One-Pot Synthesis of Dendritic Polyamide. 2. Dendritic Polyamide from 5-[3-(4-Aminophenyl)propionylamino]isophthalic Acid Hydrochloride

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ABSTRACT: Dendritic polyamides having a high degree of branching and a narrow polydispersity were synthesized by a "one-pot" procedure which consists of successive activation of carboxyl groups followed by condensation with an aminodicarboxylic acid, as the AB_2 monomer. 5-[3-(4-Aminophenyl)propionylamino]isophthalic acid hydrochloride (**4**) was used, as the AB_2 monomer, without a protecting group. The carboxyl group of trimesic acid (**8**) was activated with an equimolar condensing agent diphenyl (2,3-dihydro-2-thioxo-3-benzoxazolyl)phosphonate (DBOP) to produce the corresponding active amides 1,3,5-benzenetris(3-carbonylbenzoxazoline-2-thione). Then, 3 equiv of **4** was added to **8** and condensed. The dendritic polyamides were synthesized divergently by repeating these activations and condensations. The terminal carboxyl groups were end-capped by diethylamine and the products were isolated. Dendritic polyamides obtained were characterized by IR and NMR spectroscopies and GPC. Number-average molecular weights (M_n) of dendritic polyamides estimated by the end group analysis were in good agreement with the calculated values. The degrees of branching and the polydispersities M_w/M_n were 0.8−0.9 and 1.2−1.5, respectively.

Introduction

Dendrimers are well-defined, highly branched, three-dimensional compounds with a large number of reactive end groups. Therefore, they are receiving interest as new polymeric materials, whose properties should differ significantly from those of conventional polymers.[1]

There are two general approaches to dendrimer synthesis, namely the divergent[2] and convergent[3] methods. Both involve a series of stepwise protection/deprotection reactions and extensive purification steps. This makes dendrimers expensive and difficult to produce on a large scale.

Development of precise and rapid synthetic methods for dendrimers are one of the significant aspects of current work in this field. Several authors have published papers on rapid synthetic approaches of the dendrimers. Fréchet et al.[4] prepared regular dendritic poly(ether urethane)s through the growth of two generations in a single synthetic operation. They also reported the rapid synthesis of dendrimers using a AB_4 monomer.[5] On the other hand, orthogonal synthesis of the dendrimers was reported by Zimmerman et al.[6] Two different building blocks in two orthogonal coupling reactions are used sequentially, wherein each synthetic step adds a generation to the existing dendrimer. In this process, the protection or activation steps are eliminated. Yu et al.[7] reported a similar orthogonal synthesis of poly(phenylenevinylene) dendrimers.

In contrast, hyperbranched polymers[8] are generally prepared via a one-step polymerization method, where multifunctional AB_n ($n \geq 2$) monomers are allowed to react together in an uncontrolled manner, forming nonideally grown dendritic structures. This leads to an extremely broad molecular weight distribution and a low degree of branching (DB) around 0.5. As they can be easily prepared, a wide variety of hyperbranched polymers have been reported in the literature such as polyesters,[9] polyethers,[10] polyphenylenes,[11] poly(ether ketone)s,[12] and polyamides.[13] However, hyperbranched polymers cannot be expected to possess ultimate properties with respect to solubility, solution and melt viscosity, and accessibility of terminal groups based on a precise structure.

Several studies related to control of AB_2 polymerization have been reported. For example, a pseudo-one-step procedure,[14] utilization of specific AB_2 monomers[15] and slow monomer addition method.[16]

We are interest in a simple synthetic method of the dendritic polymers by a "one-pot" procedure. The one-pot procedure consists of an alternating activation of carboxyl groups and a condensation with an AB_2 monomer. Reactions characterized by 100% conversion are essential for producing perfect dendrimers. The condensing agent diphenyl (2,3-dihydro-2-thioxo-3-benzoxazolyl)phosphonate[17] (DBOP) used for chemoselective polyamidation[18] and synthesis of ordered polyamides[19] was applied to this procedure, where the carboxyl group is converted to the activated amide by treatment with an equivalent amount of DBOP. The active amide then reacts with an equivalent amount of aminodicarboxylic acid as an AB_2 monomer. Several research groups used

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5-aminoisophthalic acid (**2**) as the AB_2 monomer for synthesis of dendrimers[20] and hyperbranched polymers.[13,21] In previous work,[22] we also used **2**; however, the nucleophilicity of amino group of **2** is very low due to the existence of two electron-withdrawing carboxyl groups. Furthermore, the yield of the second-generation dendrimer was very low due to the steric hindrance. So 4-aminophenylpropionic acid was used as a spacer unit between the each generation, and dendritic polyamides were synthesized by alternative condensation of **2** and 4-aminophenylpropionic acid.

To eliminate these problems, a new AB_2 monomer, 5-[3-(4-aminophenyl)propionylamino]isophthalic acid hydrochloride (**4**) was designed and used instead of **2**. In this article, we describe the successful synthesis of novel dendritic polyamides by a one-pot procedure using **4**, as an AB_2 monomer.

Experimental Section

General Methods. IR spectra were recorded on a Perkin-Elmer FT-IR spectrometer PARAGON 1000. ^{1}H and ^{13}C NMR spectra were recorded in DMSO-d_6 on a JEOL JNM-LA600. GPC was performed using TOSOH 8020 HPLC apparatus (column, TSKgel αMx2; standard, polystyrene; solvent, DMF containing 0.4 wt % LiCl; *T*, 60 °C). Thermal analyses were performed on a MAC Science DSC 3200S at a heating rate of 10 K min^{-1} and Yamato Melting Point apparatus MP-21.

N-Methyl-2-pyrrolidinone (NMP) was distilled under reduced pressure and then stored over 4-Å molecular sieves. Triethylamine (TEA) was purified by the usual method.[23] The condensing agent diphenyl (2,3-dihydro-2-thioxo-3-benzoxazolyl)phosphonate (DBOP) was prepared according to the reported procedure.[24] The other reagents were obtained commercially and used as received.

5-[(4-Nitrocinnamoyl)amino]isophthalic Acid (3). A solution of compound **2** (9.06 g, 50 mmol) and TEA (5.06 g, 50 mmol) in NMP (45 mL) was cooled in an ice bath. To this solution was added dropwise a solution of 4-nitrocinnamoyl chloride (**1**) (10.58 g, 50 mmol) in NMP (50 mL). The mixture was stirred at room temperature for 6 h, and then poured into water (1 L). The precipitate was collected by filtration, washed with acetone, and dried to afford a pale yellow powder. The yield was 14.7 g (83%). Melting point: 307−308 °C. IR (KBr): 3380 (N−H), 3108, 1700 (C═O), 1630 (C═O), 1602, 1565, 1518, 1344, 1185. ^{1}H NMR (DMSO-d_6): δ 6.98 (d, 1H, J = 15.7 Hz, CH), 7.70 (d, 1H, J = 15.7 Hz, CH), 7.88 (d, 2H, J = 8.4 Hz, ArH), 8.18 (s, 1H, ArH), 8.26 (d, 2H, J = 8.4 Hz, ArH), 8.52 (s, 2H, ArH), 10.77 (s, 1H, NH). ^{13}C NMR (DMSO-d_6): δ 123.7, 124.0, 125.1, 126.1, 128.7, 132.0, 138.2, 139.7, 141.1, 147.6, 163.2 (CONH), 166.7 (COOH). Anal. Calcd for $C_{17}H_{12}N_2O_7$: C, 57.31; H, 3.39; N, 7.86. Found: C, 57.19; H, 3.71; N, 7.93.

5-[3-(4-Aminophenyl)propionylamino]isophthalic Acid Hydrochloride (4). The mixture of **3** (2.4 g, 6.75 mmol), 5% palladium/carbon (1.4 g), and 36% hydrochloric acid (2.4 mL) in *N*,*N*-dimethylformamide (DMF) (24 mL) and ethanol (48 mL) was vigorously stirred at room temperature under an atmosphere of hydrogen overnight. The catalyst was filtered off, and the solvent was distilled under reduced pressure. The target monomer was obtained by addition of water to the residue. Recrystallization from ethanol and water yielded a pale green powder. The yield was 1.58 g (71%). Melting point: 269−270 °C. IR (KBr): 3425 (N−H), 3021, 2553, 1709 (C═O), 1688 (C═O), 1567, 1509, 1463, 1284, 1233, 1182. ^{1}H NMR (DMSO-d_6): δ 2.71 (t, 2H, J = 7.7 Hz, CH_2), 2.90 (t, 2H, J = 7.7 Hz, CH_2), 7.30 (d, 2H, J = 8.0 Hz, ArH), 7.39 (d, 2H, J = 8.0 Hz, ArH), 8.15 (s, 1H, ArH) 8.45 (s, 2H, ArH), 10.51 (s, 1H, NH). ^{13}C NMR (DMSO-d_6): δ 30.1 (CH_2), 37.7 (CH_2), 123.1, 123.5, 124.5, 128.7, 129.6, 129.9, 131.7, 139.9, 141.0, 166.5 (COOH), 170.9 (CONH). Anal. Calcd for $C_{17}H_{17}N_2O_5Cl$: C, 55.97; H, 4.70; N, 7.68. Found: C, 55.59; H, 4.79; N, 7.52.

General Procedure for the One-Pot Synthesis of Dendritic Polyamide. To a solution of trimesic acid (**8**) in NMP was added TEA (3 equiv) and DBOP (3.09 equiv). The activation of the carboxyl groups was carried out at room temperature for 30 min. Then, **4** (3 equiv) was added to the solution, and the condensation was performed at room temperature for 30 min. These activations and condensations were repeated alternately for 1−5 times. Finally, the terminal carboxyl groups were end-capped with an excess amount of diethylamine and DBOP. The reaction mixture was poured into a 1 wt % aqueous $NaHCO_3$ solution, and the precipitate was collected by filtration. The product was washed with methanol and dried in vacuo.

One-Pot Synthesis of a Third-Generation Dendritic Polyamide. DBOP (47.3 mg, 0.124 mmol) was added to a solution of **8** (8.41 mg, 0.04 mmol) and TEA (33.5 μL, 0.24 mmol) in NMP (0.48 mL). After this solution was stirred at 25 °C for 30 min, **4** (43.7 mg, 0.12 mmol) was added, and the solution was stirred for 30 min. NMP (0.48 mL), TEA (66.9 μL, 0.48 mmol), and DBOP (94.7 mg, 0.247 mmol) were then added, and the solution was stirred for 30 min whereupon, **4** (87.5 mg, 0.24 mmol) was added. After this solution was stirred for 30 min, NMP (0.96 mL), TEA (134 μL, 0.96 mmol), and DBOP (189.4 mg, 0.494 mmol) were added and stirred for 30 min, followed by adding **4** (174.9 mg, 0.48 mmol). The solution was stirred for 30 min. Finally, NMP (1.92 mL), TEA (134 μL, 0.96 mmol), DBOP (404.4 mg, 1.056 mmol), and diethylamine (199 μL, 1.92 mmol) were added. After 1 h, the reaction mixture was poured into a 1 wt % aqueous $NaHCO_3$ solution. The precipitate was filtered, washed with water and methanol, and dried in vacuo. Yield 100%. IR (KBr): 3282 (N−H), 1654 (C═O), 1597, 1516, 1440, 1411, 1317, 1278. ^{1}H NMR (DMSO-d_6): δ 1.08 (CH_3), 2.65, 2.92 (CH_2), 6.91, 7.25, 7.62, 7.68, 7.92, 8.08, 8.10, 8.15, 8.30, 8.67 (ArH) 10.18, 10.29, 10.37, 10.55 (NH). ^{13}C NMR (DMSO-d_6): δ 12.7 (CH_3), 13.9 (CH_3), 30.1 (CH_2), 30.6 (CH_2), 38.0 (CH_2), 38.7 (CH_2), 42.8 (CH_2), 116.6, 118.0, 120.3, 121.0, 128.3, 128.7, 135.9, 136.4, 137.0, 137.9, 139.1, 164.9 (CONH), 168.9 (CON), 170.8 (CONH). Anal. Calcd for $C_{462}H_{516}N_{66}O_{66}$: C, 68.94; H, 6.46; N, 11.48. Found: C, 69.01; H, 6.27; N, 11.31.

Second-Generation Dendritic Polyamide. Yield 99%. IR (KBr): 3289 (N−H), 1654 (C═O), 1597, 1516, 1440, 1411, 1317, 1278. ^{1}H NMR (DMSO-d_6): δ 1.09 (CH_3), 2.65, 2.91 (CH_2), 6.92, 7.25, 7.62, 7.68, 7.93, 8.07, 8.09, 8.15, 8.30, 8.67 (ArH) 10.18, 10.28, 10.37, 10.54 (NH). ^{13}C NMR (DMSO-d_6): δ 12.7 (CH_3), 13.9 (CH_3), 30.1 (CH_2), 30.6 (CH_2), 38.0 (CH_2), 38.7 (CH_2), 42.8 (CH_2), 116.6, 118.0, 120.3, 121.0, 128.4, 128.7, 135.9, 136.3, 137.0, 137.9, 139.1, 164.9 (CONH), 168.9 (CON), 170.8 (CONH). Anal. Calcd for $C_{210}H_{240}N_{30}O_{30}$: C, 68.83; H, 6.60; N, 11.47. Found: C, 68.85; H, 6.45; N, 11.22.

Fourth-Generation Dendritic Polyamide. Yield 93%. IR (KBr): 3276 (N−H), 1654 (C═O), 1596, 1515, 1438, 1411, 1317, 1278. ^{1}H NMR (DMSO-d_6): δ 1.09 (CH_3), 2.65, 2.91 (CH_2), 6.92, 7.25, 7.62, 7.68, 7.92, 8.08, 8.10, 8.15, 8.30, 8.68 (ArH) 10.18, 10.28, 10.40, 10.54 (NH). ^{13}C NMR (DMSO-d_6): δ 12.8 (CH_3), 14.0 (CH_3), 30.2 (CH_2), 38.1 (CH_2), 38.8 (CH_2), 42.9 (CH_2), 116.7, 118.1, 120.4, 121.1, 128.5, 136.0, 136.5, 137.0, 138.0, 139.2, 165.0 (CONH), 169.0 (CON), 170.9 (CONH). Anal. Calcd for $C_{966}H_{1068}N_{138}O_{138}$: C, 68.98; H, 6.40; N, 11.49. Found: C, 68.85; H, 6.22; N, 11.45.

Fifth-Generation Dendritic Polyamide. Yield 94%. IR (KBr): 3279 (N−H), 1654 (C═O), 1596, 1516, 1438, 1411, 1316. ^{1}H NMR (DMSO-d_6): δ 1.09 (CH_3), 2.65, 2.91 (CH_2), 6.92, 7.25, 7.63, 7.68, 7.92, 8.08, 8.10, 8.15, 8.30, 8.69 (ArH) 10.18, 10.29, 10.36, 10.55 (NH). ^{13}C NMR (DMSO-d_6): δ 12.8 (CH_3), 14.0 (CH_3), 30.2 (CH_2), 38.1 (CH_2), 38.8 (CH_2), 42.9 (CH_2), 116.7, 118.1, 120.4, 121.0, 128.5, 136.0, 136.5, 137.0, 138.0, 139.2, 165.0 (CONH), 169.0 (CON), 170.9 (CONH). Anal. Calcd for $C_{1974}H_{2172}N_{282}O_{282}$: C, 69.00; H, 6.37; N, 11.50. Found: C, 68.84; H, 6.22; N, 11.44.

5-[(3-Phenylpropionyl)amino]isophthalic Acid (9). A solution of **2** (9.96 g, 55 mmol) and TEA (5.57 g, 55 mmol) in NMP (50 mL) was cooled with an ice bath. To this solution was added dropwise a solution of phenylpropionyl chloride (9.27 g, 55 mmol) in NMP (50 mL). The reaction mixture was

stirred at 25 °C for 12 h. Compound **9** was isolated as a white powder by the same procedure as that used for the synthesis of **3**. Yield: 16.1 g (94%). Melting point: 278−279 °C. IR (KBr): 3285 (N−H), 1694 (C═O), 1667 (C═O), 1604, 1544, 1453, 1408, 1282. ^{1}H NMR (DMSO-d_6): δ 2.69 (t, 2H, J = 7.8 Hz, CH_2), 2.94 (t, 2H, J = 7.8 Hz, CH_2), 7.18−7.30 (5H, ArH), 8.15 (s, 1H, ArH), 8.44 (s, 2H, ArH), 10.31 (s, 1H, NH). ^{13}C NMR (DMSO-d_6): δ 30.6 (CH_2), 37.9 (CH_2), 123.3, 124.3, 125.9, 128.2, 128.3, 131.6, 139.7, 140.9, 166.4 (COOH), 170.8 (CONH). Anal. Calcd for $C_{17}H_{15}NO_5$: C, 65.17; H, 4.83; N, 4.47. Found: C, 64.76; H, 5.06; N, 4.95.

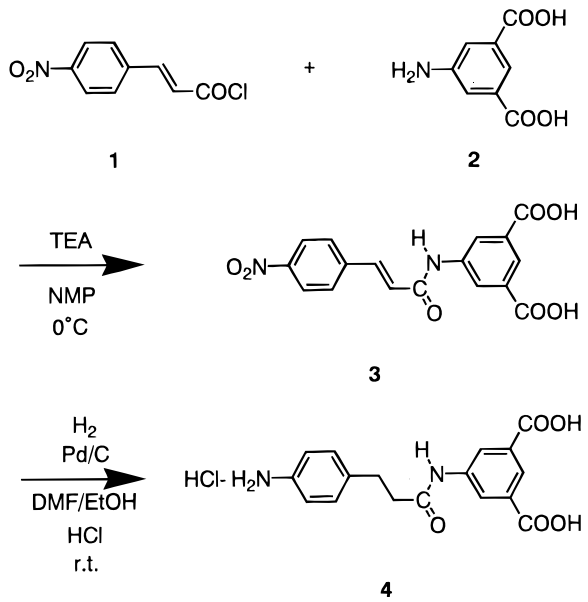
Dimethyl 5-[(4-Nitrocinnamoyl)amino]isophthalate (10). This compound was prepared from dimethyl 5-aminoisophthalate and **1** in the manner described above and yielded as a pale yellow powder. Yield: 6.67 g (72%). Melting point: 295−296 °C. IR (KBr): 3356 (N−H), 1721 (C═O), 1688 (C═O), 1545, 1515, 1444, 1342, 1257, 1167. ^{1}H NMR (DMSO-d_6): δ 3.89 (s, 6H, CH_3), 6.97 (d, 1H, CH), 7.74 (d, 1H, CH), 7.91 (d, 2H, ArH), 8.20 (s, 1H, ArH), 8.30 (d, 2H, ArH), 8.60 (s, 2H, ArH). Anal. Calcd for $C_{19}H_{16}N_2O_7$: C, 59.38; H, 4.20; N, 7.29. Found: C, 59.27; H, 4.41; N, 7.57.

Dimethyl 5-[(4-Aminophenylpropionyl)amino]isophthalate Hydrochloride (11). The mixture of **10** (5.00 g 13 mmol), 5% palladium/carbon (2.77 g), 36% hydrochloric acid (5.0 mL), DMF (50 mL), and ethanol (100 mL) was vigorously stirred under hydrogen atmosphere for 12 h. The catalyst was filtered, and the solvent was distilled in vacuo. Compound **11** was obtained as a white powder by addition of water to the residue. Yield: 2.34 g (50%). Melting point: 228−230 °C. IR (KBr): 3266 (N−H), 2882, 1725(C═O), 1663 (C═O), 1606, 1556, 1514, 1342, 1255. ^{1}H NMR (DMSO-d_6): δ 2.71 (t, 2H, J = 7.5 Hz, CH_2), 2.96 (t, 2H, J = 7.5 Hz, CH_2), 3.89 (s, 6H, CH_3), 7.31 (d, 2H, J = 7.5 Hz, ArH), 7.38 (d, 2H, J = 7.5 Hz, ArH), 8.13 (s, 1H, ArH), 8.50 (s, 2H, ArH). ^{13}C NMR (DMSO-d_6): δ 29.9 (CH_2), 37. 6 (CH_2), 52.4 (CH_3), 122.9, 123.3, 123.8, 129.4, 129.9, 130.5, 140.0, 140.8, 165.2 ($COOCH_3$), 170.8 (COOH). Anal. Calcd for $C_{19}H_{21}N_2O_5Cl$: C, 58.09; H, 5.39; N, 7.13. Found: C, 58.26; H, 5.33; N, 6.99.

Preparation of Dendritic Model: 5-(3-Phenylpropionylamino)-*N*′,*N*′-bis[4-[*N*-[(3,5-di(methoxycarbonyl)phenyl]propanamido]phenyl]isophthalamide (12). TEA (279 μL, 2 mmol) and DBOP (421 mg, 1.1 mmol) were added to the solution of **9** (157 mg, 0.5 mmol) and **11** (393 mg, 1 mmol) in NMP (4 mL). The mixture was stirred at 25 °C for 2 h and poured into a 1 wt % aqueous $NaHCO_3$ solution. The precipitate was filtered and dried in vacuo. Compound **12** was purified by reprecipitation with acetone and water to afford a white solid. Yield: 433 mg (84%). Melting point: 129−131 °C. IR (KBr): 3322 (N−H), 1727 (C═O), 1672 (C═O), 1598, 1532, 1515, 1441, 1344, 1253. ^{1}H NMR (DMSO-d_6): δ 2.67 (6H, CH_2), 2.93 (6H, CH_2), 3.90 (12H, CH_3), 7.2−7.4 (9H, ArH), 7.69 (4H, ArH), 8.15 (3H, ArH), 8.29 (2H, ArH), 8.49 (4H, ArH), 10.34 (1H, NH), 10.37 (2H, NH), 10.40 (2H, NH).^{13}C NMR (DMSO-d_6): δ 30.1 (CH_2), 30.7 (CH_2), 37.9 (CH_2), 38.0 (CH_2), 52.5 (CH_3), 120.4, 120.9, 121.1, 123.4, 123.8, 126.0, 128.2, 128.3, 128.4, 130.6, 136.0, 136.4, 137.0, 139.5, 140.1, 141.0, 165.0 (CONH), 165.3 ($COOCH_3$), 170.9 (CONH), 171.0 (CONH). Anal. Calcd for $C_{55}H_{51}N_5O_{13}$: C, 66.73; H, 5.19; N, 7.07. Found: C, 66.38; H, 5.14; N, 7.09.

Preparation of Terminal Model: 5-(3-Phenylpropionylamino)-*N*′,*N*′,*N*″,*N*″-tetraethylisophthalamide (13). TEA (139 μL, 1 mmol) and DBOP (421 mg, 1.1 mmol) were added to the solution of **9** (157 mg, 0.5 mmol) and diethylamine (114 μL, 1.1 mmol) in NMP (4 mL). Compound **13** was isolated as a white powder by the same procedure as that used for the synthesis of **12**. Yield: 167 mg (79%). Melting point: 144−145 °C. IR (KBr): 3276 (N−H), 2979, 1632 (C═O), 1586, 1563, 1439. ^{1}H NMR (DMSO-d_6): δ 1.10 (12H, CH_3), 2.68 (2H, CH_2), 2.94 (2H, CH_2), 3.38 (8H, CH_2), 6.94 (1H, ArH), 7.2−7.4 (5H, ArH), 7.66 (2H, ArH), 10.21 (1H, NH). ^{13}C NMR (DMSO-d_6): δ 12.7 (CH_3), 13.9 (CH_3), 30.5 (CH_2), 37.9 (CH_2), 42.8 (CH_2), 116.6, 118.0, 125.9, 128.1, 128.2, 137.9, 139.1, 140.9, 168.9 (CON), 170.8 (CONH). Anal. Calcd for $C_{25}H_{33}N_3O_3$: C, 70.89; H, 7.85; N, 9.92. Found: C, 70.60; H, 7.80; N, 9.70.

Scheme 1



Result and Discussion

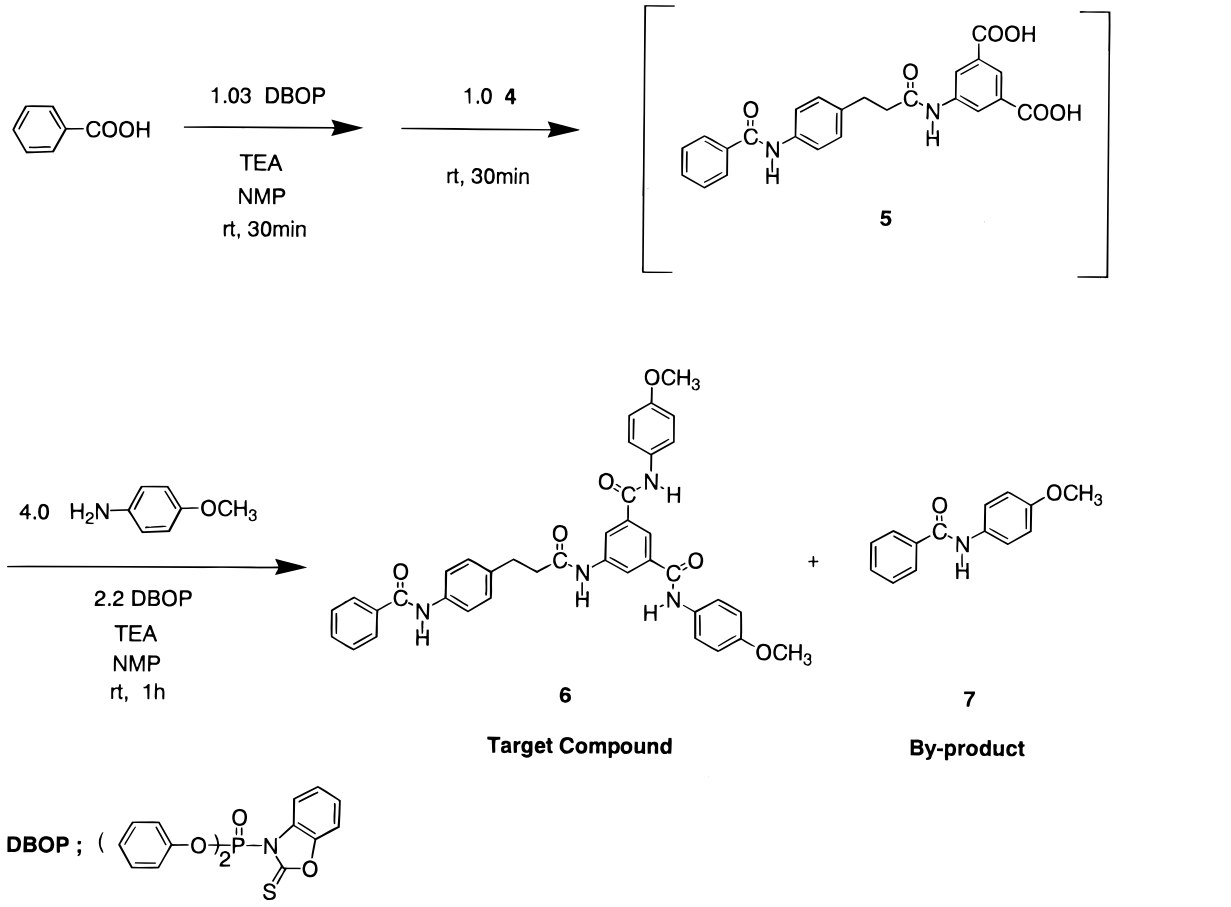
Monomer Synthesis. For a one-pot procedure, an aminodicarboxylic acid without protecting groups as an AB_2 monomer is required. From considerations of our previous results[22] and results presented by others,[13,20,21] we designed the new aminodicarboxylic acid, 5-[3-(4-aminophenyl)propionylamino]isophthalic acid hydrochloride (**4**) which might have both higher nucleophilicity and less steric congestion compared to 5-aminoisophthalic acid (**2**). The nucleophilicity of amino groups will be increased due to its isolation from carboxyl groups. The flexible methylene unit in its structure avoids potential steric congestion. Monomer **4** was easily prepared via a two-step reaction from commercially available 4-nitrocinnamoyl chloride (**1**) and **2** as shown in Scheme 1.

Condensation of **1** with **2** was carried out in NMP at 0 °C, giving 5-[(4-nitrocinnamoyl)amino]isophthalic acid (**3**) in excellent yield. Reduction of **3** with H_2 in the presence of palladium/carbon as a catalyst in DMF/ethanol and a hydrochloric acid solution then produced **4** in good yield. The structure of **4** was confirmed by elemental analysis and IR, ^{1}H, and ^{13}C NMR spectroscopies. Aliphatic aminodicarboxylic acids such as glutamic acid are insoluble in organic solvents; however, **4** was soluble in polar aprotic solvents, such as NMP, DMF, and DMSO.

Model Reaction. The model reaction, shown in Scheme 2, was carried out to confirm the reactivity of **4**. The reaction of benzoic acid and DBOP in the presence of TEA in NMP at 25 °C for 30 min produced an active amide, 3-benzoylbenzoxazoline-2-thione, which then reacted with **4** at 25 °C for 30 min to give amide **5**. Finally, two carboxyl groups of **5** were capped by excess amounts of *p*-anisidine in the presence of DBOP.

The reaction mixture was poured into a 1 wt % aqueous $NaHCO_3$ solution. The precipitate was characterized by IR and ^{1}H NMR spectroscopies. It was found that the precipitate was a mixture of **6** and **7**. The product ratio of the desired product **6** and the undesired byproduct **7** was estimated from the integrated intensities of amide protons at 10.21 and 10.14 ppm, and was 9:1. The reaction of 3-benzoylbenzoxazo-

Scheme 2



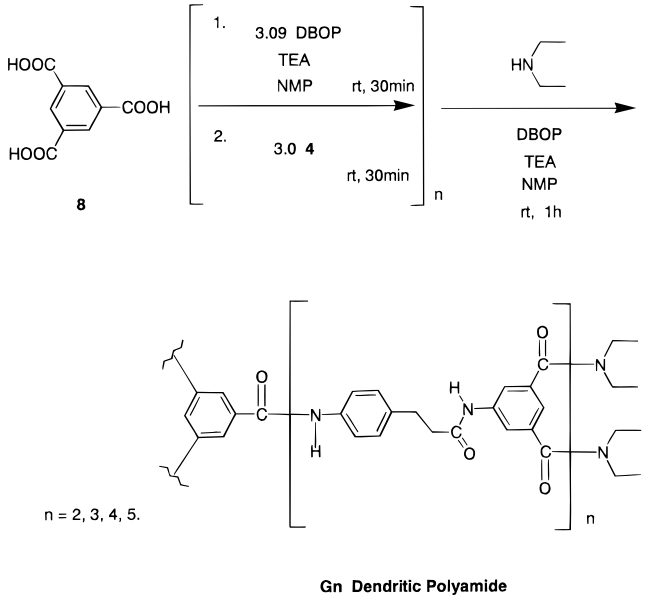
line-2-thione with **2** required 24 h for completion. Thus, the nucleophilicity of amino groups of **4** is found to be very high showing that it is suitable as the AB_2 monomer. On the other hand, the byproduct of the reaction was comparable to that of using **2**.

One-Pot Synthesis. Synthesis of dendritic polyamides was carried out in NMP at 25 °C. Trimesic acid (**8**) was used as a trifunctional core molecule (Scheme 3).

The carboxyl groups of **8** were activated by 3.09 equiv of DBOP for 30 min, followed by condensation with 3.0 equiv of **4** for 30 min in which 6 equiv of triethylamine were added to accept hydrogen chloride of **4**. This alternating activation and condensation was repeated 2−5 times for production of the second- through fifth-generation dendritic polyamides. Terminal carboxyl groups were end-capped with excess amounts of diethylamine and DBOP for the determination of the degree of branching (DB) by end group analysis. The concentration of carboxyl groups in the reaction was kept at 0.25 and 0.125 mol/L at the synthesis of second and third generations and fourth and fifth generations, respectively, by adding NMP at each step. All reactions proceeded homogeneously, and the products were precipitated with a 1 wt % aqueous $NaHCO_3$ solution. The precipitate was recovered by filtration, washed with methanol, and dried in a vacuum. Dendritic polyamides of each generation were obtained in essentially 100% yield. The desired structure of the second-generation dendrimer is shown in Scheme 4.

Characterization. Each dendritic polyamide was characterized by IR and NMR spectroscopies and GPC. The results are summarized in Table 1.

Scheme 3



The IR spectra of all dendritic polyamides showed characteristic absorptions attributable to N−H, amide I, and amide II bands in the range of 3200−3300, 1650−1660, and 1510−1520 cm^{-1}, respectively. No carbonyl signals due to the carboxyl group at 1700 cm^{-1} and the active amide at 1720 cm^{-1} were detected, thereby confirming that all terminal carboxyl groups were end-capped with diethylamine.

The dendritic polyamides obtained contain the dendritic, terminal, and linear units in their structures as

Scheme 4

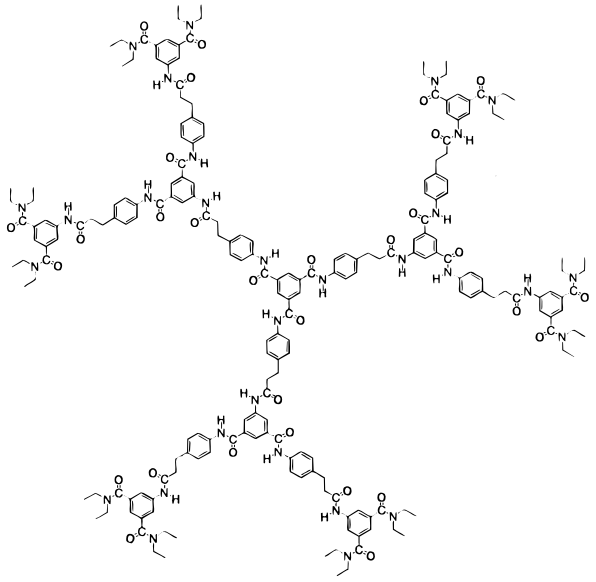


Table 1. One-Pot Synthesis of Dendritic Polyamide

generation	yield, %	M^a calcd	$M_n{}^b$	$M_w/M_n{}^c$	DB^b	DB′^{b}
2	99	3 660	4 040	1.29	0.81	0.71
3	100	8 040	11 900	1.34	0.84	0.81
4	93	16 800	17 800	1.40	0.87	0.86
5	94	34 320	30 400	1.55	0.89	0.88

[a] Calculated molecular weight. [b] Estimated by ^{1}H NMR spectroscopy. [c] Measured by GPC using DMF containing 0.4 wt % LiCl as eluents.

shown in Figure 1. The defect of branching is estimated by the degree of branching (DB), which is 0 for a linear polymer and 1 for a perfect dendrimer. The DB is defined as the following equation:[25]

$$\mathrm{DB} = \frac{(\text{the number of dendritic units} + \text{the number of terminal units})}{\text{the total number of units}}$$

The number of each unit can be estimated by the integrated intensity of the ^{1}H NMR signals of aromatic ring *2* (see Figure 1). ^{1}H NMR spectrum of the fourth-generation dendritic polyamide is shown in Figure 2a. The signals at 7.69 and 7.25 ppm are attributed to the protons of aromatic ring *1*. However, the chemical shifts of protons for aromatic ring *2* will vary according to the type of unit. Thus, to know the chemical shift of these protons for each type of unit, two model compounds **12** and **13** for dendritic and terminal units respectively, were prepared as shown in Scheme 5.

^{1}H NMR spectra of dendritic model compound **12** shown in Figure 2b displayed two peaks at 8.29 and 8.15 assignable to the protons d_2 and d_1 of aromatic ring *2*. While the corresponding protons t_2 and t_1 of terminal model compound **13** appeared at 7.66 and 6.94 ppm (Figure 2c). Assignment of corresponding signals in ^{1}H NMR of dendritic polyamide (Figure 2a) was done on the basis of these data. On using an aromatic or primary aliphatic amine as end-capping agent, these signals overlap each other making the estimation of DB impossible. Therefore, a secondary aliphatic amine was selected as the end-capping agent. The estimated DBs of each dendritic polyamide were in the range of 0.8−0.9.

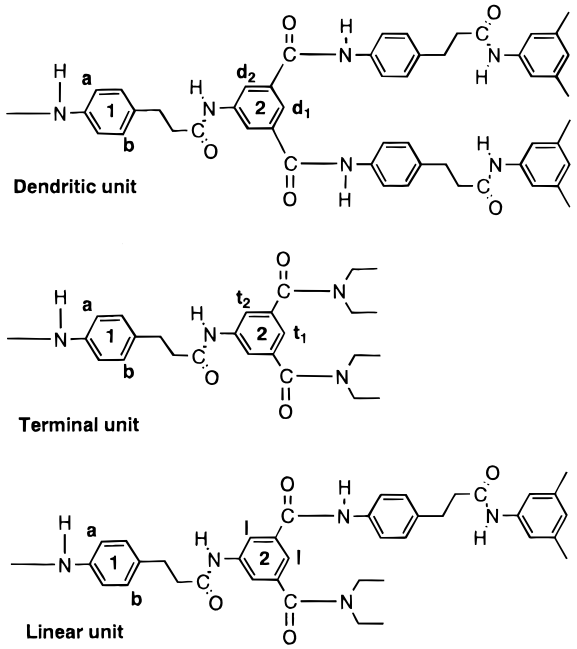


Figure 1. Structure of repeat unit in the dendritic polyamide.

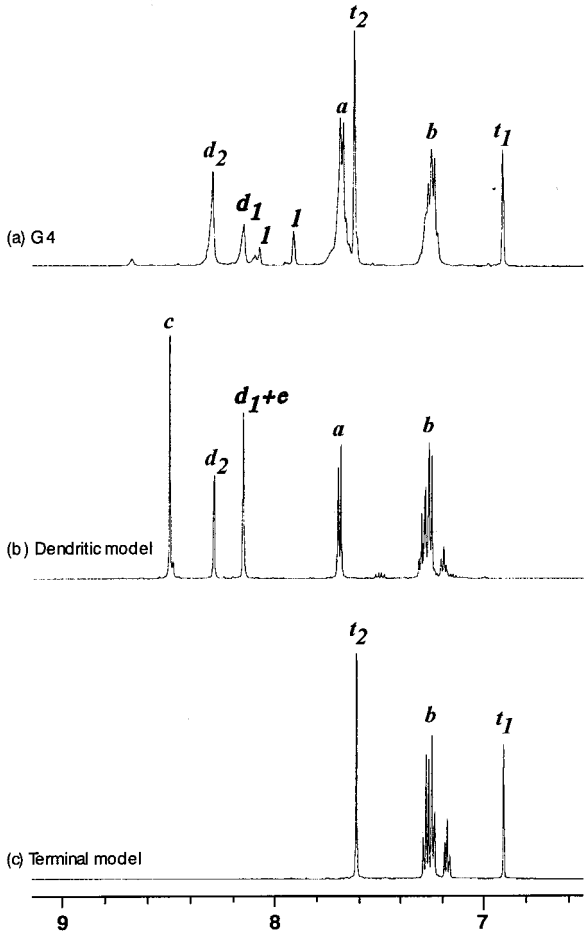
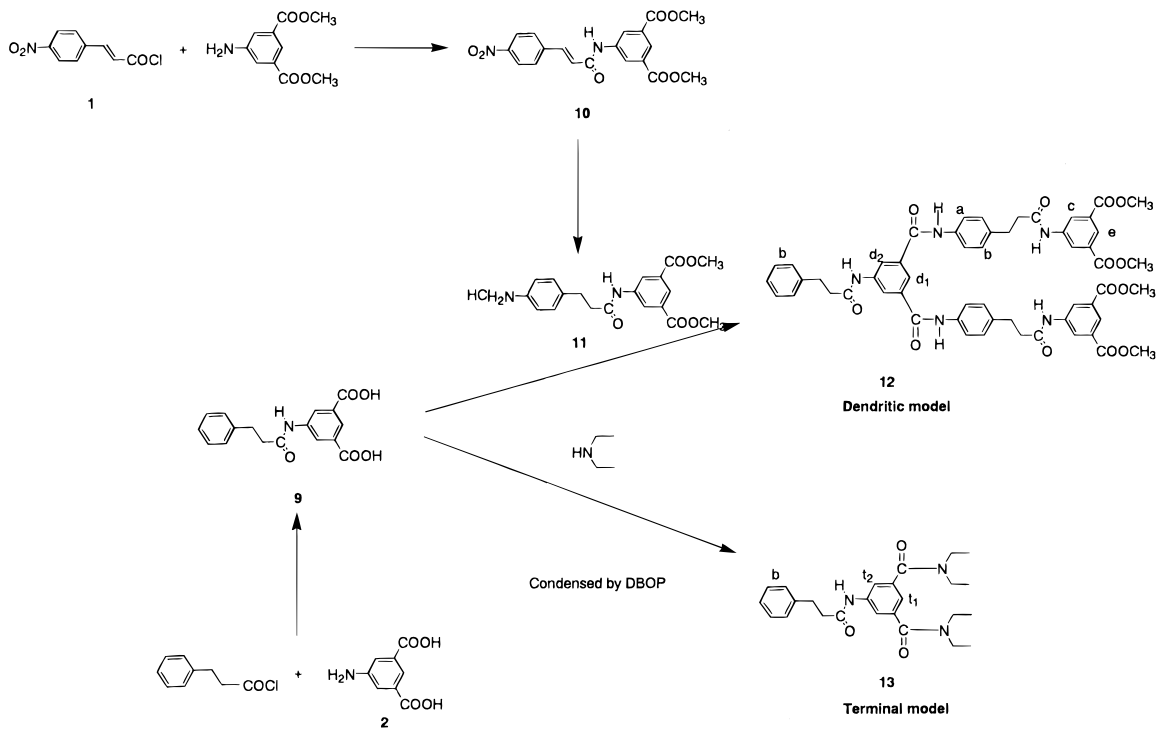


Figure 2. ^{1}H NMR spectra of fourth-generation dendritic polyamide (a) and model compounds **12** (b) and **13** (c).

The DB was found to increase with increase in the generation and reached to a maximum of 0.9. This value is consistent with the purity of the model reaction.

Recently, Frey et al.[26] pointed out that the equation proposed by Fréchet et al. leads to an overestimation of the DB for low molecular weight molecules. They

Scheme 5



proposed another equation for calculation of DB:

$$\mathrm{DB} = \frac{(2 \times \text{the number of dendritic units})}{(2 \times \text{the number of dendritic units} + \text{the number of linear units})}$$

We estimated the DBs of each dendritic polyamide on the basis of their equation and results obtained are given in Table 1 as DB′. As predicted by Frey et al., the DB′ of the second-generation dendritic polyamide calculated by using their equation was lower than that obtained by Fréchet's equation. Whereas no such difference was observed for the fourth- and fifth-generation dendritic polyamides. The DB′ of high generation dendritic polyamides was found to be 0.9.

As described above, the DB of a perfect dendrimer is 1.0, and that of hyperbranched polymers prepared by one-step polymerization is 0.5 with several exceptions.[14−16] It is noteworthy that the new process one-pot procedure investigated by us is not only easy, it realized significantly high DB also.

Molecular weight distribution is also important to evaluate the regularity of dendritic macromolecules. The M_w/M_n was measured by GPC in DMF containing 0.4 wt % LiCl as an eluent. GPC traces of dendritic polyamides are shown in Figure 3. The M_w/M_ns of dendritic polyamides were in the range of 1.2−1.5 and increased with increasing the generation. As dendrimers synthesized by the conventional method have a polydispersity less than 1.1, this one-pot procedure needs to be improved to obtain dendrimers with a narrower polydispersity.

The correct molecular weight of dendritic macromolecules cannot be obtained by GPC measurement using polystyrene as a standard. Therefore, number-average molecular weight (M_n) of dendritic polyamides was estimated by the end group analysis. The integrated intensity of terminal and linear units bonding with diethylamine was used for this purpose. M_n of all dendritic polyamides was found to be close to the calculated values.

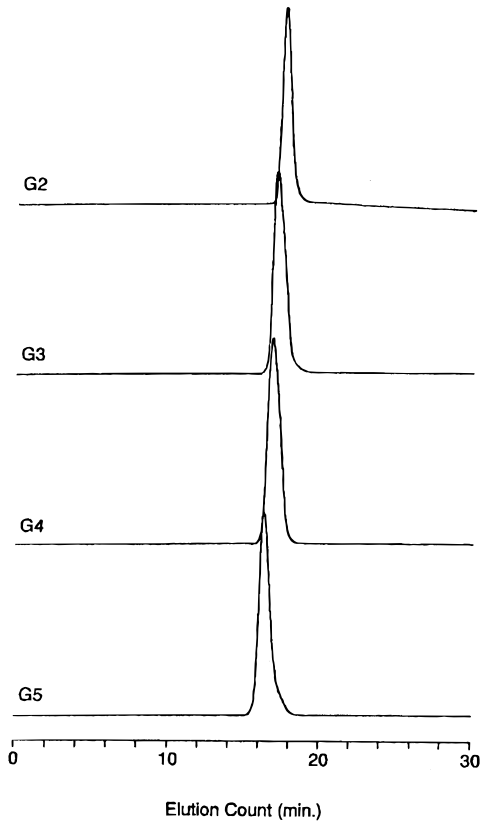


Figure 3. GPC traces of the dendritic polyamides.

Conclusions

One-pot synthesis of dendritic polyamides using the condensing agent DBOP was demonstrated. This procedure consists of successive activation of carboxyl

groups, followed by condensation with aminodicarboxylic acid **4.** Each reaction was completed within 30 min. Dendritic polyamides obtained had the DB values in the range of 0.8−0.9 and the molecular weights (M_n) close to the calculated values. The molecular weight distributions were 1.2 and 1.5 in the second and fifth generation dendritic polyamides, respectively.

This easy and rapid one-pot procedure gave the dendritic polyamides with the controlled high DB and the narrow polydispersity. When a complete coupling reaction is realized, the perfect dendrimer without the structural defect will be obtained.

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