Synthesis of Poly(thymol) via Oxidative Coupling Polymerization

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The oxidative polymerization of thymol was performed using a copper chloride(I) catalyst with a bulky 2-(p-tolyl)pyridine ligand in toluene under oxygen atmosphere; the reaction produced linear poly(thymol) (PPETh) with a number average molecular weight ($M_n$) and its distribution ($M_w/M_n$) of 43,000 and 1.6, respectively. The resulting polymer consists of an almost perfect C–O linkage with good solubility, such as in toluene, chloroform, tetrahydrofuran, and N-methylpyrrolidone, when the polymerization was conducted below 40 °C. The resulting PPETh is an amorphous polymer with glass transition temperature ($T_g$) and 5 wt% loss temperature in nitrogen ($T_d5$) of 130 °C and 402 °C, respectively. The transparent pale-yellow film was obtained by solvent casting method.

Keywords: Oxidative Polymerization, Thymol, High Temperature Polymer, Thermoplastic, Biopolymer

1. Introduction

Engineering plastics are widely accepted as a useful substitute for metals and ceramics owing to their high processability and characteristic properties, such as optical transparency and high-impact strength. Poly(2,6-dimethyl-1,4-phenylene oxide) (PPE26) was developed by GE in 1956 using the oxidative polymerization of 2,6-dimethylphenol (26DMP), after which numerous research papers have been published [1–5]. The manufacturing process is a green process owing to high atom economy (87.0%) and a nontoxic byproduct (i.e., H₂O). Currently, the use of environmentally harmful organic solvents is decreasing [6–8]. PPE26 has excellent insulating and mechanical properties; however, its relatively low glass transition temperature ($T_g$) and poor processability complicate its use in industrial applications. Therefore, blending with polystyrene is performed to improve the toughness and processability of PPE26. Despite these research efforts, there are still critical issues to be solved. Because the oxidative polymerization process proceeds via radical mechanism, substituents at 2 and 6 positions are always required to prepare linear PPE that is free from branching structures. Hay et al. have reported that catalysis using CuCl with 2-alkyl pyridine derivatives, such as 2-tridecylpyridine, was effective for the synthesis of high-molecular-weight poly(o-cresol) (PPEOC) [9]; however, branching could not be completely excluded. Higashimura et al. have reported the use of a tridentate copper catalyst, a $\mu-\eta^2:\eta^2$-peroxodicopper(II) complex, in conjunction with bulky 2,6-diphenylpyridine for the oxidative polymerization of 2,5-dimethylphenol (25DMP). The resulting polymer, poly(2,5-dimethyl-1,4-phenylene ether) (PPE25), had a number average molecular weight ($M_n$) of 4 kDa [10]. Although this catalytic system can be applied to the polymerization of other phenol derivatives (e.g., o-cresol [11], m-cresol [12], and p-phenoxypbenol [13]), perfect regioselectivity (RS) has not been realized yet. A mesoporous supported copper–amine catalyst was prepared and applied to the oxidative polymerization of 26DMP [14] and 25DMP [16]; using this reaction, a perfectly regiocontrolled polymer was obtained. A simpler and more homogeneous catalytic system, which is based on CuCl(I) with 100 equiv of 2-(p-tolyl)pyridine, was also used for the polymerization and resulted in excellent RS of the resulting PPE25; the melting temperature and the degree of

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crystallinity of PPE25 were 310 °C and 42%, respectively.

Polyphenols have attracted considerable attention owing to their wide availability in food and beverages; strong antioxidant properties, potential anticancer activity, and anticarcinogenic, antimicrobial, and anti-inflammatory properties make them useful for the prevention of diseases [17–19]. Glycoside β-arbutin (βArb) is one of the main polyphenol components in pears; recently, we reported the selective C–C oxidative polymerization of βArb using a conventional copper catalyst in a buffer solution to produce corresponding poly(arylb) with \( M_n \) values reaching 10 kDa [20]. In addition, we investigated the introduction of \( n \)-alkyl groups to poly(arylb) via addition reactions between \( n \)-alkyl isocyanate and the phenolic group, which produces corresponding alkylated polymers \( \text{poly(arylb)}-R_x \) (R: alkyl group, x: degree of substitution) [21]. Thymol, which is found in varying amounts in the essential oil of several plants belonging to the genera *Thymus* (Thyme), *Origanum* (Origanum), and *Carum* (Ajowan), is another naturally occurring phenol, which has been widely used to treat several helminth infections in people during the early periods of this century [22]. Thymol is a phenol derivative with isopropyl and methyl substituents at 2 and 5 positions; therefore, we expected that thymol can be polymerized with our oxidative polymerization catalyst to form a novel bio-based linear and soluble polymer as the PPE family. Here, we report the regiocontrolled synthesis of poly(thymol) (PPETh) using CuCl(I), with a bulky 2-(\( p \)-tolyl)pyridine ligand and its properties (Scheme 1).

![Scheme 1. Polymerization of thymol.](image)

2. Experimental

2.1. Reagents and solvents

Thymol was purchased from Kanto Chemical Co., Inc., and purified by sublimation. 25DMP was purchased from Tokyo Chemical Industry Co., Ltd., and purified by recrystallization from hexane, followed by sublimation, and stored under \( \text{N}_2 \) atmosphere. CuCl(I) (99.99%) was purchased from Strem Chemicals, Inc., and used as received. 2-(\( p \)-Tolyl)pyridine was purchased from Tokyo Chemical Industry Co., Ltd., and used as received. All other reagents and solvents were also used as received.

2.2. Polymerization

Typical procedure: A total of 0.099 g (10 mol% relative to the monomer) of CuCl(I), 6.77 g of (40 equiv relative to CuCl(I)) 2-(\( p \)-tolyl)pyridine, and 15 mL of toluene were added into a two-necked flask. The flask was purged with oxygen twice and stirred for 30 min. The polymerization was initiated by the addition of the monomer (1.500 g, 10.00 mmol), and the solution was vigorously stirred at 40°C for 24 h. The resulting viscous solution was poured into 300 mL of methanol containing 5 mL of concentrated hydrogen chloride to precipitate the polymer. The precipitate was dissolved in chloroform and reprecipitated in methanol. The polymer was collected, washed with methanol, and vacuum-dried at 100°C for 12 h to give PPETh in a 25% yield as pale-yellow fibers.

2.3. Measurement

Fourier-transform infrared (IR) spectra were obtained using a Jasco IR-5500 spectrometer (Jasco Co., Ltd.) and KBr tablets. \( ^1\text{H} \) and \( ^13\text{C} \) nuclear magnetic resonance (NMR) analyses were conducted using a Bruker AC-400P spectrometer at 400 and 125 MHz, respectively. Deuterated chloroform (CDCl\(_3\)) was used as the solvent. The number- and weight-averaged molecular weights (\( M_n \) and \( M_w \), respectively) were measured using Tosoh HLC-8120 GPC equipped with consecutive polystyrene gel columns (TSK-GEL GMHHR-M and GMHHR-N) at 40 °C eluted with chloroform at a flow rate of 1.0 mL min\(^{-1}\) calibrated by standard polystyrene samples. Thermogravimetric analysis was conducted using the HITACHI TG/DTA7220 system at a heating rate of 10 °C/min under exposure to air or \( \text{N}_2 \). Differential scanning calorimetry (DSC) was performed using the HITACHI X-DSC7000 system at a heating rate of 20 °C/min under nitrogen.

3. Results and discussion

3.1. Polymer synthesis

In the oxidative polymerization of 2,5-disubstituted phenol monomers, the selection of ligand for the Cu(I) catalyst is critical to realize the regiocontrolled reaction. In our previous study using 25DMP as a monomer, the CuCl(I)-pyridine catalyst produced a cross-linked gel, whereas 100 equiv of 2-phenylpyridine relative to CuCl(I) produced soluble linear PPE25. A bulkier ligand, 2-
(p-tolyl)pyridine, produced crystalline PPE25, with \( T_g \) and melting temperature \( (T_m) \) of 149.5 and 310 °C, respectively. However, the resulting PPE25 has a symmetric structure which is too high, resulting only in a low-molecular-weight product without solubility in any organic solvent. Thus, despite this well-controlled polymerization technique, the PPE25 polymer does not currently have any industrial output. Thymol is a naturally occurring 2,5-disubstituted phenol derivative, and it has a bulky isopropyl group at the 2 position. Therefore, this compound was suitable for the polymerization with our bulky catalyst. The results of the oxidative polymerization of thymol are summarized in Table 1. Owing to the bulky isopropyl group next to the phenolic OH function, the rate of the polymerization of thymol seems smaller than that of 25DMP (runs 1, 2, 4, and 5). Then, polymerization was conducted with a smaller amount of expensive 2-(p-tolyl)pyridine compared with the 25DMP polymerization. However, the use of 40 equiv of the ligand both at 50 °C and 60 °C produced cross-linked brown-colored products (runs 3, 6, and 7). Below 40 °C, using the ligand, soluble pale-yellow products were obtained (runs 8–16). The use of larger quantity of the ligand, which arise steric repulsion between the catalyst and the monomer, and lower polymerization temperature, which decrease the probability of collision, resulted in lower polymerization rate, which led to lower yield and lower \( M_n \) values. It appears that polymerization using 10 mol% CuCl(I) with 5 equiv of the 2-(p-tolyl)pyridine ligand at 40 °C resulted in high yield (57%) and high \( M_n \) value of over 40 kDa with reasonable \( M_w/M_n \) (run 11).

Figure 1 presents the IR spectra of thymol and the polymer (runs 8 and 11 in Table 1). Compared with the strong OH vibration at 3200 cm\(^{-1}\) for thymol, the polymer exhibits no absorption at the wavelength region especially in the PPETh (run 8). In addition, while the characteristic tri-substituted C–H bending of thymol is observed at 834 cm\(^{-1}\), tetra-substituted C–H bending is observed at 933 cm\(^{-1}\). These results suggested that polymerization proceeded at 1,4 C–O linkage free from the unfavorable C–C coupling reaction.

To evaluate the effect of RS on polymerization, the \(^1\)H NMR spectra were acquired in a CDCl\(_3\) solvent. Figure 2 presents the \(^1\)H NMR spectra of (a) thymol, and PPETh obtained in (b) run 11 and (c) run 8 shown in Table 1. Signals assignable to proton \( e \) (Ar-H) and \( g \) (O-H) are appeared at 7.08 and 4.63

### Table 1. Polymerization results of thymol with the Cu(I) catalyst\(^a\).

| Run | CuCl (mol\%) | Base (equiv) | Temp (°C) | Yield\(^b\) (%) | \( M_n \) (\( \times 10^4 \)) | \( M_w/M_n \) | Remarks |
|-----|--------------|--------------|-----------|----------------|-----------------|-------------|---------|
| 1   | 3            | 150          | 70        | <1             | -               | -          | -       |
| 2   | 3            | 150          | 60        | <1             | -               | -          | -       |
| 3   | 10           | 40           | 60        | 78             | 0.32            | 1.3        | gel     |
| 4   | 3            | 150          | 50        | 3              | -               | -          | -       |
| 5   | 3            | 100          | 50        | 5              | -               | -          | -       |
| 6   | 10           | 40           | 50        | 58             | 3.6             | 2.0        | gel     |
| 7   | 10           | 5            | 50        | 55             | 3.1             | 1.3        | -       |
| 8   | 10           | 40           | 40        | 25             | 3.1             | 1.6        | -       |
| 9   | 10           | 30           | 40        | 25             | 3.2             | 1.5        | -       |
| 10  | 10           | 20           | 40        | 54             | 3.5             | 1.7        | -       |
| 11  | 10           | 5            | 40        | 57             | 4.3             | 1.9        | -       |
| 12  | 10           | 40           | 30        | 19             | 0.53            | 1.6        | -       |
| 13  | 10           | 30           | 30        | 18             | 0.39            | 1.7        | -       |
| 14  | 10           | 20           | 30        | 10             | 0.42            | 1.5        | -       |
| 15  | 10           | 10           | 30        | 35             | 0.40            | 1.4        | -       |
| 16  | 10           | 5            | 30        | 25             | 0.35            | 1.5        | -       |

\(^a\) Conditions: 3 or 10 mol% CuCl(I), \([M]_0 = 0.70 \text{ mol/L}, \text{ toluene, O}_2.\ ^b\) MeOH-insoluble part. \(^c\) Determined by GPC (CHCl\(_3\), PST).
ppm as a doublet and singlet peaks, respectively, in the spectrum of the thymol monomer, and these are disappeared after the polymerization. Surprisingly, the synthesized two polymers exhibit considerably different spectra. Though these two polymers have similar GPC result, the PPETh in run 8 seems to be consisted of more ideal C-O coupled structure than the counterpart. The integration values of each signal for PPETh (run 8) are reasonable, and there are no unknown signals in it.

![Fig. 3](image)

Fig. 3. $^{13}$C NMR spectra of poly(thymol) obtained in (a) run 11 and (b) run 8 presented in Table 1.

The $^{13}$C NMR spectra also indicated the difference in $\Delta S$ in these two polymers (Fig. 3); PPETh (run 8) has dominant C–O linkage in its structure. From the methyl signal 3, $\Delta S$ can be estimated to be roughly 95% (determined by inverse gate $^1$H decoupling method). Minor signals are also observed around aromatic region (115–138 ppm), which are arisen from branching structure, but not correctly identified yet. As the results, using 40 equiv of the ligand at 40 °C gave the corresponding C-O coupled polymer (PPETh) effectively. Gelation can be occurred at the 6 position of the monomer, and this can be completely suppressed by the addition of 40 equiv of the ligand to form the sterically demanded catalytic site and the appropriate polymerization temperature. Relatively low yield (about 30%) of the products as a condensation polymer may be attributable to the formation of diphenoquinone at the early stage of the polymerization, or redistribution/rearrangement reactions, typically observed in PPE synthesis.

3.2. Polymer properties

The solubility of the resulting PPETh is summarized in Table 2. As expected, PPETh exhibits good solubility in ordinary organic solvents, such as toluene, chloroform, tetrahydrofuran, and N-methylpyrrolidone, at 1 mg/mL concentration at 20°C.

Figure 4 depicts the TGA curves of PPE polymers under nitrogen.

A commercially available PPE26 polymer shows excellent thermostability ($T_d5 = 435$ °C). 2,5-Disubstituted PPE polymers are slightly lower thermostability, but they show similar thermal degradation temperature, indicating the secondary isopropyl substituent does not affect the thermal degradation. The PPE25 polymer has the highest char yield of 29% at 800 °C, probably because of the crystalline nature of the polymer.

Figure 5 depicts the DSC profiles of these three PPE polymers. As seen in this Figure, it is clear that the PPETh polymer is amorphous just like PPE26. In spite of the symmetric arrangement of the substituents at 2 and 5 positions, the bulky isopropyl group may prevent the crystallization, while PPE25 shows typical crystalline polymer behavior in DSC measurement. The order of the $T_g$ of these three PPE polymers is as follows: PPE26 > PPE25 > PPETh.

![Fig. 4](image)

![Fig. 5](image)

![Table 2](image)
3.3. Structural study

Figure 5 presents the optimized geometry and the estimated cross-sectional diameter (D) of the octamers of PPE families. We thought this parameter D is a good indicator to evaluate the polymer as a low k material, since the material needs low relative permittivity (\(\varepsilon_r\)), which is correlated with polymer density; \(\varepsilon_r\) can be decreased with decreasing the D value. The PPE\(_N\) model has a unique screw-sense structure with a large D value of 8.05 Å. PPE\(_{OC}\) and PPE\(_{25}\) exhibit a rather flat structure with the smaller D of 5.5–5.9 Å. PPE\(_{26}\) is known to be a good insulating material (low-k dielectric) with \(\varepsilon_r\) of 2.4 and tan \(\delta\) of 0.002 at 1 GHz owing to the two bulky methyl substituents with low polarity, i.e., the phenylene ether group. From the D values presented in Fig. 5, it is determined that PPE\(_N\) and PPE\(_{Th}\) may be good candidates for such low-k material; however, PPE\(_N\) is a crystalline polymer with poor solubility and low molecular weight. The relatively low thermal stability is a critical issue. However, thus far, PPE\(_{Th}\) seems to be a potential candidate as the next-generation low-k material.

![Figure 5. DSC profiles of (a) PPE\(_{Th}\), (b) PPE\(_{25}\), and (c) PPE\(_{26}\) under N\(_2\) at a heating rate of 20 °C/min.](image)

![Figure 6. Optimized geometry of octamers and the cross-sectional diameter (D) of PPE families using MM2 calculations.](image)

4. Conclusion

We demonstrated the synthesis of linear thermoplastic poly(thymol) PPE\(_{Th}\) via controlled oxidative polymerization using CuCl(I) with the 2-(p-toly)pyridine catalyst at 40 °C under oxygen atmosphere. An almost perfect RS was attained. The resulting PPE\(_{Th}\) is an amorphous high-molecular-weight green polymer with a \(T_g\) of approximately 130 °C. The PPE\(_{Th}\) film prepared by solution-casting method shows good transparency with slightly yellowish color.
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