Synthesis of novel AB_2 monomers for the construction of highly branched macromolecular architectures

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Abstract

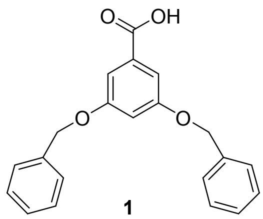
A series of novel, structurally related AB_2 monomers was synthesized and incorporated into branched materials. Size exclusion chromatography was used to compare these systems based on their relative hydrodynamic volumes. The results of these studies indicated an increased hydrodynamic volume of bis-benzyl amine based AB_2 monomer relative to analogous bis-benzyl ether structures. In order to further explore the bis-benzyl amine AB_2 structural motif, additional monomers were synthesized, leading to new branched materials and hyperbranched polymer structures.

Keywords: Monomers, branched macromolecules, hyperbranched polymer, dendrimers

Introduction

Highly branched macromolecular structures such as dendrimers[1] and hyperbranched polymers[2] have gained considerable attention for their potential in applications such as drug delivery,[3] molecular recognition,[4] catalysis,[5] and organic electronic devices.[6] To expand the repertoire of highly branched systems with varying functionalities, new monomers need to be synthesized and analyzed. The AB_2 motif is common in macromolecules due to its branching and symmetry. For example, Fréchet introduced the bis-benzyl ether AB_2 monomer **1** for the synthesis of dendrimers[7] and hyperbranched polyesters.[8] Using the bis-benzyl ether monomer **1** as a starting point, new monomers **2-6** were designed to increase the variety of AB_2 building blocks for use in macromolecular design. Herein, the synthesis of these novel monomers is reported, and studies involving the preparation of highly branched structures from **2-6** are disclosed.

Initially, **2-4** were targeted because of their similarity to the known bis-benzyl ether monomer **1**: **2** has reversed the ether linkage position relative to **1**, **3** is the bis-cyclohexyl analog, and **4** is the corresponding bis-amine analog. It was hypothesized that modest changes embodied by **2-4** would lead to differences in the resulting macromolecular properties. To test this hypothesis, branched materials constructed from **2-4** were prepared and studied as a first step towards designing more advanced AB_2 monomers for larger hyperbranched structures.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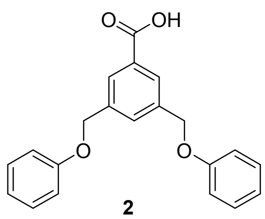
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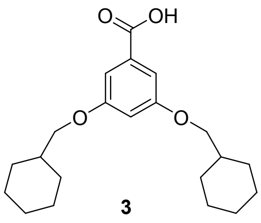
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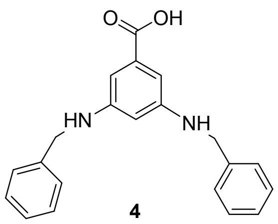
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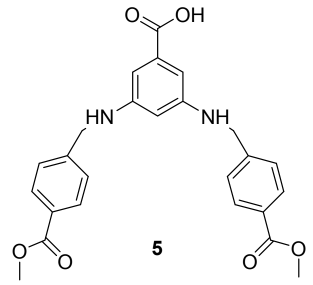
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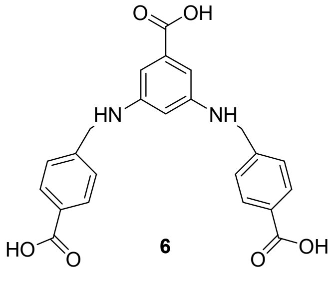
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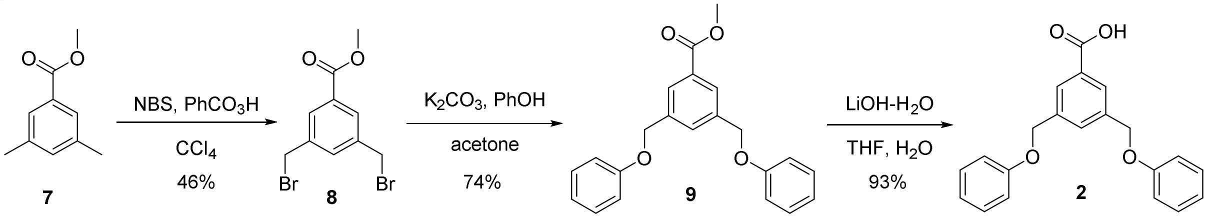
Results and Discussion

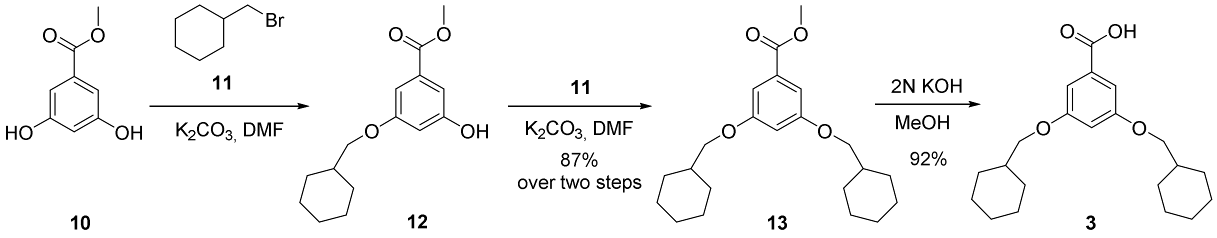
The synthesis of monomer **2** was previously reported as an intermediate step in the preparation of glucokinase activators.[9] In this previous disclosure, methyl 3,5-bis(hydroxymethyl)benzoate, an expensive starting material, underwent a Mitsunobu reaction with two equivalents of phenol as the key step in the synthesis of **2**. In the present study, an alternative approach was used in order to use a more economical starting material and avoid the triphenylphosphine oxide by-product from the Mitsunobu reaction (Scheme 1).



Scheme 1. Preparation of AB_2 monomer **2** from commercially available **7**.

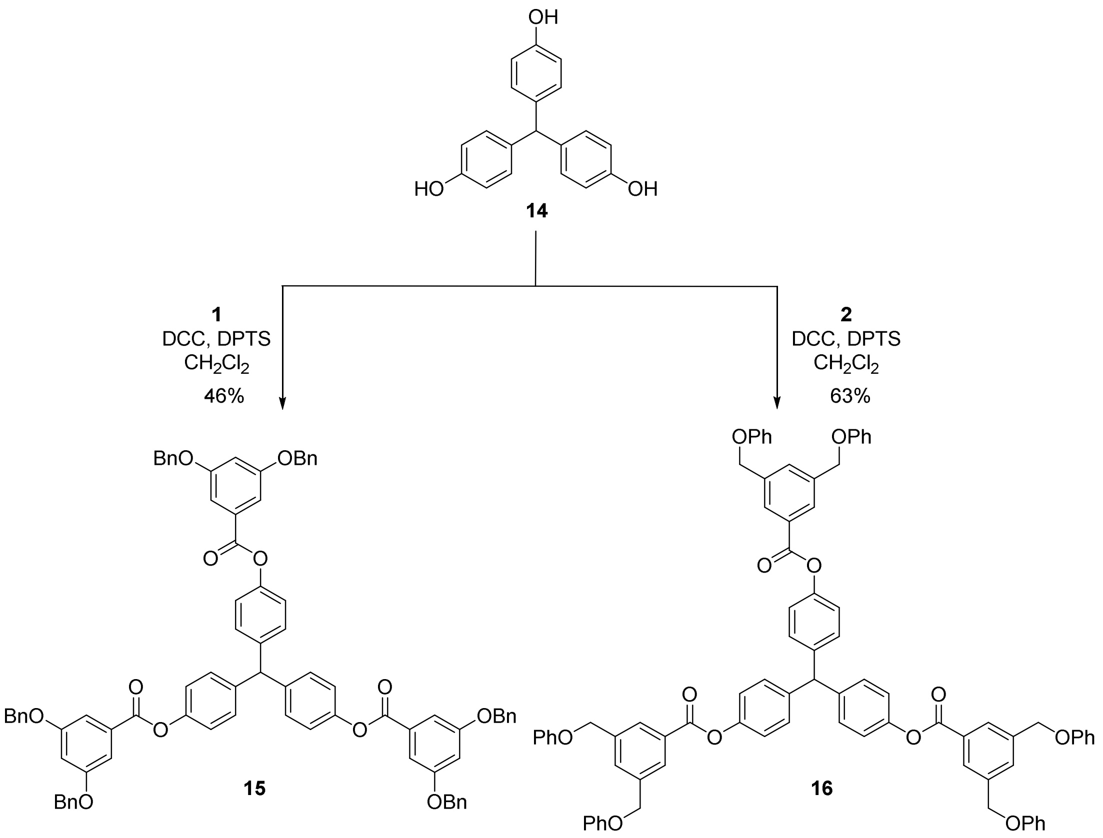
Beginning with methyl 3,5-dimethylbenzoate **7**, a free radical halogenation reaction afforded the dibromide **8**[10] which was reacted with two equivalents of phenol in the presence of potassium carbonate to provide the diether **9**. Hydrolysis of the methyl ester in **9** resulted in the carboxylic acid monomer **2**.

Monomer **3** was prepared as described in Scheme 2. Dialkylation of methyl 3,5-dihydroxybenzoate **10** with excess of bromomethyl cyclohexane (**11**) proceeded slowly relative to alkylation of **10** with benzyl bromide. This rate difference presumably is due to the increased steric bulk of bromomethyl cyclohexane and its reduced solubility in polar solvents. In practice, it was more convenient to isolate the mono-alkylated product **12** by column chromatography (SiO_2) and then subject this intermediate to an alkylation with **11**, giving the desired **13** as a crystalline solid upon trituration.[11] Hydrolysis of **13** to form **3** required higher temperatures compared with similar conditions used to prepare the standard benzyl ether monomer **1**.[7] The difference in hydrolysis reactivity is proposed to be due to the hydrophobic cyclohexane rings reducing solubility of the parent methyl ester. The bis-benzyl amine monomer **4** and its synthesis were reported in an earlier publication.[12]

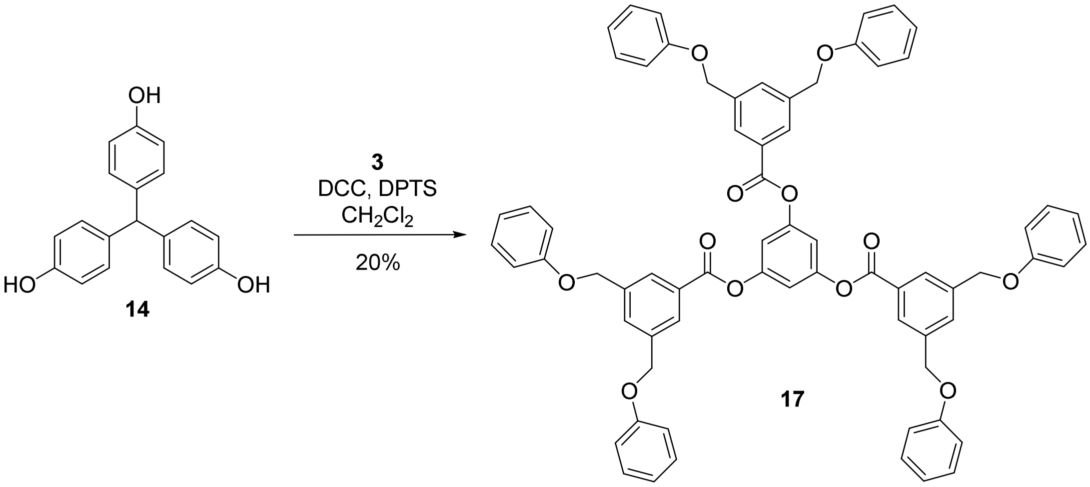


Scheme 2. Preparation of AB_2 monomer **3** containing cyclohexane units.

Monomers **1-3** were combined with 1,1,1-tris(4-hydroxyphenyl)methane **14**, DCC and (dimethylamino)pyridinium 4-toluenesulfonate (DPTS),[13] to form the branched materials **15-17**, respectively (Schemes 3 and 4) which were purified by either column chromatography (SiO_2) or size exclusion chromatography (SEC).[14] The triphenylmethane core employed in the synthesis of **15-17** has been used previously used in the synthesis of hyperbranched polymers[15] and self-assembled liquid crystals.[16] Its use in the synthesis of benzyl ether-type dendrimers has not been described, although structures closely related to **15** have been reported.[7] Thus, **15-17** represent novel structures which have not been disclosed elsewhere.



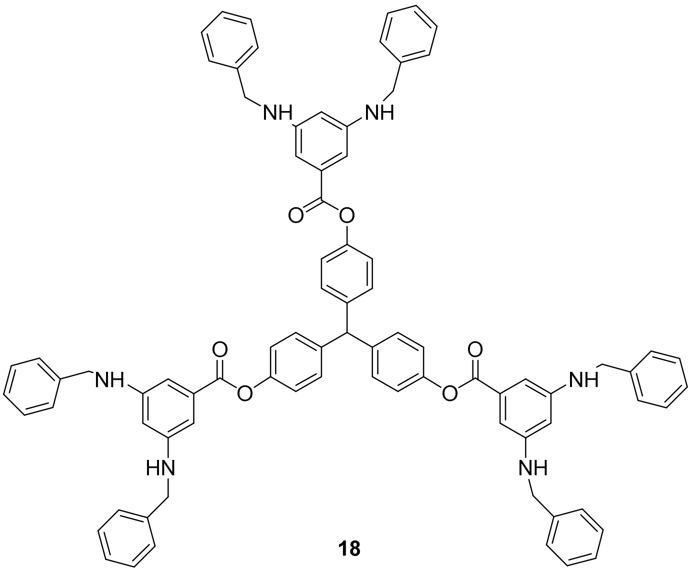
Scheme 3. Preparation of branched materials **15-16** via DCC coupling conditions.



Scheme 4. Preparation of branched material **17** via DCC coupling conditions.

The preparation of the benzyl amine **18** from monomer **4** and **14** was accomplished using our previously described method.[12] Branched materials were also synthesized from monomers **2** and

3 with two other tri-phenol cores (**19** and **20**) and their experimental data are reported in the supplemental information.[17] Benzyl amine based branched structures were not obtained from the reaction of **4** with cores **19** and **20** since it appeared that macromolecules were formed but underwent degradation before isolation was possible.



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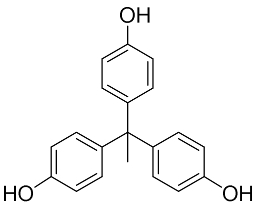

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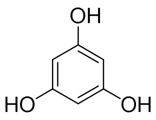

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The model branched materials **15-18** were compared using analytical SEC (Figure 1) using styrene divinylbenzene columns in series and THF as the eluent. Typically a macromolecule with a higher molecular weight has a larger hydrodynamic volume, leading to an earlier retention time.[18] Upon running the SEC, the two benzyl ether positional isomers **15** and **16** eluted with identical retention times. The cyclohexyl system **17** and benzyl amine system **18** shifted to shorter retention times, corresponding to larger apparent molecular weights. These results could be explained by examining the correlation between SEC retention time and hydrodynamic volume.[18] Branched materials **15-16** have the same molecular weights (Table 1) and thus presumably a similar hydrodynamic volume and retention time. The smaller retention time of **17** relative to **15-16** can be justified by the larger molecular weight of **17** and the greater steric demand of the cyclohexyl groups, leading to a larger hydrodynamic volume.

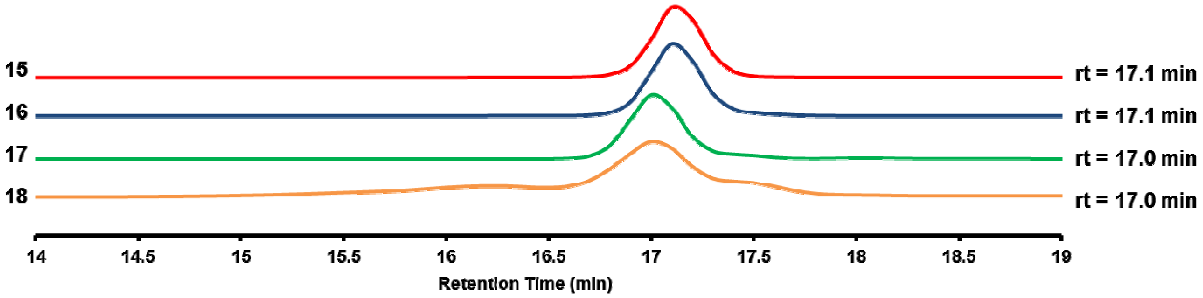


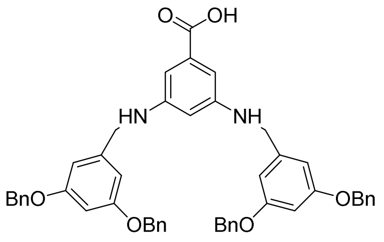
Figure 1. Analysis of the branched materials **15-18** by analytical SEC.

The rationale of the smaller retention time of the benzyl amine system **18** was less clear, especially since the molecular weights of **15**, **16**, and **18** are very similar. Based on the experimental data, **18** should have a smaller hydrodynamic volume relative to the cyclohexane system **17** due to its lower molecular weight. However, the two compounds eluted at nearly identical times on SEC. It is possible that increased repulsions between the internal amine groups within the branches of **18** in THF lead to a more extended conformation and subsequently a larger hydrodynamic volume. Thus, the branched structure constructed from the bis-benzyl amine **4** appeared to have unique properties which warrant further study of the bis-benzyl amine AB_2 motif in novel branched macromolecular structures.

Table 1. Comparison of SEC retention times, SEC derived molecular weights and calculated molecular weights (g/mol) of **15-18**. SEC derived molecular weights were determined using a calibration curve obtained from polystyrene standards[17]

Compound	Retention Time (min)	Apparent MW	Calculated MW
15	17.13	1326.78	1240.44
16	17.11	1340.58	1240.44
17	17.02	1447.39	1277.69
18	17.02	1447.96	1235.50

As noted above, the reaction of other tri-phenol cores such as **19** and **20** with monomer **4** in the presence of DCC and DPTS did not lead to branched materials. Two strategies were devised to obtain new branched systems from the bis-benzyl amine AB_2 motif. First, hybrid monomer **21** was prepared containing both ether and amine functionalities. Hybrid dendrimers were successfully synthesized from this monomer, and the results of these studies are reported elsewhere.[12] In another approach, an amide bond between **4** and the core was proposed to improve the stability of the resulting system relative to the ester linkages in **18**. A new branched material **22** was designed in which amide bonds link the core with the monomer.



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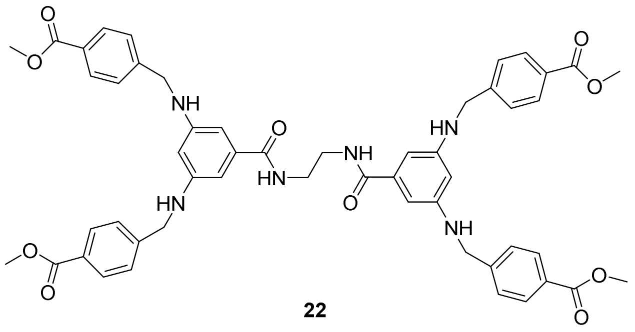

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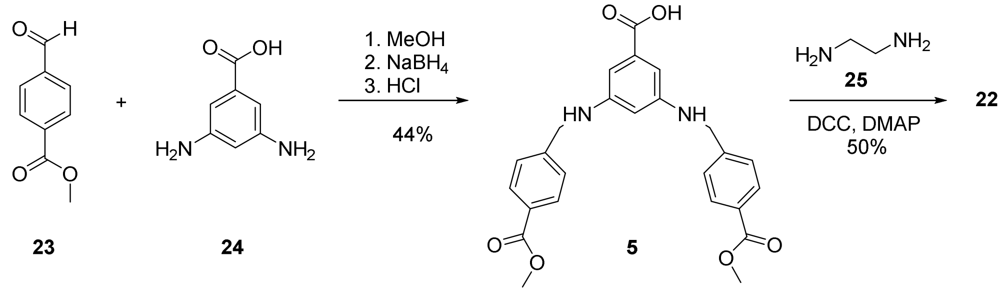
Ethylenediamine was utilized as the core because it was hypothesized that amide bonds to an alkyl amine containing core would be more stable than amide bonds with a di- or tri- aniline containing core. The methyl ester groups present at the periphery of **22** were incorporated to provide a functional handle to build larger dendrimers and hyperbranched structures.

Monomer **5**, designed for the synthesis of the model system **22**, was prepared following Scheme 5. Two equivalents of aldehyde **23** were condensed with 3,5-diaminobenzoic acid (**24**) and the resulting mixture was treated with $NaBH_4$ followed by concentrated HCl. The desired bis-benzylamine monomer **5** was isolated in 44% yield with sufficient purity that additional chromatographic purification was not required. To form the two arm system **22**, a DCC coupling reaction was performed using two equivalents of monomer **5** and ethylenediamine (**25**). Purification by column chromatography (SiO_2) resulted in **22** and its purity was confirmed by SEC (Figure 2).



Scheme 5. Preparation of bis-amine branched system **22** via DCC coupling conditions.

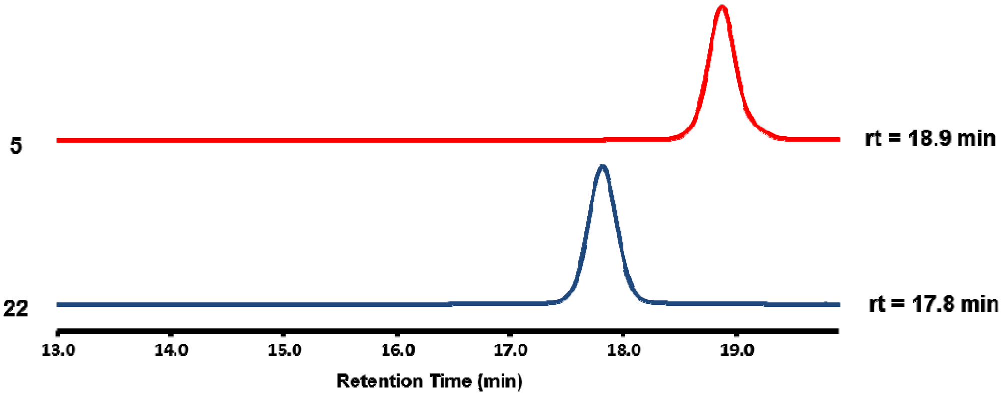
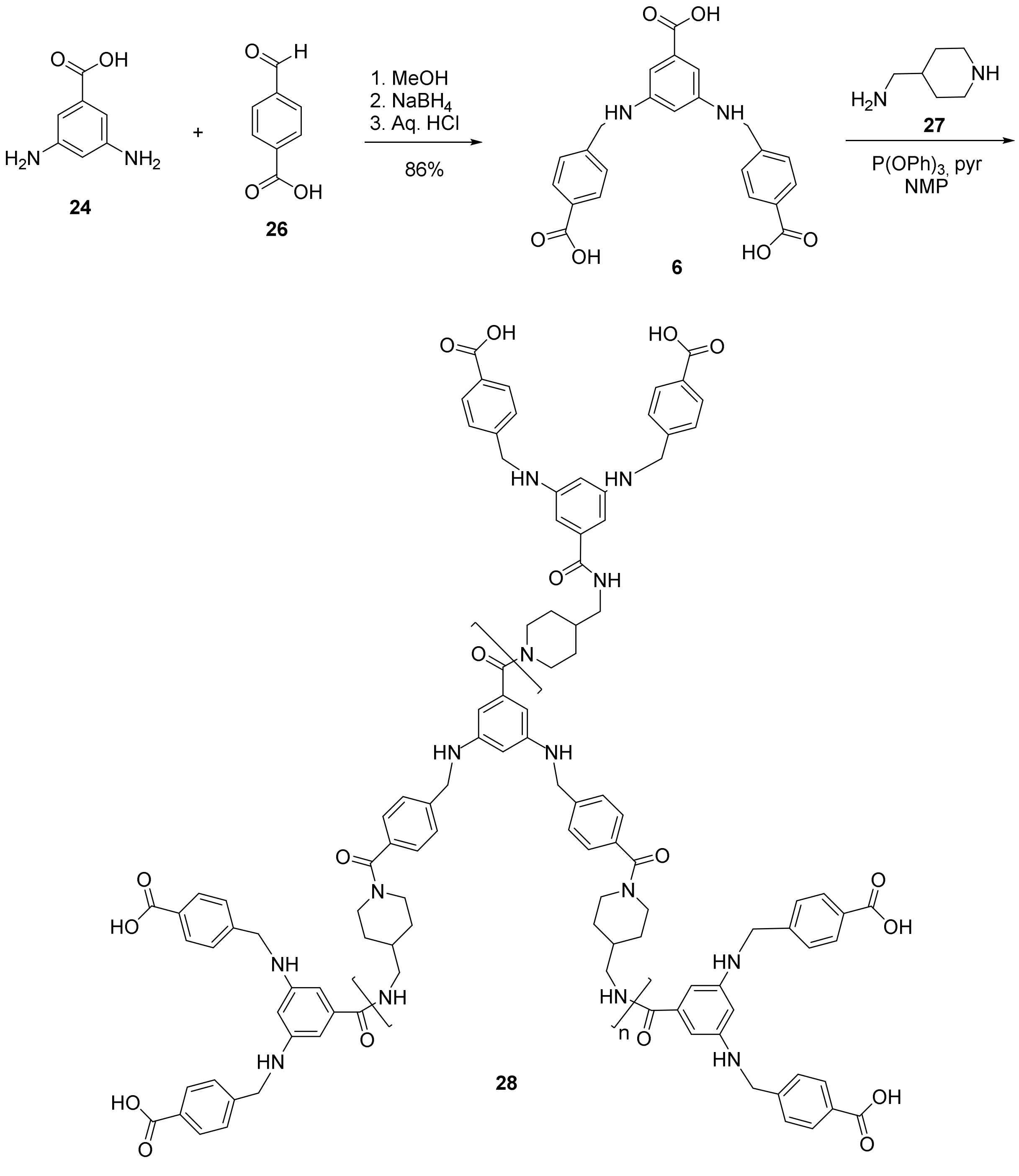


Figure 2. Analysis of branched material **22** and the parent monomer **5** using SEC.

Branched material **22** had improved chemical stability compared to **18** and thus could be isolated and characterized. The improved stability of **22** was evident by SEC analysis which showed a single peak comparable in peak shape to the parent monomer **5**. In contrast, the ester-linked bis-benzyl amine system **18** exhibited peak broadening (Figure 1). The improved stability of **22** suggested that larger branched architectures could be constructed from bis-benzyl amine monomers constructed through amide bonds to a core. Additional branched macromolecular structures were designed based on the bis-benzyl amine monomer motif to make more stable macromolecules. A hyperbranched polymer was proposed from the polycondensation of the tri-acid monomer **6** and a diamine. Novel hyperbranched polymers containing amine groups are of interest because they are proposed to have favorable properties for applications such as encapsulation, drug delivery, and waste water remediation.[19]



Scheme 6. Preparation of hyperbranched polymer **28** by condensing **6** with **27**.

Monomer **6** was prepared according to Scheme 6. Condensation of 3,5-diaminobenzoic acid (**24**) with two equivalents of 4-carboxybenzaldehyde **26** was followed by an *in situ* reduction of the resulting imine intermediate with $NaBH_4$. After acidification with 2N HCl, **6** was isolated in 86% yield by filtration with no additional purification required. Polycondensation of **6** with 4-(aminomethyl) piperidine **27** was attempted in the presence of $P(OPh)_3$ and pyridine using NMP as a solvent[20] and the reaction was monitored over 24 hours. As time progressed a polymer was visually observed to precipitate. After 24 hours, a white precipitated solid and clear supernatant were observed (Figure 3).

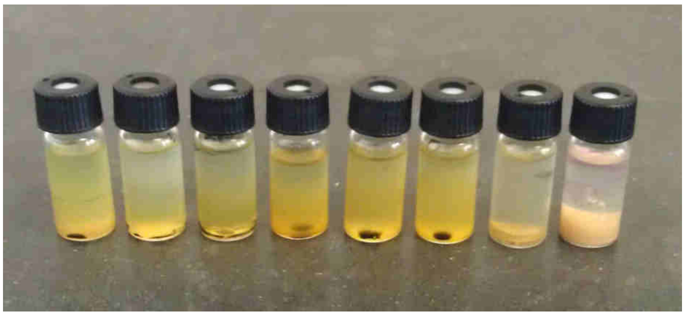


Figure 3. Formation of a precipitated polymer from the reaction of monomer **6** and 4-(aminomethyl) piperidine **27.** Aliquots taken from the polymerization reaction over time. From left to right, aliquots from 0.5 h, 1 h, 1.5 h, 2 h, 2.5 h, 3 h, 12 h, 24 h time points are compared.

Although the solubility of the polycondensation reaction product was limited in organic solvents, preliminary analysis using SEC and ^1H Nuclear Magnetic Resonance (NMR) spectroscopy was attempted. Unfortunately, the polymer was not sufficiently soluble in THF or other suitable solvents to give reliable SEC traces. NMR analysis revealed significant peak broadening, suggesting that higher molecular weight structures formed. One possible product of the polycondensation reaction is represented by structure **28**. Studies were done to examine the stability of the resulting polymer in the presence of different solvents. The polymer was found to be stable under various organic and aqueous solvents, even upon extensive sonification. Degradation began after the polymer was in the presence of concentrated HCl at 25 ˚C for 24 hours.

Conclusions

Several novel AB_2 monomers were synthesized and incorporated into branched materials. These branched materials were used as model systems to make direct comparisons between structures resulting from the different monomers. Analytical SEC indicated that **17**, constructed from the bis-benzylamine monomer **4**, had a larger hydrodynamic volume than analogous ether systems, even though it had a smaller molecular weight. Based on this finding, monomers **5** and **6** were efficiently synthesized in order to study further the formation and properties of macromolecular structures containing the benzyl amine AB_2 motif. The bis-benzyl amine monomer **5** could be introduced into a branched system successfully through amide linkages with an aliphatic core. Furthermore, the amide-linked structure **22** exhibited improved stability relative to the ester-linked structure **18**. A polycondensation reaction between monomer **6** and an aliphatic diamine lead to the formation of a hyperbranched polymer. Dendrimers and other branched macromolecules based on the bis-benzyl amine AB_2 monomer have the potential for unique properties and applications involving encapsulation, host-guest complexation, and waste water remediation.[19] Studies are underway to explore further the formation of dendrimers and other hyperbranched macromolecules containing the bis-benzyl amine motif, and these structures will be exploited for the removal of common environmental pollutants.

Experimental Section

General. All reactions were performed under an argon gas atmosphere with oven-dried glassware unless otherwise noted. Reagents were obtained from Aldrich or TCI America. 2-(Dimethylamino)pyridinium *p*-toluenesulfonate (DPTS) was prepared as reported previously.[13] Solvents and reagents were used without further purification except for the following: CH_2Cl_2 was distilled from CaH_2, phloroglucinol dihydrate was azeotroped five times with toluene prior to use, and *N*-bromosuccinimide was recrystallized from water and dried *in vacuo* prior to use. Reactions were monitored by TLC using silica gel 60 F_{254} glass plates. TLC bands were visualized by UV and phosphomolybdic acid (PMA) stain. Eluent solvent ratios are reported in v/v.

^1H NMR spectra were recorded at 300 MHz and ^{13}C NMR spectra were recorded at 75 MHz on a Bruker AV-300 high performance digital NMR spectrometer. Chemical shifts were reported in parts per million (ppm) and coupling constants were reported in Hertz (Hz). ^1H NMR spectra obtained in acetone-d_6 were referenced to 2.50 ppm, spectra obtained in $CDCl_3$ were referenced to 7.26 ppm, and spectra obtained in DMSO-d_6 were referenced to 2.05 ppm. ^{13}C NMR spectra obtained in acetone-d_6 were referenced to 29.84 ppm, $CDCl_3$ were referenced to 77.2 ppm and DMSO-d_6 were referenced to 39.50 ppm. Mass spectra were obtained from University of Illinois Mass Spectrometry Center (Micromass Q-TOF Ultra, ESI). Preparative size exclusion chromatography (SEC) was performed using a 2 cm × 50 cm column of Bio-Rad BioBeads S-X1 beads (200-400 mesh) in toluene. Analytical SEC data was obtained using a Dionex Ultimate 3000 with Styragel HR 3 (7.8 × 300 mm) and Styragel HR 4E (7.8 × 300 mm) columns in series in THF. Melting points were obtained using an OptiMelt Automated Melting Point System and are uncorrected.

Benzyl ether branched system 15. The synthesis proceeded according to methods previously reported.[7] Branched structure **15** was obtained as a white solid. ^1H NMR ($CDCl_3$): δ 7.46-7.35

(m, 36H, ArH), 7.18 (app quart, *J* 8.8, 12H, ArH), 6.88 (t, *J* 2.1, 3H, ArH), 5.14 (s, 12H, OCH_2Ph), 5.52 (s, 1H, CH). ^{13}C NMR ($CDCl_3$): δ 164.8, 159.9, 149.1, 146.2, 136.3, 131.4, 129.8, 128.6, 128.2, 127.6, 121.1, 70.4, 51.7. HRMS-ESI: *m/z* $[M+Na]^+$ calcd for $C_{83}H_{66}O_{12}Na$ 1277.4452; found 1277.4409.

“Reverse” benzyl ether monomer and corresponding branched material synthesis

Methyl 3,5-bis(bromomethyl)benzoate (8). Synthesis proceeded as reported by Sivakumar and Nasar.[10] Silica gel column chromatography was performed under different conditions (15:1 ligroin/EtOAc) to produce the white solid **8** in 46% yield. Spectral data are consistent with literature values. Dibenzylbromide **8** was used in the experimental procedures below to produce **9** and **2**. The synthesis and characterization of **2** and **9** were reported previously by Hayter *et al.*[9]

Methyl 3,5-bis(phenoxymethyl)benzoate (9).[9] To a solution of K_2CO_3 (0.81 g, 5.85 mmol) in acetone (15 mL) was added PhOH (0.55 g, 5.85 mmol) and the reaction was stirred at 25 ˚C for 1 h. Dibenzylbromide **8** (0.94 g, 2.93 mmol) was added and the reaction was heated to reflux for 24 h. After cooling to 25 ˚C, the solvent was evaporated *in vacuo* leaving a white solid. The solid was dissolved in CH_2Cl_2 (60 mL), and the organic layer was washed with saturated Na_2CO_3(aq) (3 × 30 mL), H_2O (30 mL), and brine (30 mL). After drying over Na_2SO_4, and removal of solvent, the resulting white solid was purified by silica gel chromatography (8:1, ligroin:EtOAc) to afford **9** (1.08 g, 74%) as a white solid, mp 65.6-68.9 ºC; ^1H NMR ($CDCl_3$): δ 8.08 (d, *J* 1.1, 2H, ArH), 7.74 (t, *J* 2.2, 1H, ArH), 7.33-7.26 (m, 4H, ArH), 7.00-6.97 (m, 6H, ArH), 5.10 (s, 4H, CH_2OPh), 3.94 (s, 3H, CO_2CH_3). ^{13}C NMR ($CDCl_3$): δ 166.8, 158.6, 138.2, 130.8, 128.2, 121.4, 115.0, 69.4, 52.4. HRMS-ESI: *m/z* $[M + H]^+$ calcd for $C_{22}H_{21}O_4$ 349.1440; found 349.1441.

3,5-bis(phenoxymethyl)benzoic acid (2).[9] To a solution of **9** (0.21 g, 0.66 mmol) in THF (12.5 mL) was added LiOH (0.083 g 1.97 mmol) and H_2O (12.5 mL). The mixture was stirred at 25 ˚C for 24 h; THF was then removed *in vacuo*. The resulting clear solution was acidified to pH 2 by slow addition of 1N HCl and the product was extracted with EtOAc (3 × 40 mL). The combined organic layers were dried over Na_2SO_4 and solvent was removed to leave **2** as a white solid (0.19 g, 93%). mp 155.5-158.2 ºC; ^1H NMR (acetone-d_6): δ 8.11 (d, *J* 1.3, 2H, ArH), 7.86 (t, *J* 1.7, 1H, ArH), 7.35-7.27 (m, 4H, ArH), 7.06 (app d, *J* 7.8, 4H, ArH), 6.95 (tt, *J* 7.2, 2H, ArH), 5.24 (s, 4H, CH_2OPh). ^{13}C NMR (acetone-d_6): δ 166.0, 158.3, 138.1, 130.7, 130.4, 129.3, 129.1, 127.5, 120.5, 114.4, 68.4.

“Reverse” benzyl ether branched system 16. To a solution of **2** (0.25 g, 0.75 mmol) in CH_2Cl_2 (2.5 mL) was added **14** (0.24 mmol) and DPTS (0.23 g, 0.82 mmol). After 15 min, DCC (0.17 g, 0.82 mmol) was added, and the reaction mixture was stirred until TLC (10% MeOH in CH_2Cl_2) indicated that the reaction was complete. The reaction mixture was passed through a short silica gel plug and washed with CH_2Cl_2 (100 mL). After the solvent was removed *in vacuo*, the resulting solid was purified by size exclusion chromatography in $PhCH_3$ to obtain **16** as a white foam (0.18 g, 63%). ^1H NMR ($CDCl_3$): δ 8.24 (s, 6H, ArH), 7.84 (s, 3H, ArH), 7.35-7.29 (t, *J* 8.0, 12H, ArH), 7.21 (app quart, *J* 3.7, 12H, ArH), 7.01 (app d, *J* 7.1, 18H, ArH), 5.67 (s, 1H, CH), 5.17 (s, 12H, CH_2OPh). ^{13}C NMR ($CDCl_3$): δ 164.8, 158.4, 149.4, 141.1, 138.3, 131.4, 130.5, 130.3, 129.6, 128.6, 121.6, 121.3, 114.9, 69.2. HRMS-FAB: *m/z* $[M]^+$ calcd for $C_{82}H_{64}O_{12}$ 1240.4398; found 1240.4395.

Cyclohexane based monomer and corresponding branched material synthesis

Methyl 3,5-bis(cyclohexylmethoxy)benzoate (13).[11] To methyl 3,5-dihydroxybenzoate (5.00 g, 29.7 mmol) in DMF (37.5 mL) was added K_2CO_3 (8.50 g, 61.5 mmol) and the mixture was stirred at 25 ˚C for 2 h. Bromomethylcyclohexane (8.80 mL, 63.1 mmol) was added over 10 min, the reaction was heated at 80 ºC for 3 h. The reaction flask was cooled to 25 ˚C, EtOAc (100 mL) was added and the organic layer was washed with H_2O (5 × 70 mL) and brine (70 mL). After drying over Na_2SO_4 and removal of the solvent, the resulting product was purified by silica gel column chromatography (1:1 pet ether:Et_2O) to separate the desired dialkylated product and the monoalkylated species. The mono-alkylated product was subjected to the above conditions to obtain additional product. Trituration with ice-cold pet ether afforded **13** (4.36 g, 87%) as a white solid. ^{1}H NMR ($CDCl_3$): δ 7.15 (d, *J* 2.3, 2H, ArH), 6.63 (t, *J* 2.3, 1H, ArH), 3.91 (s, 3H, CO_2CH_3), 3.77 (d, *J* 6.2, 2H, OCH_2Cy), 1.88-1.03 (m, 22H, Cy). ^{13}C NMR ($CDCl_3$): δ 167.0, 160.3, 131.8, 107.6, 106.5, 73.8, 52.2, 37.7, 29.9, 26.5, 25.8. HRMS-ESI: *m/z* $[M + H]^+$ calcd for $C_{22}H_{33}O_4$ 361.2392; found 361.2390.

3,5-Bis(cyclohexylmethoxy)benzoic acid (3). To a solution of **13** (0.50 g, 1.39 mmol) in MeOH (30 mL) was added of 2 N KOH (6 mL). The reaction was heated to reflux for 1.5 h before the solvent was removed *in vacuo*. To the residual solid was added DI H_2O (25 mL) and 2 N HCl was added dropwise until the solution reached pH 4. The aqueous layer was extracted with EtOAc (3 × 30 mL) and the combined organic layers dried with $MgSO_4$. Removal of the solvent *in vacuo* gave **3** as a white solid (0.44 g, 92%), mp 182.5-184.6 ºC; ^{1}H NMR ($CDCl_3$): δ 7.21 (d, *J* 2.3, 2H, ArH), 6.68 (t, *J* 2.3, 1H, ArH), 3.78 (d, *J* 6.2, 4H, OCH_2Cy), 1.88-1.69 (m, 10H, Cy), 1.38-1.18 (m, 6H, Cy), 1.02-0.99 (m, 4H, Cy). ^{13}C NMR (acetone-d_6): δ 161.2, 133.2, 108.4, 106.4, 74.1, 38.4, 30.4, 27.1, 26.4. HRMS-ESI: *m/z* $[M + H]^+$ calcd for $C_{21}H_{31}O_4$ 347.2222; found 347.2222.

Cyclohexane branched system 17. To a solution of **3** (0.25 g, 0.72 mmol) in 10 mL of CH_2Cl_2 was added 0.24 mmol of **14** and 0.20 g (0.72 mmol) of DPTS. After 15 min, DCC (0.15 g, 0.72 mmol) was added and the reaction mixture was stirred 25 ˚C for 15 min until TLC (1:1 pet ether:EtOAc) indicated that the reaction was complete. The mixture was filtered and washed with cold CH_2Cl_2. After solvent removal *in vacuo*, the residual solid was purified by silica gel column chromatography (1:1 pet ether:EtOAc) to obtain **17** as a white solid (0.18 g, 20%). ^{1}H NMR ($CDCl_3$): δ 7.30 (d, *J* 2.3, 6H, ArH), 7.18 (app quart, *J* 8.9, 12H, ArH), 6.70 (t, *J* 2.3, 3H, ArH), 5.57 (s, 1H, CH), 3.79 (d, *J* 6.2, 12H, OCH_2Cy), 1.89-1.69 (m, 42H, Cy), 1.36-1.18 (m, 22H, Cy), 1.11-1.00 (m, 12H, Cy). ^{13}C NMR ($CDCl_3$): δ 165.1, 160.4, 149.5, 141.0, 131.1, 130.4, 121.6, 108.1, 107.1, 73.8, 37.6, 29.8, 26.5, 25.8. HRMS-FAB: *m/z* $[M + H]^+$ calcd for $C_{82}H_{101}O_{12}$ 1277.7293; found 1277.7289.

Benzyl amine based monomer and corresponding branched material synthesis

3,5-Bis[[4-(methoxycarbonyl)benzyl]amino]benzoic acid (5). To a heterogeneous solution of **24** (0.10 g, 0.66 mmol) in MeOH (10 mL) was added **23** (0.23 g, 1.38 mmol). After 20 min, the reaction was cooled to 0 ºC and 0.08 g of $NaBH_4$ was added in three portions. The reaction was slowly warmed to 25 ˚C and stirred overnight. The reaction was cooled to 0 ºC and H_2O (1 mL) added dropwise before 2N HCl was added dropwise until the solution reached pH 3. The resulting precipitate was vacuum-filtered and washed with cold MeOH. Upon drying, **5** was obtained as a light gray solid (0.13 g, 44%). mp 182.6-184.7 ºC. ^{1}H NMR (DMSO-d$_6$): δ 12.4 (broad s, 1H, COOH), 7.85 (d, *J* 8.1, 4H, ArH), 7.37 (d, *J* 8.1, 4H, ArH), 6.43 (s, 2H, ArH), 6.35 (t, *J* 5.9, 2H, ArH), 5.90 (s, 1H, NH), 4.25 (d, *J* 5.7, 4H, $NHCH_2Ph$), 3.83 (s, 6H, CO_2CH_3). ^{13}C NMR ($CDCl_3$): δ 168.5, 167.2, 150.4, 147.1, 132.8, 130.3, 129.7, 128.0, 104.7, 101.3, 52.3, 47.8. HRMS-ESI: *m/z* $[M + H]^+$ calcd for $C_{25}H_{25}N_2O_6$ 449.1713; found 449.1717.

Benzylamine branched system 22. To **5** (0.25g, 0.056 mmol) in 5 mL of CH_2Cl_2 was added ethylenediamine (0.020μL, 2.99×10^{-4} mmol) and DMAP (0.068 g, 0.557 mmol). After 15 min, DCC (0.12 g, 0.56 mmol) was added and the reaction was stirred for 48 h. The mixture was filtered and the solid was thrice washed with cold CH_2Cl_2. After the solvent from the filtrate was removed *in vacuo*, the resulting solid was purified by silica gel column chromatography (EtOAc) to obtain **22** as an off-white solid (0.13 g, 50%). ^{1}H NMR (acetone-d$_6$): δ 7.87 (d, *J* 8.1, 8H, ArH), 7.79 (broad s, 2H, NH), 7.41 (d, *J* 8.1, 8H. ArH), 6.52 (d, *J* 2.0, 4H, ArH), 6.00 (t, *J* 2.0, 2H, ArH), 5.54 (t, *J* 6.1, 4H, NH), 4.37 (app d, *J* 5.8, 8H, $NHCH_2Ph$), 3.86 (s, 12H, CO_2CH_3), 3.48-3.44 (m, 4H, $NHCH_2CH_2NH$). ^{13}C NMR (acetone-d$_6$): δ 167.2, 150.3, 147.1, 130.3, 128.0, 102.3, 52.3, 46.2. HRMS-ESI: *m/z* $[M + H]^+$ calcd for $C_{52}H_{53}N_6O_{10}$ 921.3823; found 921.3810.

4,4'-[[(5-Carboxy-1,3-phenylene)bis(azanediyl)]bis(methylene)]dibenzoic acid (6). To a heterogeneous solution of 3,5-diaminobenzoic acid (**24**) (0.5 g, 3.28 mmol) in MeOH (45 mL) was added aldehyde **26** (1.00 g, 6.89 mmol). After 20 min, the reaction was cooled to 0 ºC and $NaBH_4$ (0.46 g) was added in three portions. The reaction was slowly warmed to 25 ˚C and stirred overnight. The reaction was cooled to 0 ºC and H_2O (5 mL) added dropwise before 2N HCl was added dropwise until the solution reached a pH 1. The resulting precipitate was vacuum-filtered and washed with cold MeOH. Upon drying, **6** was obtained as a dark gray solid (1.19 g, 86%), mp >250 ºC (dec.); ^{1}H NMR (DMSO-d$_6$): δ 12.7 (broad s, 3H, COOH), 7.98 (d, *J* 8.1, 4H, ArH), 7.45 (d, *J* 8.1, 4H, ArH), 6.44 (d, *J* 1.4, 2H, ArH), 6.29 (app t, *J* 1.4, 1H, ArH), 4.26 (s, 4H, OCH_2Ph). ^{13}C NMR (DMSO-d$_6$): δ 168.2, 167.1, 149.2, 145.8, 131.8, 129.3, 129.2, 127.0, 102.6, 99.9, 46.3. HRMS-ESI: *m/z* $[M + H]^+$ calcd for $C_{23}H_{32}N_2O_6$ 421.1400; found 421.1402.

Polymer 28. To NMP (4.75 mL) was added 4-(aminomethyl)piperdine (66.1 μL, 0.59 mmol), pyridine (0.45 mL, 5.56 mmol), and $P(OPh)_3$ (1.6 mL, 6.11 mmol). After the reaction was heated to 80 ºC, 0.25 g (0.59 mmol) of **6** was added. Aliquots were removed every 30 min to monitor the reaction. After 24 h, 20 mL of H_2O and 15 mL of CH_2Cl_2 was added. The resulting precipitate was filtered and dried to obtain of a brown solid 0.31 g. Characterization was not performed as the product was insoluble in organic or inorganic solvents.

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