}$ at λ_{\max} of 284 nm and $12,500 \text{ M}^{-1}\text{cm}^{-1}$ at λ_{\max} of 342 nm.

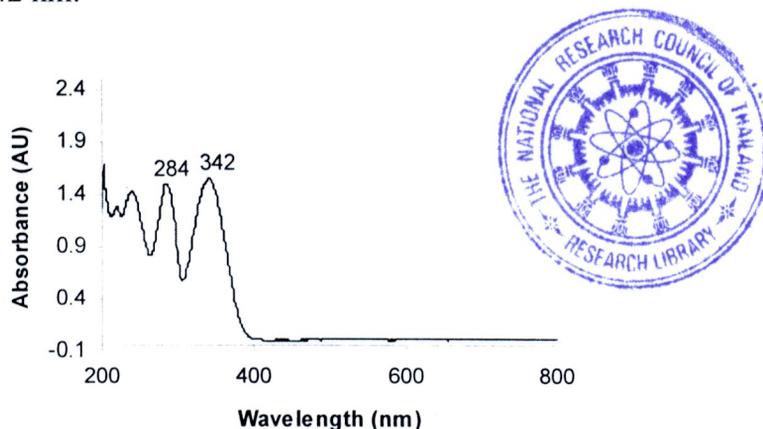


Figure 3.5 UV spectrum of 1.24×10^{-4} mol of chromophore/L of the grafted product obtain from 90°C reaction in ethanol.

When measured in ethanol the grafted product; poly[(vinyl 2,4,5-trimethoxy cinnamate)(vinyl alcohol)] copolymer showed small hypsochromic shift (2 nm) of the UV absorption when compared to 2,4,5-trimethoxycinnamic acid precursor. The molar extinction coefficients of the chromophores in the grafted product are similar to 2-ethylhexyl-2,4,5-trimethoxycinnamate ($\lambda_{\max} = 290 \text{ nm}$; $\epsilon = 12,400 \text{ M}^{-1}\text{cm}^{-1}$ and $\lambda_{\max} = 349 \text{ nm}$; $\epsilon = 14,200 \text{ M}^{-1}\text{cm}^{-1}$) (32). This is reasonable because similar chromophore should give similar UV absorption properties.

As mentioned earlier that upon esterification from 2,4,5-trimethoxycinnamic acid to poly[(vinyl 2,4,5-trimethoxycinnamate)(vinyl alcohol)] copolymer, -2 nm hypsochromic shift was observed. However, in previous study, upon esterification from 2,4,5-trimethoxycinnamic acid to 2-ethylhexyl-2,4,5-trimethoxycinnamate, +5 nm bathochromic shift was observed (32). The reason for this difference may lie on the fact that the grafted product contains many hydrophilic hydroxyl groups and those groups can hydrogen bond with the carbonyl moiety of the chromophore. This kind of

interaction may affect the excited state configuration in the way that increase its energy level compared to the excited state of ethylhexyl esterification product. The application can also be that such interaction somehow increases the gap between the ground state and the excited state of the grafted product.

In addition, the grafted product was subjected to photostability test. The tests were done in ethanol (results shown in Figure 3.7 and Figure 3.8). The UVA and UVB absorption efficiency of the grafted product decreased as the compound was exposed to UV-light. The decreased in UV absorption upon UV exposure agreed with the previous studies (28-30) which have shown that the lost in UV absorption efficiency was caused by *trans* to *cis* isomerization. The $^1\text{H-NMR}$ spectrum of the UV-exposed grafted product was shown in Figure 3.6. Obvious *trans* to *cis* photoisomerization could be seen from this NMR spectrum.

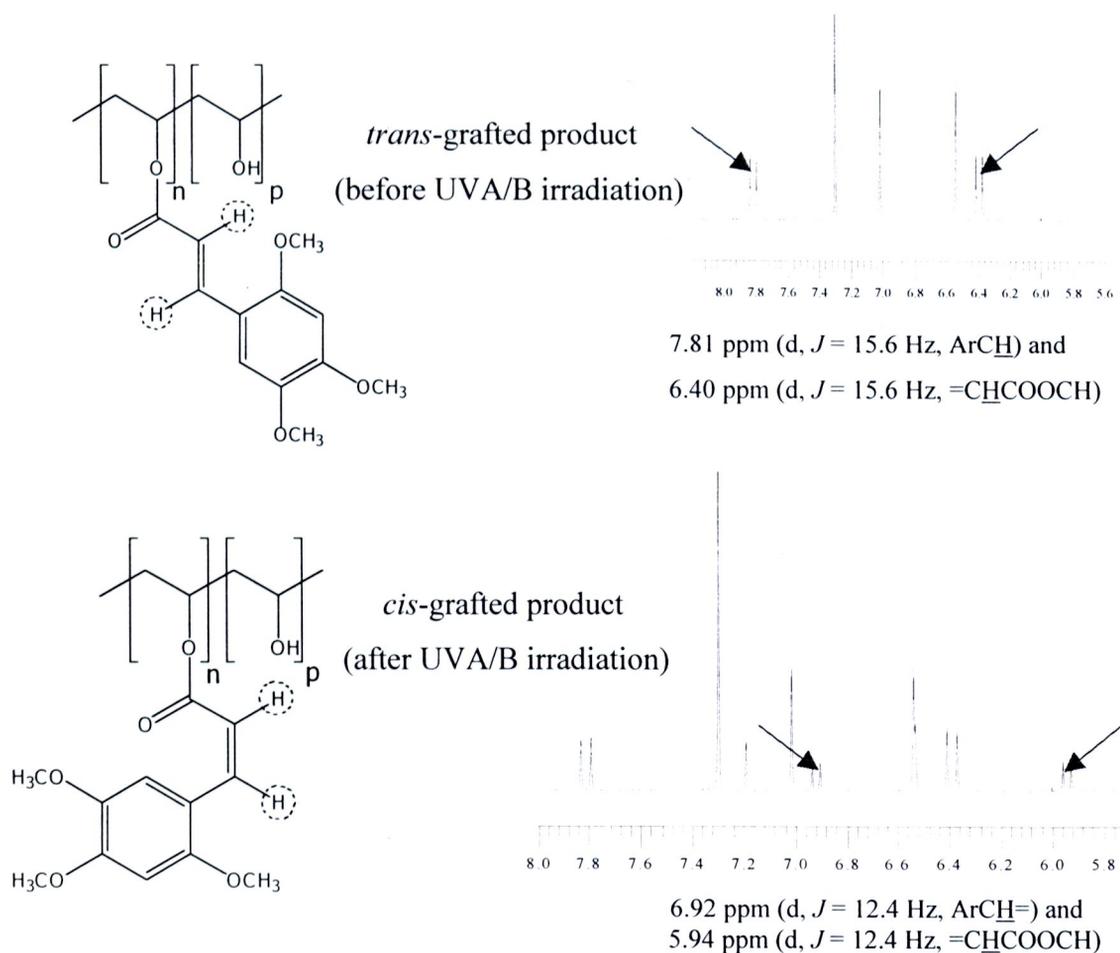


Figure 3.6 $^1\text{H-NMR}$ spectrum of the grafted product obtains from 90°C reaction after UVA/UVB irradiation; the irradiation was done for 30 min at 1.10 mw/cm^2 UVA and 0.07 mw/cm^2 UVB.

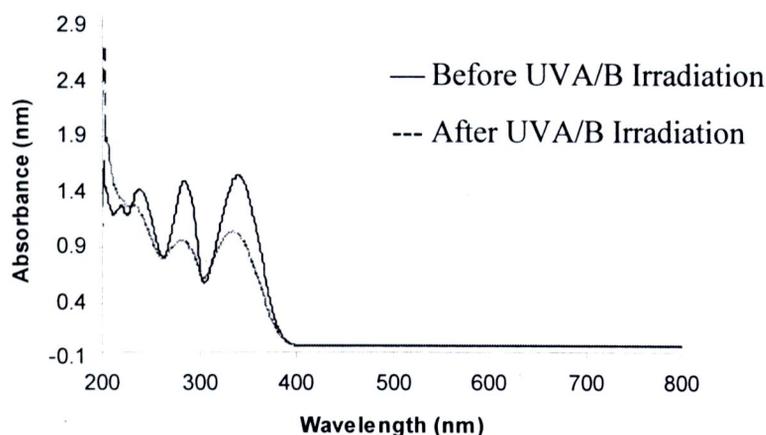


Figure 3.7 UV spectrum of 1.24×10^{-4} mol of chromophore/L of the grafted product obtain from 90°C reaction in ethanol before and after irradiation; the irradiation was done for 30 min at 1.10 mw/cm^2 UVA and 0.07 mw/cm^2 UVB.

As can be seen in Figure 3.8, the poly[(vinyl 2,4,5-trimethoxycinnamate) (vinyl alcohol)] copolymer and the free 2,4,5-trimethoxy cinnamic acid showed moderated photostability. And as mentioned earlier, the decreased in UV absorption efficiency was due to *trans* to *cis* photoisomerization (28-30). From the graph, decrease in UV absorption was very obvious for both free chromophore and grafted chromophore. The grafted chromophore showed less photostability which indicated more *trans* to *cis* configurational changes for the chromophoric moieties in the grafted environment. This may be a result from polar hydroxyl groups on the polymeric chain. Previous study has shown that the *trans* to *cis* configurational change of this chromophore was directly effected by polarity of the solvent. More *trans* to *cis* configurational change was found at photostationary equilibrium in more polar solvent (31). Further study on formulation, transdermal absorption and skin irradiation of the compound should be done.

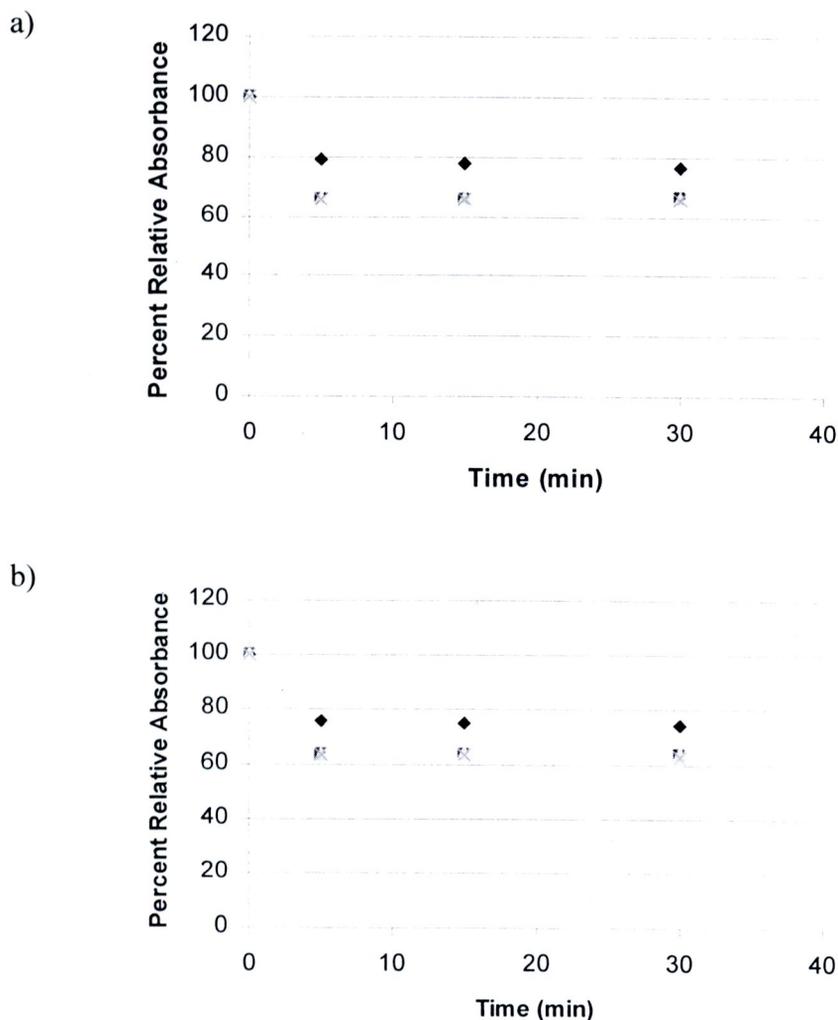


Figure 3.8 Photostability of 2,4,5-trimethoxycinnamic acid and the grafted product in ethanol a) UVA region ($\lambda = 342$ nm) and b) UVB region ($\lambda = 284$ nm); the irradiation was done for 30 min at 1.10 mw/cm^2 UVA and 0.07 mw/cm^2 UVB.

- ◆ 5.00×10^{-5} M of 2,4,5-trimethoxycinnamic acid
- 9.34×10^{-5} mol of chromophore/L of the grafted product
- ▲ 1.24×10^{-4} mol of chromophore/L of the grafted product
- × 1.55×10^{-4} mol of chromophore/L of the grafted product

3.3 Spectroscopic Data of All Synthesized Compounds

The structures of all synthesized compounds were well characterized using various spectroscopic techniques including ^1H , ^{13}C -NMR, IR and GPC (gel permeation chromatography). Spectroscopic spectra of all compounds are shown in Appendix B.

3.3.1 Infrared Spectroscopy

Poly(diethylbenzalmalonate vinyl ether) displays the characteristic of common functional groups in IR spectra. The absorption band around 2983 cm^{-1} corresponds to C-H stretching of aliphatic hydrocarbons. The C=O stretching vibrations are shown at 1730 cm^{-1} . The C=C (next to aromatic ring) stretching vibration at 1504 cm^{-1} and C=C stretching of the aromatic ring at $1600\text{-}1420\text{ cm}^{-1}$ are also detected. The C-O stretching vibration is detected at 1247 cm^{-1} .

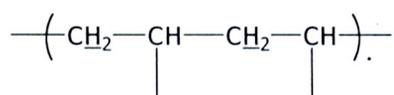
In the case of the grafted product, the poly[(vinyl 2,4,5-trimethoxycinnamate) (vinyl alcohol)] copolymer, O-H stretching vibrations of alcohol is presented around 3257 cm^{-1} (br). The C=C (next to aromatic ring) stretching vibration and C=C ring stretching were detected at $1600\text{-}1452\text{ cm}^{-1}$.

3.3.2 NMR Spectroscopy

$^1\text{H-NMR}$

For NMR spectroscopy, CDCl_3 was used as solvent for all compounds. The $^1\text{H-NMR}$ spectrum of poly(diethylbenzalmalonate vinyl ether) shows two doublet of doublet signals with each of 1H integration at 6.68 ppm ($J = 14.04, 6.24\text{ Hz}$), 4.92 ($J = 14.04, 0\text{-}1\text{ Hz}$) and 4.58 ppm ($J = 6.24, 0\text{-}1\text{ Hz}$) which correspond to $\text{CH}_2=\text{CH-O-Ar}$. Signals that were detected at 7.48, 7.03 ppm can be assigned for aromatic protons. The singlet signal at 7.72 ppm corresponds to $\text{Ar-CH}=\text{C}(\text{COOC}_2\text{H}_5)$.

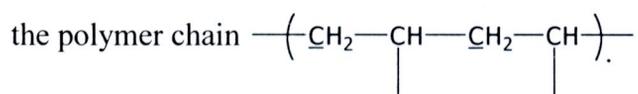
Similarly, the $^1\text{H-NMR}$ spectrum of poly[(vinyl 2,4,5-trimethoxycinnamate) (vinyl alcohol)] copolymer (90°C grafted product), displays two double signals with each of 1H integration at 7.81 ppm ($J = 15.6\text{ Hz}$) and 6.40 ppm ($J = 15.6\text{ Hz}$) which correspond to $\text{Ar-CH}=\text{CH-COOCH-}$ (H-a and H-b). The coupling constant absolutely indicates *trans*-geometry in the molecule. Signals that were detected at 7.00, 6.53 ppm and 3.94, 3.89, 3.88 ppm can be assigned for aromatic and methoxy protons respectively. Signal at 2.05-1.11 ppm was assigned for polyvinyl back bone



^{13}C -NMR

The ^{13}C -NMR spectrum of poly(diethylbenzmalonate vinyl ether) displays signals belonging to olefinic carbon at 141.30 ppm ($\text{Ar}-\underline{\text{C}}\text{H}=\text{C}(\text{COOC}_2\text{H}_5)$). The signals of aromatic carbons were detected at 116.88 and 131.49 ppm respectively. The spectrum also shows signals of vinylic carbon atom at 97.11 ($\underline{\text{C}}\text{H}_2=\text{CH}-\text{O}-\text{Ar}$) and 61.77 ($\text{O}\underline{\text{C}}\text{H}_2$) ppm and alkyl carbons around 13.98-14.20 ppm.

In the case of poly[(vinyl 2,4,5-trimethoxycinnamate)(vinyl alcohol)] copolymer (90°C grafted product), the two signals of olefinic carbons were detected at 97.03 and 111.39 ppm. Signals at 111.40 and 135.50 ppm were assigned for aromatic carbons. The spectrum shows signals of methoxy carbons at 56.41-56.04 ppm. Moreover, signals at 33.98-24.93 ppm were assigned for carbon back bone of the polymer chain



3.3.3 Gel Permeation Chromatography

The weight average molecular weight (\overline{M}_w) of both products were determined by gel permeation chromatography (GPC) (see Appendix B). Table 3.2 summarized the results of the \overline{M}_w of each product.

Table 3.2 \overline{M}_w of products

Compounds	\overline{M}_w	Polydispersity
Poly(diethylbenzmalonate vinyl ether)	1943	1.30
Grafting of the UV filter chromophore on poly(vinyl alcohol)	31557	1.69