Synthesis of a Hyperbranched Polymer with Perfect Branching Based on Piperidine-4-one

Warapon Sinananwanich, Tomoya Higashihara, and Mitsuru Ueda*

Department of Organic & Polymeric Materials, Graduate School of Science & Engineering, Tokyo Institute of Technology, 2-12-1-H120, O-okayama, Meguro-ku, Tokyo, 152-8552 Japan

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ABSTRACT: A new class of a hyperbranched polymer with 100% degree of branching has been successfully prepared by using 1-(3-phenoxypropyl)piperidine-4-one as an AB_2 monomer in the presence of methanesulfonic acid. This hyperbranched polymer is based upon a piperidine-4-one ring and is designed to react with aromatic nucleophiles to give an irreversibly formed diarylated compound. The electrophilicity of piperidine-4-one is enhanced by through-space electrostatic repulsion and an inductive effect. The kinetics of the model reaction between 1-ethylpiperidine-4-one and anisole was examined. The reaction followed second-order kinetics, indicating that the first reaction, that is, the formation of the intermediate from the reaction between 1-ethylpiperidine-4-one and anisole, is considerably slower than the second one, that is, the reaction of the generated intermediate with anisole. On the basis of this observation, a new monomer, which was expected to produce a 100% branched hyperbranched polymer, was designed and synthesized. The obtained polymer was characterized by ^{1}H and ^{13}C NMR spectroscopy, which affirmed the 100% degree of branching of the hyperbranched polymer.

Introduction

Dendrimers have attracted much interest during the past decade,[1] mainly due to their unusual, globular, perfectly branched structures, and monodispersity. The production of dendrimers, however, requires multistep syntheses, with cumbersome purifications between each step, making it a costly and time-consuming process. Hyperbranched polymers, in contrast, are often far easier to prepare under less drastic reaction conditions. Although they have less perfect branching structures than those of dendrimers, such systems retain a high degree of functionality, high solubility, low viscosity, and higher segment density compared to linear analogs.[2] Therefore, hyperbranched polymers provide a less expensive alternative to dendrimers for various applications, such as the production of blended components, photosensitive materials, nonlinear optics, light harvesting, drug delivery, and use as catalysts.[3] Hyperbranched polymers are generally prepared by one-pot self-polycondensation of an AB_x monomer. Here, A and B are two functionalities that can react with each other but not with themselves. Theoretically, for polymers derived from an AB_2 monomer, the degree of branching (DB) is determined by statistics and only reaches around 50%; this value is assumed based on the equal reactivity of the B functional groups of the AB_2 monomer.[4] To approach 100% branching, a characteristic property of dendrimers, several workers have reported methods for improving the DB, such as slow monomer addition,[5] polymerization in the presence of polyfunctional core molecules,[6] and the use of polyfunctional AB_x monomers.[7] All these approaches are restricted by the use of an AB_x monomer with equal B group reactivity and are therefore still subject to the statistical determination of the DB. Such 100% hyperbranched polymers can be obtained when the first reaction step of an AB_2 monomer activates the second reaction.[8] Recently, hyperbranched polymers with 100% DB have been synthesized by the polymerization of an AB_2-type monomer, using a "criss-cross" cycloaddition, with a maleimide group as the functional A group and with azine groups as the 2 B groups,[9] and by acid-catalyzed polycondensation of isatins or acenaphthenequinones with aromatic compounds.[10] During the course of our study on the synthesis of a hyperbranched polymer with 100% branching, we have reported that a such hyperbranched polymer could be prepared in an acidic medium by using 2-(4-phenoxyphenoxy)-fluorenone as a monomer.[11] Moreover, a 100% branched polythioketal which was synthesized by acid-catalyzed polycondensation of an AB_2 monomer, 2-[4-(4-mercaptobutoxy)phenoxy]-9*H*-fluoren-9-one, has been developed by our research group.[12] An alternate type of AB_2 monomer which can form a 100% branched hyperbranched polymer is ultimately desirable for developing this research area.

There are a lot of examples in physical-organic studies that use through-space electronic interactions to control regio- and stereospecificity.[13,14] Molecules such as 4-substituted bicyclo-[2.2.0]octane-1-carboxylic acid were developed to determine the Coulombic interaction between a polar substituent and carboxylic acid. The through-space electrostatic interaction between these groups perturbs the pK_a of the carboxylic acid group.[15] Seto et al. have described this physical-organic strategy to control the potency of enzyme inhibition. They found that the piperidine-4-one ring system is the most reactive toward nucleophilic attack by water or thiols.[16] Recently, Klumpp et al. utilized this activation for the synthesis of aryl-substituted piperidines by the Friedel-Craft type reaction of a piperidine-4-one with benzene.[17] The proposed reaction mechanism was that the origin of this enhanced reactivity is located at the base site nitrogen atom and that protonated nitrogen induces the electrophilicity of a carbonyl group, which is sufficiently condensed with aromatic nucleophiles. This activation may arise from inductive effects or by through-space electrostatic effects.[18] Furthermore, when an alcohol intermediate is formed in an acidic solution, it will readily react with another aromatic compound to give a diarylated product. However, thermodynamically favorable disubstituted products have been found to be poorly reversible in acid hydrolysis.[19] Despite the importance of these studies, we have noted that through-space interactions are rarely used as a rational design element in polymer synthesis. Therefore, a reaction based upon a piperidine-4-one structure has brought to our attention the possibility of applying a physical-organic concept in designing a novel class of AB_2 monomer for 100% hyperbranched polymer synthesis.

* To whom all correspondence should be addressed. Telephone: +81-3-57342127. Fax: +81-3-57342127. E-mail: ueda.m.ad@m.titech.ac.jp.

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Herein, we report the synthesis of a hyperbranched polymer with a 100% DB by polycondensation of a 1-(3-phenoxypropyl)piperidine-4-one as an AB_2 monomer in the presence of methanesulfonic acid (MSA). Moreover, a model reaction between 1-ethylpiperidine-4-one and anisole was studied to investigate the reactivity of the second B versus that of the first B of the AB_2 monomer.

Experimental Section

Materials. All reagents were purchased from TCI (Japan) and used without further purification. THF was dried over sodium/benzophenone and distilled before use under nitrogen.

Measurements. The FT-IR spectra were measured on a Horiba FT-720 spectrophotometer. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX-300 spectrometer at 300 MHz for ^{1}H and 75 MHz for ^{13}C measurement. Static light scattering (SLS) measurements were performed with an Ootsuka Electronics SLS-2000 instrument equipped with a He−Ne laser (633 nm) in $CHCl_3$ at 25 °C. The refractive index increment (dn/dc) in $CHCl_3$ at 25 °C was determined with a Optilab rEX operating at 633 nm. Thermogravimetry (TG) was performed using a Seiko TG/DTA 6300 thermal analysis system at a heating rate of 10 °C/min under nitrogen. Differential scanning calorimetry (DSC) was performed using a Seiko EXSTAR 6000 DSC 6200 at a heating rate of 5 °C/min under nitrogen.

Model Reaction. To a solution of 1-ethylpiperidine-4-one (0.30 g, 2.35 mmol) and anisole (0.76 g, 7.07 mmol) was added methanesulfonic acid (2.35 mL, 24.45 mmol), and then the solution was stirred at room temperature for 5 h. The solution was poured over several grams of ice. The aqueous solution was then made basic by addition of $NaHCO_3$, and the products were extracted into $CHCl_3$. The organic solution was then wash with water and brine, dried with $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography eluting with hexane/ethyl acetate (5:5), to give 1-ethyl-4,4-bis(4-methoxyphenyl)piperidine: coloress liquid, 0.75 g (98%). IR (neat, υ, cm^{-1}): 3039, 2938, 2830, 1604, 1511, 1457, 1380, 1295, 1249, 1180, 1141, 1033, 941, 825. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.14 (d, J = 9.0 Hz, 4 H), 6.80 (d, J = 9.0 Hz, 4 H), 3.74 (s, 6 H), 2.50 (m, 6 H), 2.37 (q, J = 7.2 Hz, 4 H), 1.08 (t, J = 7.2 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm): 157.3, 128.0, 113.6, 55.0, 52.3, 50.1, 43.4, 36.2, 11.9. Anal. Calcd for $C_{21}H_{27}NO_2$: C, 77.50; H, 8.36; N, 4.30. Found: C, 77.06; H, 8.34; N, 4.26.

For measuring the progress of reaction, to a solution of 1-ethylpiperidine-4-one (0.22 g, 1.73 mmol), and anisole (0.27 g, 2.52 mmol) in dichloromethane (3.00 mL) was added methanesulfonic acid (1.00 mL, 15.40 mmol) and then the solution was stirred at room temperature for 8 h. Dodecane (0.11 mL, 0.70 mmol) was added as an internal standard to the reaction mixture. After the solution was well mixed, then 0.2 mL of it was transferred to a NMR tube and subsequently added dichloromethane-d_2 (0.4 mL). The reaction was sampled and monitored by using ^{1}H NMR spectroscopy every 30 min.

Synthesis of 4,4-Bis(4-methoxyphenyl)piperidine. Piperidine-4-one hydrochloride (0.20 g, 2.01 mmol) was suspended in anisole (0.45 g, 4.23 mmol) and methanesulfonic acid, or trifluoromethane sulfonic acid, (2.0 mL) was added. The reaction was stirred at room temperature for 5 h, after which the reaction was poured over several grams of ice. The aqueous solution was then made basic by addition of $NaHCO_3$. The precipitate was collected by filtration, washed with water, and dried in vacuo at 50 °C for 6 h. The desired product was obtained in 0.59 g, 98%. Mp: 88−91 °C. IR (KBr, υ, cm^{-1}): 3448, 3031, 2946, 2830, 1612, 1565, 1511, 1465, 1411, 1288, 1249, 1180, 1033, 825. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.15 (d, J = 8.70 Hz, 4 H), 6.81 (d, J = 8.70 Hz, 4 H), 3.76 (s, 6 H), 2.90 (t, J = 5.40 Hz, 4 H), 2.32 (t, J = 5.40 Hz, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm): 157.5, 128.1, 113.8, 55.3, 43.8, 43.0, 37.2.

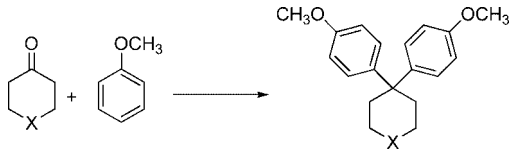
Synthesis of 1-Ethyl-4-(4-methoxyphenyl)piperdine-4-ol (3). The Grignard reagent was prepared from magnesium powders (0.20 g, 8.25 mmol) in dry tetrahydrofuran (15.00 mL) and 4-bromoanisole (1.47 g, 7.86 mmol) in dry tetrahydrofuran (5.00 mL) at 80 °C for 1 h. 1-(3-Phenoxypropyl)piperidine-4-one (0.50 g, 3.93 mmol) was added to the cooled Grignard solution. Then the mixture was refluxed for 6 h. The reaction mixture was neutralized with saturated ammonium chloride solution, extracted with ethyl acetate, washed with brine, dried with $MgSO_4$, and concentrated under reduced pressure. A yellow solid 0.68 g (73%) was isolated after purification by using silica gel column chromatography eluting with hexane/ethyl acetate (6:4). Mp: 95−98 °C. IR (KBr, υ, cm^{-1}): 3340, 3178, 2954, 2823, 1604, 1511, 1457, 1303, 1249, 1149, 1103, 1033, 925, 833, 771. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.42 (d, J = 9.0 Hz, 2 H), 6.86 (d, J = 9.0 Hz, 2 H), 3.79 (s, 3 H), 2.88 (m, 2 H), 2.55 (m, 4 H), 2.20 (m, 2 H), 1.78 (m, 2 H), 1.16 (t, J = 7.2 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm): 158.5, 140.4, 125.8, 113.6, 70.5, 55.2, 52.4, 49.0, 37.9, 11.6. Anal. Calcd for $C_{14}H_{21}NO_2$: C, 71.46; H, 8.99; N, 5.95. Found: C, 71.01; H, 9.12; N, 5.77.

Synthesis of 1-(3-Phenoxypropyl)piperidine-4-one (5). A mixture of piperidin-4-one hydrochloride (4.00 g, 40.35 mmol), (4-bromobuthoxy)benzene (7.02 mL, 44.38 mmol), and potassium carbonate (22.30 g, 161.40 mmol) in dehydrated DMF (50.0 mL) was heated at refluxed for overnight. Then the mixture was cooled, diluted with water, and extracted with ethyl acetate. The combined organic extracts were washed with brine, dried with $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography eluting with hexane/ethyl acetate (7.5:2.5), to give an AB_2 monomer 8.20 g (87%). IR (neat, υ, cm^{-1}): 3039, 2954, 2807, 1720, 1596, 1496, 1380, 1295, 1241, 1133, 1033, 964, 887, 755. H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.30 (m, 2 H), 6.92 (m, 3 H), 4.06 (t, J = 6.0 Hz, 2 H), 2.78 (t, J = 6.0 Hz, 4 H), 2.65 (t, J = 7.2 Hz, 2 H), 2.46 (t, J = 6.0 Hz, 4 H), 2.00 (m, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm): 209.3, 159.0, 129.5, 120.8, 114.5, 65.9, 54.1, 53.2, 41.3, 27.4. Anal. Calcd for $C_{14}H_{19}NO_2$: C, 72.07; H, 8.21; N, 6.00. Found: C, 71.66; H, 8.32; N, 5.89.

Synthesis of 4,4-Bis(4-methoxyphenyl)-1-(3-phenoxypropyl)-piperidine (7). A mixture of 1-(3-phenoxypropyl)piperidine-4-one (0.50 g, 2.14 mmol) and anisole (2.31 g, 21.43 mmol) was added methanesulfonic acid (3.00 mL, 46.20 mmol). The reaction was stirred at room temperature for 5 h. The solution was poured over several grams of ice. The aqueous solution was then made basic by addition of $NaHCO_3$, and the products were extracted into $CHCl_3$. The organic solution was then washed with water and brine, dried with $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography eluting with hexane/ethyl acetate (7:3) to provide a coloress liquid 0.46 g (50%). IR (neat, υ, cm^{-1}): 3062, 2946, 2830, 1604, 1511, 1465, 1380, 1295, 1249, 1180, 956, 825, 755. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.25 (m, 2 H), 7.15 (d, J = 9.0 Hz, 4 H), 6.90 (m, 3 H), 6.80 (d, J = 9.0 Hz, 4 H), 3.97 (t, J = 6.0 Hz, 2 H), 3.75 (s, 6 H), 2.46 (m, 10 H), 1.95 (m, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm): 159.0, 157.3, 129.4, 128.1, 120.6, 114.5, 113.6, 66.3, 55.4, 55.2, 50.7, 43.5, 36.6, 27.0. Anal. Calcd for $C_{28}H_{33}NO_3$: C, 77.93; H, 7.71; N, 3.25. Found: C, 77.50; H, 7.74; N, 3.28.

Synthesis of 4-(4-Methoxyphenyl)-1-(3-phenoxypropyl)piperidine-4-ol (8). The Grignard reagent was prepared from magnesium powders (0.06 g, 2.70 mmol) in dry tetrahydrofuran (7.00 mL) and 4-bromoanisole (0.48 g, 2.57 mmol) in dry tetrahydrofuran (2.00 mL) at 80 °C for 1 h. 1-(3-Phenoxypropyl)piperidine-4-one (0.30 g, 1.28 mmol) was added to the cooled Grignard solution. Then the mixture was refluxed for 6 h. The reaction mixture was neutralized with saturated ammonium chloride solution, extracted with ethyl acetate, washed with brine, dried with $MgSO_4$, and concentrated under reduced pressure. A pale yellow solid 0.35 g (80%) was isolated after crystallization from ethyl acetate. Mp: 132−134 °C IR (KBr, υ, cm^{-1}): 3417, 3139, 2946, 2823, 1604, 1504, 1457, 1388, 1303, 1241, 1172, 1118, 1049, 971, 833, 755. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.43 (d, J = 9.0 Hz, 2 H), 7.28 (m, 2 H), 6.91 (m, 5 H), 4.06 (t, J = 6.0 Hz, 2 H), 3.80 (s, 3 H), 2.82 (m, 2 H), 2.60 (m, 2 H), 2.47 (m, 2 H), 2.10 (m, 4 H), 1.77 (m, 2 H), 1.59 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm): 159.1, 158.6, 129.5, 125.8, 120.7, 114.6, 113.7, 71.0, 66.3, 55.5,

Table 1. Model Reaction between a Ketone and Anisole



entry	X	catalyst	product
1	CH_2	CH_3SO_3H	no disubstitution reaction
2	NH_2^+	CH_3SO_3H	97%
3	CH_2	CF_3SO_3H	no disubstitution reaction
4	NH_2^+	CF_3SO_3H	98%

55.4, 49.8, 38.7, 27.1. Anal. Calcd for $C_{21}H_{27}NO_3$: C, 73.87; H, 7.97; N, 4.10. Found: C, 73.85; H, 8.01; N, 4.13.

Hyperbranched Polymer Synthesis. A solution of 1-(3-phenoxypropyl)piperidine-4-one (0.05 g, 0.21 mmol) in methanesulfonic acid (2 mL) was stirred at room temperature for 16 h, and then a mixture was poured into 30% KOH aqueous solution (50 mL). After filtration, a solid was washed successfully with water. The polymer was collected (0.48 g, 94%) and dried at 85 °C for 8 h under vacuum. IR (KBr, υ, cm^{-1}): 3099, 2946, 2807, 1712, 1604, 1511, 1465, 1380, 1241, 1180, 1133, 1033, 964, 825. ^1H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.30 (br, proton 1 of dendritic unit), 7.12 (br, proton 8 of periphery), 6.81 (br, proton 2 of dendritic unit, proton 9 of periphery), 4.00 (br, proton 3 of dendritic unit, proton 10 of periphery), 2.55 (br, proton 5, 6, and 7 of dendritic unit, proton 12, 13, and 14 of periphery), 1.98 (br, proton 4 of dendritic unit, proton 11 of periphery). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm): 209.3, 158.2, 156.7, 134.4, 133.4, 128.1, 126.0, 120.2, 120.0, 114.3, 114.2, 66.4, 66.2, 66.0, 65.9, 55.4, 55.2, 54.1, 53.4, 53.2, 50.7, 50.5, 43.5, 41.2, 36.6, 28.2, 27.4, 27.2, 27.0.

Modification of Polymer 6. When the polymerization reaction was reached into a desired reaction time, an octane thiol (0.11 mL, 0.64 mmol) was directly added into reaction mixture. After extended it stirring for 5 h, the mixture was poured into 30% KOH aqueous solution (50 mL). The precipitate was collected by filtration and then washed with hexane to remove an excess amount of octane thiol. IR (KBr, υ, cm^{-1}): 3039, 2923, 2815, 1612, 1511, 1465, 1380, 1303, 1249, 1187, 1041, 825, 771. ^1H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.32 (br, Ar−H), 7.10 (br, Ar−H), 6.83 (br, Ar−H), 4.02 (CH_2 of dendritic unit), 3.11−2.50 (S−CH_2− of octane thiol, CH_2 of dendritic unit), 2.45−1.94 (CH_2 of dendritic unit), 1.62 (−CH_2−CH_2− of octane thiol), 1.44−1.08 (−CH_2−CH_2− of octane thiol), 0.86 (-CH_3 of octane thiol). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm): 157.42, 127.69, 126.03, 114.20, 65.75, 55.22, 55.02, 49.75, 49.50, 48.31, 43.00, 39.47, 39.22, 36.29, 35.60, 35.05, 34.40, 31.87, 29.23, 29.13, 29.06, 28.58, 28.35, 25.84, 22.70, 22.66, 14.19, 11.03.

Results and Discussion

To know whether the efficient ketone group of piperidine-4-one is suitable for the synthesis of a 100% hyperbranched polymer, the following requirements should be clarified: (1) the ketone group needs to be activated toward aromatic nucleophilic substitution in an acidic medium; (2) the rate constant of the second substitution should be faster than that of the first.

Initially, a model reaction was carried out at room temperature between piperidine-4-one or cyclohexanone and anisole with catalysts of different acidity, MSA and trifluoromethanesulfonic acid (TFSA) (Table 1).

We found that diarylated piperidines were isolated in excellent yield in the case of both MSA and TFSA but in contrast, no disubstitution reaction occurred when cyclohexanone was reacted with aromatic nucleophiles in an excess amount of acidic catalysts. This result indicated that the ketone group of piperidine-4-one is more electrophilic than standard ketones. Two possible factors increase their reactivity.[18,20] First, in the presence of acid, unfavorable through-space charge-dipole repulsion occurred between a positively charged ammonium group and a partial dipole of a carbonyl group. This interaction destabilizes the ketone, but is dissipated by the addition of nucleophiles because the reacting carbonyl carbon goes from sp^2 to sp^3 hybridization and carries a partially negative charge. Second, a protonated amine also acts as an electron-withdrawing group, which relies on through-bond inductive effects (Figure 1).

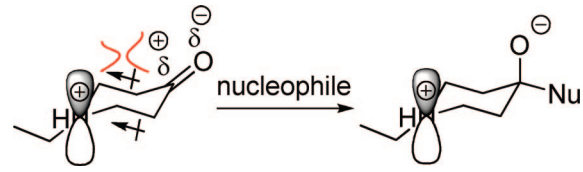
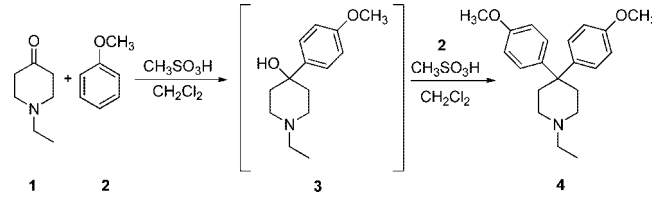


Figure 1. Electrostatic model proposed for substitution by aromatic nucleophiles in the presence of acid catalyst.

Scheme 1. Model Reaction between 1-Ethylpiperidine-4-one and Anisole



This observation suggested that the Friedel−Craft reaction of piperidine-4-one can be exploited to synthesize a 100% hyperbranched polymer. According to the same results in the case of both acids, MSA was selected for further studies so as to avoid using the costly and highly toxic TFSA.

To the best of our knowledge, the formation of diarylated products from a hydroxyalkylation reaction proceeds via alcohol intermediates, which are expected to react immediately with other aromatic nucleophiles. To follow the progress of this reaction, the model reaction between 1-ethylpiperidine-4-one (**1**) and anisole (**2**) was investigated in dichloromethane in the presence of MSA at room temperature (Scheme 1).

The reaction proceeded in a homogeneous state. The model reaction was monitored by using ^1H NMR spectroscopy.

The ^1H NMR spectra (Figure 2) show the formation of expected diarylated compound (**4**) with characteristic signals at 1.31 and 3.72 ppm, corresponding to the methyl and methoxy protons, respectively; unconverted **1** should also be noted. For reference, the alcohol intermediate was synthesized by the reaction of **1** with 4-methoxyphenyl magnesium bromide. No peaks were observed due to the intermediate (**3**) and other side reaction products, suggesting that the condensation of **1** and **2** proceeds via intermediate **3**, whose reactivity is much greater than that of starting ketone **1**.

Moreover, a comparison of the ^1H NMR spectrum measurements before and after the addition of acid supported our assumption that the protonation of nitrogen occurred due to the peak of the methyl group shifting to a lower field. This is good evidence that the charge-dipole repulsion was the driving force in the nucleophilic aromatic substitution reaction of piperidine-4-one.

The changes in the consumption of starting material **1** and **2** and the yield of product **4** were plotted against the reaction time, as shown in Figure 3. The graph indicated that one equiv of **1** condensed with two equiv of **2** to afford one equiv of **4**.

The concentration curve of the starting material decreases, but that of the product increases in the time range from 0 to 5 h, after which they reach a plateau. These results show a complementary relationship, also indicating that no side

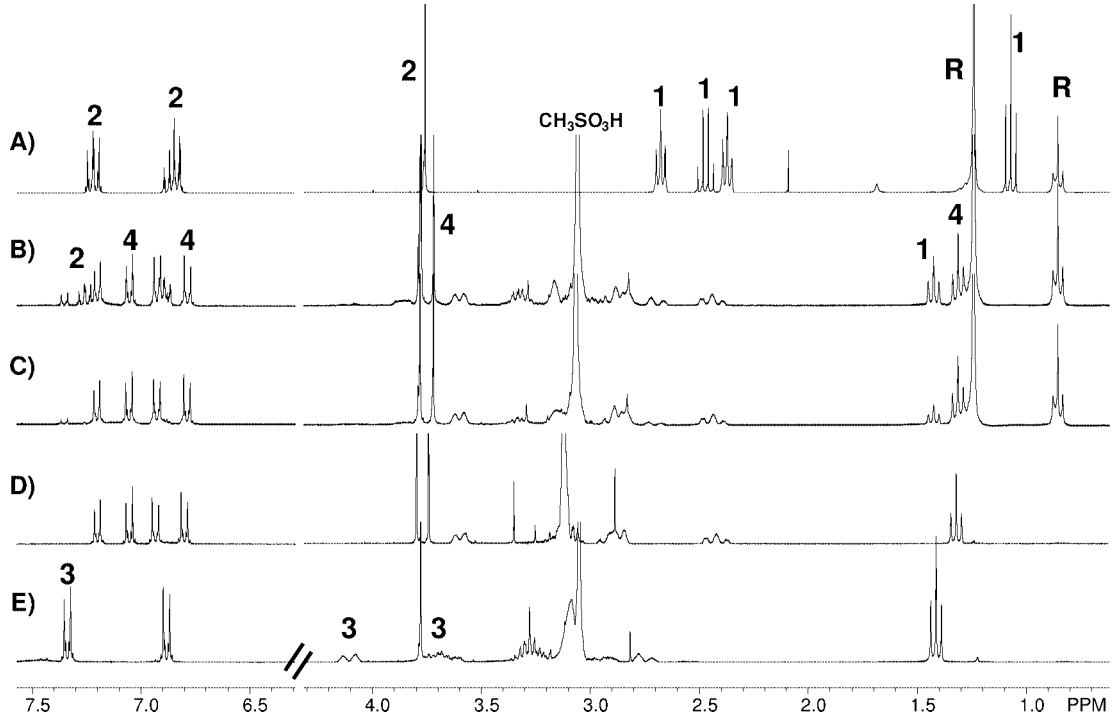


Figure 2. ^{1}H NMR spectra of products obtained by the model reaction between 1-ethylpiperidine-4-one (1.73 mmol) and anisole (2.52 mmol) in the presence of CH_3SO_3H (1 mL) in CD_2Cl_2 of A) absence of acid, B) $t = 2$, C) $t = 6$ h, D) diarylated product **4** in the presence of CH_3SO_3H, E) intermediate **3** in the presence of CH_3SO_3H. R is reference, dodecane.

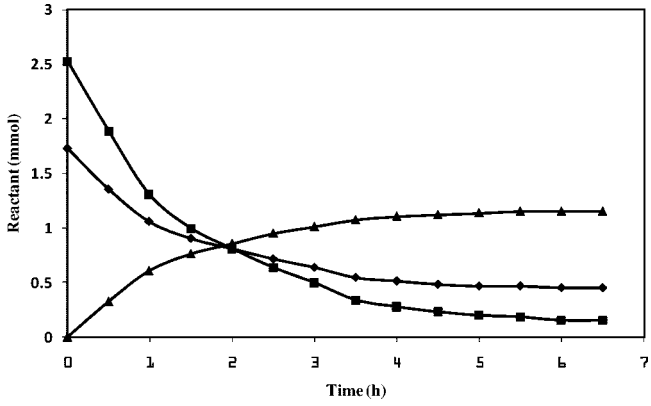


Figure 3. Relationship between amounts of the reactants, that is, **1** (♦) and **2** (■), and the product **4** (▲) with the reaction time in the model reaction between 1-ethylpiperidine-4-one (1.73 mmol) and anisole (2.52 mmol) in the presence of CH_3SO_3H (1 mL).

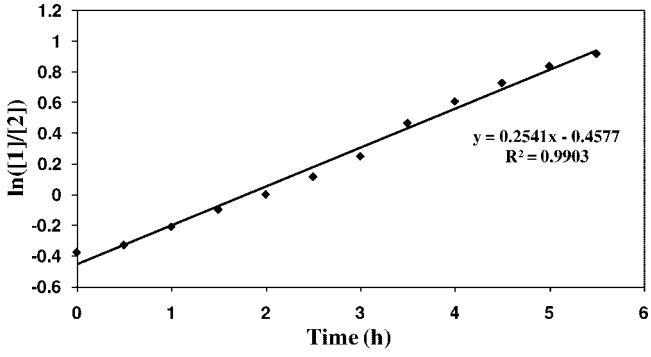
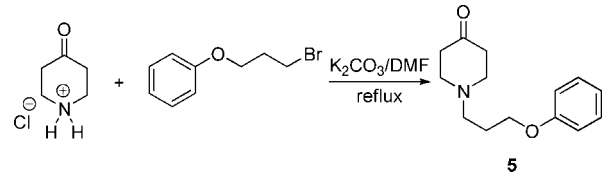


Figure 4. Second-order kinetic plot for the condensation of **1** and **2** in the model reaction between 1-ethylpiperidine-4-one (1.73 mmol) and anisole (2.52 mmol) in the presence of CH_3SO_3H (1 mL).

reactions occur during this condensation. Consequently, the reaction rate constant of the second step, i.e., the reaction of alcohol **3** with anisole, is considerably higher than that of the first step.

Scheme 2. Monomer Synthesis



Furthermore, the kinetic measurement of the model reaction was studied to consider the reaction mechanism in more detail, which is based on the following equation:

$$\mathbf{1} + \mathbf{2} \xrightarrow{k_1} \mathbf{3}$$

$$\mathbf{3} + \mathbf{2} \xrightarrow{k_2} \mathbf{4}$$

where **3** is an intermediate. Moreover,

$$-\mathrm{d}[2]/\mathrm{d}t = k_1[\mathbf{1}][\mathbf{2}] + k_2[\mathbf{3}][\mathbf{2}] \quad (1)$$

$$-\mathrm{d}[\mathbf{1}]/\mathrm{d}t = k_1[\mathbf{1}][\mathbf{2}] \quad (2)$$

$$\mathrm{d}[\mathbf{3}]/\mathrm{d}t = k_1[\mathbf{1}][\mathbf{2}] - k_2[\mathbf{3}][\mathbf{2}] \quad (3)$$

and

$$\mathrm{d}[\mathbf{4}]/\mathrm{d}t = k_2[\mathbf{3}][\mathbf{2}] \quad (4)$$

if $k_1 \ll k_2$, the amount of intermediate **3** can be ignored in the steady state. Thus,

$$\mathrm{d}[\mathbf{3}]/\mathrm{d}t = 0 \quad (5)$$

From eqs 3 and 5, the concentration of **3** can be expressed as follows:

$$[3] = k_1/k_2[1] \quad (6)$$

Equation 4 can then be expressed using (6) as

$$d[\mathbf{4}]/dt = k_1[\mathbf{1}][\mathbf{2}] \quad (7)$$

The concentrations of **1** and **2** are given by

$$[\mathbf{1}] = [\mathbf{1}]_0 - [\mathbf{4}] \quad \text{and} \quad [\mathbf{2}] = [\mathbf{2}]_0 - 2[\mathbf{4}]$$

Therefore, eq 7 is written as

$$d[\mathbf{4}]/dt = k_1([\mathbf{2}]_0 - 2[\mathbf{4}])([\mathbf{1}]_0 - [\mathbf{4}])$$

This expression can be integrated under the condition that [**4**] = 0 when time $t = 0$ as follows:

$$\ln([\mathbf{1}]/[\mathbf{2}]) = (2[\mathbf{1}]_0 - [\mathbf{2}]_0)k_1 t + \ln([\mathbf{1}]_0/[\mathbf{2}]_0)$$

Figure 4 shows the linear relationship between ln ([**1**]/[**2**]) and the reaction time; the overall reaction rate (k) and the correlation coefficient were estimated to be 0.2717 $L \cdot mol^{-1} \cdot h^{-1}$ and 0.9903, respectively. These results suggest that the first reaction, i.e., the reaction between **1** and **2**, is the rate-determining step.

According to the results of all experiments described above, all requirements are satisfied—the reactive species of piperidine-4-one is formed after activation by acid catalyzed and then condensed with anisole nucleophiles to produce alcohol intermediates whose reactivity is much higher than that of the starting material. Therefore, we have devised a new type of AB_2 monomer which combines the piperidine-4-one and anisolyl functions as B_2 and A functionalities, respectively, in order to synthesize a hyperbranched polymer with a DB of 100%. The synthesis of the expected AB_2 monomer, 1-(3-phenoxypropyl)-piperidine-4-one (**5**) can be easily accomplished in a one-step synthesis by using a base- catalyzed N-alkylation reaction (Scheme 2).

The structure of the AB_2 monomer was confirmed by FT-IR, NMR spectroscopy, and elemental analysis. The FT-IR spectrum of **5** showed characteristic absorptions at 3039, 1596, and 1720 cm^{-1} which can be assigned to aromatic C−H, aromatic C−C and carbonyl group stretching, respectively. The ^{1}H NMR spectrum of **5** can be fully assigned, as shown in Figure 5.

The self-polycondensation of **5** was carried out in the presence of MSA at room temperature for 16 h, and the monomer concentration of 100 mg/4 mL was applied (Scheme 3).

The polymer was isolated by pouring the polymer solution into a 30% KOH aqueous solution and was washed successively with water. The obtained polymer was partially soluble in chloroform at room temperature. The molecular weight could be improved by increasing the reaction time and temperature, however the resulting high molecular-weight polymer (37 h,

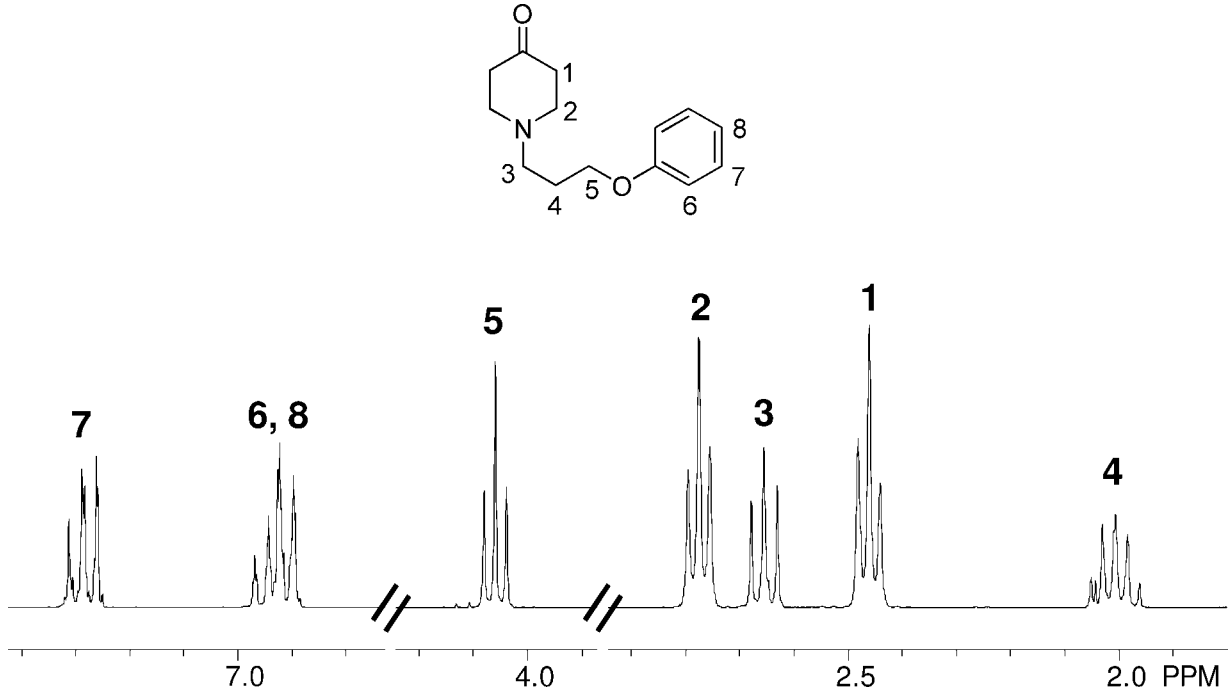
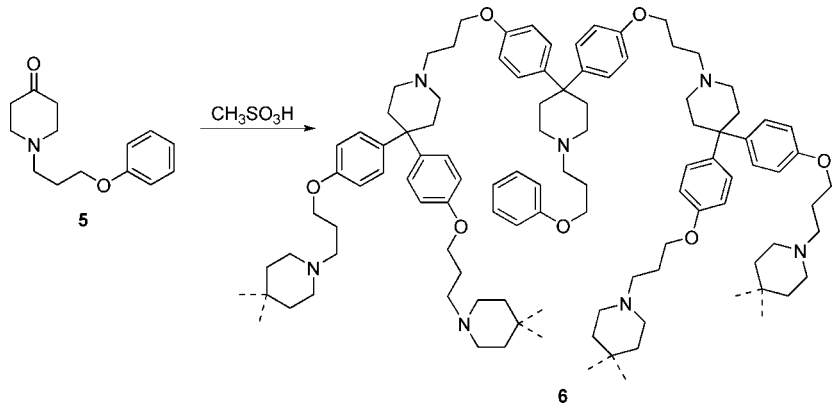


Figure 5. ^{1}H NMR spectrum of AB_2 monomer **5.**

Scheme 3. 100% Hyperbranched Polymer Synthesis



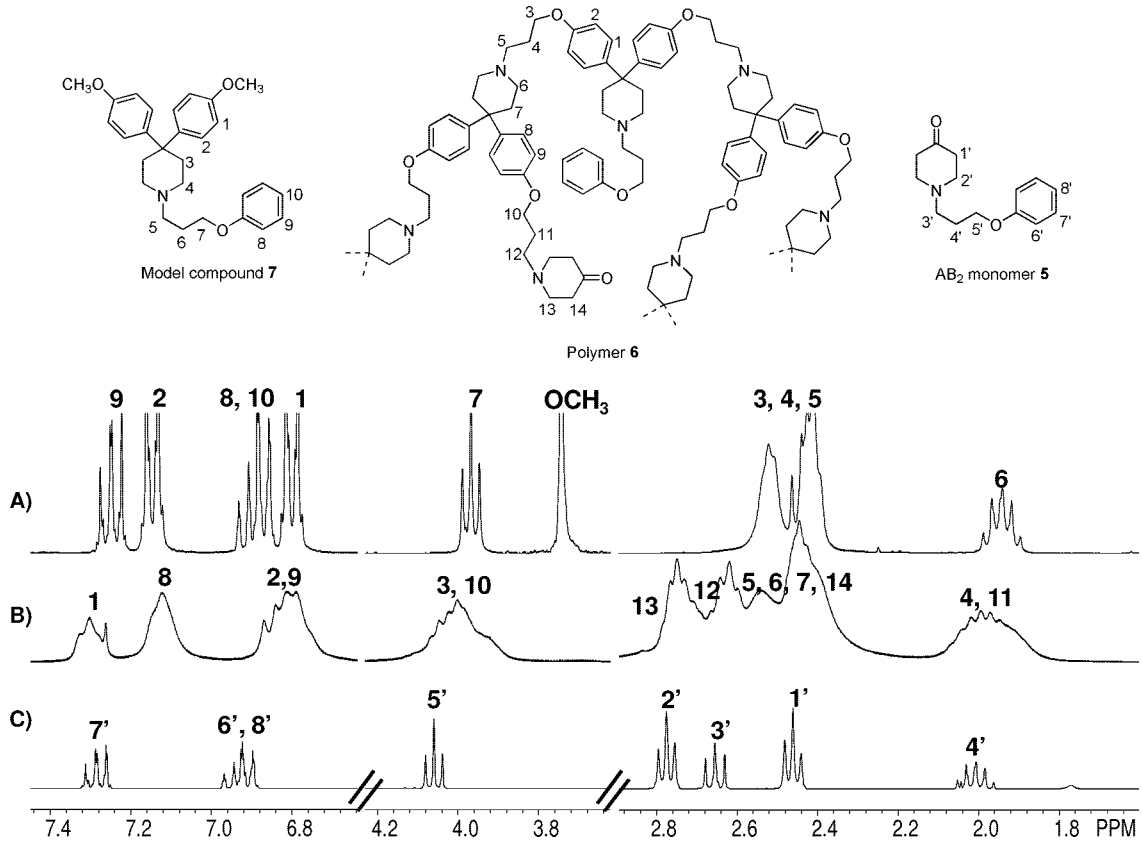


Figure 6. [1]H NMR spectra of (A) model compound **7**, (B) polymer **6**, and (C) AB_2 monomer **5** in $CDCl_3$.

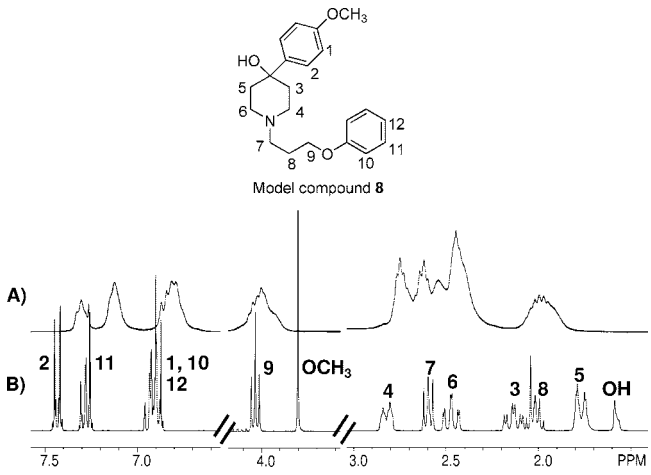
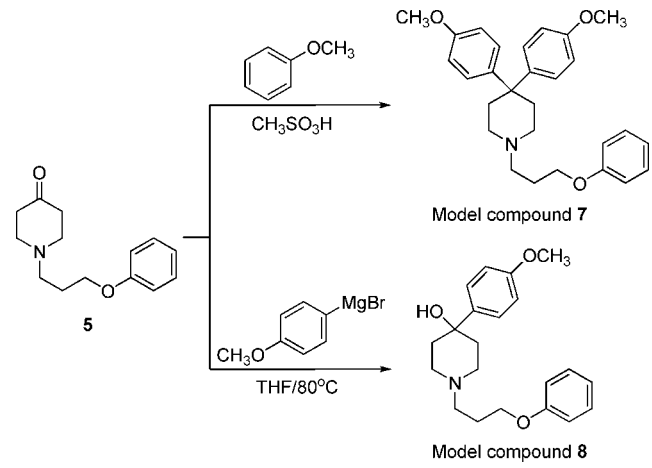


Figure 7. [1]H NMR spectra of (A) polymer **6** and (B) model compound **8**.

Scheme 4. Synthesis of Dendritic and Linear Units



room temperature) showed poor solubility in common organic solvents. To improve its solubility, octane thiol was added into the reaction mixture so that the ketone terminal units were converted to thioketal functional groups in the presence of MSA. The modified polymer was soluble in dichloromethane, chloroform and 1-methyl-2-pyrrolidinone. The absolute weight-average molecular weight and radius of gyration (R_g) of the modified polymer were measured by static light-scattering to obtain values of 7.86×10^4 g/mol and 14.8 nm, respectively.

In general, polycondensation of the AB_2 monomer provides a hyperbranched polymer containing three unit types in its structure—dendritic (D), linear (L), and terminal (T) units. To determine the abundance of these units in the obtained polymer, model compound **7**, 4,4-bis(4-methoxyphenyl)-1-(3-phenoxypropyl)piperidine, corresponding to the dendritic unit, was prepared by a reaction of **5** with anisole in the presence of MSA. Furthermore, model compound **8**, 4-(4-methoxyphenyl)-1-(3-phenoxypropyl)piperidine-4-ol, used as a representative for the linear unit, was synthesized by 4-methoxyphenyl magnesium bromide, together with **5** (Scheme 4).

Polymer **6** was characterized by FT-IR and NMR spectroscopy. In the FT-IR spectrum, characteristic absorption of carbonyl groups and aromatic carbon−carbon bonds appeared at 1712, 1604, and 1511 cm^{-1}, respectively. The [1]H NMR spectra of AB_2 monomer **5**, model compound **7**, and polymer **6** are presented in Figure 6.

By comparing the chemical shifts of monomer **5** and model compound **7**, the signals of polymer **6** were completely assigned. Unfortunately, no separated characteristic proton signals of the terminal and dendritic units were observed.

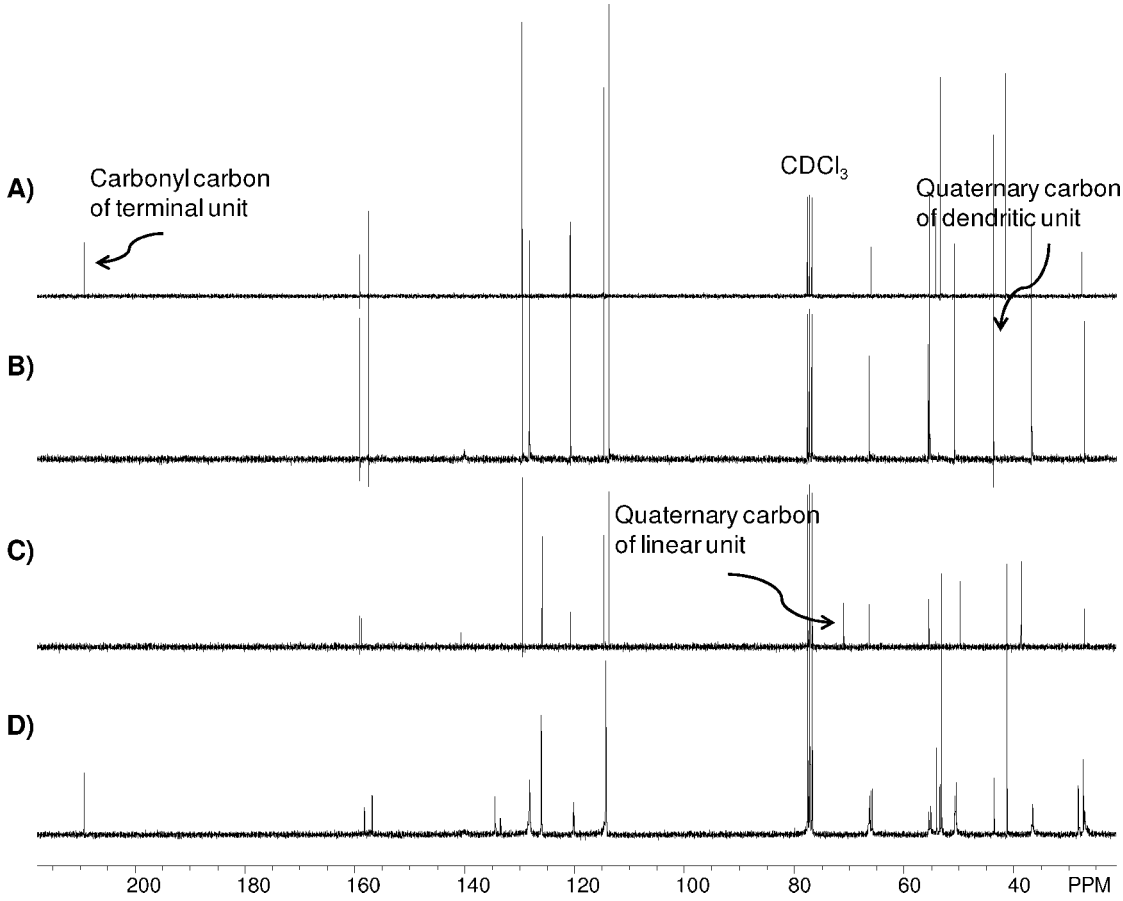


Figure 8. ^{13}C NMR spectra of (A) AB_2 monomer **5**, (B) model compound **7**, (C) model compound **8**, and (D) polymer **6** in $CDCl_3$.

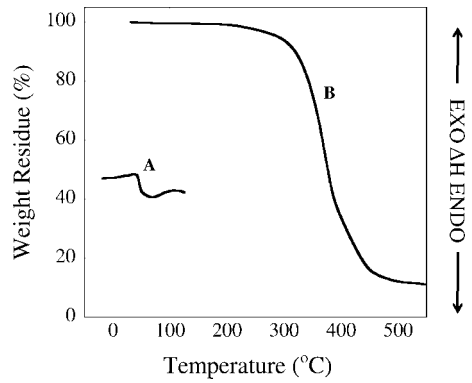


Figure 9. (A) TGA curve of polymer **6** at a heating rate of 10 °C min^{-1}. (B) TG curve of polymer **6** at a heating rate of 5 °C min^{-1}.

For further confirmation, the ^1H NMR spectrum of polymer **6** and model compound **8** are compared in Figure 7. It was found that no peaks corresponding to the linear unit at 1.77, 2.82, and 7.43 ppm appeared in the polymer spectrum.

Furthermore, polymer **6** was further investigated by ^{13}C NMR spectroscopy, and the result is shown in Figure 8. There are two characteristic peaks at 209.3 and 43.5 ppm, which can be assigned to carbonyl carbon of the terminal unit and quaternary carbon of the dendritic unit, respectively. In particular, the signal appearing at 71.0 ppm, which corresponded to quaternary carbon of the linear unit, could not be found in the spectrum of polymer **6**. All NMR spectroscopic data were consistent with our hypothesis that the synthesized polymer possessed 100% branching and no traces of linear units were incorporated.

Despite the architecture of a hyperbranched polymer having 100% branching, its structure is still not perfect, like a dendrimer. Hobson and Feast[21] pointed out that there are many architectures existing for 100% branching polymers from AB_2 monomers, such as the perfectly hyperbranched polymers, the dendrimer wedge and quasi-linear polymer.

The thermal stability of polymer **6** was determined by TGA. Polymer **6** is stable up to 300 °C in a nitrogen atmosphere, as shown in Figure 9. The glass transition temperature (T_g) was noted at 45 °C in a DSC thermogram. The absence of rigid structures in the polymer causes a low T_g.

Conclusions

We demonstrated that through-space electrostatic interactions can be the basis for a useful and predictable design of a monomer for the construction of a hyperbranched polymer with 100% branching. Protonation at the base site nitrogen atom induces electrostatic repulsion between the ammonium cation and the ketone in piperidine-4-one. This activation provides reactive species which sufficiently react with anisole to form a diarylated piperidine. Moreover, the results from the model reaction indicate that the rate constant of the second substitution is much faster than that of the first. On the basis of a combination of these results, a 100% branched hyperbranched polymer was successfully prepared in a one-step synthesis. Further research toward the application of this synthesized hyperbranched polymer is currently ongoing.

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