

Rapid Communication

**SYNTHESIS AND CHARACTERIZATION OF HYPERBRANCHED
POLY(ESTER-AMIDE)S BASED ON GALLIC ACID AND
DL-2-AMINOBUTYRIC ACID**

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Abstract A novel AB₃-type monomer was prepared from gallic acid and DL-2-aminobutyric acid, and used for the synthesis of the biocompatible hyperbranched poly(ester-amide)s by self-polycondensation. The polymers were characterized via FTIR and NMR spectroscopy and thermal analysis, and the average degree of branching of the polymers was estimated to be 0.75. The polymers with abundant acetyl end groups were found to be amorphous with lower intrinsic viscosity, better thermal stability and excellent solubility.

Keywords Hyperbranched polymer, Biocompatible, Gallic acid, Hyperbranched poly(ester-amide)s

INTRODUCTION

Highly branched macromolecules including dendrimers and hyperbranched polymers are interesting materials with unique molecular structures and potential applications^[1–5]. The two types of polymers have many analogous physical and chemical properties such as high solubility, low viscosity and abundance of terminal groups. The former attracts much attention of researchers due to its perfect monodisperse architecture, but its preparation is generally tedious because of various protection, deprotection and purification steps. For hyperbranched polymers, one-step polycondensation can be used with AB_x-type monomers. Since Kim and Webster synthesized the first highly branched polymers in 1990^[6], hyperbranched polymers with the advantages of special structure and properties have been widely investigated. Their applications include blend components, additives, coating components, liquid crystals, medicine, and so on.

Kricheldorf and coworkers synthesized homo- and copolyesters from gallic acid and β -(4-hydroxyphenyl)-propionic acid^[7, 8] in connection with their investigation of biodegradable hyperbranched polymers. This type of polymer may be of interest as neat materials for medical applications or as reinforcing component of biodegradable composites. To our best knowledge, however, no hyperbranched polymer prepared from both gallic acid and amino acid has been reported. In this paper, we report new hyperbranched poly(ester-amide)s from the natural substances gallic acid and amino acid, which widely occur in the metabolism of numerous plants and animals. These polymers might be used as a drug-delivery system due to their low toxicity and excellent biocompatibility. Furthermore, the incorporation of amino acids into the backbone makes these polymers potentially useful as degradable, biocompatible delivery devices.

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EXPERIMENTAL

Materials

Gallic acid and *DL*-2-aminobutyric acid were purchased from Aldrich and used as received. *N,N*-Dimethylacetamide (DMAc) was purified by vacuum distillation over phosphorus pentoxide, and triethylamine was distilled over molecular sieves. Other solvents and reagents were of analytically pure grade and used without further purification.

Measurements

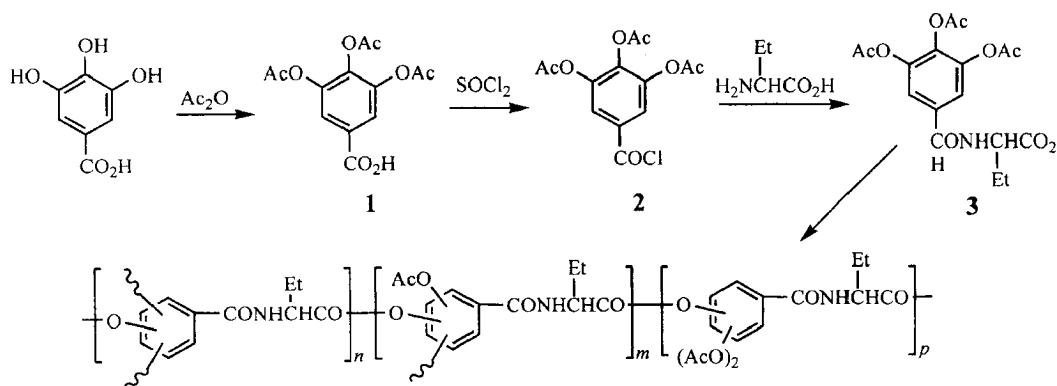
The FTIR spectra were recorded from KBr pellets using a Bio-Rad FTS-135 spectrophotometer. The NMR spectra were performed on a Bruker AV 300 MHz spectrometer. The inherent viscosities were measured with an Ubbelohde Viscosimeter thermostated at 30 °C in DMAc. The DSC measurements and thermogravimetric analyses (TGA) were conducted on a Perkin-Elmer Pyris 1 Differential Scanning Calorimeter and a Perkin-Elmer Pyris 1 Thermogravimetric Analyzer, respectively, using heating and cooling rates of 10 K/min in nitrogen. Gel permeation chromatography (GPC) was performed with a Waters 2414 fitted with polystyrene columns (Styragel HT3 THF).

Synthesis of Monomers

Triacetylalloyl chloride was prepared according to the procedure described by Kricheldorf^[7–9]. A 30 mmol amount of triacetylalloyl chloride and a 10% excess of *DL*-2-aminobutyric acid (33 mmol) were dissolved in dry DMAc in a 100 mL round-bottomed flask with side tube. Triethylamine (36 mmol) were added dropwise with syringe pump. The reaction mixture was stirred for 24 h at room temperature. After filtration, the filtrate was evaporated under reduced pressure and then precipitated in water, filtered, and washed with water. After drying, 7.39 g of the product was obtained as a white powder. Yield: 65%. m.p. 176–178 °C. ¹H-NMR (DMSO-*d*₆): δ 0.94 (t, 3H, CH₃), 1.80 (q, 2H, CH₂), 2.31 (s, 3H, CH₃), 4.27 (m, 1H, CH), 7.75 (s, 2H, Ar-H), 8.71 (s, 1H, NH), 12.64 (s, 1H, COOH). ¹³C-NMR (DMSO-*d*₆): δ 11.3, 20.3, 20.8, 24.5, 54.8, 120.9, 132.5, 137.9, 143.5, 164.8, 167.5, 168.5, 173.9.

Polycondensations

The monomers and a catalytic amount of magnesium oxide (MgO) were weighed into a cylindrical glass reactor equipped with a mechanical stirrer and gas-inlet and gas-outlet tubes. The reactor was flushed with a slow stream of nitrogen and placed in an oil bath preheated at 160 °C. The homogeneous melt had formed in a few minutes with the temperature increasing. The mixture was stirred at the desired condensation temperature for a period. Finally vacuum was applied for 1 h. The crude product was dissolved in DMAc, precipitated into water and isolated to dry at 60 °C in vacuum. Yields were about 40%–60%.



Scheme 1 Synthesis of monomer and polymers

RESULTS AND DISCUSSION

AB₃-type monomer **3** was successfully prepared in three steps from gallic acid as shown in Scheme 1. The synthesis of **2** was performed by the acetylation of gallic acid with excess of acetic anhydride and a catalytic amount of pyridine under reflux, followed by acyl chloride formation. Reaction of **2** with *DL*-2-aminobutyric acid in the presence of triethylamine produced monomer **3** in a yield of ca. 65%. The melting point of the monomer **3** was 176–178 °C, which was very low for successful polycondensation in bulk. The structure of monomer **3** was characterized by ¹H-NMR, ¹³C-NMR, and FTIR spectra.

Table 1. The reaction conditions and properties of hyperbranched poly(ester-amide)s

Entry	<i>T</i> (°C)	Time ^a (h)	Yield (%)	η_{inh}^b (dL/g)	<i>M_w</i> (g/mol)	PDI	<i>T_g</i> ^c (°C)	<i>T_d</i> ^{5d} (°C)	Solubility ^e			
									DMSO	DMAc	THF	CHCl ₃
1	180	1.5 + 1 V	40	0.04	1839	1.22	119	230	++	++	++	--
2	180	3.0 + 1 V	52	0.05	1955	1.28	131	261	++	++	++	--
3	180	5.5 + 1 V	53	0.08	1937	1.21	144	262	++	++	++	--
4	180	7.0 + 1 V	59	0.10	2417	1.28	178	268	++	++	++	--
5	190	7.0 + 1 V	59	0.11	2678	1.31	206	270	++	++	+-	--

^a V means vacuum was applied;

^b Measured at 30 °C with *c* = 4 g/L in DMAc;

^c From DSC measurements with a heating/cooling rate of 10 K/min in nitrogen (2nd heating);

^d From TGA measurements with a heating rate of 10 K/min in nitrogen;

^e ++ soluble, +- partly soluble, -- insoluble

In the presence of MgO as transesterification catalyst, the hyperbranched poly(ester-amide)s were synthesized by self-polycondensation of the AB₃-type monomer **3** which was prepared from natural products gallic acid and amino acid. The polymerization results are summarized in Table 1. The ¹H-NMR and ¹³C-NMR spectra of the monomer and the polymer sample (Entry 3) are shown in Fig. 1 and 2. The spectra of the polymer became more complicated than that of the monomer due to the changes of the chemical environments. Two types of methyl group of the monomer were observed at δ = 0.94 and 2.31 (H_a and H_c in Fig. 1). As shown in Fig. 1, the single peak of H_a obviously split into four peaks (δ = 1.29, 0.93, 0.73, 0.60) in the spectrum of the polymer, which indicates there are four different structures for H_a. However, it is difficult to assign them to a particular kind of structural unit (dendretic, semidendric, linear or terminal unit) due to the complex structure of the polymer. The same changes occurred to the phenyl group (H_e) and amide group (H_f). Moreover, a similar split was observed in ¹³C-NMR spectra (Fig. 2), which also proves that there are branched structures in the polymer. The degree of branching (DB) is an important characteristic of hyperbranched polymer design. It can be calculated according to the relative amounts of each type of hydrogen atom or carbon atom. According to the chemical environments^[10], we can find the four units of C_f (δ = 120.9) and C_i (δ = 143.5), namely, the signals from the high field to the low field belong to terminal, linear, semidendric and dendritic units, respectively (designated C_f^T, C_f^L, C_f^{SD}, C_f^D, and C_i^T, C_i^L, C_i^{SD}, C_i^D, respectively). The DB was defined as the ratio of the sum of branched and terminal units versus total units^[11]. For our work, the branched units contain semidendric and dendritic units^[12]. The DB was determined to be 0.72 and 0.78 by calculating the integration ratio of the four peaks of C_f and C_i, respectively, and the average DB was 0.75.

Various attempts were made to polycondense monomer **3** in the maximum temperature range of 180–210 °C using MgO as transesterification catalyst. Completely soluble product was obtained at 180–190 °C, slightly crosslinking was found at a reaction temperature of 200–210 °C. On comparison of entries 4 and 5, we find that high reaction temperature is propitious for yielding high molecular weight hyperbranched polymers prepared from self-polycondensation of AB₃ monomer **3**. Under the same reaction temperature, the molecular weights of the hyperbranched poly(ester-amide)s increased steadily with reaction time. The apparent molecular weights were relatively low determined by GPC, using linear polystyrene as standard. The actual molecular weights should be three to five times higher than the obtained values since highly branched polymers are known to have

smaller hydrodynamic volume than their linear analogues^[13–15]. In general, the polydispersities of hyperbranched polymers prepared from self-polycondensation of AB_x monomers, according to Flory's prediction^[16], are broad, whereas we obtained some narrow molecular weight distribution. The similar results have been reported by other research groups^[17, 18]. The low inherent viscosities are consistent with the properties of hyperbranched polymers which usually have a lower inherent viscosity than their linear analogues with similar molecular weight.

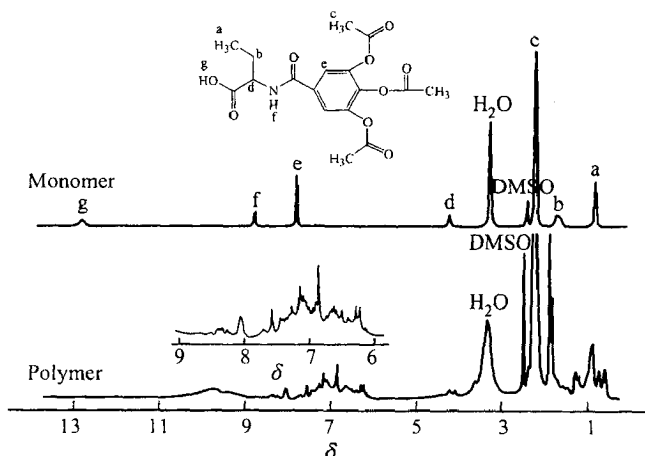


Fig. 1 ¹H-NMR spectra of the monomer and the polymer

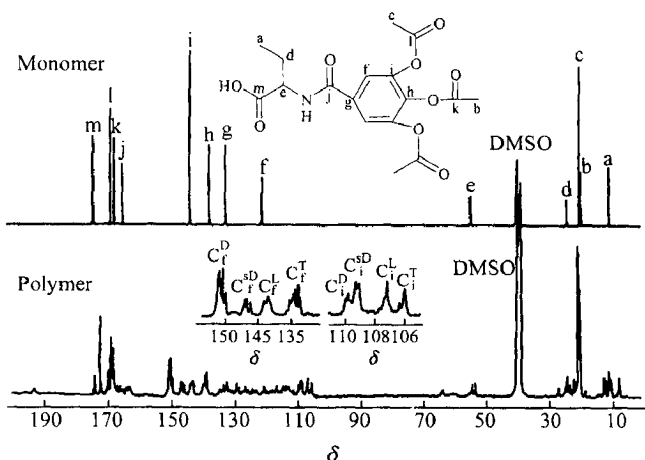


Fig. 2 ¹³C-NMR spectra of the monomer and the polymer

No crystallization and melting peaks in the DSC graph were observed, suggesting that the hyperbranched polymers obtained are amorphous. The hyperbranched poly(ester-amide)s from natural products display high thermal stability. The glass transition temperatures (T_g) ranged from 119°C to 178°C, and the decomposition temperature at 5% weight-loss (T_d^5) increased from 230°C to 270°C with the increase of molecular weight.

CONCLUSION

The synthesis and characterization of the hyperbranched poly(ester-amide)s containing acetyl end groups from natural products was reported. The resulting poly(ester-amide)s have low inherent viscosities, high degree of branching (0.75), and excellent thermal stability. The poly(ester-amide)s might have more promising applications as biocompatible components because they are prepared from natural materials, and contain both ester linkages and amide bonds, unlike the polymers reported by Kricheldorf.

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