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ARTICLE

Base-Catalyzed Synthesis of a 100% Hyperbranched Polymer on the Basis of an Indolin-2-one Unit

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ABSTRACT: A novel synthetic method of a hyperbranched polymer possessing 100% branching was successfully developed by using 3,3-dibromo-1-hexyl-5-hydroxyindolin-2-one as a monomer in the presence of sodium hydride. The structure of the monomer is based upon an indolin-2-one core having geminal dibromide and hydroxyl functional groups which are designed to react together to form an irreversible ketal compound. A kinetic model reaction between 3,3-dibromo-1-hexylindolin-2-one with 4-methylphenol was studied in a base medium. The reaction followed second-order kinetics, indicating that the first reaction, that is, the formation of an intermediate from a reaction between 3,3-dibromo-1-hexylindolin-2-one and sodium 4-methylphenolate, is considerably slower than the second one—a reaction of the generated monobromide ether with sodium 4-methylphenolate. Therefore, a new monomer was designed and synthesized, aiming at a 100% hyperbranched polymer. The isolated polymer was characterized by ^{13}C NMR spectroscopy, which confirmed the 100% branching of the hyperbranched polymer.

Introduction

Dendritic macromolecules can generally be divided into two types: dendrimers and hyperbranched polymers. Dendrimers are synthesized by two complementary general approaches, the divergent and convergent methods, and have a globular shape, perfectly branched structures, and also well-defined monodispersity.[1] However, the synthesis of a dendrimer requires a tedious multistep procedure with repetitive protection−deprotection and purification processes in each generation of the dendrimer synthesis, making it a costly and time-consuming process. Hyperbranched polymers, in contrast, are usually the product of a one-pot polymerization procedure and therefore exhibit an irregular architecture with incompletely reacted branch points throughout the structure, leading to an extremely broad polydispersity and a low degree of branching, when compared with dendrimer analogues.[2] Hyperbranched polymers provide a less expensive alternative to dendrimers for various applications due to the fact that such a system retains a high degree of functionality, high solubility, low viscosity, and higher segment density compared to a linear counterpart.[3] The majority of hyperbranched polymer syntheses involves a step-growth polycondensation reaction employing monomers of the AB_x type, where A and B represent two different functional groups. In this respect, the degree of branching (DB) has been discussed as one of the key parameters for the characterization of hyperbranched polymers, which is controlled by the reactivity of the functional groups involved in the synthesis. Theoretically, for polymers derived from an AB_2 monomer, the DB is determined by statistics and only reaches around 50%, assuming it is based on equal reactivity of the two B functional groups of the AB_2 monomer.[4] Recently, several groups have reported methods for increasing the DB of hyperbranched polymers to achieve 100% branching and the characteristic property of dendrimers.[5] All these approaches are restricted by the use of an AB_x monomer with equal reactivity of the B group 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.[6] Komber et al. reported the first example of a 100% hyperbranched polymer which was synthesized by the polymerization of an AB_2-type monomer, using "criss-cross" cycloaddition.[7] Afterward, Smet et al. applied acid-catalyzed polycondensation of isatins or acenaphthenequinones with aromatic compounds to provide a 100% hyperbranched polymer.[8] During the course of our study on 100% hyperbranched polymer synthesis, we reported that such a hyperbranched polymer could be prepared in an acidic medium by using 2-(4-phenoxyphenoxy)fluorenone as the monomer.[9] Moreover, a 100% branched polythioketal by acid-catalyzed polycondensation of 2-[4-(4-mercaptobutoxy)phenoxy]-9*H*-fluoren-9-one was prepared by our group.[10] Recently, we applied a physical organic concept, the charge−dipole interaction, to design an AB_2 monomer for synthesis of a 100% hyperbranched polymer.[11] To date, only acid-catalyzed 100% hyperbranched polymer syntheses have been reported, so it is highly desirable and challenging to seek new strategies toward 100% hyperbranched polymers under a base medium.

In general, the highest molecular weight of a linear polymer in step-growth polymerization is obtained with an exact stoichiometric amount of monomers, but a stoichiometric imbalance in the monomer feed ratio decreases the degree of polymerization.[12] However, a stoichiometric imbalance practically enhances the molecular weight of a polymer in step polymerization, in which the first condensation of a bifunctional monomer enhances the second condensation. In other words, the degree of polymerization can be increased when it proceeds via a reactive intermediate. By applying this concept, Endo et al. reported that a linear polyorthocarbonate with high molecular weight was prepared by polycondensation of a 0.7 equiv excess of 2,2-dichloro-1, 3-benzodioxole with bisphenol A. They found that the rate of

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the first nucleophilic displacement was 27 times slower than that of the second reaction.[13] In addition, the reaction of bisphenol A with methylene bromide in the presence of sodium hydroxide produced a high-molecular-weight aromatic polyformal. The proposed reaction mechanism was that the reaction occurred via a bromomethyl ether intermediate which is much more reactive than the monomer, methylene dibromide.[14] Ueda et al. also studied the kinetics of the polycondensation of 4,4-thiobisbenzenethiol and dibromomethane and found that this polymerization is a stoichiometric imbalance-enhanced polymerization.[15] Therefore, it was envisioned that a geminal dihalide functional group has the possibility of being applied to B_2 groups in the AB_2 monomer structure for the synthesis of 100% hyperbranched polymers.

Herein, we report the synthesis of a hyperbranched polymer with 100% branching by self-nucleophilic substitution of a 3,3-dibromo-1-hexyl-5-hydroxyindolin-2-one as the AB_2 monomer in the presence of sodium hydride. Moreover, a model reaction between 3,3-dibromo-1-hexylindolin-2-one and 4-methylphenol 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. Molecular weight measurement was performed via gel permeation chromatography with JASCO PU-2080Plus with two polystyrene gel columns (TSK GELs; GMH_{HR}-M). *N*,*N*-Dimethylformamide (DMF) containing 0.01 M LiBr was used as a solvent at a flow rate of 1.0 mL/min. The M_n and M_w were calibrated by standard polystyrene samples. Thermogravimetry (TG) was performed using a Seiko TG/DTA 6300 thermal analysis system at a heating rate of 10 °C/min under nitrogen.

Synthesis of 1-Hexylindolin-2-one. A mixture of oxindole (5.00 g, 37.5 mmol), hexyl iodide (9.55 g, 45.1 mmol), and potassium carbonate (25.95 g, 187.8 mmol) in tetrahydrofuran (50.0 mL) was stirred at room temperature overnight. The mixture was then diluted with water and extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography eluting with hexane/ethyl acetate (9:1) to provide a colorless liquid, 3.80 g (47%). IR (neat, ν, cm^{-1}): 3054.6, 2927.4, 2857.9, 1716.3, 1612.2, 1465.6, 1357.6, 1195.6, 1095.3, 1018.2, 948.8, 748.2. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.16 (m, 2 H), 6.92 (td, J = 7.5, 1.0 Hz, 1 H), 6.73 (d, J = 7.8 Hz, 1 H), 3.59 (t, J = 7.4 Hz, 2 H), 3.41 (s, 2 H), 1.57 (m, 2 H), 1.22 (m, 6 H), 0.78 (t, J = 6.9 Hz, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm): 175.0, 144.8, 127.8, 124.8, 124.5, 122.1, 108.4, 40.1, 35.9, 31.6, 27.5, 26.7, 22.6, 14.1.

Synthesis of 3,3-Dibromo-1-hexylindoline-2-one. To a solution of 1-hexylindolin-2-one (3.00 g, 13.8 mmol) in ethyl acetate (100 mL) was added copper bromide (12.3 g, 55.2 mmol), and then the mixture was refluxed at 90 °C for 3 h. After the mixture cooled down, it was extracted with ethyl acetate, washed with brine, and dried over $MgSO_4$. The crude product was purified by silica gel column chromatography eluting with hexane/ethyl acetate (8.5:1.5) to give a pale red liquid, 3.2 g (62%). IR (neat, ν, cm^{-1}): 3058.5, 2927.4, 2857.9, 1735.6, 1608.3, 1469.4, 1353.7, 1176.3, 1099.2, 902.5, 809.9, 748.2. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.63 (dd, J = 7.8, 1.1 Hz, 1 H), 7.34 (td, J = 7.9, 1.5 Hz, 1 H), 7.17 (td, J = 7.7, 1.5 Hz, 1 H), 6.83 (d, J = 8.1 Hz, 1 H), 3.73 (t, J = 7.5 Hz, 2 H), 1.72 (m, 2 H), 1.33 (m, 6 H), 0.88 (t, J = 7.0 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm): 169.9, 139.3, 131.6, 131.2, 126.1, 123.9, 109.4, 45.5, 40.9, 31.4, 27.0, 26.3, 22.5, 14.0.

Synthesis of 1-Hexyl-3,3-diphenoxyindolin-2-one. A mixture of 3,3-dibromo-1-hexylindolin-2-one (0.30 g, 0.80 mmol) and phenol (0.16 g, 1.76 mmol) in tetrahydrofuran (2.00 mL) was added sodium hydride (0.04 g, 1.92 mmol) or diaza(1,3)bicyclo-[5.4.0]undecane (0.29 g, 1.92 mmol). The reaction mixture was stirred at room temperature for 3 h, after which the reaction was 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 (9:1) to give a 1-hexyl-3,3-diphenoxyindolin-2-one, 0.31 g (97%); mp 65−66 °C. IR (KBr, ν, cm^{-1}): 3054.6, 2931.2, 2854.1, 1731.7, 1612.2, 1488.7, 1369.2, 1292.0, 1195.6, 1106.9, 1018.2, 987.3, 902.5, 759.8, 694.2. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.18 (m, 11 H), 6.80 (m, 3 H), 3.65 (t, J = 7.3 Hz, 2 H), 1.57 (m, 2 H), 1.26 (m, 6 H), 0.86 (t, J = 6.6 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm): 169.1, 153.7, 142.9, 131.2, 129.2, 126.0, 124.6, 124.2, 122.4, 122.3, 109.0, 100.6, 40.1, 31.5, 27.1, 26.5, 22.6, 14.1.

Model Reaction. Sodium hydride (0.1 g, 3.99 mmol) was added to a solution of 3,3-dibromo-1-hexylindoline-2-one (0.50 g, 1.33 mmol) and 4-methylphenol (0.36 g, 3.33 mmol) in tetrahydrofuran (2.00 mL), and then the solution was stirred at room temperature for 3 h. The solution was poured into water, and the products were extracted into ethyl acetate. The organic solution was then 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 (9:1) to give 1-hexyl-3,3-bis(4-tolyloxy)indolin-2-one: a colorless liquid, 0.55 g (96%). IR (neat, ν, cm^{-1}): 3031.5, 2927.4, 2857.9, 1739.4, 1612.2, 1504.2, 1469.4, 1365.3, 1199.5, 1114.6, 1037.5, 937.2, 821.5, 752.1. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.26 (m, 1 H), 7.01 (m, 8 H), 6.80 (m, 3 H), 3.62 (t, J = 7.4 Hz, 2 H), 2.26 (s, 6 H), 1.55 (m, 2 H), 1.24 (m, 6 H), 0.86 (t, J = 6.6 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm): 169.2, 151.3, 142.7, 134.0, 130.9, 129.6, 126.0, 124.2, 122.2, 108.9, 100.5, 39.9, 31.5, 27.1, 26.4, 22.5, 20.8, 14.0.

For monitoring the progress of reaction, in a two-necked flask equipped with a septum rubber and nitrogen inlet and outlet tubes was placed a solution of 3,3-dibromo-1-hexylindoline-2-one (0.40 g, 1.06 mmol) and 4-methylphenol (0.17 g, 1.59 mmol) in tetrahydrofuran (3.00 mL). Dodecane (0.07 g, 0.42 mmol) was added as an internal standard to the reaction mixture. Then to the solution was added sodium hydride (0.046 g, 1.92 mmol) and left it stirring at room temperature for 4 h. After the solution was well mixed, then 0.2 mL of it was transferred to a NMR tube and subsequently added chloroform-d_3 (0.4 mL). The reaction was sampled and monitored by using ^{1}H NMR spectroscopy every 20 min.

Synthesis of 4-(Hexylamino)phenol. 2-Propanol (300.0 mL) was added to a flask containing Pd/C (2.34 g, 21.99 mmol). Ammonium formate (46.22 g, 733.07 mmol) dissolved in water (50.0 mL) was transferred to the same flask. The reaction mixture was stirred for 1 min to activate Pd/C. Then 4-aminophenol (8.0 g, 73.30 mmol) and hexanal (8.95 mL, 73.30 mmol) were subsequently added. The reaction mixture was stirred at room temperature for 2 h. After completion of the reaction based on TLC monitoring, the Pd/C catalyst was filtered off on Celite, and the solvent was removed by rotary evaporation. The reaction mixture was diluted with dichloromethane and washed with brine. The organic phase was collected, dried with $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography eluting with hexane/ethyl acetate (8:2) providing mono-*N*-hexylation product, 12.3 g (86%). IR (KBr, ν, cm^{-1}): 3286.1, 2927.4, 2850.2, 1600.6, 1519.6, 1434.7, 1376.9, 1226.5, 1072.2, 902.5, 825.3. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm): 6.70 (d, J = 9.0 Hz, 2 H), 6.53

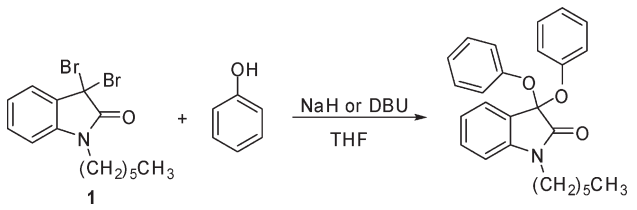
(d, J = 9.0 Hz, 2 H), 3.04 (t, J = 7.2 Hz, 3 H), 1.56 (m, 2 H), 1.31 (m, 6 H), 0.89 (t, J = 6.8 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm): 147.7, 142.9, 116.2, 114.3, 45.2, 31.8, 29.7, 27.0, 22.7, 14.2.

Synthesis of 2-Chloro-*N*-hexyl-*N*-(4-hydroxyphenyl)acetamide. A biphasic mixture of the 4-(hexylamino)phenol (4.00 g, 20.69 mmol) and potassium hydroxide (2.32 g, 41.38 mmol) in ethyl acetate (50 mL) and water (40 mL) was cooled to 0 °C using an ice bath. To the vigorously stirred mixture, chloroacetyl chloride (2.46 mL, 31.04 mmol) was added in small portions over 5 min. Stirring was continued at 0 °C for 30 min, at which point the reaction mixture was transferred to a separatory funnel. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated with the aid of a rotary evaporator. The residue was purified by silica gel column chromatography eluting with hexane/ethyl acetate (8:2) to give the amide product, 4.56 g (81%); mp 78−80 °C. IR (KBr, ν, cm^{-1}): 3239.8, 3004.5, 2927.4, 2857.9, 1635.3, 1592.9, 1511.9, 1446.3, 1365.3, 1272.7, 1226.5, 1145.5, 1099.2, 929.5, 836.9, 790.6. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm): 6.96 (m, 4 H), 3.79 (s, 2 H), 2.19 (t, J = 7.7 Hz, 2 H), 1.45 (m, 2 H), 1.17 (m, 6 H), 0.76 (t, J = 6.6 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm): 167.4, 157.4, 132.3, 128.9, 117.0, 50.5, 42.0, 31.5, 27.3, 26.4, 22.6, 14.0. Anal. Calcd for $C_{14}H_{20}ClNO_2$: C, 62.33; H, 7.47; N, 5.19. Found: C, 62.18; H, 7.25; N, 5.12.

Synthesis of 1-Hexyl-5-hydroxyindolin-2-one. An oven-dried Schlenk tube equipped with a magnetic stir bar and a Teflon stopcock was evacuated while hot and cooled under nitrogen. The tube was charged with palladium acetate (0.05 g, 0.22 mmol), 2-(di-*tert*-butylphospino)biphenyl (0.03 g, 0.11 mmol), and 2-chloro-*N*-hexyl-*N*-(4-hydroxyphenyl)acetamide (2.0 g, 7.41 mmol). The tube was evacuated and backfilled with nitrogen (repeated three times), and the Teflon stopcock was replaced with a rubber septum. Anhydrous triethylamine (1.54 mL, 11.12 mmol) was added, followed by anhydrous toluene (7.50 mL). The septum was replaced by the Teflon stopcock under a positive pressure of nitrogen, and the sealed tube was placed in an oil bath preheated to 110 °C. After 9 h, the reaction was allowed to cool to room temperature and was diluted with ethyl acetate. The mixture was filtered through Celite and concentrated on a rotary evaporator. The crude product was purified by silica gel column chromatography eluting with hexane/ethyl acetate (7:3) to give a white solid, 1.20 g (69%); mp 120−121 °C. IR (KBr, ν, cm^{-1}): 3185.8, 2927.4, 2857.9, 1666.2, 1596.7, 1488.7, 1400.0, 1369.2, 1284.3, 1234.2, 1187.9, 1149.3, 944.9, 798.3, 721.2. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm): 6.85 (m, 1 H), 6.79 (dd, J = 8.1, 2.4 Hz, 1 H), 6.84 (d, J = 8.7 Hz, 1 H), 3.67 (t, J = 7.5 Hz, 2 H), 3.49 (s, 2 H), 1.65 (m, 2 H), 1.30 (m, 6 H), 0.87 (t, J = 6.9 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm): 175.3, 152.4, 137.5, 126.1, 114.0, 113.0, 109.1, 40.4, 36.3, 31.5, 27.5, 26.7, 22.6, 14.1. Anal. Calcd for $C_{14}H_{19}NO_2$: C, 72.07; H, 8.21; N, 6.00. Found: C, 72.23; H, 8.25; N, 5.92.

Synthesis of 3,3-Dibromo-1-hexyl-5-hydroxyindolin-2-one. To a solution of 1-hexyl-5-hydroxyindolin-2-one (0.8 g, 3.58 mmol) in ethyl acetate (40.0 mL) was added copper bromide (3.20 g, 14.3 mmol), and then the mixture was refluxed at 90 °C for 3 h. After the mixture cooled down, it was extracted with ethyl acetate, washed with brine, and dried over $MgSO_4$. The crude product was purified by silica gel column chromatography eluting with hexane/ethyl acetate (8.5:1.5) to give the AB_2 monomer, 0.54 g (38%); mp 134−135 °C. IR (KBr, ν, cm^{-1}): 3282.2, 2927.4, 2869.5, 1697.0, 1600.6, 1500.3, 1481.0, 1365.3, 1334.5, 1288.2, 1187.9, 1157.0, 817.6. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.25 (d, J = 2.7 Hz, 1 H), 6.89 (dd, J = 2.7, 8.4 Hz, 1 H), 6.69 (d, J = 8.7 Hz, 1 H), 6.48 (s, 1 H), 3.70 (t, J = 7.2 Hz, 2 H), 1.70 (m, 2 H), 1.31 (m, 6 H), 0.87 (t, J = 6.7 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm): 170.2, 153.4, 132.2, 132.1, 118.4, 114.0, 110.4, 45.8, 41.2, 31.4, 27.0, 26.4, 22.6, 14.1. Anal. Calcd for $C_{14}H_{17}Br_2NO_2$: C, 42.99; H, 4.38; N, 3.58. Found: C, 42.83; H, 4.37; N, 3.17.

Scheme 1. Model Reaction between 3,3-Dibromo-1-hexylindolin-2-one and Phenol in the Presence of a Different Base



Hyperbranched Polymer Synthesis. To a solution of 3,3-dibromo-1-hexyl-5-hydroxyindolin-2-one (0.05 g, 0.13 mmol) in 1-methyl-2-pyrolidinone (0.5 mL) was added sodium hydride (3.68 mg, 0.15 mmol) at 0 °C. The solution was warmed to room temperature and stirred for 18 h, and then the solution was poured into water. After filtration, a solid was washed successfully with water followed by diethyl ether. The polymer was collected and dried at room temperature for 4 h under vacuum. IR (KBr, ν, cm^{-1}): 2954.4, 2927.4, 2869.5, 1716.3, 1619.9, 1461.7, 1365.3, 1268.9, 1180.2, 1110.8, 809.9, 732.8. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.11 (br, Ar−H), 6.76 (br, Ar−H), 6.56 (br, Ar−H), 3.57 (br, −N−CH_2 of dendritic and terminal units), 1.57 (br, −CH_2− of dendritic and terminal units), 1.18 (br, −CH_2− of dendritic and terminal units), 0.74 (br, −CH_3 of dendritic and terminal units). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm): 198.7, 170.0, 164.2, 153.5, 140.7, 140.6, 132.1, 131.8, 118.3, 113.9, 110.3, 105.8, 54.5, 53.3, 45.9, 41.0, 31.4, 27.0, 26.2, 22.5, 13.9.

Results and Discussion

As mentioned in the Introduction, the rate constant of the second reaction must be faster than that of the first; therefore, we began to find a suitable monomer which is expected to produce a 100% hyperbranched polymer. It is based upon an AB_2 monomer containing two identical B groups which should be located in the same position. We anticipated that if the reaction of the first B group occurs, it will affect the remaining B group with higher reactivity, e.g., by a resonance effect, inductive effect, neighboring group participation, or rearrangement.[7] Significantly, when the first B group reacts with A, it generates an unstable intermediate which readily reacts with the second B group to form a stable and irreversible product under the reaction conditions employed. In this study, nucleophilic substitution of geminal dibromide with a hydroxyl group was brought our attention in designing a novel system of an AB_2 monomer for base-catalyzed 100% hyperbranched polymer synthesis.

To elucidate whether the geminal dibromide group of the indolin-2-one core is appropriate for utilizing as the two B groups, the following requirements should be clarified: (1) the geminal dibromide group reacts with a hydroxyl group to give only a disubstituted product; (2) the rate constant of the second substitution should be faster than that of the first.

Initially, a model reaction between 3,3-dibromo-1-hexylindolin-2-one (**1**) and phenol was carried out in the presence of sodium hydride (NaH) or diaza(1,3)bicycle[5.4.0]undecane (DBU) at room temperature (Scheme 1). We found that only disubstituted products were isolated in excellent yield without the observation of monosubstituted compounds in the case of both NaH and DBU, although the reaction required a longer reaction time when DBU was used. Then the stronger inorganic base, NaH, was selected for further studies. This result indicates that a nucleophilic substitution reaction of geminal dibromide with a hydroxyl group can be employed for 100% hyperbranched polymer synthesis.

Based on these findings, the ketal formation from nucleophilic substitution of geminal dibromide with a hydroxyl group

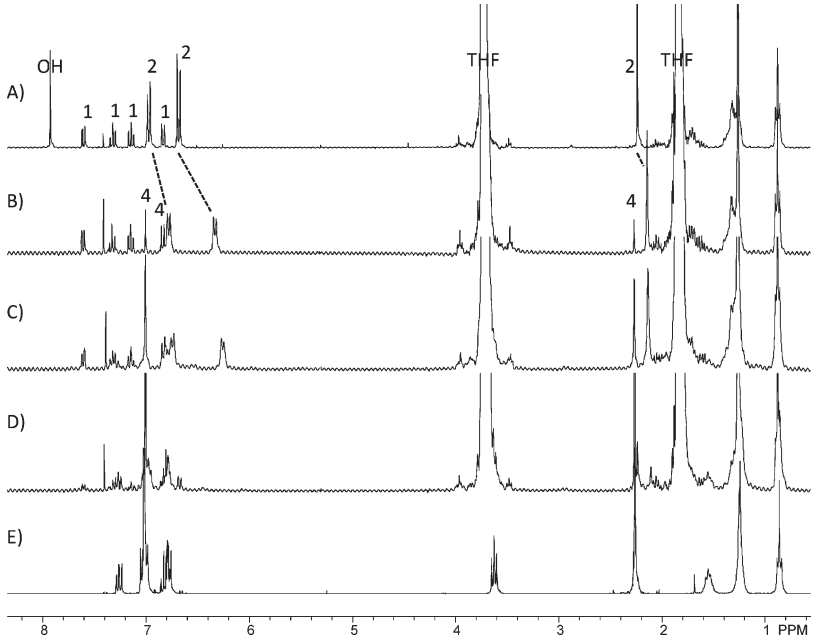
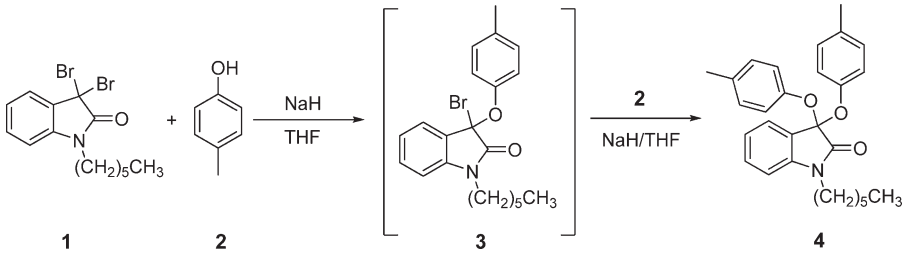


Figure 1. ^{1}H NMR spectra of products obtained by the model reaction between 3,3-dibromo-1-hexylindolin-2-one (1.07 mmol) and 4-methylphenol (1.60 mmol) in the presence of NaH (0.048 g) in $CDCl_3$: (A) absence of base (t = 0), (B) t = 35, (C) t = 95, (D) t = 200 min, (E) disubstituted product **4**.

Scheme 2. Model Reaction between 3,3-Dibromo-1-hexylindolin-2-one and 4-Methylphenol



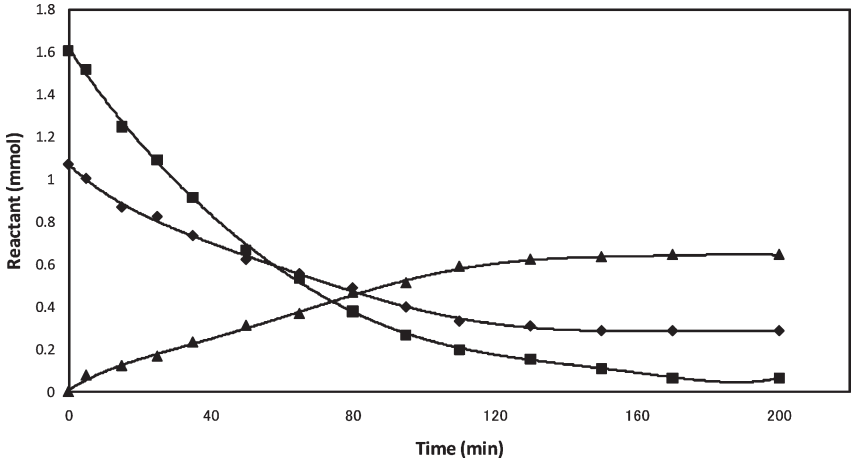


Figure 2. Relationship between amounts of reactants, that is, **1** (◆) and **2** (■), and the product **4** (▲) with the reaction time in the model reaction between 3,3-dibromo-1-hexylindolin-2-one (1.07 mmol) and 4-methylphenol (1.60 mmol) in the presence of NaH (0.048 g).

proceeded via an intermediate, which was expected to react with other nucleophiles immediately. To follow the progress of this reaction, a model reaction between **1** and 4-methylphenol (**2**) was studied in tetrahydrofuran in the presence of sodium hydride at room temperature (Scheme 2).

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

The ^{1}H NMR spectra (Figure 1) show the formation of the expected ketal compound with characteristic signals at 2.26 and 7.02 ppm, corresponding to methyl and aromatic protons, respectively; unconverted **1** should also be noted. No peaks were observed corresponding to intermediate (**3**) or other side-reaction products, suggesting that the condensation of **1** and **2** proceeds via intermediate **3**, whose reactivity is much higher than that of

geminal dibromide compound **1**. Moreover, when compared to the ^{1}H NMR spectra before and after the addition of NaH, the signals of 4-methylphenol were shifted to a higher field, indicating that sodium 4-methylphenolate was generated in the reaction medium.

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

The concentration curve of the starting material decreases, and that of the product increases in a time range from 0 to 3 h, after which they reach a plateau. These results show a complementary relationship, also indicating the absence of side reactions during this substitution. Consequently, the reaction rate constant of the second step, i.e., the reaction rate of monobromide ether **3** with sodium 4-methylphenol, is considerably higher than that of the first step.

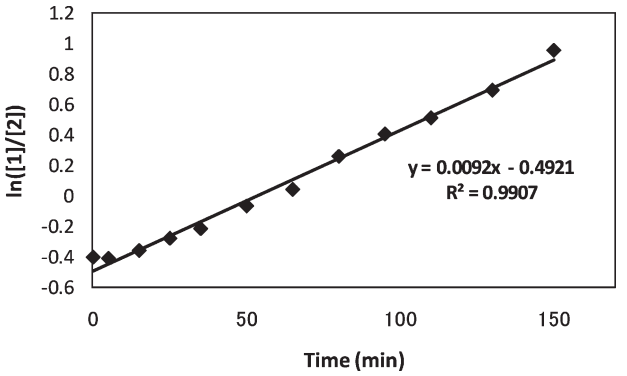


Figure 3. Second-order kinetic plots for the condensation of **1** and **2** in the model reaction between 3,3-dibromo-1-hexylindolin-2-one (1.07 mmol) and 4-methylphenol (1.60 mmol) in the presence of NaH (0.048 g).

In order to consider the reaction mechanism of the model reaction in more detail, the kinetic measurement was studied. We derived a kinetic equation,[9−11] which was based on

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

The linear relationship between ln ([**1**]/[**2**]) and the reaction time was observed in Figure 3; the overall reaction rate (k) and the correlation coefficient were estimated to be 0.2717 L mol^{-1} min^{-1} and 0.9907, respectively. These results indicate that the first reaction, i.e., the reaction between **1** and **2**, is the rate-determining step.

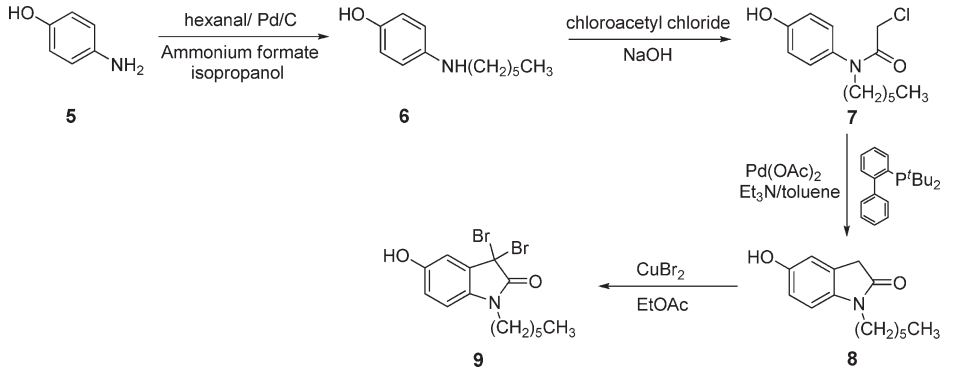
According to the results of all experiments described above, all requirements were satisfied. The reactive monobromide ether intermediate, whose reactivity was higher than the dibromide starting material, was generated after the first nucleophilic substitution occurred; then it was readily attacked again by other nucleophiles to form the stable ketal compound. To synthesize a 100% hyperbranched polymer, we designed a new structure of an AB_2 monomer containing geminal dibromide and hydroxyl groups as B_2 and A functionalities, respectively. The synthetic

Table 1. Molecular Weight of Hyperbranched Polymers 10[a]

run	NMP (mL)	time (h)	temp (°C)	M_n[b]	M_w/M_n[b]	yield (%)
1	1	3	RT	4200	2.7	72
2	1	6	RT	9700	2.7	75
3	1	15	RT	19000	3.2	78
4	1	18	RT	22000	2.9	77
5	0.5	18	RT	29000	2.6	76
6	0.5	10	40	insoluble		82

[a] Polymerization was carried out with 0.05 g (0.13 mmol) of **9**. [b] Estimated by GPC and eluted with DMF using the polystyrene standard.

Scheme 3. Monomer Synthesis



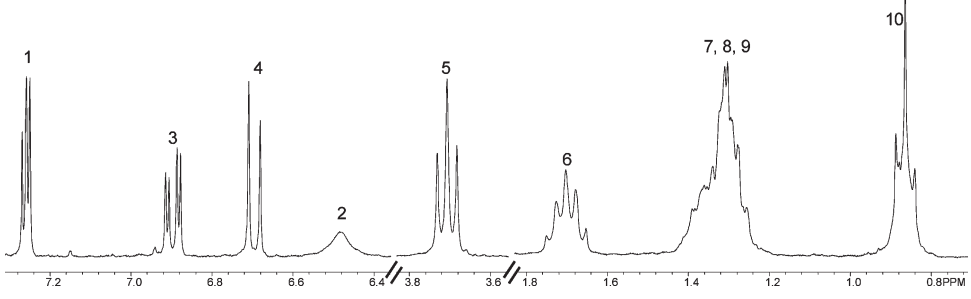


Figure 4. ^{1}H NMR spectrum of AB_2 monomer in $CDCl_3$.

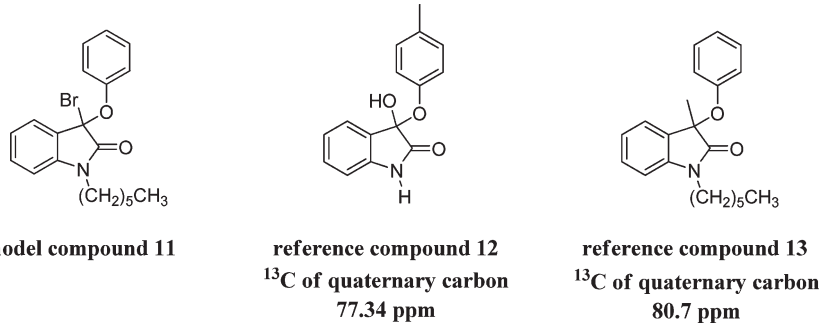
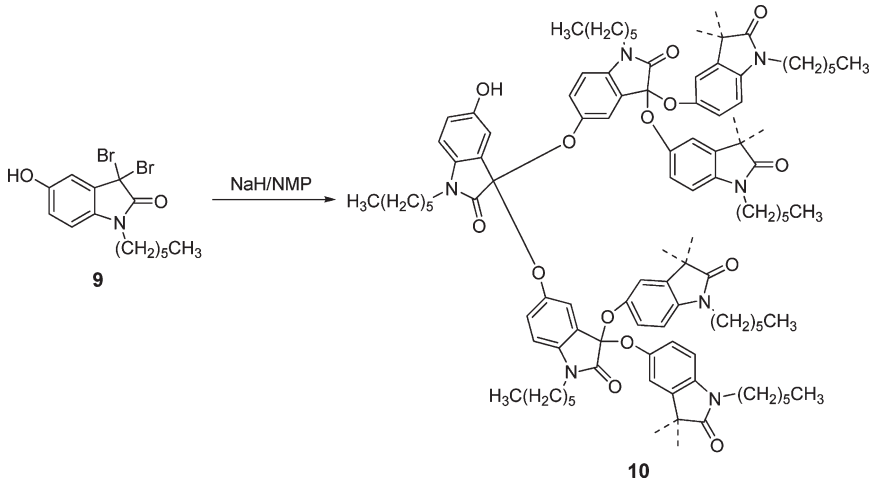


Figure 5. Model and reference compounds.

Scheme 4. 100% Hyperbranched Polymer Synthesis



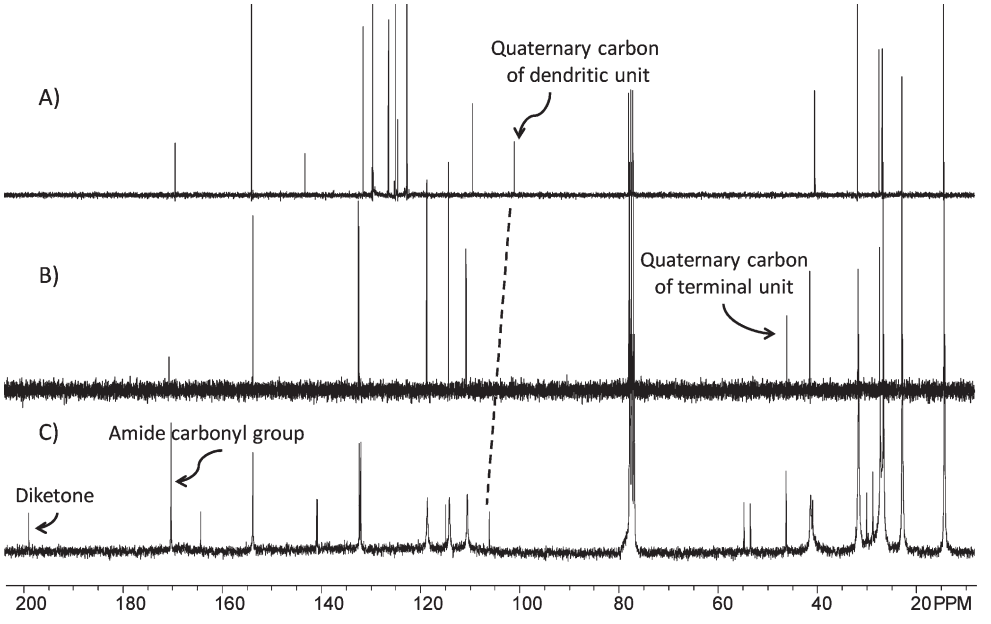
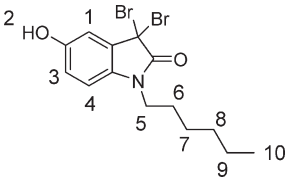


Figure 6. ^{13}C NMR spectra of (A) 1-hexyl-3,3-diphenoxyindolin-2-one, (B) AB_2 monomer, and (C) polymer **10** in $CDCl_3$.

procedure toward the AB_2 monomer is outlined in Scheme 3. First, the reductive mono-N-alkylation of 4-aminophenol with hexanal was carried out by using Pd/C as a catalyst. Acylation of compound **6** with chloroacetyl chloride was performed chemoselectively at aniline nitrogen in the presence of sodium hydroxide to give amide product **7**. Cyclization of compound **7** by way of an intramolecular Friedel−Crafts procedure using a palladium catalyst occurred regioselectivity to yield **8**. The desired AB_2 monomer was prepared by refluxing compound **8** with $CuBr_2$ in ethyl acetate.

The structure of the AB_2 monomer was characterized by FT-IR, NMR spectroscopy, and elemental analysis. The characteristic signals appeared at 3282.2, 1697.0, and 1600.6 cm^{-1} in the FT-IR spectrum, corresponding to hydroxyl, carbonyl group,

and aromatic C=C stretchings, respectively. The ^{1}H NMR spectrum of the monomer was fully assigned, as shown in Figure 4.



Then, the inorganic base NaH (1.2 equiv) was applied for the self-nucleophilic substitution polymerization of **9** (Scheme 4). The results are summarized in Table 1. When the concentration of the monomer was increased or the polymerization time was prolonged, the molecular weight of the polymers increased. However, polymerization at high temperature produced an insoluble polymer. The polymer was isolated by pouring the polymer solution into water, and then a low-molecular-weight residue was successfully removed by washing with diethyl ether. The resulting polymer was soluble in dichloromethane, THF, DMSO, DMF, and NMP at room temperature. The highest molecular weight of the hyperbranched polymer was obtained at a monomer concentration 100 mg/mL of NMP at room temperature for 15 h. The molecular weight and polydispersity index are 2.9×10^4 g/mol and 2.6, respectively. The thermal stability of polymer **10** was measured by TGA. Polymer **10** exhibited low 10% weight loss temperature ($T_{10\%}$) at 218 °C under a nitrogen atmosphere because of geminal dibromide terminal groups.

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 polymer structure, 1-hexyl-3,3-diphenoxyindolin-2-one, whose quaternary carbon signal appeared at 100.6 ppm, was used as the model compound of D. We attempted to synthesize a model compound, **11**, which can be represented as a linear unit; however, this compound was unstable under laboratory conditions. Thus, a structure similar to that of **11** was used as a reference for the signal of the quaternary carbon of the linear unit[16] (Figure 5).

The structure of polymer **10** was confirmed by FT-IR and NMR spectroscopy. In the FT-IR spectrum, characteristic absorption of the carbonyl groups and carbon−oxygen ether bonds was observed at 1716 and 1110 cm^{-1}, respectively. Unfortunately, no separate characteristic proton signals of the terminal and dendritic units were observed when the ^{1}H NMR spectra of the AB_2 monomer and polymer were compared with each other. Then, the structure of polymer **10** was investigated by ^{13}C NMR spectroscopy, and the spectra are shown in Figure 6. There are three characteristic peaks at 170.0, 105.9, and 45.8 ppm, which can be assigned to be the carbonyl carbon of the amide group, the quaternary carbon of the dendritic unit, and the quaternary carbon of the terminal unit, respectively. The extra signal of the carbonyl group appeared at 198.8 ppm because some of the geminal dibromide terminal groups were hydrolyzed to be diketone functional groups by precipitating in water. On the other hand, the signal corresponding to the quaternary carbon of the linear unit could not be found in the range of 60.0−100.0 ppm in the spectrum of polymer **10**.

The ^{13}C NMR spectrum and kinetic model reaction studies were consistent with our hypothesis that a 100% hyperbranched polymer with no trace of linear units can be prepared based on nucleophilic substitution of geminal dibromide by the hydroxy group.

Conclusions

We demonstrated the first example of base-catalyzed synthesis of a hyperbranched polymer with 100% branching based on an indolin-2-one core. This polymerization relied on the nucleophilic substitution reaction of geminal dibromide and a hydroxyl group, and it was found that only disubstituted products were isolated without the formation of a monosubstitued one. We assume that the reaction proceeds via a reactive monobromide ether species, whose reactivity is higher than that of dibromide. Furthermore, the results from kinetic studies of the model reaction indicated that the first substitution is the rate-determining step. On the basis of these findings, a 100% hyperbranched polymer was successfully prepared in a one-step synthesis under a base condition.

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