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ORIGINAL PAPER

The Lewis Acid-Catalyzed Synthesis of Hyperbranched Oligo(glycerol–diacid)s in Aprotic Polar Media

Victor T. Wyatt · Gary D. Strahan · Alberto Nuñez

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Abstract The Lewis acid, titanium (IV) butoxide [15% (w/w; catalyst/reactants)], was used to catalyze the condensation of 0.05 mol glycerol with 0.10 mol of succinic acid, glutaric acid, and azelaic acid to produce oligomers. The reactions were refluxed in dilute solutions of dimethylsulfoxide (DMSO) or dimethylformamide (DMF) for 24 h. The oligomers were obtained, on average, in 84% yield and were soluble in polar organic solvents. Analysis by gel permeation chromatography determined that the oligomers had a number of average molecular weights (M_n) ranging from 2,118 to 3,245 g/mol, with degrees of polymerization (DOP) ranging from 12.2 to 13.4 repeat units. The oligomers had low polydispersities (M_w/M_n) that averaged $\approx$1.33. Degrees of branching were determined by one-dimensional and two-dimensional ^{1}H NMR and ^{13}C NMR and varied from 25 to 80%. Like M_n and the DOP values, the degrees of branching were dependent on the aliphatic chain length of the diacid. MALDI-TOF mass spectrometry was used to detect ionated species that were unique to branched molecules. It was also used to validate NMR studies that suggested that some diacids were terminated with dimethylamine, generated from the hydrolysis of DMF, by as much as 36%.

Keywords Diacids · Hyper-branching · Glycerol · Polymers

Introduction

The principle co-product from the transesterification process by which biodiesel is made is crude glycerol. For every 9 kg of biodiesel produced, about 1 kg of crude glycerol is formed [1, 2]. According to the National Biodiesel Board, biodiesel production in the United States increased dramatically from 500,000 gallons in 1999 to over 700 million gallons in 2008. Commercial grades of glycerol suitable for applications in the food, drug, cosmetic, and tobacco industries are available but there is no additional need for glycerol in those markets. It is therefore important to find new outlets for biodiesel-derived glycerol in an effort to curtail glycerol waste and decrease biodiesel production costs by adding value to the glycerol co-product [3–7].

Glycerol-based polymers could serve as an outlet for excess glycerol if appropriate uses can be identified. One benefit to synthesizing polymers from glycerol is that several molecules of glycerol will be consumed at once. However, very little literature on producing polyglycerols with glycerol-derived repeat units is available because glycerol is not as popular as some other multifunctional acyl acceptor reagents, such as glycidol, as a major propagating unit [1, 8].

Since glycerol is a trifunctional monomer, it can be used to synthesize hyperbranched polymers. Hyperbranched polymers are related to the family of highly branched molecules known as dendrimers. Dendrimers are highly branched monodispersed macromolecules typically produced by multi-step syntheses whereas hyperbranched

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V. T. Wyatt (✉) · G. D. Strahan · A. Nuñez
US Department of Agriculture, Agricultural Research Service, Eastern Regional Research Center, 600 East Mermaid Lane, Wyndmoor, PA 19038, USA
e-mail: victor.wyatt@ars.usda.gov

polymers are randomly branched macromolecules typically prepared by a simple one-step reaction. Hyperbranched polymers commonly exist as AB_2 branched polymers where A and B represent different functional groups [9–13]. AB_2 monomers are not readily available but kinetic calculations show that the first condensation reaction between A_2 and B_3 monomers produces an AB_2 dimer that is functionally equivalent to an AB_2 monomer. This condensation is faster than subsequent polymer propagation; therefore, the remainder of the reaction progresses as polycondensations between AB_2 type species prior to the gel point.

One of the earliest studies on hyperbranched polymers was performed by Flory [14], in which he described the critical gel-point for AB_2 hyperbranched polymers produced from AB_2 monomers. Since that time, several methods have been employed to avoid gelation in direct condensation reactions between of di-functional (A_2) monomers such as diacids and tri-functional (B_3) monomers such as glycerol by performing the reactions in dilute solutions [9, 12, 13] or by reacting them in the absence of solvent while monitoring the viscosity of the system [10]. Others have shown that gelation, branching, and molecular weight can be controlled by lipase-catalyzed, bulk polycondensations [11].

We have reported results supporting the production of linear and branched poly(diacid–glycerol) oligomers. Previous research, including results from our laboratory, has been reported on the neat synthesis of diacid–glycerol oligomers [10, 15]. Further research in this area is currently ongoing in our laboratory in a continuing effort to find new uses for glycerol. This paper describes reactions that were performed in aprotic polar solvents (DMSO or DMF) to determine if increased branching and elongation of the propagating chains could be achieved before the gel point was reached [9, 12, 13]. Esterification reactions between glycerol and diacids are typically run above 150 °C. Accordingly, these solvents were chosen because they have boiling points that are high enough to facilitate esterifications and are sufficiently polar to dissolve the reactants. Aprotic polar solvents such as these are also generally not expected to participate in acid-catalyzed nucleophilic substitution reactions because they are unable to form hydrogen bonds with the nucleophile.

Glycerol-based polymers are expected to render new surgical materials that are useful in orthopedic and ophthalmic applications, reconstructive surgery and as drug delivery agents [16–18]. These biocompatible polymers also are of interest for their potential uses as cosmetics, food additives, surfactants, lubricants, and azeotropic phase separators [19]. Previous research, including results from our laboratory, has been reported on the neat synthesis of linear and branched oligo(glycerol–diacid)s [10, 15]. This study is intended to provide an additional demonstration of the potential for using monomeric glycerol as a propagating monomer by synthesizing polyesters in a polar solvent with the intent to reduce or eliminate the production of crosslinked polymers.

The advantage of making oligomers by the method described here is two-fold. It addresses the need for co-product (glycerol) utilization while producing oligomers that are not crosslinked. In the absence of crosslinks, oligomeric products have the ability to be further processed for use in many applications. Because non-crosslinked resins are soluble, they can be used as additives in such things as paints and varnishes or they may be further polymerized or functionalized for use as adhesives, rubbers, and foams. Toward this goal, a series of diacids was reacted with glycerol in polar solvents and the characteristics (yields, molecular weights, degrees of polymerization, degrees of branching) of the polymers obtained.

Materials and Methods

Materials

Azelaic acid (98%), glutaric acid (99%), and reagent grades of glycerol (99.9%), titanium (IV) butoxide [$Ti(OC_4H_9)_4$] (97%) and *N,N*-dimethylformamide (DMF ≥99.9%) were purchased from Sigma-Aldrich (St. Louis, MO). HPLC grades of acetone, chloroform, and acetonitrile were purchased from J.T. Baker (Phillipsburg, NJ). Spectroscopic grade dimethylsulfoxide (DMSO 99.9%) and succinic acid (99%+) were from Aldrich Chemical Co. (Milwaukee, WI). Deuterated nuclear magnetic resonance (NMR) solvent, dimethylsulfoxide-d_6, was ordered from Cambridge Isotope Laboratories (Andover, MA). Polystyrene standards (Easycal A) were obtained from Polymer Laboratories (Amherst, MA) and a series of mono-, di-, and tri-oleins and palmitates were obtained from Nu-Chek Prep, Inc. (Elysian, MN).

Polymerizations in Dilute Solutions

A diacid (0.10 mol) was added to DMF or DMSO (90 mL) and stirred at room temperature until the solid was completely dissolved. DMSO or DMF (45 mL), glycerol (0.05 mol) and 0.15% w/w (titanium IV) butoxide (catalyst/reactants) were placed in a 3-neck 250-mL round bottom flask and heated to 150 °C. Heat was provided by an oil bath wrapped with a heating strap controlled by a variable AC transformer. The diacid mixture subsequently was added drop-wise over a 2-h period and once it was all added, the mixture was allowed to react for another 22 h at 150 °C. The solvent was removed from the crude reaction products by

rotary evaporation. Qualitative solubility studies using various solvents revealed that chloroform could be used to extract the oligo(glycerol–azelaic acid) from unreacted azelaic acid. Once the unreacted azelaic acid was filtered off and weighed, the filtrate solution was condensed via rotary evaporation. The resulting product was washed three times with water to remove residual catalyst and glycerol, lyophilized and weighed. Qualitative solubility studies did not reveal solvent systems suitable for the extraction of the oligo(glycerol–succinic acid) and the oligo(glycerol–glutaric acid) products from the starting materials. Therefore, the DMF or DMSO was removed from the product via rotary evaporation, lyophilized and weighed.

Gel Permeation Chromatography

Gel permeation chromatography (GPC) was performed on a Polymer Laboratories (Amherst, MA) PL-GPC 120 high temperature chromatograph equipped with a refractive index detector. Succinic acid–glycerol, glutaric acid–glycerol, and azelaic acid–glycerol oligomers were dissolved in THF in concentrations of approximately 10^{-4} mg/mL, and 20–30 mL were injected onto a Polymer Laboratories (Amherst, MA) PLgel 5 μM guard (50 × 7.5 mm) and two Polymer Labs PLgel 3 μM MIXED-E (300 × 7.5 mm) columns. A Holland spark Midas auto-sampler was employed. Data were collected and processed on a Windows 98 Micron Pentium 2 computer running Cirrus GPC online GPC/SEC software, version 1.11. Chromatographic runs were made using an isocratic flow rate (1 mL/min) of tetrahydrofuran at 40 °C. All parameters, including M_n, M_w, and PDI, were calculated by the Cirrus software using a third order polynomial derived from a standard curve. The standard curve was generated from a series of polystyrene molecular weight standards and a series of mono-, di-, and tri-oleins and palmitates.

Mass Spectrometry

Matrix-assisted laser desorption/ionization with time of flight (MALDI-TOF) mass spectra were acquired with a 4,700 Proteomics Analyzer mass spectrometer (Applied Biosystems, Framingham, MA) in the positive reflector mode with a 200-Hz Nd-YAG 355-nm laser. Spectra were obtained by averaging 1,000 acquired spectra in the MS mode. An aliquot (1 μL) of polymer solution (1 mg/mL in H_2O) was mixed with 24 μL of 2,5-dihydroxybenzoic acid (DHB) matrix solution (10 mg/mL, acetonitrile–water 50:50 v/v) and 0.5 μL of the resulting solution was spotted on the MALDI plate for analysis. The TOF analyzer in the reflectron mode can provide a resolution between 15,000 and 20,000 full width half-maximum (FWHM) with error in the mass determination below 50 ppm.

Nuclear Magnetic Resonance

All solution-state NMR spectra were recorded at 9.4 Tesla on a Varian (Palo Alto, CA) INOVA NMR Spectrometer operating at 27 °C, using a 5-mm indirect-detect probe with *Z*-axis pulsed field gradient. All samples were dissolved in d_6-DMSO and referenced to the residual solvent. The 1D proton (^{1}H) spectra (400 MHz) were acquired with a spectral width of 6,000 Hz, a 90° pulse angle and a 2.5-s relaxation delay. The ^{13}C spectra (100 MHz) were acquired with a spectral width of 25–30 kHz, a pulse angle of 45°, a relaxation delay of 20 s, 128 k data points, and 6–18 k transients. To allow for accurate integration of ^{13}C signals, these 1D-^{13}C spectra were recorded with proton decoupling only during the acquisition periods (“inverse-gating”), to avoid non-uniform enhancement of carbon signals from proton NOE effects. In addition, a delay of 20 s (greater than 5 times the longest carbon T_1), and a small excitation angle of 45°, were employed to ensure that virtually all ^{13}C atoms returned to their equilibrium states after each excitation.

Resonance assignments utilized the distortionless enhancement polarization transfer (DEPT) spectra, as well as 2D-NMR. A fully edited DEPT experiment was run using the standard flip angles of 45°, 90°, and 135°, followed by mathematical manipulation to generate separate CH, CH_2, and CH_3 ^{13}C spectra. The 2D-NMR studies included gradient enhanced versions of correlation spectroscopy (COSY), Heteronuclear Single Quantum Correlation (HSQC) or Heteronuclear Multiple Quantum Correlation (HMQC), Heteronuclear Multiple Bond Correlation (HMBC) (8 and 16 Hz coupling) and Total Correlation Spectroscopy (TOCSY) (80-ms mixing time). The proton homonuclear COSY and TOCSY (80-ms mixing time) 2D experiments were recorded with spectral widths of 6 or 8 kHz in both dimensions, using 4,096 points in the directly detected dimension, and 512 increments in the second dimension; 16 transients per fid were collected with a 2-s delay between scans.

The ^{1}H–^{13}C heteronuclear experiments, HSQC, HMQC, and HMBC (8 and 16 Hz coupling), were recorded using 4,096 data points and spectral widths of 6 or 8 kHz in the proton dimension (directly detected). For the carbon (indirectly detected) dimension, 512 increments were acquired with a spectral width of 25 or 30 kHz, a 2-s delay between scans, and 32 or 64 transients per fid. All 2D spectra were analyzed using SPARKY 3 [20] NMR assignment and integration software.

Results and Discussion

Polymerizations in Dilute Solutions

Oligomers resulting from the copolymerization of glycerol with diacids having three different carbon chain lengths

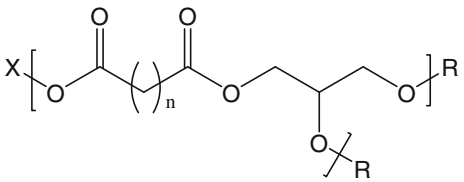


Fig. 1 Hyperbranched oligomers produced from the condensation of diacids with glycerol $n = 2$ oligo(succinic acid–glycerol), $n = 3$ oligo(glutaric acid–glycerol), $n = 7$ oligo(azelaic acid–glycerol). X=H or Ester linkage to glycerol, R=H or Ester linkage to diacid

were synthesized (Fig. 1). Consistent with previous studies of this type [10, 15], gelation was controlled by reaction time and/or reactant concentration. Purification and characterization of the oligomers were performed based on the solubility differences of the individual oligomers. Qualitative solubility studies were performed for the neat glutaric acid–glycerol product to determine the most effective method for product extraction and characterization by spectroscopic analysis. As expected, the glutaric acid–glycerol product conformed to the previously reported solubility trend for oligo(glycerol–succinic acid) and oligo(glycerol–azelaic acid) [15]. Water solubility of the oligomers decreased with increasing chain length of the diacid monomers used in preparing the oligomers. The glutaric acid–glycerol product was soluble in polar solvents such as acetonitrile and methanol but insoluble in non-polar solvents such as toluene.

The reactions conducted in dilute solutions gave polymer yields, on average, of 84% based on the weights of the starting materials and final product. The mass balance is likely due to the loss of small volatile anhydrides and the loss of water. Additionally, up to 6% of unreacted starting material was recovered by extraction of the azelaic acid product with chloroform. It was difficult to remove the solvent from the dark, tar-like DMSO-derived oligomers; whereas, DMF-derived products were amber in color and did not have any odor due to residual solvent. Therefore, further analysis was focused on DMF-derived products.

Attempts to perform analogous neat reactions for the purpose of comparison resulted in solid materials that were insoluble and; therefore, could not be analyzed by MALDI-TOF mass spectroscopy or GPC. The neat-derived products swelled in the presence of solvent and were characterized by NMR showing significant increases in degrees of branching. This data will be included in a forthcoming paper that will compare the physical and mechanical properties of neat and solvent-derived hyperbranched polyesters. Previously published molecular weights for neat-derived hyperbranched oligo(diacid–glycerol)s [15] were inappropriate for comparison here because significantly longer reaction times were used in these experiments.

Table 1 M_n as determined by gel permeation chromatography (GPC) data for glycerol-based oligomers

Co-monomer	M_n	DOP	PDI
Succinic acid	2,118	12.2	1.06
Glutaric acid	2,402	12.8	1.09
Azelaic acid	3,245	13.4	1.84

M_n number average molecular weight, *PDI* polydispersity index, *DOP* degree of polymerization

GPC Analysis

Table 1 lists the number average molecular weight (M_n), polydispersity and degree of polymerization for each oligomer as determined by GPC. The average molecular weights, M_n, for the reactions performed in dilute solutions ranged from 2,188 Da for succinic acid-derived oligomers to 3,245 Da for azelaic acid-derived oligomers with relatively low polydispersities. Owing to the differences in the molecular weights of the diacid monomers, the best way to determine the extent of reaction is to normalize the molecular weights by determining degrees of polymerization. Such comparisons show that the degrees of polymerization for the three diacids with glycerol were similar, ranging from 12.2 (succinic acid-derived oligomers) to 13.4 (azelaic acid-derived oligomer). This trend suggests that the length of the aliphatic unit of the diacid chain has a positive affect on the degree of polymerization.

MALDI Analysis

MALDI-TOF mass spectroscopy was used in these experiments to prove the presence of branched species. If branched products are formed as the result of esterification at the primary and secondary glycerol hydroxyl groups, the spectrum of the branched trisubstituted oligomers will show characteristic ion masses that differ from those of the linear disubstituted structures (Tables 2, 3, 4, 5). The addition of glycerol at the terminal carboxylic acids of branched structures will produce isomeric structures indistinguishable by mass spectrometry from the linear polymers. However, the presence of some branched species is easily detectable because their molecular weights cannot be duplicated by linear structures. Structures having more than two free acid functionalities at the end-terminals can occur only after branching.

Previous MALDI-TOF spectra of polymer samples produced after reacting succinic acid or azelaic acid as a copolymer with glycerol, produced masses that matched the calculated weights of branched and linear oligomeric species [15]. These masses were separated by 174 and 244 Da, respectively. The mass differences were consistent with the elongation of oligomeric chains with repeating

Table 2 Calculated nominal masses for the glutaric acid (A)–glycerol (G) linear polymerization

n	A–G–(A–G)$_n$–A		A–G–(A–G)$_n$–A–G		G–(A–G)$_n$–A–G	
	$(M + Na)^+$	$(M + K)^+$	$(M + Na)^+$	$(M + K)^+$	$(M + Na)^+$	$(M + K)^+$
1	531.17	547.14	605.21	621.18	491.17	507.24
2	719.24	735.21	793.27	809.25	679.24	695.31
3	907.30	923.28	981.34	997.32	867.31	883.37
4	1,095.37	1,111.35	1,169.41	1,185.38	1,055.38	1,071.44
5	1,283.44	1,299.41	1,357.48	1,373.45	1,243.45	1,259.51
6	1,471.51	1,487.48	1,545.55	1,561.52	1,431.51	1,447.58
7	1,659.58	1,675.55	1,733.61	1,749.59	1,619.58	1,635.65
8	1,847.64	1,863.62	1,921.68	1,937.66	1,807.65	1,823.71
9	2,035.71	2,051.69	2,109.75	2,125.72	1,995.72	2,011.78

Table 3 Calculated mass for the succinic acid (A)–glycerol (G) linear polymerization

n	A–G–(A–G)$_n$–A		A–G–(A–G)$_n$–A–G		G–(A–G)$_n$–A–G	
	$(M + Na)^+$	$(M + K)^+$	$(M + Na)^+$	$(M + K)^+$	$(M + Na)^+$	$(M + K)^+$
1	489.12	505.10	563.16	579.13	637.20	653.17
2	663.18	679.15	737.21	753.19	811.25	827.22
3	837.23	853.20	911.27	927.24	985.30	1,001.28
4	1,022.28	1,038.26	1,085.32	1,101.29	1,159.36	1,175.33
5	1,185.34	1,201.31	1,259.37	1,275.35	1,333.41	1349.38
6	1,359.39	1,375.36	1,433.43	1,449.40	1,507.46	1,523.44
7	1,533.44	1,549.42	1,607.48	1,623.45	1,681.52	1,697.49
8	1,707.49	1,723.47	1,781.53	1,797.51	1,855.57	
9	1,881.55		1,955.58			

Table 4 Calculated mass for the azelaic acid (A)–glycerol (G) linear polymerization

n	A–G–(A–G)$_n$–A		A–G–(A–G)$_n$–A–G		G–(A–G)$_n$–A–G	
	$(M + Na)^+$	$(M + K)^+$	$(M + Na)^+$	$(M + K)^+$	$(M + Na)^+$	$(M + K)^+$
1	455.24	471.21	773.39	789.37	603.30	619.27
2	699.37	715.34	1,017.53	1,033.50	847.43	863.41
3	943.50	959.47	1,261.66	1,277.63	1,091.56	1,107.54
4	1,187.63	1,203.60	1,505.79	1,521.76	1,335.69	1,351.67
5	1,431.76	1,447.73	1,749.92	1,765.89	1,579.82	1,595.80
6	1,675.89	1,691.87	1,994.05	2,010.02	1,823.96	1,839.93
7	1,920.02	1,936.00	2,238.18	2,254.15	2,068.09	2,084.06
8	2,164.15	2,180.13	2,482.31	2,498.29	2,312.22	2,328.19
9	2,408.28	2,424.26	2,726.44	2,742.42	2,556.35	2,572.32

units in the form –(A–B)–; where A represents a diacid unit and B represents a glycerol unit.

New spectra of oligomers produced by the condensation of glutaric acid with glycerol also showed characteristic masses that were consistent with elongation of oligomeric chains separated by 188 Da due to repeating units in the form –(A–B)–. Masses determined with MALDI-TOF for the individual oligomeric chains of diacid–glycerol products correlated, within experimental error, with the calculated mono-isotopic masses of the linear and branched oligomeric structures reported in Tables 2, 3, 4 and 5. MALDI-TOF mass spectral data are not valid below 500 Da due to matrix interference; therefore, the reported masses only include oligomeric structural masses above

Table 5 Suggested structures and predicted mono-isotopic masses of the sodium and potassium adducts for the branched form of co-oligomerized diacids (A) with glycerol (G)

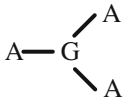
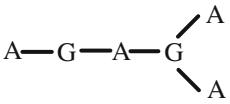
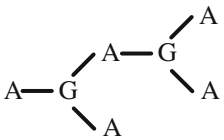
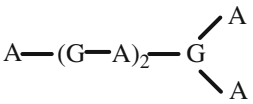
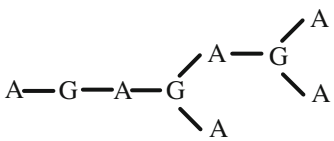
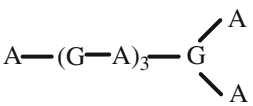
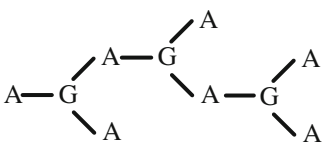
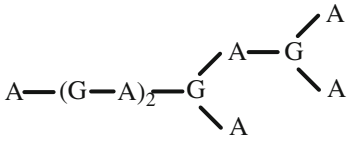
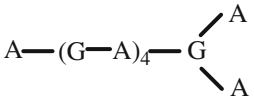
Entry	Suggested oligomeric structure	Succinic acid $(M + Na)^+$ $(M + K)^+$	Glutaric acid $(M + Na)^+$ $(M + K)^+$	Azelaic acid $(M + Na)^+$ $(M + K)^+$
1		–	–	625.33 641.30
2		589.14 605.11	645.20 661.17	869.45 885.43
3		689.16 705.13	759.23 775.20	1,039.56 1,055.53
4		763.19 779.17	833.27 849.24	1,113.58 1,129.56
5		863.21 879.18	947.30 963.27	1,283.68 1,299.65
6		937.25 953.22	1,021.34 1,037.31	1,357.71 1,373.69
7[a]		963.23 979.20	1,061.33 1,077.30	1,453.79 1,469.76

Table 5 continued

Entry	Suggested oligomeric structure	Succinic acid $(M + Na)^+$ $(M + K)^+$	Glutaric acid $(M + Na)^+$ $(M + K)^+$	Azelaic acid $(M + Na)^+$ $(M + K)^+$
8		1,037.26 1,053.24	1,135.37 1,151.34	1,527.81 1,543.78
9		1,111.30 1,127.27	1,209.40 1,225.34	1,601.84 1,617.82

Only masses above 500 Da are reported

[a] Ions not detected by MALDI-TOF analysis of the oligomeric product

500 Da. Nonetheless, the most intense ions for these oligomeric products were closer to the lower limit of 500 Da, while no ions were detected above 2,500 Da.

The mass spectra of the oligomeric products confirm the presence of branched species. For example, the presence of calculated masses (Table 5) that are unique to branched molecules of the azelaic acid-derived product are detected by he MALDI-TOF spectrum for oligo(azelaic acid–glycerol) (Fig. 2). There was evidence of crosslinking as shown by some species differing by 18 Da, indicating the loss of one water unit. However, given the reaction conditions and ease of solubility, the degree of crosslinking is assumed to be minimal. Large cyclic cavities in the middle and the ends of oligomer chains, as seen in the synthesis of iminodiacetic acid–glycerol oligomers [15], were not observed.

NMR and Degree of Branching Analysis

The diacids may react with the glycerol at any of its three different alcohol positions. Depending on which combinations of primary and secondary alcohols react, the hyperbranched structure may consist of glycerol units which are trisubstituted dendritic (*D*), disubstituted linear (*L*), or terminal (*T*). Each of these general categories may be subcategorized as depicted in Fig. 3. While MALDI-TOF mass spectroscopy can prove the presence of branched

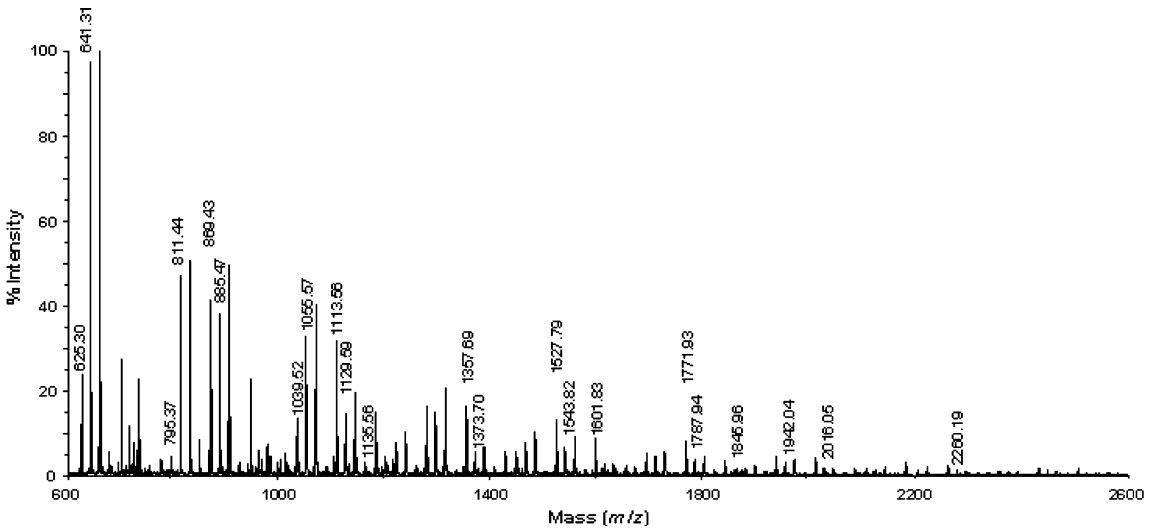


Fig. 2 Representative MALDI-TOF mass spectrum of K^+ and Na^+ adducts of oligo(azelaic acid–glycerol)

species, it is not a reliable method for determining the percentage of a molecule that is branched [21]. NMR spectroscopy, however, can determine how many glycerol units have reacted and at which of the primary or secondary alcohol positions the diacids are located. Therefore, it can characterize the types of branching patterns and measure their relative occurrence. This information can be summarized as a degree of branching ratio (DB%).

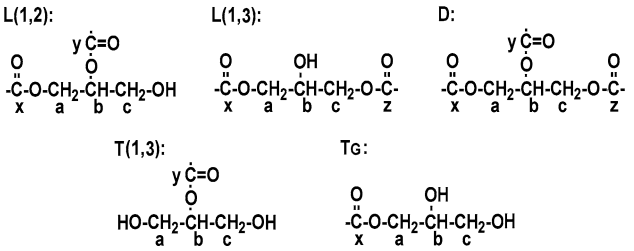


Fig. 3 Substitution patterns for the glycerol backbone after reaction with one or more diacids. Carbons are labeled according to their NMR spectral assignments, where *a*, *b*, and *c* refer to the carbons at glycerol branch-points, and *x*, *y*, and *z* refer to diacid carbons

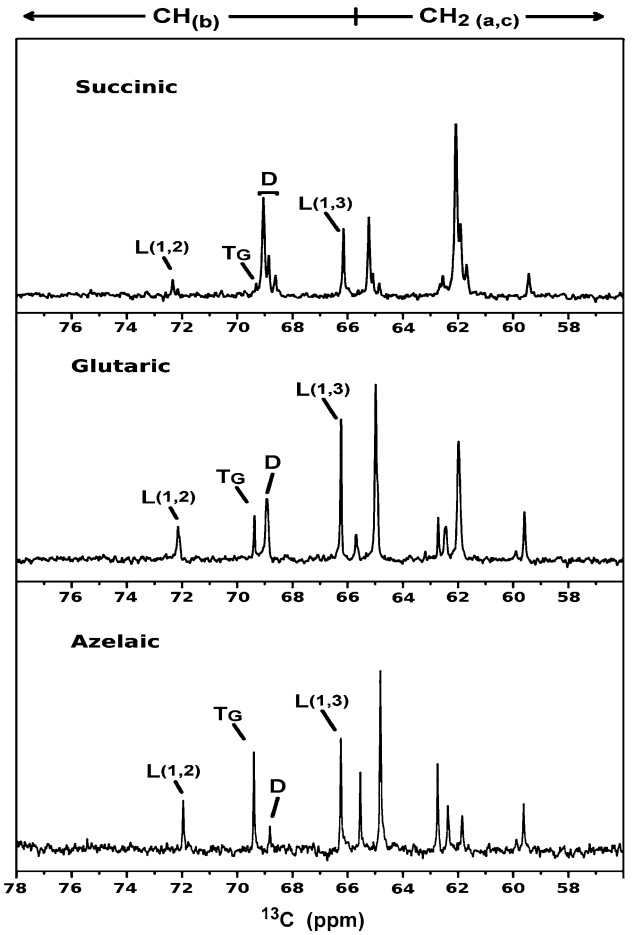


Fig. 4 Expanded inverse gated ^{13}C-NMR spectra of the indicated diacid copolymerized with glycerol

Determining the degree of branching (DB%) by NMR relies upon the ability to distinguish between the different glycerol units by accurately assigning the carbons at each of the glycerol branch points and the terminal positions as also shown in Fig. 3 (labeled C_a, C_b, and C_c). The ^{13}C NMR resonance peaks for these units were then assigned (Fig. 4), integrated, and used to calculate the degree of branching according to Eq. 1 [10, 11, 22–26]:

$$\mathrm{DB}\% = \frac{2D}{2D + \left(L_{1,2} + L_{1,3}\right)} \times 100 \quad (1)$$

where D refers to the integrated NMR intensity of the dendritic branching pattern, and $L_{1,2}$ and $L_{1,3}$ refer to the intensities of the two types of linear substitution patterns (Fig. 3).

Table 6 Experimentally determined NMR resonance assignments for glycerol branching patterns shown in Fig. 3

	D	$L_{1,2}$	$L_{1,3}$	T_G	$T_{1,3}$
Succinic					
H_a	4.24	4.22	4.04	4.03	3.52
H_b	5.23	4.99	3.92	3.69	4.77
H_c	4.24	3.55	4.04	3.39	3.52
C_a	62.05	62.50	65.16	65.94	59.75
C_b	68.94–69.07	72.35	66.13	69.41	75.97
C_c	62.05	59.45	65.16	62.70	59.75
C_x=O	171.7	171.9	171.9	172.0	–
C_y=O	171.4	171.3	–	–	NA
C_z=O	171.7	–	171.9	–	–
Glutaric					
H_a	4.25	4.22	4.05	4.03	3.52
H_b	5.25	5.01	3.92	3.69	4.79
H_c	4.25	3.55	4.05	3.39	3.52
C_a	61.87	62.31	65.05	65.61	59.69
C_b	69.10	72.27	66.56	69.43	75.68
C_c	61.87	59.50	65.05	62.98	59.69
C_x=O	172[b]	171.9	172[a]	172[a]	–
C_y=O	171.8	172.1	–	–	NA
C_z=O	172[b]	–	172[a]	–	–
Azelaic					
H_a	4.20	4.18	4.01	4.00	3.49
H_b	5.21	4.97	3.89	3.66	4.75
H_c	4.20	3.52	4.01	3.37	3.49
C_a	61.88	62.35	64.86	65.57	59.92
C_b	68.93	72.00	66.31	69.48	75.52
C_c	61.88	59.58	64.86	62.88	59.92
C_x=O	172.6	172.7	172.8	173.0	–
C_y=O	172.3	172.4	–	–	172.8
C_z=O	172.6	–	172.8	–	–

NA Not assigned

[a] Not all of the peaks are visible on the scale depicted in the Figures

[b] Spectral overlap inhibited more accurate resonance assignment

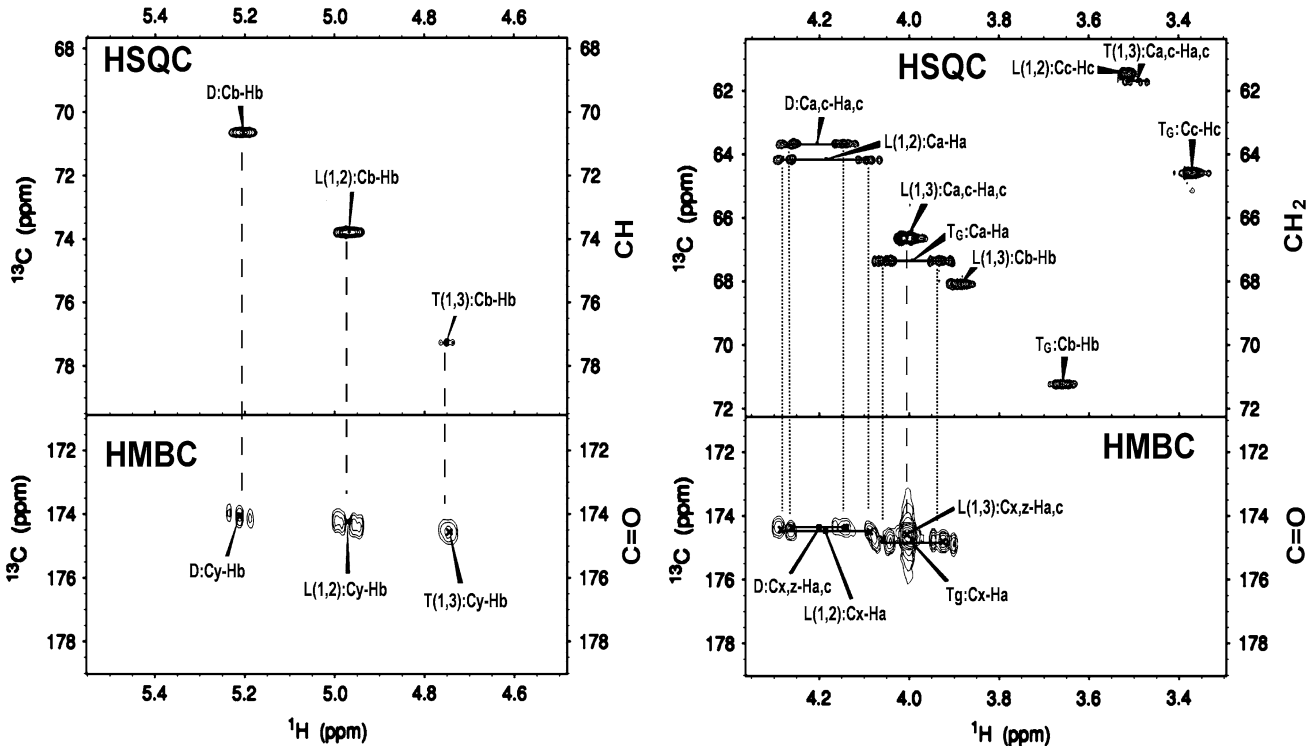


Fig. 5 The 2D-gHSQC and gHMBC (8 Hz) of the azelaic polymer, demonstrating the carbon–proton correlations across the ester oxygen

In this work, the complete assignment of the resonances was determined by analysis of the ^{13}C-DEPT and 2D-NMR spectra to determine the through-bond chemical connectivities within the polymers. This approach is superior to assignments based solely on chemical shift analyses, which are less reliable and can be misleading. ^{1}H- and ^{13}C-NMR assignments for the glycerol region are listed in Table 6. A review of the literature reveals that the exact assignment of the carbons, and in particular, that of T_G versus $L_{1,2}$, may be dependent upon the chemical composition of the branched chains. Thus, the HMBC experiment was of particular importance, as it definitively established the chemical connectivity from the carbonyl carbons of the diacid to the glycerol carbons, through the ester linkage (Fig. 5). The resulting assignments are largely consistent with those of the polymers studied by Kulshrestha et al. [11], but differed from those studied by Stumbe and Bruchmann [10].

It was observed that the amount of $L_{1,2}$ branching increased with increasing diacid length, and that shorter diacids yield greater amounts of dendritic branching (Table 7). The succinic and glutaric oligomers show two peaks near 69 ppm (Table 6), which are attributed to standard dendritic branching, as well as crosslinking, As we could not distinguish between these two types, they were integrated together for the purpose of calculating the degree of branching. These extra peaks are not seen in the azelaic acid derivative. It is likely that such crosslinking (and possible cyclization) occurs more easily with the smaller diacids.

Table 7 Relative amounts of dendritic, linear, and terminal units present in oligo(glycerol–diacids) as determined from integrated ^{13}C NMR resonance peaks

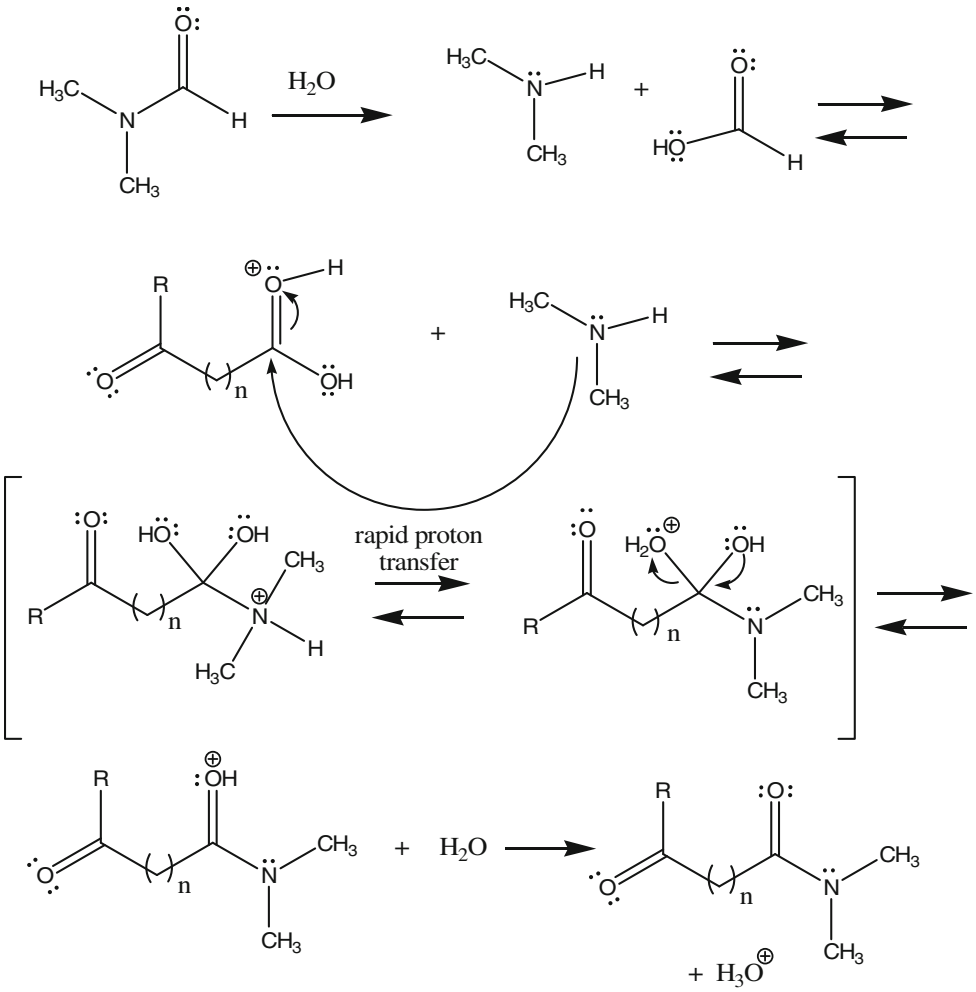
Diacid	D	$L_{1,2}$	$L_{1,3}$	T_G	$T_{1,3}$	DB%
Succinic	66	7	26	3	ND	80
Glutaric	32	17	37	13	ND	54
Azelaic	10	19	39	32	ND	25

Degree of branching (DB) is calculated using Eq. 1

ND Not determined

DMF Reactivity with Propagating Oligomer Chains

The NMR spectra revealed resonances that could be attributed to the presence DMF that had reacted with the oligomer chains, as well as of unremoved (free) DMF. Analysis of the two-dimensional HMBC spectra indicated that some chains terminated with $–CH_2–C(O)–N(CH_3)_2$. This was evidenced in the HMBC spectra by through-bond couplings between the methyls of the $–N(CH_3)_2$ and the adjacent diacid CH_2, through the diacid carbonyl. DMF is a useful common organic solvent because it is a resonance stabilized molecule with a low dissociation constant.



Scheme 1 Proposed mechanism for the formation of a dimethyl amine derivative of hyperbranched oligo(diacid–glycerol)s and formic acid. *R* represents an ester linkage to a glycerol along the oligomeric chain. $n = 2$ oligo(succinic acid–glycerol), $n = 3$ oligo(glutaric acid–glycerol), $n = 7$ oligo(azelaic acid–glycerol)

However, in the presence of water, DMF hydrolyses to form dimethylamine (DMA) and formic acid. It is likely that water produced from the esterifications caused the hydrolysis of DMF, which enabled the production of these DMA-terminated polyesters, as shown in Scheme 1.

The resonances of the bound DMA and free DMF were determined by spiking the samples with a small aliquot of pure DMF. It was possible to determine the extent of overall DMA incorporation by comparing the integrated areas of the $-N(CH_3)_2$ methyl protons to those of the central CH_2 in the diacid chains. This ratio revealed that only a small percentage of the azelaic acid-derived oligomers reacted with DMF ($\sim$4%), while succinic acid- (14%) and glutaric acid- (36%) derived oligomers showed higher degrees of DMF reactivity to the polymer. This putative chain-length dependence may be important in future analyses, as they may correlate directly to the esterification rate of each diacid with glycerol.

Analysis of the MALDI-TOF mass spectrometry data also indicated that the masses detected for the ionated polyester species represented molecules that were DMA-terminated. This is observed in the MALDI-TOF mass spectroscopy as a net MW increase of 27 corresponding to the replacement of the hydroxyl group from the diacid with the dimethyl amine. Ionated species corresponding to formic acid-terminated glycerols were not detected.

Summary

Oligo(diacid–glycerol)s were successfully synthesized in DMF. These oligomers were soluble in many polar solvents which suggest that crosslinking was avoided or present in negligible quantities for 24-h reactions. Although not discussed in detail, neat reactions performed under similar conditions gave solid, insoluble materials that have characteristics consistent with crosslinked products. Compared to DMSO, DMF was found to be a good solvent. DMSO could not be effectively removed from the dark, tar-like products that resulted when it was used as a solvent. Conversely, DMF was easier to remove and produced clear, amber, viscous, liquids. Increasing the diacid chain length appears to be a primary factor in influencing increased degrees of branching; however, explanations for

this effect is beyond the scope of this work. The termination of the oligomers by the addition of dimethylamine demonstrates the ability to stop chain propagation. In future studies, this may allow added control of the physical and mechanical properties of such hyperbranched polymers by using the appropriate stoichiometric amount of a solvent or monofunctional monomer to incorporate terminal functionalities. The presence of DMA-termination observed in these studies is an indication that DMF is being hydrolyzed. Therefore, the removal of water from the system (i.e. by the use of molecular sieves) could eliminate or control the incorporation of DMA into the product.

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