Synthesis of novel polyamides starting from ferulic acid dimer derivative

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Abstract—Novel polyamides containing cyclobutane in the main chain were synthesized from a dimmer that was obtained by topochemical [2 + 2] photo-dimerization of *O*-acetylferulic acid crystals, using two different methods: (1) The dimer was converted into a three-dimensional network polyphenylester on heating, eliminating acetic acid. The network polymer was reacted with a diamine to afford a linear polyamide. (2) The same dimer chloride was submitted to an interfacial polycondensation with a diamine. Although the first method is a unique one to convert a network polymer to a linear polymer, the second method was found to be more practical from the viewpoints of both preparation process and the quality of the polymer obtained. These synthetic procedures into the polyamides and characterization of resulted polymers are described. The phenolic polymer showed an anti-oxidant nature when reacted with a free radical DPPH.

Keywords: *O*-Acetylferulic acid; topochemical [2 + 2] addition; three-dimensional network polymer; photo-dimerization; cyclobutane polymer; polyamides; anti-oxidizer.

1. INTRODUCTION

Various types of polymers having a cyclobutane ring either in the main chain or in the side chain, have received much attention from the viewpoint of photo-functional polymer materials for many years, since the cyclobutane ring is formed by [2 + 2] photo-dimerization, whereas the ring is cleaved into two olefin moieties both on heating and or on irradiation.

Several types of functional polyamides and polyimides having a cyclobutane ring in their main chain have been prepared by polycondensation of cyclobutane dicarboxylic derivatives with diamines [1], by polyaddition–polycondensation of

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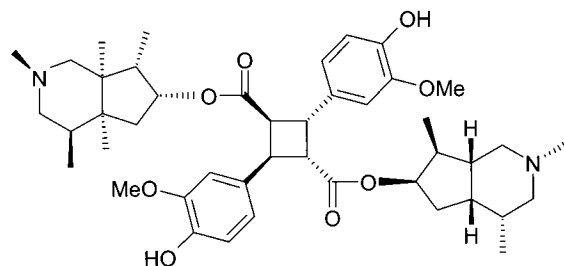
Scheme 1. Chemical structure of incarvillateine.

tetracarboxylic dianhydride with diamines [2, 3], or by ring-opening polyaddition of coumarin dimer derivatives [4, 5]. Furthermore, a large number of linear high polymer crystals have been prepared by topochemical [2 + 2] photo-polymerization of various kinds of diolefin crystals [6–9].

Recently we found that 4-acetoxy-3-methoxycinnamic acid (*O*-acetylferulic acid) undergoes [2 + 2] photo-dimerization in the crystalline state to give the corresponding dimer with a centrosymmetry (1-dimer), c-2,t-4-di(4-acetoxy-3-methoxyphenyl)-r-1,t-3-cyclobutanedicarboxylic acid (**I**) in nearly quantitative yield. As ferulic acid is produced in commercial scale, starting from rice bran [10–12] and as the acid is readily converted into **I** in a high yield, it can be a useful intermediate for new photo-functional materials and for a promising medicine as a sedative and as an anodyne, incarvillateine (Scheme 1) [13]. Furthermore, ferulic acid has recently been identified as a component of the cell walls of some plants [14–16] and it seems that it dimerizes by sun light. Its cyclodimer has been reported by Morrison *et al.* [17].

In this work, the dimer (**I**) was converted on heating into cross-linked polyphenylester (**II**) by polycondensation, eliminating 2 mol of acetic acid. The highly regular structure of the resulting network polymer (**II**) was confirmed by conventional analytical measurements. Then it was derived into a linear polyamide having a cyclobutane ring in the main chain by an ester–amide exchange reaction with hexamethylenediamine.

This article reports the synthesis of network polyphenylester (**II**) and its reaction with hexamethylenediamine to form a linear polyamide containing cyclobutane ring in the main chain, and the synthesis of the same polyamide obtained by the interfacial polycondensation between the chloride of (**I**) and the diamine.

2. EXPERIMENTAL

The synthetic route to the 3-dimensional polymer is shown in Scheme 2.

2.1. Preparation of O-acetylferulic acid

To a solution of ferulic acid (19.4 g, 0.1 mol) in acetic anhydride (400 ml) was added sodium acetate (16.4 g, 0.2 mol). After refluxing for 14 h, the reaction mixture was

Ac$_2$O

hv
dimerization

-2 CH$_3$COOH

(I)

(II)
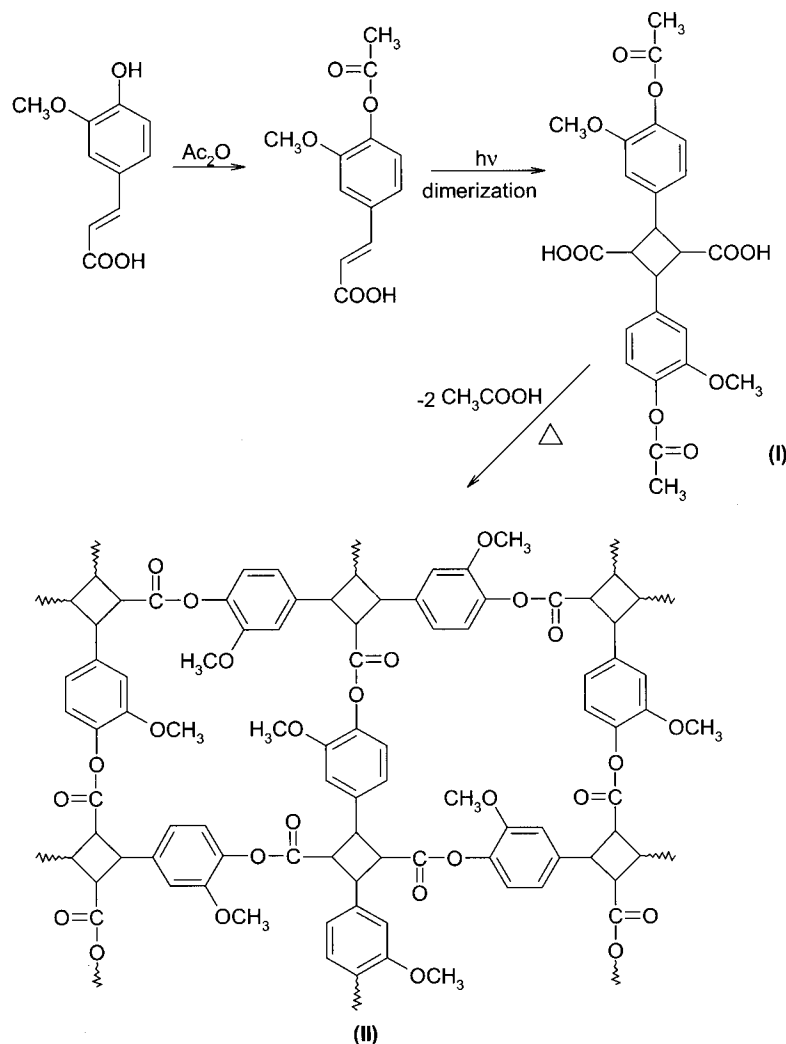
Scheme 2. Synthetic route to 3-dimensional network polyphenylester.

poured into water (500 ml). The precipitate obtained was re-crystallized from ethyl acetate, obtaining 18.7 g (0.079 mol) of acetylferulic acid (yield 79%), mp 201 °C; IR (KBr) 1762 (C=O acet.), 1689 (C=O fer.), 1632 (C=C), 985 (C=C) cm^{-1}.

2.2. Preparation of O-acetylferulic acid dimer

Purified crystals of the acetylferulic acid were ground in a mortar into fine powder, and 16 g (67.8 mmol) of the powder was suspended in 1.5 l hexane in a 2-l two-necked flask in which an Ace Glass 450-W medium pressure mercury lamp was immersed and the system was irradiated with stirring for 20 h under argon atmosphere. The precipitate was collected by filtration and washed with chloroform
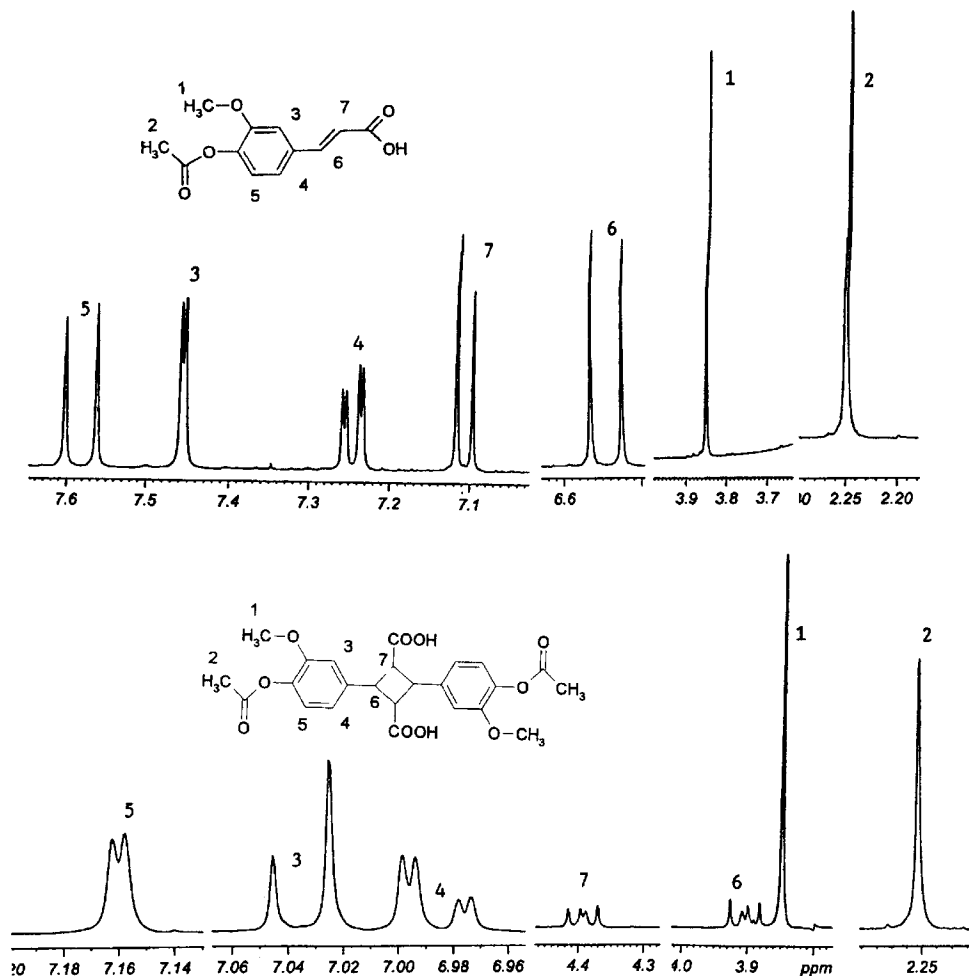
Figure 1. ^{1}H-NMR spectra of O-acetylferúlic acid and its dimer (recorded in acetone-d). The peak heights do not correspond to quantities of each proton in the form of this display.

to remove the unreacted acid and dried under vacuum. 13 g of the crude dimer was obtained (yield 81%). Recrystallization from dioxane gave fine powder crystals with mp 280°C (278°C by DSC). IR (KBr): 1756 (C=O acet.), 1698 (C=O fer.) cm^{-1}. The peaks due to the C=C of O-acetylferulic acid at 1633 and 987 cm^{-1} disappeared after dimerization. ^{1}H-NMR spectra of O-acetylferulic acid and its dimer are shown in Fig. 1. The olefinic protons of the monomer disappeared, and they appeared as the protons of cyclobutane ring.

2.3. Thermal conversion of O-acetylferulic acid dimer to net-work polyphenylester

5.5 g of benzophenone was placed in a Petri dish of diameter of 56 mm at 290°C, and 2.57 g (5.5 mmol) of the dimer was added little by little under nitrogen stream.

The dimer dissolved in benzophenone and vigorous liberation of acetic acid took place. After 20 min the system was cooled and benzophenone was removed by extraction with dichloromethane. 1.88 g of three-dimensional polymer was obtained (the theoretical yield is 1.94 g). The direct heating of the dimer without solvent caused burning of the product. Other high-boiling-point solvents, such as paraffin, were also tried, but benzophenone was found to be most suitable as the cyclic dimer is soluble in melted benzophenone.

2.4. Reaction of 3-dimensional polyphenylester (II) with n-butylamine

1 g of (**II**) was suspended in 10 ml of dimethylformamide (DMF) and 15% excess of n-butylamine was added at room temperature. The suspended powder was dissolved quickly and the transparent solution was stirred at room temperature for 24 h. The solution was poured into slightly acidic water, and the precipitate was filtered and washed with water. It was dissolved again in dimethylformamide (DMF) and precipitated in water. The yield was 60%. Recrystallization was not possible, and the product was found to be amorphous under a polarized optical microscope.

## 2.5. Preparation of polyamide (Scheme 3)

1 g (2.84 mmol) of the three-dimensional polyphenylester was ground to fine powder and suspended in 3 ml of DMAc, and 0.33 g (2.84 mmol) of hexamethylenediamine was dissolved in 3 ml of DMAc. After stirring for 18 h at 100°C, the system dissolved completely, and resulted reaction mixture was added into water (200 ml) and the system was acidified with dilute hydrochloric acid. The precipitate was filtered and dried in vacuum (0.8 g, yield 60%). $\eta_{inh} = 0.403$ dl/g (in DMF at 25°C). IR (KBr) 3373, 1644, 1518, 1279 cm^{-1}.

$$\text{II} \quad + \quad H_2N(CH_2)_6NH_2 \longrightarrow$$

(III)
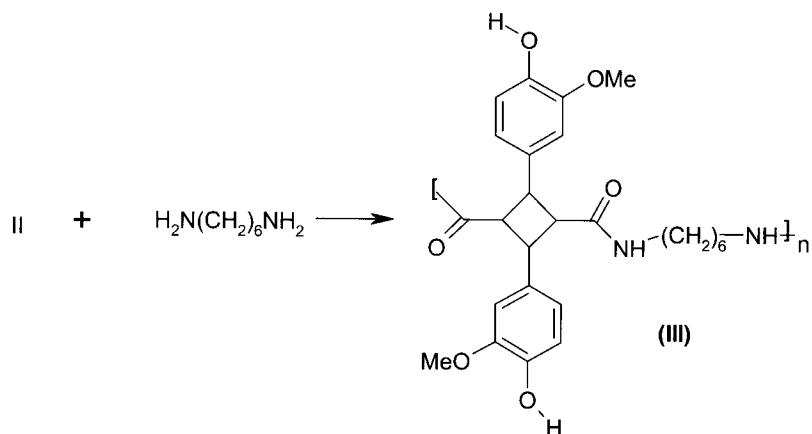
Scheme 3. Possible route to obtain polyamide from three-dimensional polymer.

2.6. Interfacial polycondensation of the dimer acid chloride with hexamethylenediamine (Scheme 4)

The dimer chloride of *O*-acetylferulic acid was prepared by the reaction of the acid dimer with oxalyl chloride and afforded the following interfacial polycondensation: to 2 g of the acid dimer chloride in 20 ml dichloroethane, an aqueous solution of an equimolecular amount of hexamethylenediamine containing sodium hydroxide (10% excess to the chloride) was added, and the polymer formed at the interface was collected. The yield was quantitative. The polymer had an inherent viscosity of 1.20 dl/g at 25°C in DMF. In order to remove the acetyl group, the obtained polymer was dissolved in DMF, a solution of hydroxide in methanol/water mixture was added and the mixture was stirred for 24 h. Then the solution was poured into dilute hydrochloric acid, the precipitated polymer was filtered, washed well with water and dried in vacuum (polymer **V**).
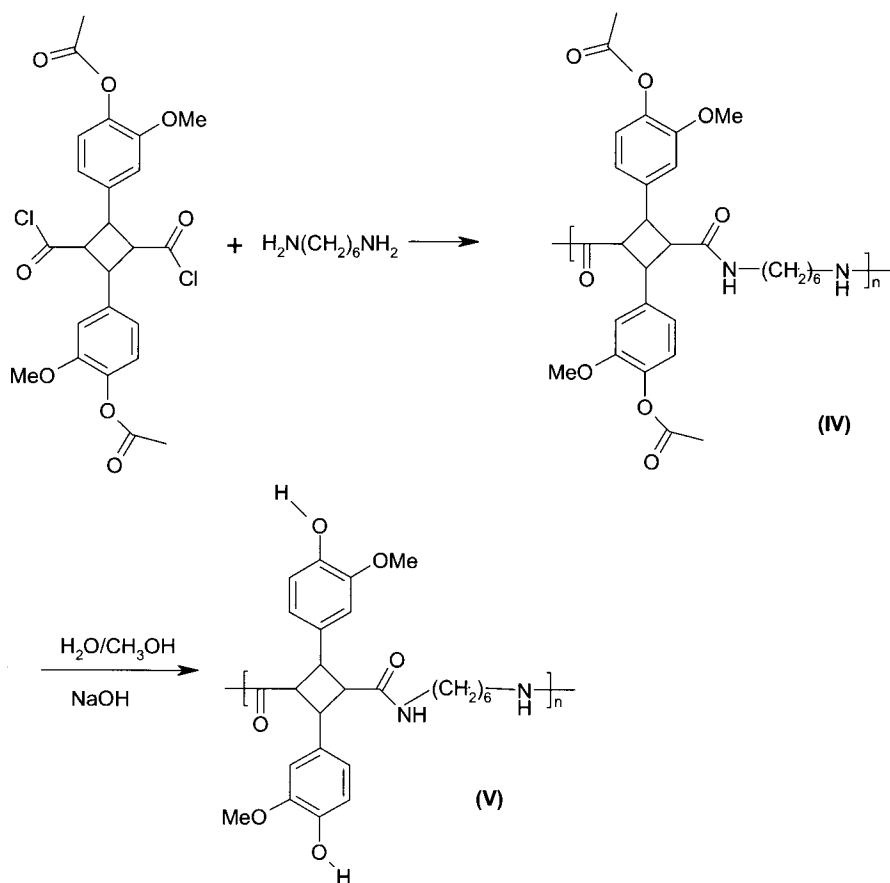
Scheme 4. Polyamides from interfacial polycondensation.

2.7. Characterization

Mass spectra of the dimer were taken using a quadrupole mass spectrometer (Extrel EXM-2000) equipped with an ion source for liquid ionization, by liquid ionization mass spectroscopy (LI-MS) [18], which is a kind of atmospheric ionization using excited argon atoms for ionizing involatile organic compounds. ^{1}H-NMR spectra were recorded using a Bruker Avance 400 MHz spectrometer. FT-IR spectra were recorded on a Nicolet 510P spectrophotometer. Differential Scanning Calorimetry (DSC) and Thermogravimetric Analysis (TGA) were carried out using a DuPont Instrument Model 910 DSC and 951 TGA, respectively. The inherent viscosities of the polyamides were determined at 25°C in DMF.

3. RESULTS AND DISCUSSION

Figure 2 shows the LI-MS spectra of the dimer (**I**). The peak of 237, which corresponds to M/2 + H$^+$ from the symmetric cleavage of (**I**), is clearly seen. In addition to this a much larger peak at 219, which corresponds to 237-H$_2$O, is also seen. On the other hand, there are neither peaks at 98 (maleic anhydride) and 116 (maleic acid), nor at 365 (3,3'-dimethoxy-4,4'-diacetoxystylbene). These three peaks should be seen, in addition to the peak of 237, if the unsymmetric cleavage of head-to-head type cyclobutane dimer (*m*-dimer) occurred [4, 19]. From these results, it is inevitably concluded that the dimer is the ï dimer with a center-symmetry (**I**), but not the one with a plane-symmetry (*m*-dimer).

The dimer (**I**) was submitted to thermal analysis (DSC and TGA). As shown in Fig. 3, the dimer (**I**) loses nearly 25% of its original weight at its melting temperature (approx. 280°C), which neatly corresponds to the elimination of 2 mol of acetic acid (the calculated weight of acetic acid to be liberated to form the network polyphenylester is 24.39%). Thus, it is conclusive from the DSC/TGA result that (**I**) was converted into three-dimensional polyphenylester (**II**), as shown in Scheme 3. The three-dimensional polymer (**II**) thus formed is neither soluble nor fusible, and starts to decompose at around 360°C.

In order to prepare the corresponding model diamide, shown in Scheme 5, **II** was reacted with *n*-butylamine in DMF. As soon as *n*-butylamine was added, the suspended **II** powder dissolved, giving a yellowish solution. After leaving to react at room temperature for several hours, the content which became brown, was poured in water, and a solid precipitated. After drying a dark brown solid was isolated with a poor yield (about 30% or less). On evaporating the mother liquor, pale brown powder soluble in water was recovered. The IR spectra of the precipitated product showed broad peaks due to −NH− and −OH groups at 3300–3500 cm^{-1}, aliphatic CH groups at 2800–3000 cm^{-1} and the amide carbonyl group at 1634 cm^{-1}. The ^{1}H-NMR spectrum of the precipitate, shown in Fig. 4, roughly corresponds to the expected product. The integration of the 2 phenolic protons at 8.75 ppm, 2 amide protons at 7.55–7.58 ppm, 6 aromatic protons at 6.57–6.86 ppm, 6 methoxy protons
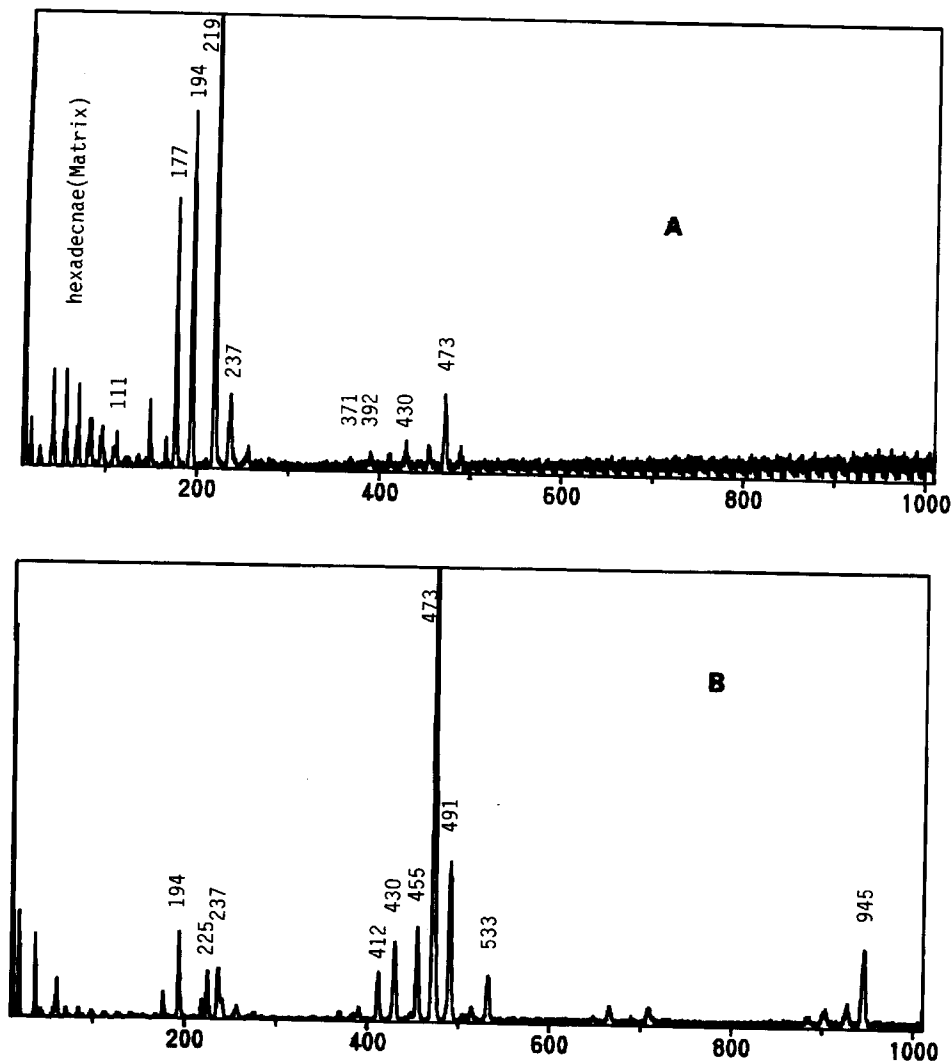
Figure 2. LI–MS of the cyclic dimer (**I**). (A) Under soft condition, (B) under decomposition condition (CID).

at 3.73 ppm and 18 protons of butyl groups at 0.67–2.89 ppm indicated that the compound is the dibutyl amide shown in Scheme 5. The peaks at 3.7–3.8 ppm and 4.1–4.2 ppm correspond to the protons of cyclobutane ring. However, the yield is rather poor, being less than 30%, and recrystallization from alcohol or DMF was not successful. Polarized optical microscope observation indicated that the product was amorphous. In order to obtain the model compound shown in Scheme 5, the cyclic dimer **I** was converted to the acid dichloride, and it was reacted with *n*-butylamine in dichloromethane. A dark colored viscous liquid product was obtained, which no longer had an acetoxy group, indicating that the acetyl group was eliminated by the
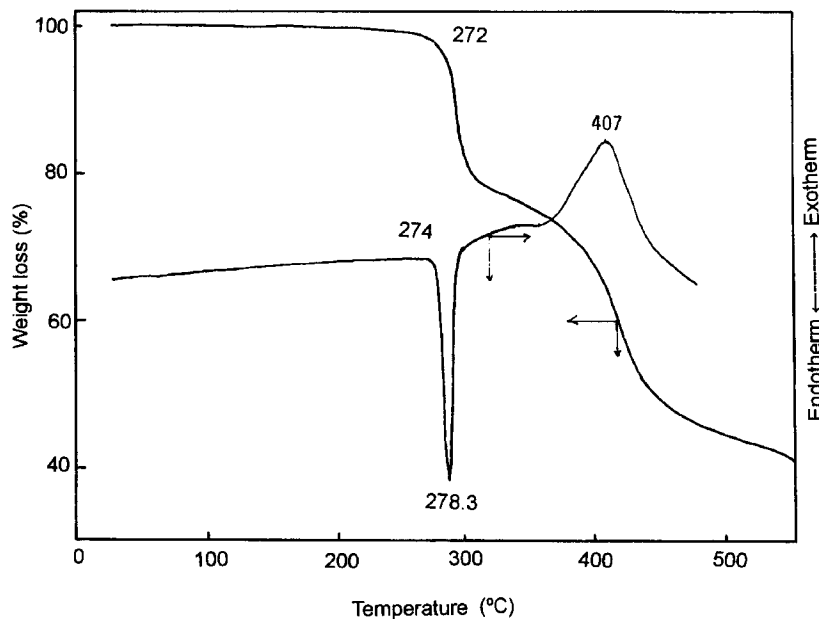
Figure 3. DSC and TGA curves of *O*-acetylferulic acid dimer.
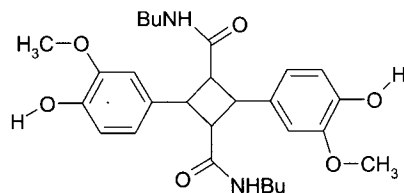
Scheme 5. Ferulic acid dimer N,N'-dibutyldiamide.

amine, as expected. It seems that the resulted phenolic group is attacked by the amine to form unsaturated carbonyl compounds.

Although the above-mentioned model reaction was not totally satisfactory, the reaction of **II** with hexamethylenediamine to obtain polymer **III** was carried out in DMF at room tempearture. The ^{1}H-NMR spectrum of the product is shown in Fig. 5. Figures 6 and 7 show ^{1}H-NMR spectra of the two polyamides obtained by interfacial polycondensation, **IV**, and its hydrolyzed product, **V**, respectively. As can be seen in Fig. 6, the methyl protons of acetoxy group are intact (at 2.2 ppm), indicating that there was no amidation of acetyl group. This is rather unexpected, because the acetoxy groups on aromatic rings are very much vulnerable to aminolysis. It can be seen in Fig. 7 that the peak due to the methyl protons of acetyl group at 2.2 ppm has completely disappeared, and a peak due to the phenolic proton appears at 887 ppm, indicating that the hydrolysis took place. The observed peaks in Figs 6 and 7 completely correspond to the structures of **IV** and **V** in Scheme 4, respectively. The integration of peaks also totally agreed with the structures. The reason why
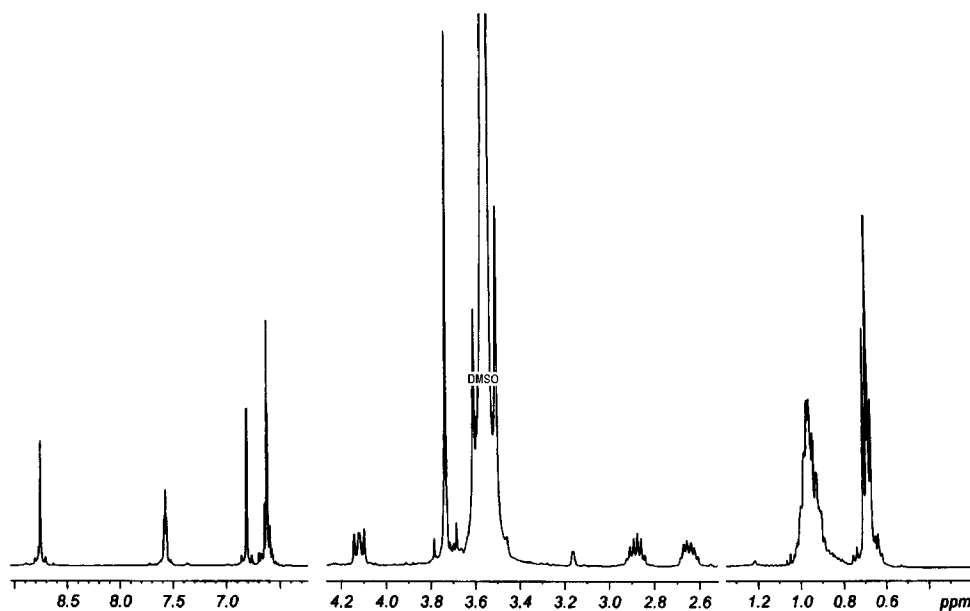
Figure 4. ^{1}H-NMR spectra of the polyamide from the 3-dimensional polymer **II** reacted with *n*-butylamine.

the acetoxy group did not undergo aminolysis is that the reaction was a interfacial reaction, and the acetoxy and the amine were in the separated phase. The integration of methoxy protons and aromatic protons gave the ratio of 1:1 for polymers **IV** and **V**. It can be seen from the NMR spectra in Figs 5 and 7 that the polyamide **III** derived from the net-work polyphenylester does not exactly coincide with the polyamide **V**. The peak of the methoxy protons at 3.7 ppm split over the region of 3.5–4.0 ppm. The signals in the aliphatic region below 1.5 ppm also changed significantly. Some other minor extra peaks suggest that the polymer **III** contains other contaminants, such as unsaturated carbonyl and quinolic rings formed during aminolysis, although the polymer was purified by repeated reprecipitation. In order to see if the phenolic group reacts with amines to form side products during the amidation, the reaction of polymer **V** with *n*-butyl amine was carried out at room temperature in DMF, and the ^{1}H-NMR spectrum of the product is shown in Fig. 8.

Significant spectral changes are seen after the treatment with *n*-butylamine. Some changes are observed at the region 3.2–3.8 ppm. The region of aromatic protons also changed significantly, showing that the polymer **V** reacted with butylamine. The peaks at 6.4–6.5 ppm can be assigned to the olefinic protons due to the olefinic group formation. The formation of C=C bonds by the cleavage of cyclobutane rings might take place, but this is rather unlikely in this case because the reaction systems were neither exposed to light nor high temperature. There are a few reports on the reactions of bases with phenolic compounds such as catechol [20, 21], but
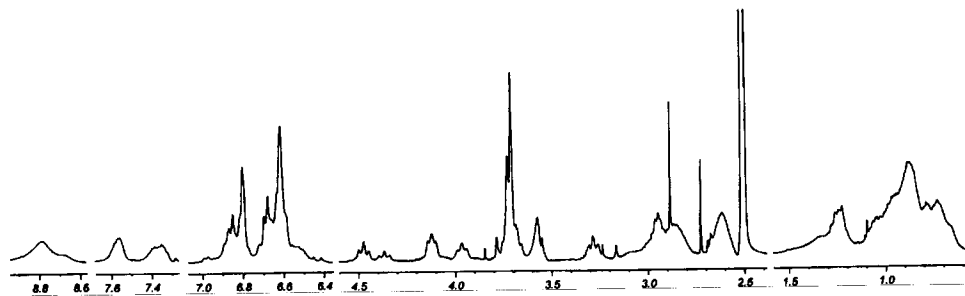
Figure 5. ^{1}H-NMR spectrum of polymer **III** in DMSO-d.
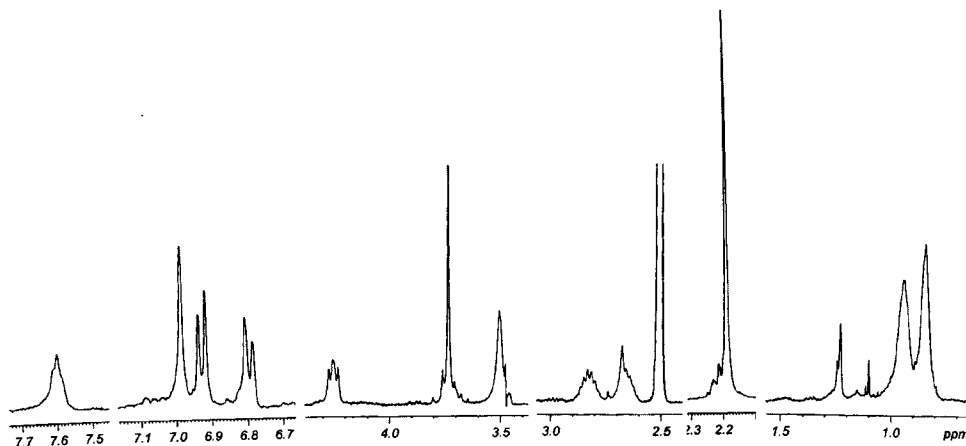

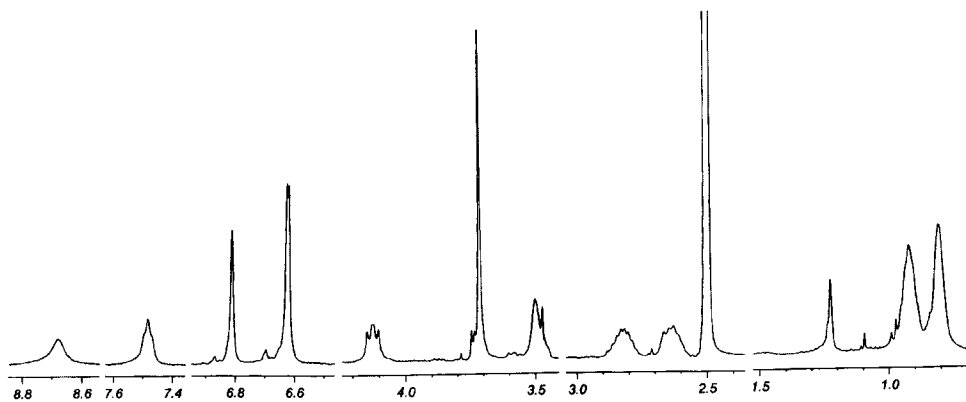**Figure 6.** ^{1}H-NMR spectrum of polymer **IV** in DMSO-d.

Figure 7. ^{1}H-NMR spectrum of Polymer **V** in DMSO-d.

the detailed reaction with amines is not known. A possible reaction is shown in Scheme 6.

IR spectra of these three polymers (**III, IV, V**) are shown in Fig. 9. The spectra correspond to each of those of NMR spectra, but it can be said that polymer **III**
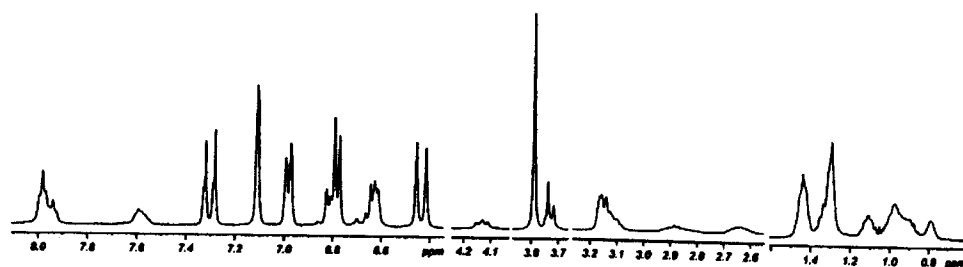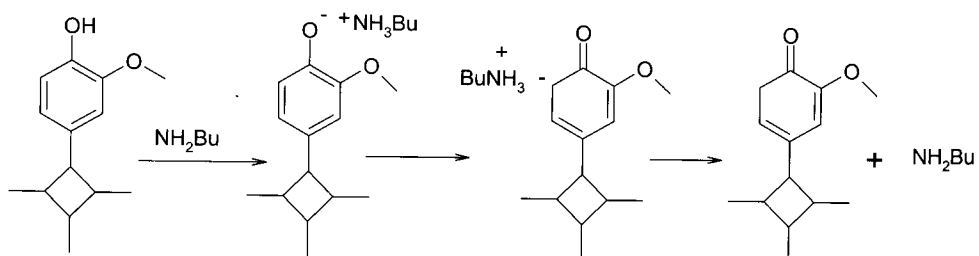
Figure 8. ^{1}H-NMR spectrum (in DMSO-d) of polymer **V** treated with n-butylamine.

Scheme 6. An example of probable reactions of phenolic group with butyl amine.
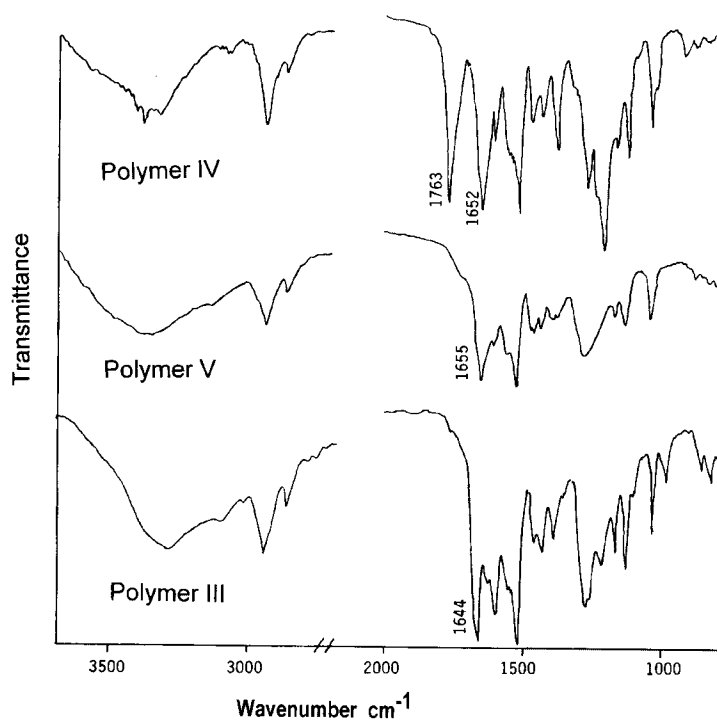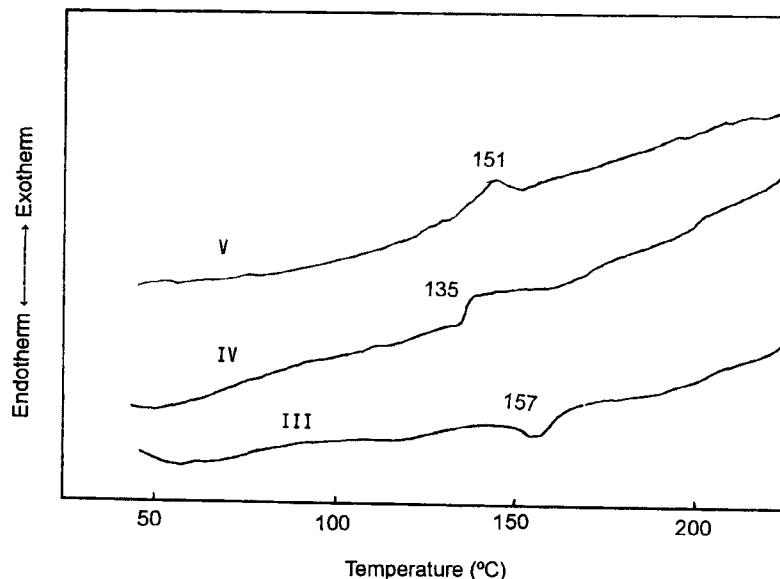

Figure 9. IR spectra of polyamides (KBr disk).

Figure 10. DSC curves and T_g of polymers.

is not exactly the same as polymer **V**. Polymer **IV** has a ester carbonyl group at 1763 cm^{-1}. All of them have peaks due to the amide carbonyl groups at around 1650 cm^{-1}. The inherent viscosity of the polymer obtained from the 3-dimensional material was low, the maximum being around 0.3 dl/g, and the cast polymer films were brittle. This is probably because the formation of the three-dimensional polymer cannot be completed to 100%. The reaction of the dimer to form the 3-dimensional material rapidly proceeds as soon as it melts, eliminating acetic acid and giving a hard material and it is difficult to stir the system. Therefore, before the reaction is completed, the material becomes infusible solid and the remaining reacting groups cannot undergo further condensation. Further heating to complete the reaction caused the coloring of the polymer, indicating that thermal decomposition can occur. The weight loss shown by TGA curve is approximately corresponds to the stoichiometric amount of acetic acid to be liberated as shown in Fig. 3. However, when larger amounts are treated, it seems difficult to complete the condensation. On the other hand, the polyamides obtained by the interfacial polycondensation are soluble in organic solvents, such as DMF, and they give transparent flexible films on casting from DMF solution.

Their DSC curves are shown in Fig. 10. The T_g of the polyamide obtained from the 3-dimensional polymer is similar to, but the T_g polymer **III** is different from that of the hydrolyzed polyamide **V** obtained by interfacial polycondensation.

The phenolic acids, such as ferulic and coumaric acids, have anti-oxidizing effects [22, 23]. Therefore, the anti-oxidant property of polymer **V** was tested using a free radical, DPPH. When the polymer solution was added to the DPPH solution, the purple color gradually faded to red, and then to yellow. The result is shown in
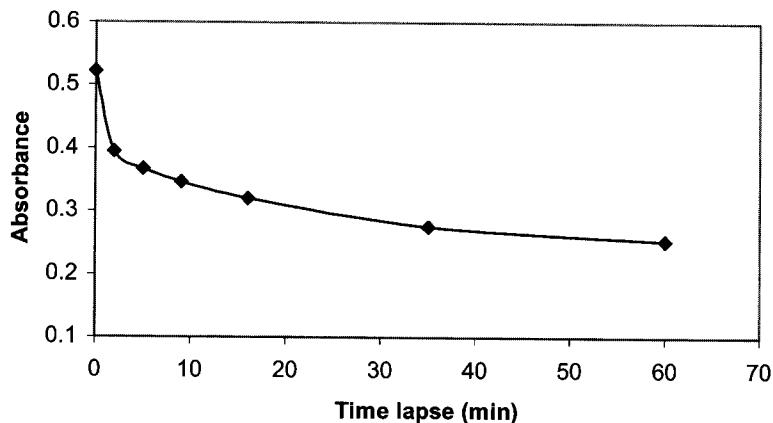
Figure 11. Anti-oxidant activity of polymer V determined at 516 nm. 0.1 ml of 2.688 mM polymer V solution was added to 3.5 ml of 0.1153 mM DPPH solution of. Molar ratio [DPPH]/[polymer] = 1.5.

Fig. 11. The polymer rapidly reacted with DPPH, indicating that it has good anti-oxidant ability.

4. CONCLUSIONS

A unique process, in which linear polymers can be obtained from a 3-dimensional polymer, was shown in this work. However, the thermal polycondensation to give the 3-dimensional polymer is inconvenient due to the difficulty in completing the reaction quantitatively. Furthermore, the polymer having phenolic groups appeared to be vulnerable to oxidation, forming unsaturated carbonyl or quinolic structures during the aminolysis. On the other hand, the interfacial polycondensation of the cyclic dimer acid chloride with other bifunctional monomers, such as diamines, will provide various new classes of polymers containing cyclobutane units to which aromatic groups are attached. The hydroxy groups of the ring can be used to give further functionality to the polymers. Polymer V, having phenolic groups, showed a promising anti-oxidant activity with DPPH.

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