Synthesis of Water Soluble Hyperbranched Polyurethanes Using Selective Activation of AB_2 Monomers

Steve P. Rannard,* Nicola J. Davis, and Ian Herbert

Unilever Research and Development Port Sunlight, Quarry Road East, Bebington, Wirral, CH63 3JW, United Kingdom

Received June 1, 2004; Revised Manuscript Received October 1, 2004

ABSTRACT: The synthesis of a novel water-soluble hyperbranched polyurethane is described. The synthetic strategy involves a new approach to hyperbranched polymerization through the selective activation of the A functionality of the unprotected of AB_2 monomer. 1,1′-Carbonyl diimidazole is added at room temperature to an amino-diol monomer with the corresponding selective formation of an active carboxamide and no detectable reaction at the hydroxyl B functional groups. The active monomer self-condenses to form hyperbranched polyurethanes with measured degrees of branching equaling 0.6 and M_n up to 11 000 Da. A series of model reactions has been conducted to confirm the polymerization mechanism, and ideally branched model molecules have been used to assign the ^{15}N NMR spectra of the hyperbranched polymers. Reaction conditions have been varied, and the factors affecting the polymerization are discussed.

Introduction

The introduction of branching into linear polymers has been the subject of intensive study by many groups for the last two decades. Specifically, structures with ideal, controlled branching such as dendrimers,[1,2] dendronized linear hybrid materials containing dendrons attached to linear polymer chains,[3,4] and statistically branched or hyperbranched polymers[5,6] have received significant attention, and a number of chemistries have been synthesized and reported.

Highly branched polyurethanes are problematic to synthesize due to the inherent difficulty in controlling the reactive chemistry that is typically used during the production of linear materials. Very few examples of ideal branching in polyurethanes have been reported with Spindler and Fréchet[7] being the first to demonstrate the synthesis of aromatic urethane dendrimers, with an alternating ether−urethane layer structure, using a convergent growth approach. Alternating aromatic−aliphatic urethane dendrimers, also containing ether links, have been synthesized by Taylor and Puapaiboon[8,9] using a modified Curtius reaction. The synthesis of aliphatic branched polyurethanes has been published by Clark et al.,[10] but only the first generation dendrimer was reported due to the complex divergent synthesis used. Aliphatic dendrimers with alternating urethane−urea links have been described up to the second generation by Peerlings et al using a novel AB−CD_2 approach, directly from a bisisocyanate AB monomer with differential reactivity.[11]

Very recently, we have reported the synthesis of the first true aliphatic homodendrimers up to the fourth generation, where the repeating structure is completely conserved from the central branching amine through to the surface groups.[12] Our convergent growth strategy relied upon the selective reaction of imidazole carboxylic esters, derived from the reaction of 1,1′-carbonyl diimidazole (CDI) and secondary alcohols, with the primary amine functionality of a new diamino-alcohol AB_2 monomer. This approach was similar to our earlier reported synthesis of polycarbonate dendrimers,[13] where the selectivity of imidazole carboxylic esters was important in directing reaction at the primary hydroxyls of a triol containing one secondary and two primary hydroxy groups.

Hyperbranched polyurethanes were also first reported by Spindler and Fréchet[14] using thermally labile blocked isocyanates. The AB_2 monomers contained a free benzyl alcohol A functionality and two phenol carbamate B groups that liberated isocyanate on refluxing in THF. Kumar and Ramakrishnan[15] have also used thermal decomposition to generate active functionality and form hyperbranched polyurethanes. In this case, 3,5-dihydroxy benzoyl azide, in the presence of catalyst at 110 °C, liberated the dihydroxy isocyanate that polymerized in 95% yield. Azide chemistry has also been utilized by Tang and co-workers[16] to form alternating ether−urethane hyperbranched polymers using a very similar strategy. More recently, Bruchmann et al. have developed a commercially viable process using the selective reaction of hindered isocyanates in a self-cross-linking reaction to form hyperbranched polyurethanes on an industrial scale.[17]

Our recent reports of reactions with carbonyl imidazole containing compounds have demonstrated the highly selective formation of urethanes,[18] carbonates,[19] and amides[18] without the need to use protection/deprotection strategies. These techniques have been used successfully to synthesize aliphatic polyamide,[20] polyurethane,[12] and polycarbonate dendrimers[13] by reacting CDI with the single focal point functionality of a dendron in convergent growth strategies. The introduction of the carbonyl imidazole group therefore has been achieved with great success, in conditions where the possibility of side reactions with other functional groups has been removed. In this study, we report the use of CDI in the selective activation of unprotected AB_2 monomers and their subsequent polymerization to form a novel class of water-soluble hyperbranched polyurethanes.

* Corresponding author. E-mail: steven.rannard@unilever.com.

10.1021/ma0489218 CCC: $27.50
Published on Web 11/17/2004

Experimental Procedures

Materials. All reagents and solvents (Aldrich Chemical Co., UK) were used as received. In all cases, the highest available purity (usually >99%) of each reagent was used. HPLC grade toluene (<0.03% v/v H_2O) and HPLC grade THF (<0.02% v/v H_2O) were used as solvents.

Characterization. ^1H, ^{13}C, and ^{15}N NMR measurements were conducted using a Bruker 300 MHz spectrometer. Mass spectrometry was conducted using either atmospheric pressure ionization (API-MS) or time-of-flight-matrix assisted laser desorption ionization (TOF-MALDI). API-MS and HPLC-MS were conducted using flow injection analysis comprised of a Hewlett-Packard 1050 series pump and autosampler linked to a VG Platform II spectrometer. TOF-MALDI was achieved using either a Kratos Kompact MALDI IV instrument operating in linear mode or a Bruker BIFLEX III TOF-MALDI instrument operating with continuous gridless extraction in the linear mode. All MALDI experiments were achieved using a gentisic acid (DHB) matrix. HPLC-ELSD was conducted using a Hewlett-Packard 1090 series chromatograph with an ACS 750/14 evaporative light scattering detector (ELSD).

Synthesis of Imidazole Carboxamide of 1-Ethylpropylamine (4). A solution of 1-ethylpropylamine (EPA, **3**) (1.08 g, 12.33 mmol) in toluene (10 mL) was added dropwise to a stirred mixture of 1,1′-carbonyl diimidazole (CDI) (2.00 g, 12.33 mmol) and toluene (50 mL). The reaction was stirred at room temperature and became clear in less than 1 min. The clear solution was left to stir overnight. The crystallized solid imidazole that formed was removed by filtration, and the filtrate was concentrated in vacuo. The residue was dissolved in CH_2Cl_2, washed three times with water, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to give the carboxamide **4** as a colorless liquid (87.4%). ^1H NMR ($CDCl_3$): 0.96 (CH_2-C***H***$_3$), 1.57 (C***H***$_2$-CH_3), 3.80 (CH_2-C***H***-CH_2), 7.00 (imidazole, CH=C***H***−N=CH), 7.71 (imidazole, C***H***=CH−N=CH), 8.21 (N***H***-CO-Imid), 8.32 (imidazole, N−C***H***=N); ^{13}C NMR ($CDCl_3$): 10.66 (CH_2-***C***H_3), 27.43 (***C***H_2CH_3), 54.98 (CH_2-***C***H-CH_2), 116.95 (imidazole, CH=***C***H−N=CH), 129.40 (imidazole, ***C***H=CH−N=CH), 136.37 (imidazole, CH=CH−N=***C***H), 149.43 (NH-***C***O-Imid); *m/z* (API-MS) 182.35 (MH^+).

N,N′*-Bis(1-ethylpropyl)urea (5).** A solution of EPA **3** (2.15 g, 24.66 mmol) in toluene (10 mL) was added dropwise to a stirred mixture of CDI (2.00 g, 12.33 mmol) and toluene (50 mL). The reaction was stirred at room temperature and became clear in less than 1 min. The clear solution was left to stir overnight. The crystallized solid imidazole that formed was removed by filtration and dried (1.67 g, 24.53 mmol. 99.5% yield of byproduct). The filtrate was concentrated in vacuo, and the residue was dissolved in CH_2Cl_2, washed three times with water, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to give the urea **5** as a colorless solid (43.7%). ^1H NMR ($CDCl_3$): 0.94 (CH_2-CH***$_3$), 1.29−1.61 (C***H***$_2$-CH_3), 3.54 (CH_2-C***H***-CH_2), 4.96 (N***H***-CO-N***H***); ^{13}C NMR ($CDCl_3$): 10.57 (CH_2-***C***H_3), 28.38 (***C***H_2CH_3), 52.92 (CH_2-***C***H-CH_2), 159.26 (NH-***C***O-NH); *m/z* (API-MS) 201.47 (MH^+).

Cyclic Carbamate of 2-Amino-2-methyl-1,3-propanediol (7). 2-Amino-2-methyl-1,3-propanediol **1** (1.00 g, 9.5 mmol) was added dropwise over 15 min to a cooled (0 °C), stirred mixture of CDI (1.55 g, 9.5 mmol) and THF (30 mL). The mixture was stirred at 0 °C for a further 4 h and then allowed to warm to room temperature. The clear reaction mixture was concentrated in vacuo, and the residue was dissolved in CH_2Cl_2, washed three times with water, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to give the cyclized carbamate as a colorless liquid (99.7%). ^1H NMR ($CDCl_3$): 1.21 (CR_3-C***H***$_3$), 3.52 (C***H***$_2$-OH), 4.02 (CH***H***-O), 4.41 (C***H***H-O-); ^{13}C NMR ($CDCl_3$): 22.74 (CR_3-***C***H_3), 59.48 (***C***R_3), 67.18 (***C***H_2-OH), 73.46 (***C***H_2-O), 160.52 (***C***=O).

Asymmetric Urea of 1-Ethylpropylamine and *N*-(3-Aminopropyl)-diethanolamine (9). The asymmetric urea **9** was synthesized through two different routes; route 1: a solution of *N*-(3-aminopropyl)-diethanolamine **2** (1.00 g, 6.16 mmol) in THF (20 mL) was added dropwise to a stirred mixture of CDI (1.00 g, 6.16 mmol) in THF (30 mL). The mixture was stirred at room temperature for 20 h forming carboxamide **8** that was not isolated. 1-Ethylpropylamine (0.54 g, 6.20 mmol) was added to the mixture, and the reaction was heated to 60 °C for 6 h and allowed to cool to room temperature. The reaction mixture was concentrated in vacuo, and the residue was dissolved in CH_2Cl_2, washed three times with water, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to give the urea **9** as a colorless gum (99.5%). Route 2: 1-ethylpropylamine (0.54 g, 6.16 mmol) was added dropwise to a stirred mixture of CDI (1.00 g, 6.16 mmol) in THF (50 mL). The reaction was stirred at room temperature for 20 h forming carboxamide **4**, which was not isolated. *N*-(3-Aminopropyl)-diethanolamine **2** (1.00 g, 6.16 mmol) was added, and the reaction mixture was stirred at room temperature for a further 18 h. The reaction mixture was concentrated in vacuo, and the residue was dissolved in CH_2Cl_2, washed three times with water, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to give urea **9** as a colorless gum (99.3%) Analysis for urea **9** was identical through routes 1 and 2: ^1H NMR (CD_3OD): 1.09 (CH_2-C***H***$_3$), 1.42−1.87 (-C***H***$_2$-), 2.78 (C***H***$_2$-N), 3.37 (C***H***$_2$−NHC=O), 3.67 (CH_2-C***H***-CH_2), 3.85 (C***H***$_2$-OH), 6.17 (N***H***-CO-N***H***); ^{13}C NMR (CD_3OD): 11.29 (CH_2-***C***H_3), 22.95 and 29.46 (-***C***H_2-), 39.91 (***C***H_2−NHC=O), 54.26 (***C***H_2N), 54.35 (***C***H), 57.99 (N***C***H_2), 61.10 (***C***H_2OH), 161.73 (NH-***C***O-NH).

Symmetric Urea of *N*-(3-Aminopropyl)-diethanolamine (10). *N*-(3-Aminopropyl)-diethanolamine **2** (1.62 g, 10.00 mmol) was added to a stirred mixture of CDI (0.81 g, 5.00 mmol) in THF (50 mL). The mixture was stirred at room temperature for 24 h and concentrated in vacuo. The crude residue was analyzed by NMR spectroscopy for evidence of carbonate, urethane, or urea formation: ^1H NMR (CD_3OD): 1.82 (CH_2-C***H***$_2$-CH2), 2.63−2.82 (NC***H***$_2$-), 3.35 (C***H***$_2$−NHC=O), 3.82 (C***H***$_2$-OH), 5.92 (N***H***-CO-N***H***); ^{13}C NMR (CD_3OD): 29.04 (CH_2-***C***H_2-CH_2), 40.18 (***C***H_2−NHC=O), 54.39 (***C***H_2N), 58.07 (N***C***H_2), 61.05 (***C***H_2OH), 161.59 (NH-***C***O-NH). Signals for the imidazole byproduct were also present.

G1 Dendron—^{t}BOC Protected 1-[*N,N*-Bis(2-hydroxyethyl)amino]-2-propanol (12). The synthesis of the G1 dendron has been previously reported.[6,11] Analytical data: ^1H NMR ($CDCl_3$): 1.11 (CH(OH)-C***H***$_3$), 1.48 (C(C***H***$_3$)$_3$), 2.56−2.95 (N-C***H***$_2$), 3.34 (CH(O***H***)CH_3), 3.73 (C***H***(OH)), 4.12 (C***H***$_2$−OC=O). ^{13}C NMR ($CDCl_3$) 20.36 (CH-***C***H_3), 28.37 (C(***C***H_3)$_3$), 54.04 (N***C***H_2CH_2), 63.86 (N***C***H_2CH), 64.40 (***C***H(OH)), 65.10 (***C***H_2-OC=O) 82.73 (***C***$(CH_3)_3$), 154.19 (***C***=O). ^{15}N NMR ($CDCl_3$, formamide standard) −91.0 (***N***$(R)_3$); *m/z* (API-MS) 364.63 (MH^+), 386.58 (MNa^+).

G2 Dendron (13). The synthesis of the G2 dendron has been previously reported.[6] Analytical data: ^1H NMR ($CDCl_3$) 1.16 (CH(OH)-C***H***$_3$), 1.29 (CH-C***H***$_3$), 1.55 (C(C***H***$_3$)$_3$), 2.52−2.92 (N-C***H***$_2$), 4.01−4.23 (C***H***(OH) and C***H***$_2$−OC=O), 4.84 (C***H***−OC=O). ^{13}C NMR ($CDCl_3$) 20.16 (CH-***C***H_3), 21.98 (***C***H_3CH-(OH)), 30.00 (C(***C***H_3)$_3$), 55.83 (N***C***H_2CH_2) 61.95 (N***C***H_2CH), 67.14 (***C***H_2OC=O), 75.82 (***C***HOC=O), 84.08 (***C***$(CH_3)_3$), 155.69 (***C***=O), 157.01 (***C***=O). ^{15}N NMR ($CDCl_3$, formamide standard) −91.0 (***N***$(R)_3$ focal point), −91.5 (***N***$(R)_3$ terminal groups). *m/z* (API-MS) 942.84 (MH^+), 964.43 (MNa^+).

G0 Dendrimer—Tris(urethane) (14). The general synthesis of the GO dendrimer **14** has been previously reported.[10] Analytical data: ^1H NMR ($CDCl_3$) 1.55 (C(C***H***$_3$)$_3$), 2.52 (NH-C***H***$_2$), 3.15 (N-C***H***$_2$), 5.38 (C=ON***H***) ^{13}C NMR ($CDCl_3$) 28.68 (C(***C***H_3)$_3$), 38.78 (NH***C***H_2CH_2) 54.47 (N***C***H_2), 79.38 (***C***$(CH_3)_3$), 156.68 (***C***=O), 157.01 (***C***=O). ^{15}N NMR ($CDCl_3$, formamide standard) −34.1 (***N***HC(=O)O),-86.8 (***N***$(R)_3$). *m/z* (API-MS) 450.64 (MH^+), 472.36 (MNa^+).

G1 Dendrimer—Carbonate—Urethane Layer Copolymer (15). A mixture of G1 dendron **12** (3.00 g, 8.23 mmol), CDI (2.01 g, 12.40 mmol), and KOH (0.2 g, 3.60 mmol) in toluene (20 mL) was heated at 60 °C for 1 h. Tris(2-aminoethyl) amine (0.40 g, 2.74 mmol) was added to the reaction, and the reaction was heated for a further 6 h. The reaction mixture was concentrated in vacuo, and the residue was dissolved in CH_2Cl_2, washed three times with water, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to give the dendrimer **15** as a colorless gum (93.1%) ^1H NMR ($CDCl_3$): 1.21 (CH-C***H***$_3$), 1.47 (C(C***H***$_3$)$_3$), 2.45−2.95 (HN-C***H***$_2$), 3.18 (N-

C***H***$_2$) 4.12 (C***H***$_2$—OC═O), 4.84 (CH_3-C***H***). ^{13}C NMR ($CDCl_3$) 18.53 (CH-***C***H_3), 27.98 (C(***C***$H_3)_3$), 39.17 (***C***H_2NH), 53.97 (N***C***H_2), 60.14 (N***C***H_2, core), 65.29 (***C***H_2OC═O), 82.10 (***C***$(CH_3)_3$), 153.75 (O***C***(═O)O), 156.69 (NHC(═O)O). ^{15}N NMR ($CDCl_3$, formamide standard) −36.2 (***N***HC(═O)O), −86.9 (***N***$(R)_3$), −89.7 (***N***$(R)_3$). *m/z* (API-MS) 1314.60 (MH^+), 1336.70 (MNa^+).

Hyperbranched Polyurethane Synthesis—General Procedure. A solution of *N*-(3-Aminopropyl)-diethanolamine (3.00 g, 18.49 mmol) in THF (30 mL) was added dropwise to a solution of CDI (3.00 g, 18.49 mmol) in THF (45 mL) and stirred at room temperature for 20 h. The reaction mixture was concentrated in vacuo to leave a residue that was heated at 90 °C for 3 h (optionally, a base such as KOH may be added prior to solvent removal). After being cooled to 40 °C, THF (60 mL) was added to the residue and heated at 60 °C for a further 1.5 h. After being cooled to room temperature, the solvent was decanted, and the residue was dried to give the polymer as a pale colorless sticky material. ^{1}H NMR (D_2O): 1.57 (CH_2-C***H***$_2$-CH_2), 2.32−2.86 (N-C***H***$_2$), 3.05 (NH(CH_2)$_2$C***H***$_2$-NR_2), 3.59 (C***H***$_2$-OH), 4.05 (C***H***$_2$—OC(═O)NH); ^{13}C NMR (D_2O): 25.99 (CH_2-***C***H_2-CH_2), 38.27 (H_2N-***C***H_2), 38.89 (***C***H_2—NHC═O), 51.74 and 52.25 (***C***H_2N), 55.34 (N***C***H_2CH_2OH), 58.89 (***C***H_2OH), 62.62 (***C***H_2OC(═O)NH), 158.19 (O-***C***O-NH). ^{15}N NMR (D_2O, formamide standard) −30.38 (***N***HC(═O)O), −80.68 (***N***$(R)_3$ dendritic fragment), −81.00 (***N***$(C_2H_4OH)(R)_2$ linear fragment), −81.24 (***N***$R(C_2H_4OH)_2$ terminal fragment) BF = 0.6. *m/z* (TOF-MALDI) repeat unit 188.23 Da.

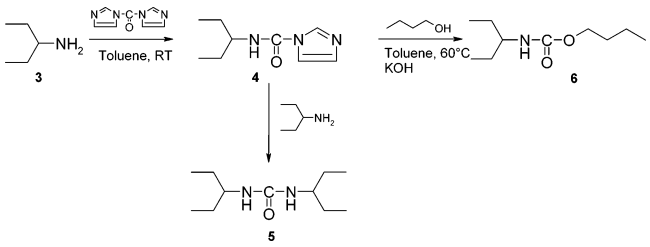
Results and Discussion

Monomer Selection. Previously, we have synthesized urethane containing materials by reacting an alcohol with CDI, to form an imidazole carboxylic ester, followed by subsequent reaction of the intermediate with a primary amine.[12] Suitable AB_2 monomers for polyurethane formation using CDI should therefore contain both primary amines and primary alcohols. Two commercially available monomers were therefore chosen for this study, 2-amino-2-methyl-1,3-propanediol **1** and *N*-(3-aminopropyl)-diethanolamine **2** (ADPE).

Model Studies. 1,1′-Carbonyl diimidazole (CDI) is a well-known coupling agent that may be used to form carbonates, ureas, amides, urethanes, and esters. To maximize the success of coupling reactions using CDI, the formation of the carbonyl imidazole containing reactive intermediates is achieved by simply stirring an amine, acid, or alcohol with CDI in an appropriate solvent with heating and base if necessary. The second reactant, amine or alcohol, may be added directly to the reaction without isolation or purification of the intermediate, and especially in the case of acid imidazolides, it is beneficial to do this as the intermediates are often hydrolytically unstable. However, the synthesis of hyperbranched polymers using conventional AB2 monomers necessarily requires the presence of the two functional groups that will be coupled to give the final polymer. CDI will only be of use for hyperbranched polymer synthesis if it can selectively activate either the A or B groups of the monomer in the presence of the other.

Ideally branched dendrimers are laborious and relatively difficult to synthesize and purify by any of the reported multistep procedures, but the characterization of each stage of growth, either divergent or convergent, is straightforward due to the need to produce only a single structure at each step. In contrast, hyperbranched polymers are usually produced using a single-pot reaction and often require little purification. The characterization of hyperbranched polymers, however, is particularly difficult due to the number of possible branched, linear, and cyclic structures that may be formed and the predominance of analytical techniques that have been developed and optimized for linear polymers. To investigate the use of CDI in hyperbranched polymer synthesis, a series of model reactions have been conducted and a number of model materials have been synthesized to aid assignment of ^{1}H, ^{13}C, and ^{15}N NMR spectra during characterization.

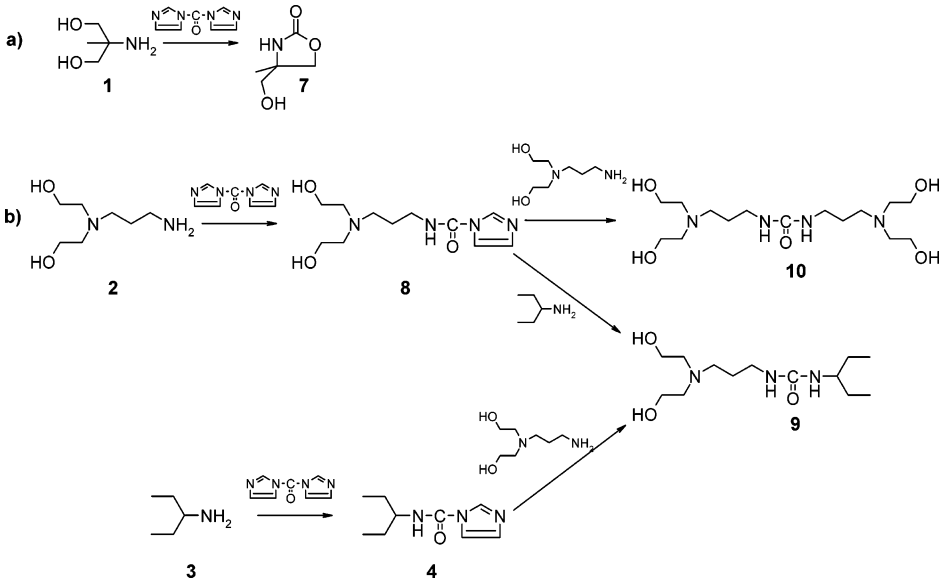
Scheme 1



Model Reactions 1: Urea and Urethane Formation using CDI. The reaction of a primary amine with CDI, and subsequent carboxamide formation, was studied to ascertain differences between amine and alcohol reactivity. Alcohols require heating and base catalysis to aid the formation of imidazole carboxylic esters.[19] To evaluate primary amine reactivity, a branched amine, 1-ethylpropylamine **3** (EPA), was added slowly to a suspension of CDI in toluene at ambient temperature with gentle stirring (Scheme 1). The reaction became completely clear after less than 1 min, indicating rapid consumption of CDI as it is not soluble in toluene. The reaction was exothermic and was left to cool overnight with stirring. If the reaction is conducted on a 1:1 (EPA/CDI) molar ratio, the reaction forms the isolated carboxamide **4** in high recovered yield (87.4%). Purification of the reaction was accomplished through filtering the crystallized imidazole followed by removal of solvent by rotary evaporation, being redissolved in dichloromethane, and being washed with water. Confirmation of carboxamide formation was accomplished through ^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectroscopy ($CDCl_3$), with a characteristic carboxamide carbonyl signal at 149.43 ppm (^{13}C NMR), the shift of the methine proton signal to 3.80 ppm (^{1}H NMR), the presence of three distinct imidazole ring proton singlets at 7.00, 7.71, and 8.32 ppm, and a doublet at 8.21 ppm corresponding to the carboxamide NH proton. Any free imidazole byproduct can be identified as it only exhibits ^{1}H NMR signals for two imidazole ring proton environments at 7.10 and 7.69 ppm. This is due to the rapid proton exchange between the two ring nitrogens that leads to the delocalization of the C═N double bond and the subsequent equivalence of the protons associated with the C═C double bond.

Increasing the ratio of EPA/CDI to 2:1, following the same synthetic procedure, gave the symmetric urea **5** at room temperature with a recovered yield of 43.7%. The imidazole that crystallizes during cooling was collected, dried, and weighed and indicated a 99.5% formation of the insoluble byproduct suggesting that much of the symmetrical urea had been lost during purification. Confirmation of urea formation was also accomplished through ^{1}H and ^{13}C NMR spectroscopy ($CDCl_3$), with a characteristic carbonyl signal at 159.26 ppm (^{13}C NMR), movement of the methine proton signal to 3.54 ppm (^{1}H NMR), and the appearance of a doublet at 4.96 ppm corresponding to the two urea NH protons.

Scheme 2



The formation of a urethane from **4** was demonstrated through the addition of 1-butanol to **4** with a catalytic amount of KOH followed by heating at 60 °C for 6 h. After purification, urethane **6** was readily isolated (58%) and characterized as previously described,[18] with a characteristic ^{13}C NMR ($CDCl_3$) carbonyl resonance at 157.14 ppm.

The reaction of carboxamides to give ureas and urethanes may proceed via the elimination of imidazole and subsequent isocyanate formation (i.e., the carboxamide is a blocked isocyanate). The recovery and purification of carboxamide **4** does suggest that these materials are relatively stable, however, and the formation of the isocyanate intermediate therefore may require specific conditions such as the presence of base or heating to induce reactivity.[22]

Model Reactions 2: Selective Reaction of CDI with the Primary Amines of Amino Alcohols. Having established the reactivity of a model primary amine with CDI and subsequent urethane formation, the selective generation of the carboxamides of **1** and **2** was studied. The carboxamides are generated in the presence of two primary hydroxyl groups, and the prevention of urethane formation will be extremely difficult during isolation and purification. By reacting the carboxamides that are formed with EPA, we aimed to trap them as the asymmetric urea and confirm the selective reaction of CDI with the primary amine functional group alone. Carbonate and urethane formation are indicative of the reaction of CDI with the primary hydroxyl groups to form an imidazole carboxylic ester and subsequent reaction with another hydroxyl group or EPA. First, **1** was added dropwise to a suspension of CDI in THF at 0 °C and stirred for 4 h. EPA was added to the mixture, and the reaction was allowed to warm to room temperature. After purification, a cyclized urethane **7** was isolated in very high yield (99.7%). This result was also achieved when **1** was added to CDI and allowed to stir without added EPA. The cyclization of **1** was not entirely unexpected as we have seen cyclic carbonate formation when reacting 1,2-diols in previous studies.[19] The formation of a cyclic urethane is probably also due to the 1,2-substitution of the amine and alcohol favoring ring closure after carboxamide formation.

Treatment of **2** in a similar procedure, however, gave the asymmetric urea **9** in high yield after purification (99.3%) (Scheme 2). The crude product mixture was analyzed in detail using ^{13}C and ^{1}H NMR spectroscopy (CD_3OD). A single carbonyl signal corresponding to urea formation was observed at 161.73 ppm, and no detectable carbonyl or proton signals corresponding to carbonate or urethane formation could be seen. To ensure correct assignment of the NMR spectra of **9**, it was also synthesized in high yield (99.5%) through reaction of EPA **3** with CDI followed by addition of **2** to the resulting carboxamide. Again, a single carbonyl signal at 161.73 ppm was observed, confirming the previous assignment. To check that symmetric urea formation was not hindered or unfavorable when using **2**, a reaction containing a 2:1 ratio of **2** to CDI was conducted at room temperature for 2 h, and the crude reaction mixture was evaporated and analyzed using ^{13}C and ^{1}H NMR (CD_3OD). The crude mixture showed exclusive formation of the symmetric urea **10**, with no evidence of residual carboxamide or unwanted urethane synthesis. The carbonyl region of the ^{13}C NMR spectrum showed a single signal at 161.59 ppm, while the ^{1}H NMR spectrum showed accurate integrals confirming the structure, a single signal for the urea NH protons at 5.89 ppm, and the presence of free imidazole. The synthesis of **10** through this facile procedure dramatically demonstrates the selectivity of carboxamide formation and the subsequent selectivity of the carboxamide for reaction with amines in the presence of hydroxyl groups.

The selectivity and reactivity of the carboxamide of **2** suggests potential problems in the use of this AB_2 monomer in hyperbranched polyurethane synthesis using CDI. The CDI/APDE stoichiometry must be kept as close to 1:1 as possible to ensure a very high conversion of amine to carboxamide. If residual amine is present after CDI consumption, the symmetrical urea **10** will be formed, leading to the uncontrolled introduction of a core terminator into the polymerization and low molecular weight polymers being formed. Excess CDI, however, would guarantee complete carboxamide formation but could also lead to carbonate groups in the final polymer through the unwanted coupling of hydroxyls with the excess CDI.

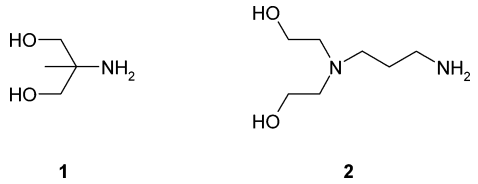


Figure 1. AB_2 monomers chosen for hyperbranched polyurethane study.

Model Materials: ^{15}N NMR Investigation of Model Branched Materials. CDI has therefore been shown to react selectively with APDE **2** to form the carboxamide in the presence of the primary hydroxyl groups. Self-condensation of the active intermediate **8** would lead to a highly branched polyurethane, but characterization of this material will be hampered by the distribution of structures and molecular weights that are generated during this uncontrolled reaction. ^{15}N NMR is the most appropriate technique to determine the degree of branching of these hyperbranched polyurethanes and has been shown to be effective in previous studies.[21] To aid the assignment of the ^{15}N NMR spectra, a number of model materials have been synthesized and analyzed, along with APDE **2** and 1-[*N*,*N*-bis(2-hydroxyethyl)amino]-2-propanol **11** (Figure 2).

^{15}N NMR spectroscopy was either carried out in D_2O (**2**) or $CDCl_3$ (**11**−**15**) using formamide as reference, 27 μs (90°) excitation pulses, and a relaxation delay of 10s. APDE **2** was analyzed using various ^{15}N NMR conditions including no proton decoupling, broadband decoupling, inverse-gated proton decoupling, and gated proton decoupling. In all cases, signals arising from the primary and tertiary amines were present at −74 and − 87 ppm, respectively, and broadband decoupling was chosen as the standard condition for analysis of further samples. The carbonate dendrons **12** and **13** were synthesized using **11** as previously reported[13] and analyzed to investigate the effect of branching on the ^{15}N shift of the tertiary nitrogen atom. A shift of 0.5 ppm from −90.5 to − 91 ppm was observed when the two primary alcohols of **11** were reacted. Forming the second-generation dendron showed no change in the shift for the tertiary nitrogen at the focus of the wedge (−91 ppm), but a further shift in the nitrogen at the surface branch was seen (−91.5 ppm). As there are no urethane links within **12** and **13**, the urethane **14** and urethane-carbonate copolymer **15** were also synthesized following reported methods[12] and analyzed to determine the position of the urethane nitrogen signal and to ascertain whether the presence of urethane groups would further

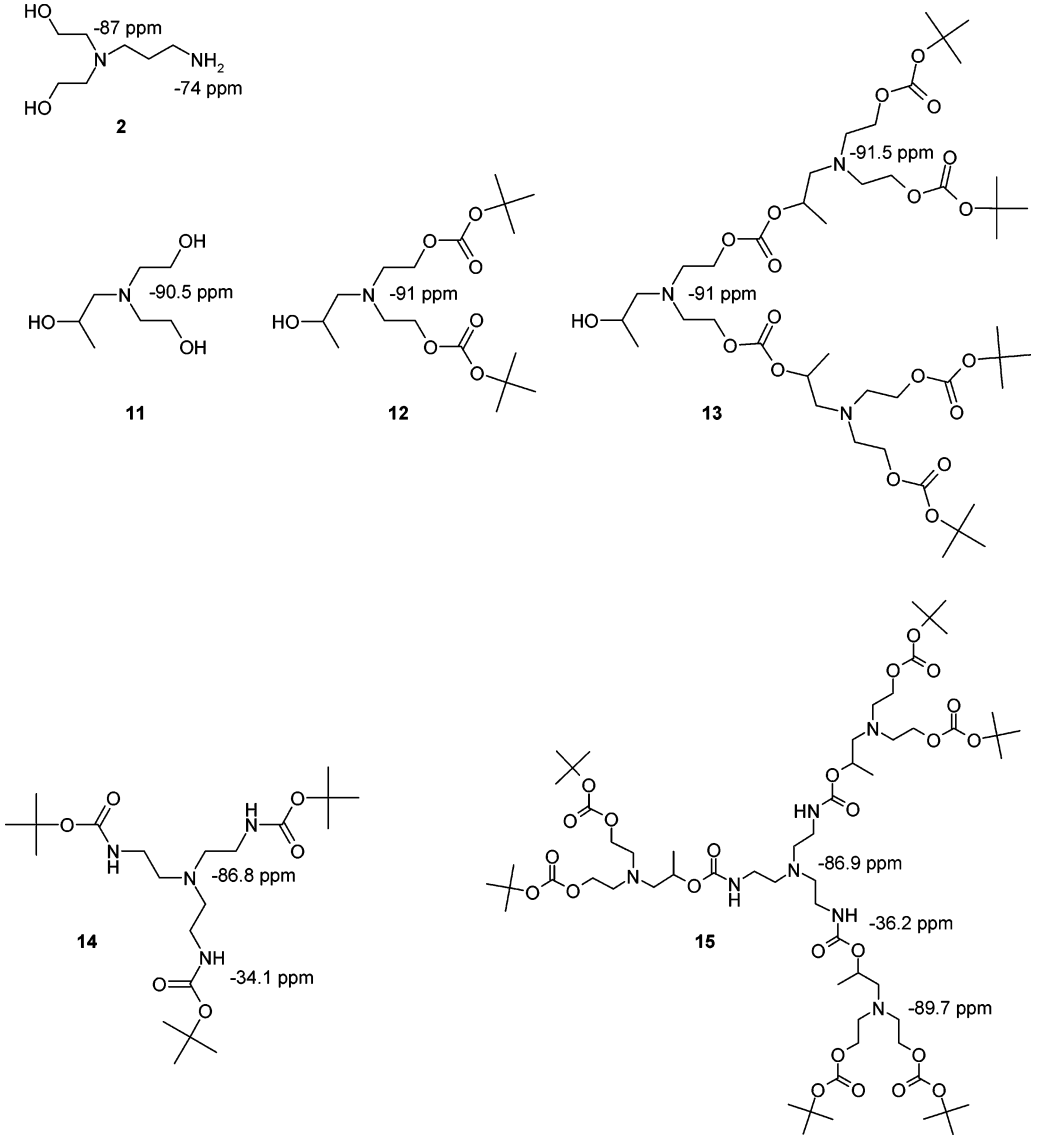
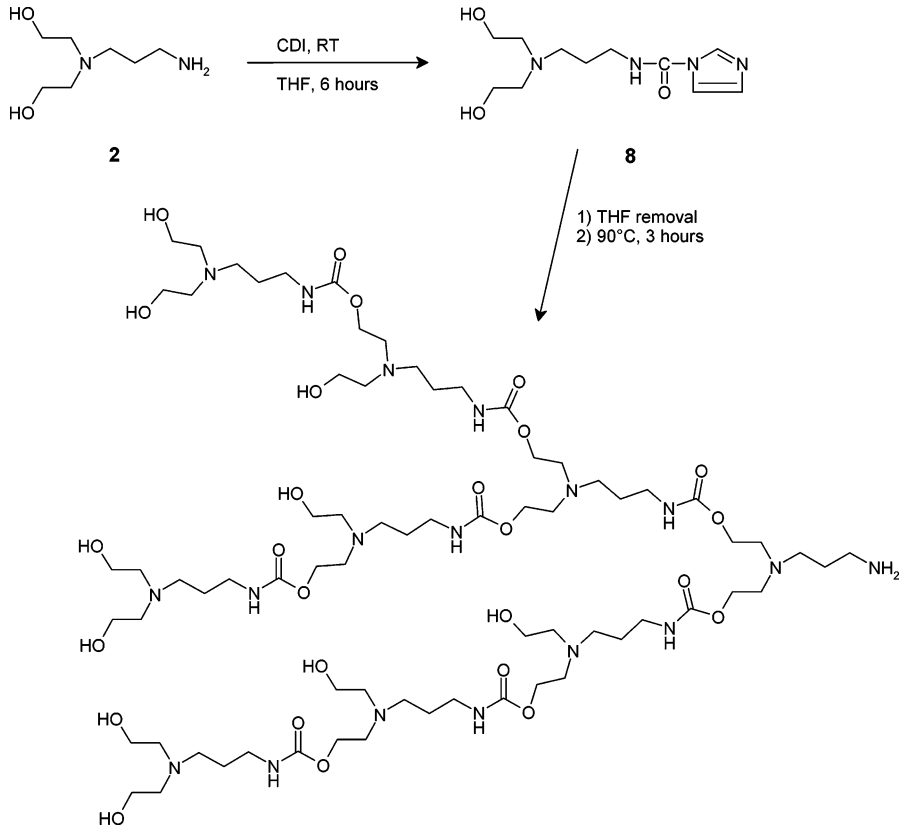


Figure 2. Model materials and the assignment of the broadband proton decoupled ^{15}N NMR signals (relative to formamide).

Scheme 3



shift the ^{15}N signal for the tertiary nitrogen of the branching unit. Compound **15** is derived from the reaction of **12** with tris(2-aminoethyl) amine, and any further shift changes of the tertiary nitrogen of the dendron **12** from −91.5 ppm in **13** can be related directly to the presence of the urethane group. The urethane NH signal was observed at −34.1 ppm and was confirmed as the NH through ^{15}N DEPT experiments. Compound **14** showed a single peak corresponding to the central tertiary nitrogen atom at −86.8 ppm, which is significantly shifted from any of the nitrogen signals of **11**−**13** (possibly due to hydrogen bonding) but very similar to that of the tertiary nitrogen of **2**. Interestingly, the copolymer **15** showed two distinct ^{15}N signals for the two different tertiary nitrogen environments (−86.8 ppm = tris urethane core, −89.7 ppm = urethane-bis carbonate surface). The difference between the shifts of the surface nitrogens of **13** and **15** of approximately 2 ppm suggests that the presence of urethane groups has a significant effect on the position of the ^{15}N signal. The 3−5 ppm difference between these peaks and the core nitrogen of **14** and **15** suggests that the number of urethanes in proximity to the nitrogen also has a significant effect.

This investigation of model compounds led us to expect measurable ^{15}N NMR differences for the tertiary nitrogens present within the linear, dendritic, and surface groups of the hyperbranched polyurethanes derived from **2**.

Synthesis and Characterization of Hyperbranched Polyurethanes Derived from APDE 2. The procedure for APDE **2** polymerization is a facile two-step process. The first step involves carboxamide synthesis and can be achieved through the dropwise addition of a THF solution of **2** to a stirred suspension of CDI in THF at room temperature. After continued stirring, the second step involves the removal of solvent, usually by rotary evaporation, followed by a melt polymerization of the residue at 90 °C for several hours (Scheme 3). Purification is achieved by stirring at 60 °C in THF to remove the imidazole byproduct. These hyperbranched polyurethanes are very water soluble and dissolved rapidly at neutral pH.

Degree of Branching Determination. The degree of branching in hyperbranched polymers is often considered the most fundamental factor that may be determined, and it is crucial to the confirmation of the hyperbranched structure and the nature of the polymerization. Deviations from the statistical degree of branching (DB = 0.49) for AB_2 monomers suggests that the mechanism is encouraging the branching process, but values lower than the theoretical value suggest that branching during polymerization is hindered and a significant fraction of linear segments are produced in the structure.

The study of model materials by ^{15}N NMR spectroscopy showed significant differences between branched nitrogen environments, and a study of hyperbranched polyurethanes was conducted using room-temperature overnight signal acquisition in D_2O (50% v/v solution of polymer), broadband proton decoupling, and a pulse width of 15 μs and a 3 s relaxation delay (formamide standard). Under these conditions, two signals were observed at −30.38 ppm (assigned as the urethane -NH) and −81.00 ppm (Figure 3 ; low molecular weight sample: M_n (NMR) = 920; DP = 5; conversion (calcd) = 73.6%).

Expansion of the signal at −81.00 ppm showed three distinct peaks at −80.68, −81.00, and −81.24 ppm. This grouping of signals was assigned using guidance from the model molecules. The tertiary amines of the terminal groups of structures **13** and **15** have ^{15}N NMR

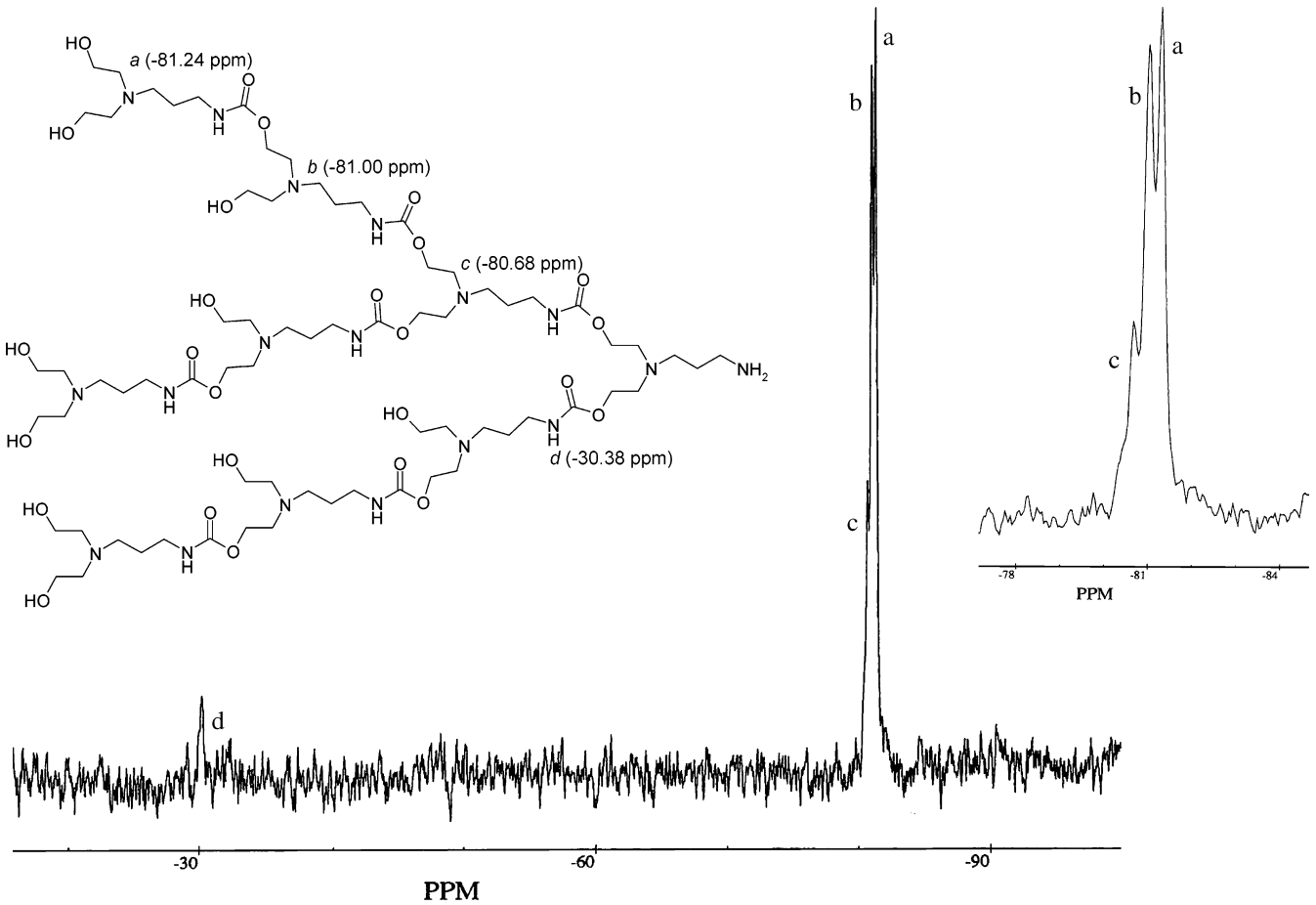


Figure 3. ^{15}N NMR spectrum of the hyperbranched polyurethane of APDE and expansion of the tertiary amine signal to showing branching. (Sample details: DP = 5; M_n (^{1}H NMR) = 920; conversion (calculated) = 73.6%.)

signals at significantly lower values than either the linear equivalent structure (focal point) within **13** or the dendritic equivalent structure (the core) of **15**. This suggests that the signal at −81.24 ppm of the hyperbranched polyurethane is indicative of the terminal units of the polymer. The dendritic core unit of **15** has a much larger shift from the terminal groups (2.8 ppm) than that shown between the terminal and the linear focal group of **13** (only 0.5 ppm). This suggests that the signal at −81.00 ppm may be assigned to the linear units and the signal at −80.68 ppm to the fully branched dendritic units. This assignment is also supported by the approximate 1:2:2 ratio of the integrals of the three signals (dendritic/linear/terminal) for the low molecular weight (DP = 5) sample shown in Figure 3 as it is not possible to generate more dendritic than terminal groups.

Although the conditions that the ^{15}N NMR spectra acquired were not completely quantitative, the integration of the three tertiary amine signals repeatedly gave a degree of branching approximately equal to 0.6 over a series of samples. This suggests that the synthesis is allowing more branching than would be expected from the statistical reaction of an AB_2 monomer although the reason for this is unclear. The formation of the first urethane at the terminal hydroxyl, however, may activate the second hydroxyl group through hydrogen bonding between the carbonyl group of the urethane and the second -OH. This may enhance the nucleophilicty of the remaining hydroxyl of linear units and favor reaction with the focal carboxamide over terminal groups.

^{1}H NMR Calculations of Conversion and Number Average Molecular Weight (M_n). The determination of conversion and number average molecular weight (M_n) has been achieved using ^{1}H NMR (D_2O). Spectra were acquired on crude samples to ensure analysis of the full reaction mixture at the end of the reaction. Imidazole was present during the analysis, but the signals from this impurity do not interfere with those assigned to the hyperbranched polyurethane. There are four distinct signals in the ^{1}H NMR spectra that are unaffected by overlap with neighboring signals or imidazole byproduct (Figure 4; M_n (^{1}H NMR) = 2980; DP = 16; conversion (calcd) = 91%) and are indicative of key features of the polymerization. The number of amines present at the beginning of the reaction is easily determined from the ^{1}H NMR as it may calculated using either of two distinct methylene signals at δ = 1.57 and 3.04 ppm that stay significantly unchanged, and free of overlap with other signals, after polymerization. These are assigned to the central methylene of the propyl chain between the primary and tertiary amines (signal b, Figure 4) and the methylene closest to the tertiary amine (signal d, Figure 4), respectively, and as these are numerically equivalent, they can both be used to minimize error during calculation. The number of amines that have successfully reacted to form urethane groups is also equal to the number of hydroxyl groups that have reacted, and a distinct signal at δ = 4.05 ppm with no overlap has been assigned to the CH_2-OCONH group (signal a, Figure 4). Using the integrals of these signals, it is possible to determine the extent of reaction (or conversion) during each polymerization through a

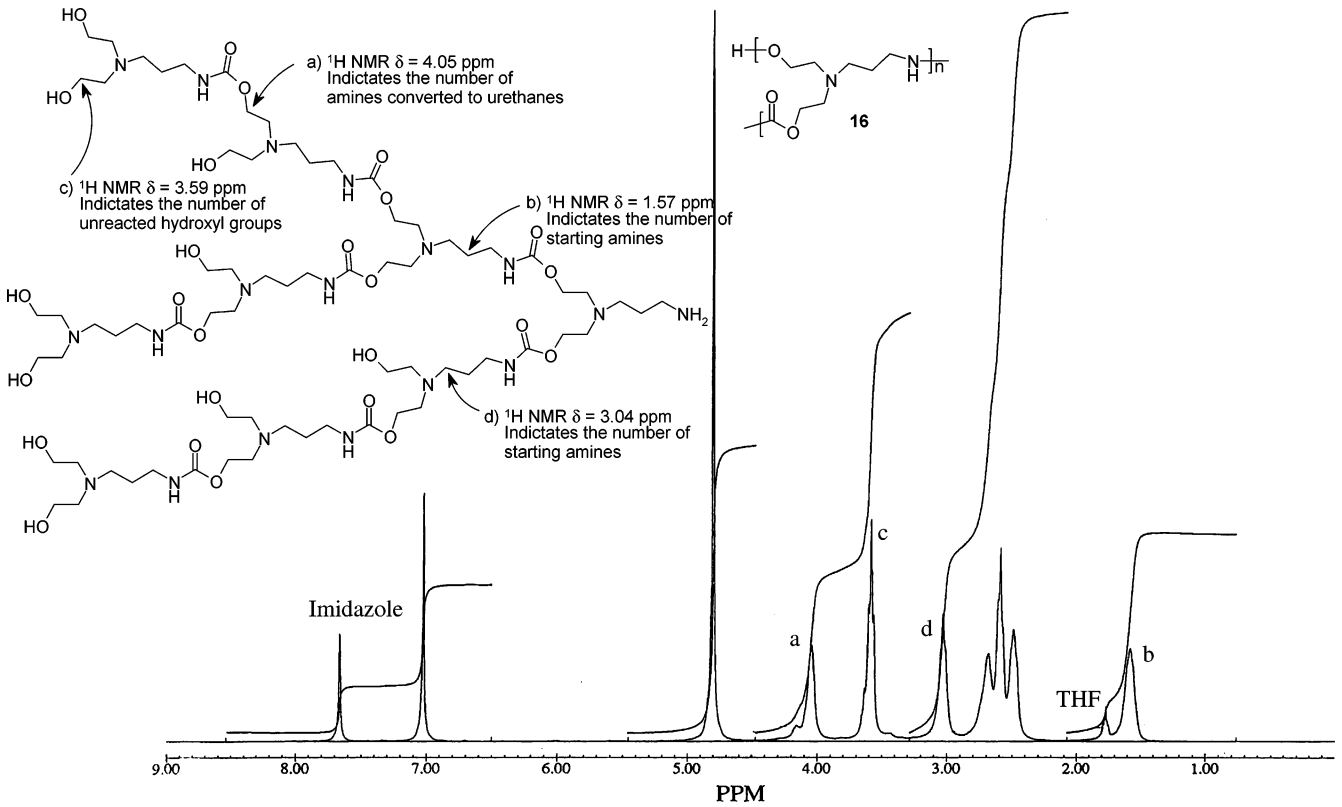


Figure 4. Crude ^{1}H NMR spectrum (D_2O) of the hyperbranched polyurethane of APDE. Assignments and repeat structures used to calculate conversion and M_n are also shown. (Sample details: DP = 16; M_n (^{1}H NMR) = 2980; conversion (calculated) = 91%.)

simple ratio a/b (or a/d). In a typical reaction, it has been possible to achieve conversions of up to 98%, although we have found that the reaction conditions are important to achieve high conversion as will be discussed later.

The end methylene of the propyl group closest to the urethane nitrogen overlaps with other signals and cannot be used directly for conversion or M_n calculation. This is also true for the focal point methylene; therefore, it is difficult to directly calculate M_n from the ^{1}H NMR. The number average degree of polymerization (DP_n) is, however, related to the average number of unreacted B functional groups per polymer, through the simple expression $B_n = DP_n + 1$. To calculate B_n, it is important to know the total number B groups present (signal c, Figure 4) and the number of polymer molecules formed during the polymerization. Care must be taken when integrating signal c as residual THF overlays with this peak. The residual THF can be accurately calculated from the signal at $\delta = 1.8$ ppm and used to accurately determine the correction to the signal c integration. As the ^{1}H NMR signal for the focal point is hidden among other signals, it is necessary to calculate the number of unreacted focal amines that are theoretically present and therefore the number of polymer molecules within the sample. It is possible to do this for the polymers in this study as the signals d and b (Figure 4) correspond to the number of starting amines, and signal a corresponds to the number of amines that have reacted. The relationship $DP_n = (c/(d - a)) - 1$ can then be used to give the number average degree of polymerization.

DP_n can be easily converted into M_n through a simple relationship M_n = (mass of repeat × DP_n) + (DP_n + 1) − 27 Da. This relationship is specific to the hyperbranched polyurethanes of this study and reflects the specific chemistry that is present within the polymer with an idealized repeat mass = 187.23 Da (**16**, Figure 4). Compound **16** is not the traditional descriptive structure used to represent hyperbranched polymers but the structure required to determine the repeat unit mass used above to calculate M_n. The function (DP_n + 1) compensates for the number of protons that need to be added to this idealized repeat structure at the terminal groups, and the subtraction of 27 Da is a correction for the lack of one carbonyl group at the terminal monomer repeat unit. Using this approach, M_n values up to 9000 Da have been determined from the ^{1}H NMR spectra of the polymers.

Mass Spectrometry and ^{13}C NMR Investigations. Matrix assisted laser desorption ionization spectrometry (TOF-MALDI) and ^{13}C NMR (D_2O) have been used to analyze the mechanism of the polymerization. The model experiments showed no urea or carbonate formation when CDI was added to APDE and exclusive formation of the carboxamide at the primary amine group. In almost all cases, the hyperbranched polyurethanes that were formed showed a single carbonyl signal in the ^{13}C NMR spectra at $\delta = 159.16$ ppm, supporting the mechanism described previously. In a number of cases, however, although the ^{1}H NMR has shown no evidence of unwanted reactions, there have been extra minor signals within the ^{13}C NMR (D_2O) spectra that indicate urea ($\delta = 161.08$ ppm) or carbonate ($\delta = 156.69$ ppm) coupling. Carbonate coupling was very rare and only seen at an extremely low concentration, but urea coupling was seen repeatedly over a number of samples (Figure 5).

Urea formation suggests that structures analogous to **10** are being formed in the early stages of the polymerization, probably during the formation of the activated

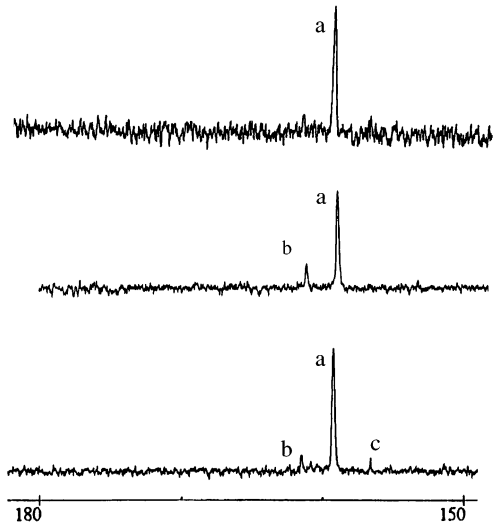


Figure 5. ^{13}C NMR spectra (carbonyl region) of hyperbranched polyurethanes showing urethane (a), urea (b), and carbonate (c) signals.

APDE **8**. This would occur if the stoichiometry of the reaction is not accurately maintained and there is either an excess of APDE or the CDI being added is not of high purity. A study of the purity of CDI was undertaken, and a number of samples from different batches, as received from the supplier, were studied using gas chromatography coupled to mass spectrometry (GC-MS) and ^1H NMR. As CDI is water sensitive, the solvents used for this study were also analyzed for trace water, and calculations of purity were made using these figures. The supplied CDI was very variable in purity and in some cases was less than 90% when delivered. Typical values of purity ranged from 99−92.5% with a single impurity identified as imidazole, the nonvolatile byproduct of CDI hydrolysis. This would account for the apparent excess of APDE and the formation of urea after CDI consumption. Urea formation was not seen in all polymerizations but was often eliminated when corrections for CDI purity were used.

TOF-MALDI analysis of the samples also supported the polymerization mechanism with a repeat unit of 188.23 Da, **16**, which is clearly seen (Figure 6).

The spectra show masses up to approximately 6500 Da (DP = 35 monomer units), but several distributions can be seen. The strongest signals are derived from the MH^+, MNa^+, and MK^+ adducts where the mass ion is derived from HBP−NH_2 (i.e., the hyperbranched polymer (HBP) with a primary amine focal group). A distribution for the HBP−Imid (polymer with the carboxamide focal group) is also often seen but mainly as the MK^+ adduct. Interestingly, distributions of signals corresponding to the MKH^{2+} of the HBP−Imid, and other doubly charged species (Figure 7), are regularly seen suggesting masses >11 000 Da (DP approximately 60 monomer units). The formation of ureas or carbonates generated through APDE coupling cannot be analyzed via TOF-MALDI as the masses of polymers linked through carbonate, urethane, or urea groups are identical and the distribution of repeat units would be the same. In several spectra, however, a grouping of signals that did not fit any theoretical series of masses was seen, even when considering the formation of cyclic species. These signals had a repeating pattern corresponding to increasing numbers of APDE monomers, with subsequent H^+, Na^+, and K^+ adducts, but were approximately 57 Da lower than the spectrum of the MH^+ series (Figure 7).

This appears to be a due to an impurity in the APDE monomer that was also used as supplied. APDE is presumably synthesized through the Michael addition of acrylonitrile to diethanolamine followed by hydrogenation. Diethanolamine has a molecular weight that is

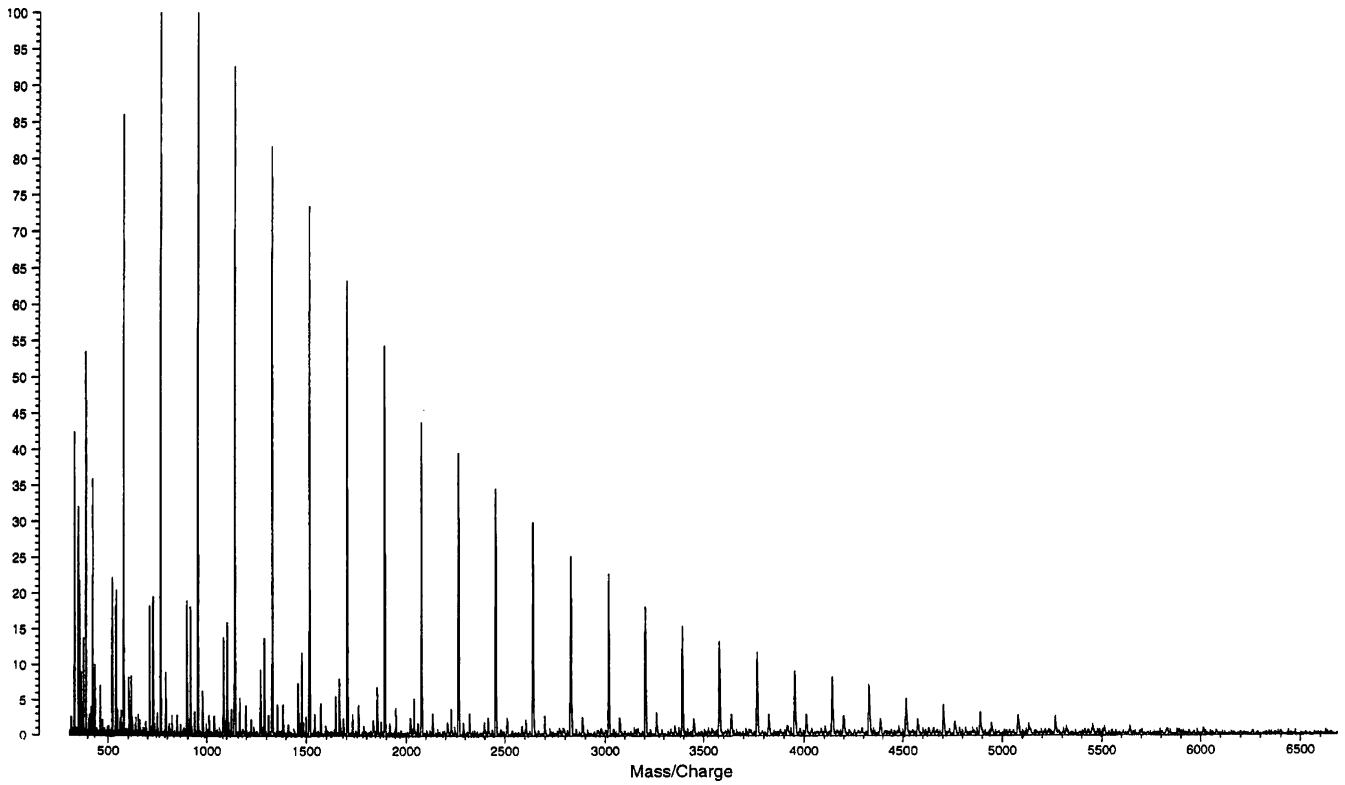


Figure 6. TOF-MALDI spectra of the hyperbranched polyurethane of APDE.

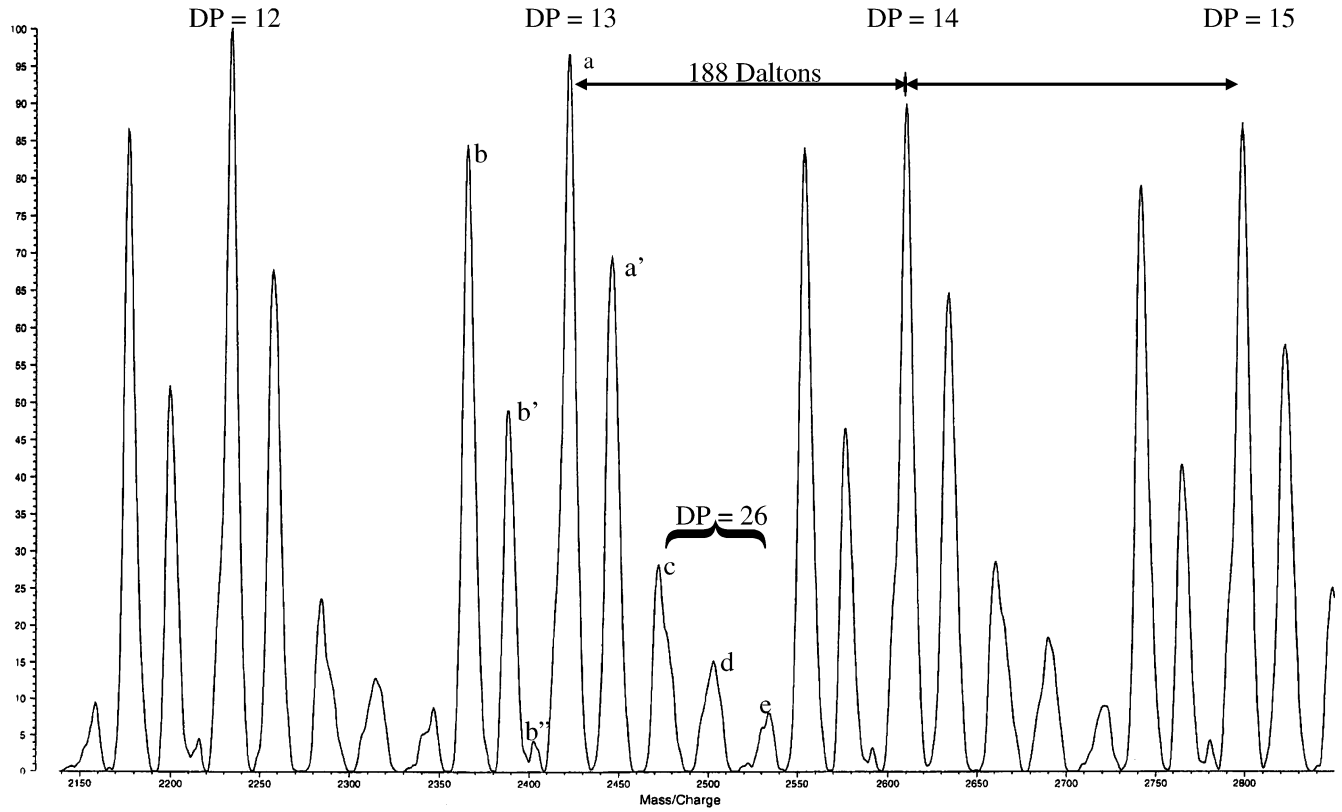


Figure 7. Expansion of the TOF-MALDI spectra of samples showing strong urea carbonyl ^{13}C signals (a, a′ = MH^+, MNa^+, amine focal point (calcd: 2421.9, 2444.0; found: 2422.0, 2445.9); b, b′, b″ = MH^+, MNa^+, MK^+, diethanol amine containing species (calcd: 2364.9, 2387.0, 2404.1; found: 2365.2, 2388.3, 2404.1); c = MKK^{2+}, amine focal point (calcd: 2473.0; found: 2474.1); d = MHK^{2+}, carboxamide focal point (calcd: 2501.0; found: 2501.8); e = $MNaK^{2+}$, diethanol containing species (calcd: 2530.6; found: 2533.2).

57.09 Da lower than APDE **2**, and this suggests that some polymer chains are terminated with or contain diethanolamine residues **17** or **18** possibly linked to the main polymer chain through an asymmetric urea link, **18**. The reaction of CDI with primary amines occurs at room temperature, whereas secondary amines require heating to form the carboxamide.[22] The primary amine carboxamide of APDE, **8**, that is formed during the initial activation stages of the polymerization may therefore react with the diethanolamine impurity resulting in the capping of the growing chains. This may either lead to a urethane linkage, which will not be discernible by NMR, or a urea link that will be discernible (Scheme 4).

This may be the most likely source of the urea resonance that can be seen in the ^{13}C NMR spectra of some polymers and may explain why the urea resonance was not always eliminated through correction for CDI purity. The presence of end-capped material will also lead to a decrease in the achievable molecular weight of the polymerization. The level of diethanolamine within the supplied sample was not easily determined, and purification was not attempted.

Effect of Reaction Conditions on Conversion and M_n: Reaction Time, Temperature, and aAddition of Base. The synthesis of urethanes via the reaction of a carboxamide and an alcohol requires the nucleophilic attack of the hydroxyl, probably as an alkoxide, at the carbonyl group. The addition of a base to the reaction would be expected to aid the polymerization reaction. However, APDE is a basic monomer containing a tertiary amine branching atom, and the imidazole byproduct that is eliminated during the initial formation of the carboxamide can also act as a base for the urethane synthesis. In previous work, we have employed KOH as a base to synthesize nonpolymeric urethanes and carbonates, but the addition of a strongly nucleophilic base may also hinder the reaction.

A series of polymerizations heated at 90 °C for 3 h with increasing KOH concentration (0−1 mol equivalent based on APDE) were conducted, and the effect on M_n (as measured by ^1H NMR) was studied. In this series of polymerizations, M_n varied dramatically from 5000 Da when no additional base was added to less than 500 Da at >0.7 mol equivalents of base (Figure 8a). Conversion appears to vary linearly with base concentration and ranged from > 97% when no extra base was added to <20% with 1 equiv of base (Figure 8a). The additional base therefore has a significant effect on the polymerization mechanism possibly through the competitive reaction of the hydroxide with the carboxamide focal group or degradation of the urethane group during the course of the polymerization. Another possibility is the addition of water to the polymerization as the KOH supplied has a significant amount of associated water (approximately 15% w/w). This would potentially lead to the degradation of the carboxamide and limit the growth of the polymer.

A comparison of reactions with added KOH (0.1 mol equiv) and polymerizations without added base was conducted to understand the role of reaction temperature and length of reaction on conversion and M_n. In all cases, the polymerizations with 0.1 mol equiv of KOH achieved significantly lower molecular weights and conversions. Reaction temperatures were varied from 60 to 145 °C, and the polymerizations were conducted

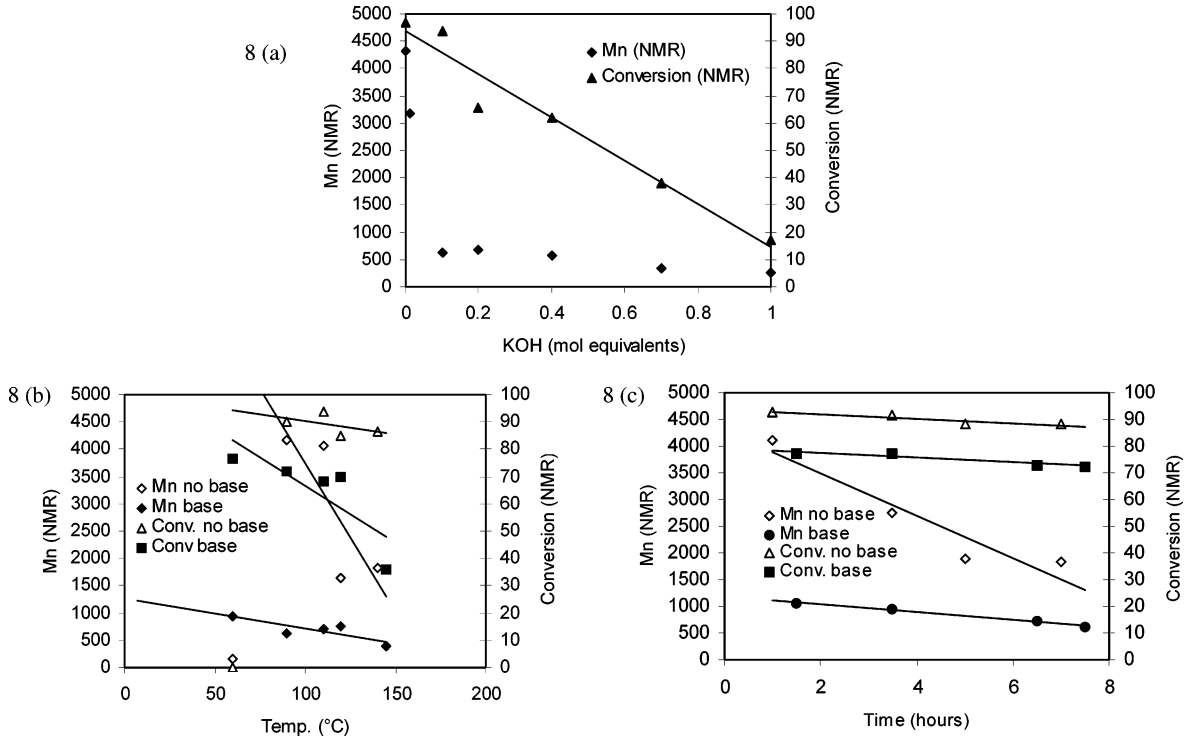
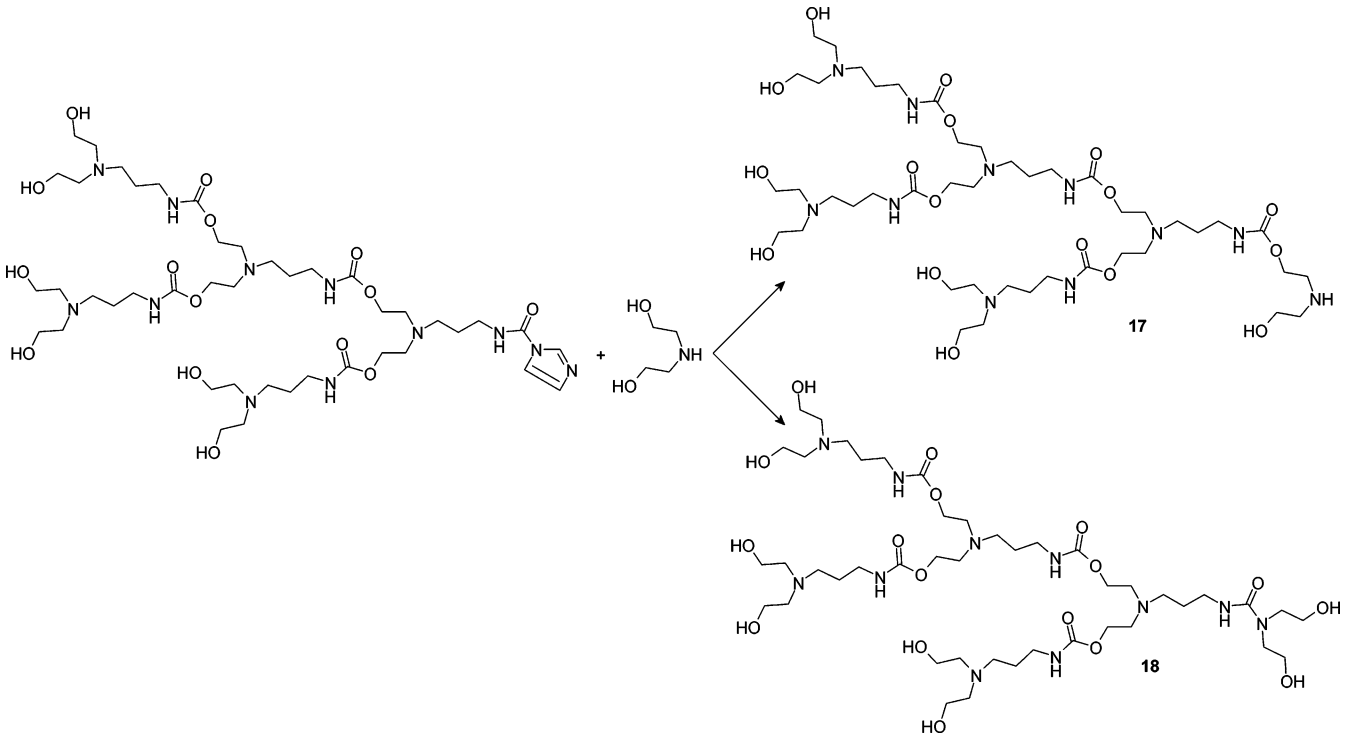


Figure 8. Effect of reaction conditions on the polymerization of APDE monomer and the formation of hyperbranched polyurethane.

Scheme 4



for 3 h as stated previously. Without added base, the polymerization at 60 °C was unsuccessful, and almost no conversion could be detected, but conversions of almost 80% (with low M_n) were achieved when KOH was added at this temperature. At temperatures >90 °C, however, the polymerizations without base showed much higher conversions and M_n than those with added KOH (Figure 8b). As the temperature of polymerization is increased, the conversions and M_n achieved decrease suggesting that either the polymer is not stable at these higher temperatures or the carboxamide is decomposing. The effect of temperature on conversion does not seem to be too dramatic in the absence of base, but a large effect is seen when base in present. This may be indicative of the hydroxide driven decomposition of the carboxamide and subsequent regeneration of primary amine at elevated temperatures, however, the carboxamide appears to be temperature sensitive under the conditions of the reaction with no added KOH. The formation of polymer appears to be faster in the absence of KOH with higher conversions being achieved at all temperatures, although the detrimental effect of higher

temperatures on M_n is more highly pronounced.

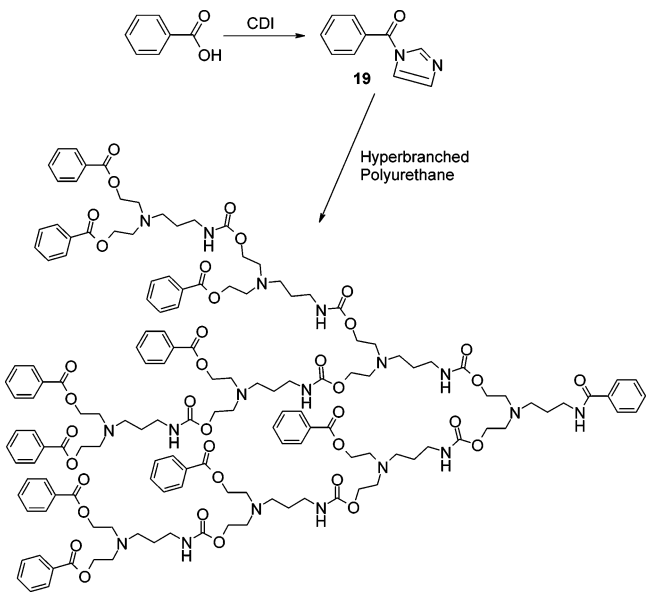
A number of polymerizations were conducted at 90 °C with either no added base or with 0.1 equiv of KOH for increasing reaction times from 1 to 7.5 h (Figure 8c). M_n decreases considerably with the extended reaction time, both in the presence and absence of added base. Conversion, however, appears to be relatively stable in both cases, and only minor differences were observed after 1 or 7.5 h. This suggests that there may be polymer degradation or cyclization reactions that are liberating low molecular weight species, although this would affect conversion if these species contained amine functionality. No evidence of cyclization was seen in the ^{1}H or ^{13}C NMR studies, and species corresponding to cyclized structures could not be observed in the TOF-MALDI spectra. It also is possible that intermolecular coupling reactions are occurring. If these lead to the elimination of low molecular weight branched oligomeric species with amine focal functionality, the number of focal groups would not change dramatically; therefore, the conversion would not be greatly affected. The overall molecular weight distribution would, however, broaden as M_n would decrease and M_w would increase. Unfortunately, reproducible aqueous GPC conditions could not be achieved for these materials during our study, and data describing M_w or polydispersity were not obtained.

Reactivity of Hydroxyl Groups—Formation of Benzoic Acid Esters. The hyperbranched polyurethanes of APDE are very water soluble presumably due to the large numbers of hydroxyl groups present combined with the tertiary amine branching atom of the repeat unit. The material should be readily modified through reaction of the hydroxyl groups to produce a range of materials, and this has been investigated through the formation of benzoate esters in an initially heterogeneous reaction in THF. Benzoic acid was treated with CDI to form benzoic acid imidazolide, which can be considered as a benzoyl chloride analogue. This was achieved through the simple stepwise addition of CDI to a solution of benzoic acid in THF. This reaction is accompanied by vigorous effervescence as CO_2 is liberated. The solution was added to a sample of hyperbranched polyurethane and stirred at 60 °C for several hours after which time a homogeneous solution had been formed, showing the solubility of the modified material in organic solvent (Scheme 5).

After purification and solvent removal, the material was analyzed by ^{1}H and ^{13}C NMR (d_6-acetone) and MALDI-TOF mass spectrometry. The resonance at δ = 3.59 ppm (^{1}H NMR), attributed to the two methylene protons next to the OH end groups (NCH_2CH_2OH), had disappeared from the spectrum and new signals at δ = 4.25 ppm (corresponding to the methylene next to a benzoate ester), and groups of aromatic protons at δ > 7.10 ppm were observed. Resonances at δ = 59.82 and 56.31 ppm (^{13}C) corresponding to these methylene carbons had also disappeared in the spectrum, and a new resonance at δ = 66.94 ppm attributed to the methylene carbon adjacent to the benzoate ester was observed. Carbonyl signals at δ = 167.48 ppm were observed, confirming the presence of the aromatic ester. Reaction of the benzoic acid imidazolide with the amine to form an aromatic amide was not observed.

MALDI-TOF analysis of the material was extremely complicated, and the clear repeat unit of the modified hyperbranched polyurethane could not be seen (expected to be 292.33 Da based on complete reaction of all hydroxyl groups). A repeating pattern of 24.01 Da, however, was apparent, which suggests multiply charged species.

Scheme 5



Conclusions

In summary, we have described the novel synthesis of a water-soluble hyperbranched polymer through the first reported selective activation of an AB_2 monomer. The reaction of 1,1′-carbonyl diimidazole with primary amines in the presence of primary alcohols has been studied using a series of model reactions and has been shown to be highly selective, forming an active carboxamide at the primary amine of an amino-diol monomer, leaving the primary alcohol groups unreacted. The water-soluble hyperbranched polyurethanes that are formed by the self-condensation of this active intermediate have been characterized using MALDI -TOF spectrometry and ^{1}H, ^{13}C, and ^{15}N NMR spectroscopy, using a number of model molecules to aid peak assignment. Polymers with M_n up to approximately 11 000 Da with degree of branching equaling 0.6 have been determined. The modification of the hydroxyl terminal groups with benzoic acid was conducted using mild conditions and reached complete formation of benzoate ester as shown by NMR spectroscopy.

Acknowledgment. The authors thank Courtaulds Corporate Technology, Coventry where the work was conducted. The expertise of Tim Jenkins and Christine Wallace at Courtaulds in chromatography/mass spectrometry and NMR spectroscopy and Amelia Jackson at Kratos Ltd is gratefully acknowledged.

Supporting Information Available: Selection of ^{1}H, ^{13}C, and ^{15}N NMR spectra for compounds **2**, **4**, **5**, **7**, and **9**−**15**. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Fréchet, J. M. J. *J. Polym. Sci. Part A* **2003**, *41*, 3713.
(2) Tomalia, D. A.; Fréchet, J. M. J. *J. Polym. Sci. Part A* **2002**, *40*, 2719.
(3) Malkoch, M.; Carlmark, A.; Woldegiorgis, A.; Hult, A.; Malmström, E. E. *Macromolecules* **2004**, *37*, 322.

(4) Santini, C. M. B.; Johnson, M. A.; Boedicker, J. Q.; Hatton, T. A.; Hammond, P. T. *J. Polym. Sci. Part A* **2004**, *42*, 2784.
(5) Voit, B. I. *C. R. Chim.* **2003**, *6*, 821.
(6) Voit, B. *J. Polym. Sci. Part A* **2000**, *38*, 2505.
(7) Spindler, R.; Fréchet, J. M. J. *J. Chem. Soc., Perkin Trans.* **1993**, *1*, 913.
(8) Taylor, R. T.; Puapaiboon, U. *Tetrahedron Lett.* **1998**, *39*, 8005.
(9) Puapaiboon, U.; Taylor, R. T.; Jai-nhuknan, *J. Rapid Commun. Mass Spectrom.* **1999**, *13*, 516.
(10) Clark, A. J.; Echenique, J.; Haddleton, D. M.; Straw, T. A.; Taylor, P. C. *J. Org. Chem.* **2001**, *66*, 8687.
(11) Peerlings, H. W. I.; Van Benthem, R. A. T. M.; Meijer, E. W. *J. Polym. Sci. Part A* **2001**, *39*, 3112.
(12) Feast, W. J.; Rannard, S. P.; Stoddart, A. *Macromolecules* **2003**, *36*, 9704.
(13) Rannard, S. P.; Davis, N. J. *J. Am. Chem. Soc.* **2000**, *122*, 11729.
(14) Spindler, R.; Fréchet, J. M. J. *Macromolecules* **1993**, *26*, 4809.
(15) Kumar, A.; Ramakrishnan, S. *Chem. Commun.* **1993**, 1453.
(16) Hong, L.; Cui, Y.; Wang, X.; Tang, X. *J. Polym. Sci. Part A* **2002**, *40*, 344.
(17) Bruchmann, B.; Königer, R.; Renz, H. *Macromol. Symp.* **2002**, *187*, 271.
(18) Rannard, S.; Davis, N. *Org. Lett.* **2000**, *2(14)*, 2117.
(19) Rannard, S.; Davis, N. *Org. Lett*. **1999**, *1(6)*, 933.
(20) Rannard, S.; Davis, N.; McFarland, H. *Polym. Int.* **2000**, *49*, 1002.
(21) Hobson, L. J.; Feast, W. J. *Polymer* **1999**, *40*, 1279.
(22) During our studies of carboxamide formation, we have observed that the addition of primary amines to stirred suspensions of CDI in toluene at room temperature form clear solutions very quickly. However, when secondary amines are added at room temperature, the suspension remains unchanged, and TLC analysis of the supernatant shows no formation of carboxamde. When the suspensions containing secondary amine are heated to 50 °C, they become clear very quickly and produce carboxamide in moderate yields (>70%). Interestingly, the carboxamides that are formed from secondary amines do not readily react with alcohols to form urethanes, or with amines to form ureas, under the conditions that we have studied. This suggests that the pathway leading to possible isocyanate intermediate formation and subsequent imidazole liberation may involve the carboxamide NH proton that is not present in examples derived from secondary amines.

MA0489218