2008

Synthesis of Higher Molecular Weight Poly(D-glucaramides) and Poly(aldaramides) as Novel Gel Forming Agents

Tyler Nations Smith
The University of Montana

SYNTHESIS OF HIGHER MOLECULAR WEIGHT POLY(D–GLUCARAMIDES) AND POLY(ALDARAMIDES) AS NOVEL GEL FORMING AGENTS

By

Tyler Nations Smith

Bachelor of Science, Mississippi College, Clinton, Mississippi, 2001

Dissertation

presented in partial fulfillment of the requirements
for the degree of

Doctor of Philosophy
in Chemistry

The University of Montana
Missoula, MT

Autumn 2008

Approved by:

Perry Brown
Assoc. Provost for Graduate Education

Donald E. Kiely, Ph.D., Chair
Chemistry

Klará Briknarová, Ph.D.
Chemistry

Jack Nunberg, Ph.D.
Biological Sciences

Ed Rosenberg, Ph.D.
Chemistry

Holly Thompson, Ph.D.
Chemistry

Smith, Tyler, Ph.D., December 2008 Chemistry

Synthesis of Higher Molecular Weight Poly(D-glucaramides) and Poly(aldaramides) as Novel Gel Forming Agents

Chairperson: Donald E. Kiely, Ph.D.

Poly(alkylene D-glucaramides) with higher molecular weights than previously reported were prepared through a multi-step process beginning with 1:1 alkylenediammonium D-glucarate salts. These salts set a precise stoichiometric equivalence between co-monomers, a necessary requirement for higher molecular weight condensation polymers. The salts were prepared by treating monopotassium D-glucarate with H^+ form ion exchange resin to give D-glucaric acid, which was then reacted with a diamine. The glucarate portion of the salt was activated for polymerization through esterification in HCl/methanol. Polymerization was initiated by basification of the resulting mixture. The molecular weights of the polymers showed strong dependence on the base used in the basification step. Sodium methoxide was a superior base to triethylamine for deprotonation of the diammonium salt and production of higher molecular weight polyamides. The molecular weights of the resulting polymers were further increased through a second polymerization reaction in a dimethylsulfoxide and ethylene glycol solvent mixture which provides greater solubility for the polymers.

The resulting poly(D-glucaramides) were found to serve as novel gel forming agents in aqueous solutions. Poly(hexamethylene D-glucaramide) formed rigid gels upon addition of water to a dimethylsulfoxide solution of the polyamide. By tailoring the water solubility profile of poly(alkylene D-glucaramides) through the use of two different diamines in the polymerization process, hydrogels were formed without dimethylsulfoxide and at low polymer concentrations (0.3-0.5%). The gelation of poly(aldaramides) is influenced by the aldaryl unit as polyamides from xylaric acid and galactaric acid have inferior gel forming ability compared to those from D-glucaric acid.

The nitric acid oxidation of D-glucose to D-glucaric acid was also investigated with emphasis on isolation and purification of the organic acid oxidation products. Oxidation reactions were carried out in an automated reactor using three and four equivalents of nitric acid to D-glucose. Removal of residual nitric acid from the organic acid products was accomplished through vacuum distillation of the reaction mixture followed by filtration through either a diffusion dialysis unit or a nanofiltration system. While nanofiltration showed higher selectivity for separating nitrate, diffusion dialysis was capable of operating at higher feedstock concentration and at low pH thus allowing nitric acid to be recycled.

.

To my wife, Adrienne, and our two boys, Elliot and Evan.

Acknowledgements

First and foremost, I would like to thank my advisor Dr. Don Kiely. I will forever be in debt to Dr. Kiely for the support and inspiration he has given me over the past five years. I have tremendous respect for Dr. Kiely, and he has had a profound impact on my life, both scientifically and personally. Thank you.

Second, I want to thank my dissertation committee for guidance and patience throughout this process.

I also want to thank the people who I have had the pleasure to work with during my graduate studies, especially my lab mates Chrissie Carpenter, Travis Denton, Kirk Hash, Sr., Michael Hinton, Kendra Kuhl, Kylie Kramer Presta, Dan Shirley, Chris Timko, and Arvind Viswanathan and my friends Brad Bessette, Ryan Boger, James Cox, Mark Hughes, Vince Schnee, Peter Slade, and Jesse Stine.

Thanks also to The University of Montana, the department of chemistry, the US Department of Agriculture, and Mrs. Doreen Shafizadeh, all for financial support.

Finally, I would like to thank my family. My wonderful wife, Adrienne, for all of her support, encouragement, and understanding, my two sons, Elliot and Evan, and my parents. Thanks Mom and Dad.

Preface

The design of industrial chemical processes traditionally focuses on cost efficiency and optimal yields. Because of the relatively low cost of petroleum and other finite resources, chemical processes have used these resources as feedstocks with little concern for the long lifetimes and detrimental effects their products have on the environment. Rising petroleum costs and awareness of negative environmental impacts have encouraged a movement toward sustainable industrial chemical processes which utilize alternative feedstock sources and reduce environmental footprints. The fundamental concepts of sustainable chemistry were outlined in the twelve guiding principles of green chemistry set forth by Anastas and Warner in 1998.[1] These interrelated principles emphasize waste reduction and the use of renewable feedstocks for producing safe and environmentally friendly products. In keeping with the ideas of green chemistry, this dissertation describes part of an on-going effort to develop a sustainable chemical process for conversion of renewable carbohydrate feedstocks into environmentally benign chemical building blocks for preparing biodegradable polymers. While green chemistry played a central theme in this work, we also wanted to stay within the boundaries of feasible industrial production in hopes of creating a commercially viable process. Therefore, a balanced approach was taken to produce environmentally friendly products from renewable resources through the use of practical industrial materials and technology.

The industrially abundant and renewable carbohydrate feedstock, D-glucose, can be chemically oxidized using nitric acid into the commercially valuable dicarboxylic acid, D-glucaric acid. Numerous efforts have been made with little success to optimize and control the oxidation reaction in attempt to increase the yields of D-glucaric acid and reduce the amounts of organic acid by-products.[2,3,4,5] Oxidation with nitric acid remains attractive despite its moderate selectivity due to the simplicity of the reaction and the low cost of the oxidizing agent. A portion of this work focuses on an effort to offset the modest yields of D-glucaric acid through isolating the organic acid by-products which have commercial potential as separate products. To this end, investigations were made into purifying the organic acid by-products from residual nitric acid.

Methods for using D-glucaric acid as a starting material for the preparation of polyhydroxypolyamides, hydroxylated nylon-type polyamides, through polycondensation with various diamines have been described but have failed to achieve high molecular weight polymers.[6,7,8,9,10] These methods rely upon gravimetric measurements for achieving equal amounts of D-glucaric acid and the diamine co-monomers, essential for producing high molecular weight condensation polymers. To improve the stoichiometric control of the co-monomers, a new method which utilizes 1:1 salts formed from D-glucaric acid and a variety of diamines as the polymer starting material will be described for preparing poly(D-glucaramides).

The final part of this dissertation describes the novel application of polyamides formed from D-glucaric and other aldaric acids as gel forming agents. The synthesis of these gel forming agents and a preliminary examination of factors influencing gel formation will be discussed.

Tyler Nations Smith

[1] Anastas, Paul T.; Warner, John C. *Green Chemistry: Theory and Practice*; Oxford University: USA, 1998.

[2] Mehltretter, C. L. Process of Making D-Saccharic Acid. *U.S. Patent 2,436,659*, Feb. 24, 1946.

[3]Mehltretter, C. L.; Rist, C. E. Sugar Oxidation, Saccharic and Oxalic Acids by the Nitric Acid Oxidation of Dextrose. *J. Agr. Food Chem.* **1953**, *1*, 779-783.

[4] Mustakas, G. C.; Slotter, R. L.; Zipf, R. L. Potassium Acid Saccharate by Nitric Acid Oxidation of Dextrose. *Ind. Eng. Chem.* **1954**, *46*, 427-434.

[5]Kiely, Donald. E.; Carter, Andy; Shrout, David P. Oxidation Process. *U.S. Patent 5,599,977*, Feb. 4, 1997.

[6]Kiely, D. E.; Lin, Tsu-Hsing. Polyhydroxypolyamides and Process for Making Same. *U.S. Patent 4,833,230*, May 23, 1989.

[7]Kiely, Donald E.; Chen, Liang.; Lin, Tsu-Hsing. Hydroxylated Nylons Based on Unprotected Esterified D-Glucaric Acid by Simple Condensation Reactions. *J. Am. Chem. Soc.* **1994**, *116*, 571-578.

[8]Kiely, Donald E.; Chen, Liang.; Lin, Tsu-Hsing. Synthetic Polyhydroxypolyamides from Galactaric, Xylaric, D-Glucaric and D-Mannaric Acids and Alkylenediamine Monomers-Some Comparisons. *J. Polym. Sci., Polym. Chem. Ed.* **2000**, 38, 594-603.

[9]Morton, David W.; Kiely, Donald E. Synthesis of Poly(azaalkylene aldaramides) and Poly(oxaalkylene aldaramides) Derived from D-Glucaric and D-Galactaric Acids. *J. Polym. Sci., Polym. Chem. Ed.* **2000**, *38*, 604-613.

[10]Nobes, Geoffrey A. R.; Orts, William, J.; Glenn, Gregory M. Synthesis and Properties of Water-Resistant Poly(glucaramides). *Ind. Crop. Prod.* **2000**, *12*, 125-135.

Table of Contents

List of Figures

List of Schemes

List of Tables

Chapter 1. Purification and Isolation of Products from the Nitric Acid Oxidation of D-Glucose.

1.1 Introduction

The 20th century witnessed unprecedented technological growth fueled in part by the isolation and refinement of petroleum. Today, however, we are witnessing the repercussions of such expansive growth. Negative environmental, political and social impacts from petroleum consumption have encouraged a global shift toward sustainable sources for fuels and chemicals. Wind, solar, and geothermal power along with biofuels derived from plant material have potential for serving as alternatives to petroleum-based energy. The use of carbon dioxide as an alternative feedstock for producing carbon-based chemicals is attractive due to the abundance of this molecule and its implication as a greenhouse gas contributing to global warming. Plants efficiently use carbon dioxide in photosynthesis to produce simple sugar (carbohydrate) molecules, making plant material an abundant and renewable chemical feedstock.

Carbohydrates in the form of polymers (polysaccharides) make up a large percentage of dry plant material. Two common polysaccharides, starch and cellulose, are composed of repeating D-glucose units and serve as energy storage and structural support polymers in plants. D-Glucose, the most naturally abundant monosaccharide, is commercially isolated through enzymatic digestion and acid catalyzed hydrolysis of starch. Because of its relative low cost and commercial availability, D-glucose is the principal monosaccharide for conversion into chemical feedstocks. An example of a successful commercial venture using D-glucose as a chemical feedstock is the production of lactic acid through fermentation.[1] Lactic acid is a platform chemical from which other valuable chemicals such as acrylic acid or propylene glycol can be made.[2] The large scale production of the compostable polyester, poly(lactic acid), by NatureWorks LLC (formerly Cargill-Dow LLC) for packaging and fiber applications underscores the commercial importance of lactic acid.

While many biological transformations involving D-glucose and other monosaccharides have the potential to be harnessed for production of chemical

intermediates and products, the utility of these transformations can be limited by the specificity of the enzymes involved. Substrate specificity of enzymes gives high selectivity in product conversion and is critical for properly functioning biological systems. However, high selectivity prevents the use of a single enzyme for converting a variety of structurally different molecules into chemical products. Therefore, a new fermentation process must be developed when the feedstock is changed. Chemical transformations offer greater flexibility in accepting a wider structural range of reactants, but this lack of discrimination usually translates into higher amounts of by-product formation. Oxidation of monosaccharides, particularly aldoses, using nitric acid is an example of a non-discriminatory chemical transformation. These oxidation reactions proceed with moderate selectivity at the terminal carbons of the aldose molecule, occurring first at the hemi-acetal group (the anomeric carbon, C_1) to give a monocarboxylic acid (aldonic acid) followed by the terminal carbon (C_5 in aldopentoses and C_6 in aldohexoses), to produce a dicarboxylic acid (aldaric acid). Historically, nitric acid oxidations of monosaccharides played a role in Fischer's elucidation of the structural identity of the five and six carbon aldoses.[3,4] The oxidation of D-glucose as an industrial process for producing D-glucaric acid was developed by USDA laboratories in the mid 20th century through the work of Mehltretter *et al.*[5,6] and the subsequent work of Mustakas *et al.*[7] in constructing a pilot plant for the reaction.

Reported uses for D-glucaric acid are numerous and include metal sequestering agent,[8,9] mordant in the dyeing of textiles, and corrosion inhibitors for metals. One of the several lactone forms of D-glucaric acid, D-glucaro-1,4-lactone, is an inhibitor of β-glucuronidase[10] enzymes and is been marketed as a nutraceutical for cancer prevention.[11] In addition to these end uses, D-glucaric acid can also be used as a starting material for the synthesis of other chemicals, particularly polyhydroxypolyamides.[12] D-Glucaric acid has been targeted by the Department of Energy as the one of the top twelve building blocks for production and development from biomass due to the high commercial potential of the compound and the availability of D-glucose starting material.[13]

Despite this potential, large scale production and commercialization of D-glucaric acid has been hindered, primarily due to competing side reactions which result in low conversion to D-glucaric acid (<50% yield) when using nitric acid as the oxidizing agent.

Oxidization methods using platinum catalyst[14] and TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl)[15,16,17] have also been explored to improve conversion of D-glucose to D-glucaric acid. The metal catalyzed reaction showed only slight improvements in yield of D-glucaric acid (54% yield), while the TEMPO-based oxidations give higher glucaric acid conversion (70-90% yield) but require expensive oxidizing agents. Biochemical production of D-glucaric acid is possible but requires a two step process beginning with fermentation of *myo*-inositol to D-glucuronic acid followed by chemical oxidation to D-glucaric acid.[18]

In spite of giving modest yields of D-glucaric acid (40-45%), nitric acid oxidation remains attractive for commercialization because of the low cost of the nitric acid which serves as both solvent and oxidizing agent. Consequently, we have continued efforts to improve the nitric acid oxidation of D-glucose with focus on reaction control and reaction work-up. Improvements to the oxidation reaction and isolation of D-glucaric acid are particularly relevant to the main topic of this dissertation concerning synthesis of poly(D-glucaramides) from monomeric D-glucaric acid. A reactor equipped with a jacketed reaction flask and an automated reactant feed was used to manage the reaction conditions through control of reaction temperature and addition of the reducing species. Gases bubbled into the reaction solution have also been shown to help remove heat from the system.[19] Use of oxygen as the cooling gas also serves to oxidize NO formed during the reaction to NO_2, and O_2 becomes the terminal oxidant, ultimately fostering regeneration of spent nitric acid and lowering the amount required. Reducing the amount of nitric acid used in the reaction can cut production costs, reduce waste, and facilitate product isolation. Vacuum distillation of the reaction solution can also reduce nitric acid waste by recovering of a large portion of the residual nitric acid as an azeotrope with water for reuse in subsequent reactions.

Unfortunately, attempts to control the nitric acid oxidation reaction have failed to significantly improve the yield of D-glucaric acid or reduce number of side products formed in the process. The major side-products observed are the monocarboxylic acids, D-gluconic acid and 5-ketogluconic acid, and the dicarboxylic acids, tartaric acid, tartronic acid, and oxalic acid which arise from oxidative carbon-carbon bond cleavage. The structural and chemical similarities of these compounds would appear to make

isolation of single product difficult; fortuitously, D-glucaric acid forms a relatively water insoluble monopotassium salt (monopotassium D-glucarate, MKG) that can be selectively precipitated from solution. A typical procedure for isolating MKG from the oxidation mixture involves basification of the nitric acid reaction solution with KOH, followed by back titration with a mineral acid to pH 3.5 to precipitate MKG. The basification step ensures that all soluble lactone forms of D-glucaric acid are hydrolyzed to the dipotassium salt prior to acidification to MKG.

To mitigate the modest yields of D-glucaric acid from nitric acid oxidations, our work described here focuses on the purification and isolation of side products from the reaction mixture. Most of the connected uses for D-glucaric acid do not require its specific molecular structure; consequently, a mixture of the oxidation products, all hydroxycarboxylic acids, could be used in place of pure D-glucaric acid. However, residual nitric acid or nitric acid salts must be separated from the organic mixture prior to use. Environmental nitrate pollution leads to excessive algae and plant growth in surface waters which, in turn, reduces the amount of oxygen (hypoxia) in the water available for fish and other aquatic organisms.[20] Nitrate in drinking water can also have negative human health effects and has been linked to hemoglobin disorders, particularly methemoglobinemia in infants.[21] Because of these environmental impacts, removing residual nitrate from the oxidation product mixture is critical for commercial development of the side-product mixture and is a central focus of this work. As previously mentioned, improvements in the nitric acid oxidation of D-glucose allow less nitric acid to be used in the reaction. Starting with lower amounts of nitric acid and using distillation to remove unconsumed nitric acid aid in achieving low nitrate levels in the product.

Initially, finding an effective analytical tool to monitor the removal of nitric acid/nitrate from the organic acids was a significant problem. Gas chromatography-mass spectrometry (GC-MS) can be used to monitor the organic product distribution from nitric acid oxidation reactions but does not show nitrate. A method using high performance liquid chromatography (HPLC) with an ion exchange column was developed to separate and visualize both nitrate and a number of the organic species.[22] Resolution was a problem with this method as a number of species gave overlapping

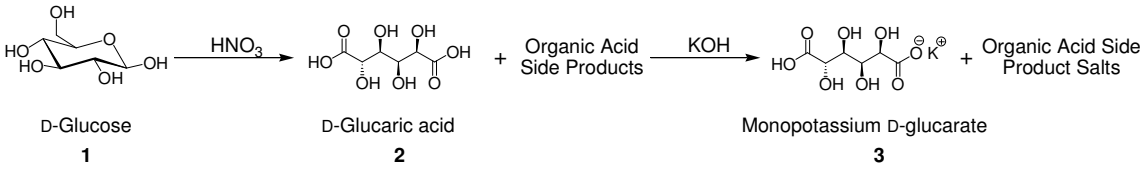
peaks. The system required a weakly acidic eluent which catalyzed lactone formation of some hydroxycarboxylic acids, giving multiple peaks for a single species. Ion chromatography (IC) shows promise for quantifying both inorganic and organic acids and preliminary investigations have shown that a majority of the components in the oxidation mixture can be resolved.[23] At this time, a standard protocol for quantifying the individual components is still being developed.

1.2 Results and Discussion

1.2.1 Oxidation Reaction

Nitric acid oxidations of D-glucose (**1**) were carried out using a computer controlled Mettler-Toledo LabMax reactor capable of automated addition of reactant solutions, reaction temperature control, and pressurization of the reaction with oxygen. A typical oxidation procedure involved charging the jacketed reactor flask with concentrated nitric acid (68%) followed by the slow addition of an aqueous D-glucose solution (62%) containing a small amount of sodium nitrite which serves as an initiator for the reaction (**Scheme 1-1**). The temperature of the exothermic oxidation reactions was closely controlled during the course of the reaction and was either held constant or slowly ramped to a higher temperature. Two different oxidation methods were employed. The first method consisted of a 30 °C reaction temperature, a 6.5 hour reaction time and the use of 4 molar equivalents of nitric acid to D-glucose. The second method consisted of a 25 °C reaction temperature, a 2.5 hour reaction time, and the use of 3 molar equivalents of nitric acid. The purpose of the first method was to drive the oxidation to completion for an optimal yield of D-glucaric acid, while the second method employed milder conditions to prevent oxidative degradation of D-glucose to undesirable small molecules such as oxalic acid and carbon dioxide.

Scheme 1-1. Nitric acid oxidation of D-glucose.



Crystalline dextrose, while high in purity, is the most expensive form of D-glucose available. Less expensive D-glucose syrups are also commercially available, and several were tested as feedstocks for the nitric acid oxidation. These aqueous syrups, collectively known as starch hydrosylates, consist of D-glucose along with oligosaccharides of D-glucose (maltose and other glucans) from incomplete hydrolysis. The syrups are differentiated by their dextrose equivalency (DE), which is a measurement of the reducing value of the mixture expressed in percent. Crystalline D-glucose (dextrose) has a DE value of 100 whereas a high molecular weight polymer of D-glucose, such as starch, has a value near 0. In this study, D-glucose syrups with DE values of 95-99 and 41-45 were evaluated as oxidation feedstocks along with pure dextrose.

1.2.2 Nitric Acid/Nitrate Removal

1.2.2.1 Distillation

The traditional work-up of the nitric acid oxidation of D-glucose requires complete neutralization of the reaction mixture with potassium hydroxide followed by back titration with a mineral acid to precipitate monopotassium D-glucarate (**3**).[6] This approach does not allow for recycling residual nitric acid. Development of an alternative work-up strategy is important in terms of commercial development and waste reduction. Nitric acid and water form a negative azeotrope with a boiling point of 120.5 °C and a composition of 68% nitric acid and 32% water. Upon completion of the oxidation reaction, the mixture was concentrated using a rotary evaporator under reduced pressure. Through distillation, approximately 60% of the initial molar amount of nitric acid can be recovered as determined by titration of the distillate with sodium hydroxide using

Figure 1-1. IC chromatogram of the reaction mixture from the nitric acid oxidation of D-glucose syrup (95-99 DE).

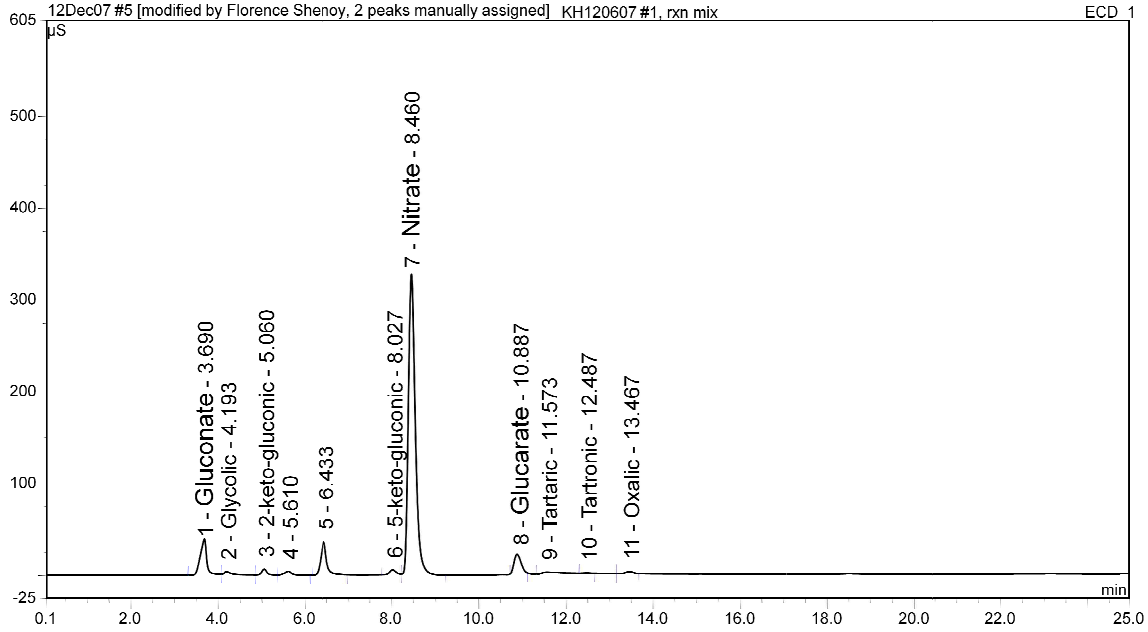
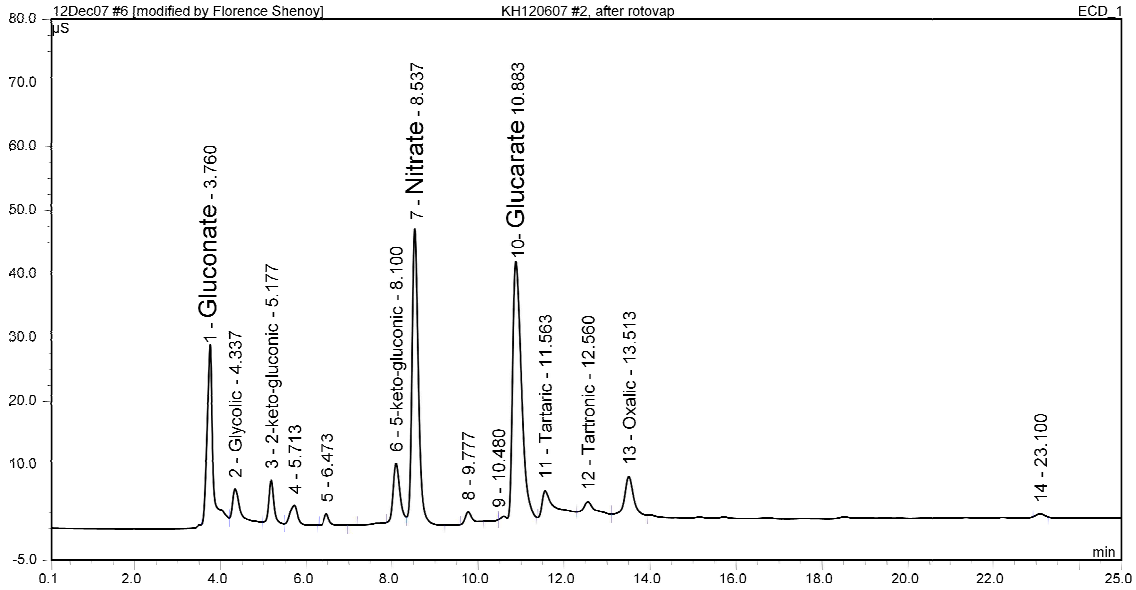


Figure 1-2. IC Chromatogram of the concentrated reaction mixture from the nitric acid oxidation of D-glucose syrup (95-99 DE).



phenolphthalein indicator. Qualitatively, the reduction of nitric acid through distillation was visualized by comparing the nitrate peak level in the IC chromatogram of the reaction mixture before (**Figure 1-1**) and after (**Figure 1-2**) distillation.

1.2.2.2 Ether Extraction

Previous work showed that an ether extraction could be used to extract a portion of the nitric acid from the aqueous reaction mixture.[24] In an effort to remove the residual nitric acid from the concentrated reaction mixture, the syrup from the distillation was treated with methyl *t*-butyl ether (MTBE) which gave a white, hygroscopic solid after several hours of stirring. The liquid ether layer contained 10% of the starting amount of acid as determined by titration. Coupling distillation with an ether extraction of the concentrate removed at least 70% of the starting nitric acid.

The ^{1}H NMR spectrum of the solid from the extraction showed a large amount of the dilactone form of D-glucaric acid, D-glucaro-1,4:6,3-dilactone. In aqueous solutions of D-glucaric acid, very little dilactone is present.[25] However, crystalline dilactone can be isolated from extensive drying of D-glucaric acid at elevated temperatures.[26] Unfortunately, attempts to crystallize the dilactone from the solid material produced in the ether extraction resulted in small amounts (~10%) of pure material.

1.2.2.3 Nanofiltration

The use of ether, a volatile and potentially explosive organic solvent, was not justified for efficient and safe removal of the residual nitric acid. As an alternative, size selective membrane filtration was tested as a way to separate inorganic nitrate salts from the organic side product salts. The feedstock solution for nanofiltration (NF) was produced from concentrated oxidation reaction mixtures that were diluted with water and made basic with sodium or potassium hydroxide. Basification of the concentrated reaction solution was carried out to prevent corrosion of the filtration system with nitric acid. A solution was fed into the nanofiltration system with applied pressure, generating two output streams, one containing components passed through the filter (permeate) and one containing components unable to pass through the filter (retentate). The HPLC chromatograms of the retentate (**Figure 1-4**) and permeate (**Figure 1-5**) in comparison to

Figure 1-3. HPLC chromatogram of the nanofiltration feedstock from nitric acid oxidation of dextrose.

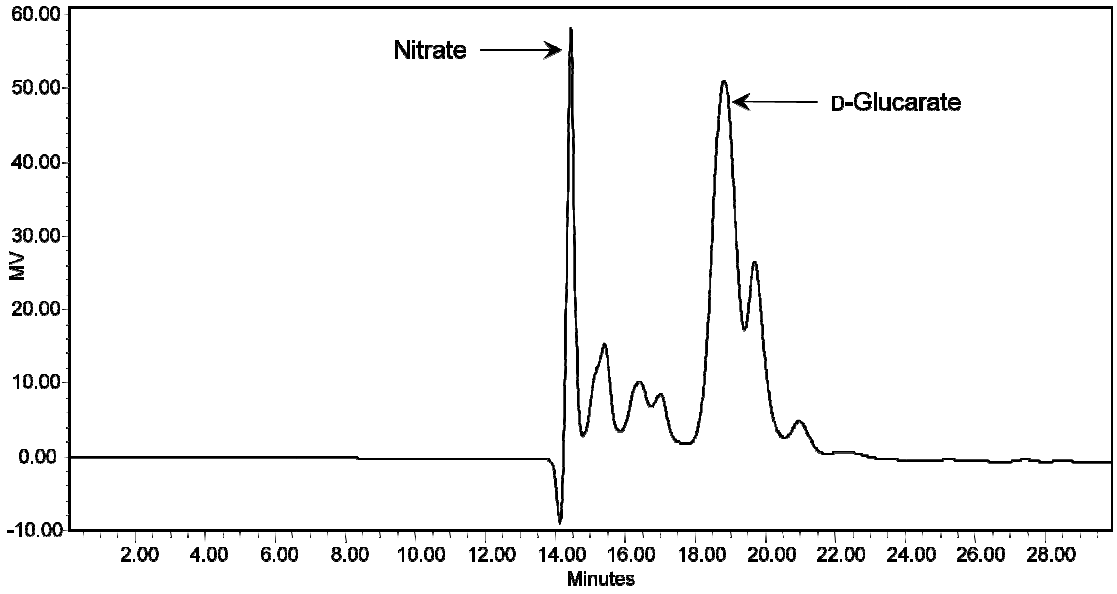


Figure 1-4. HPLC Chromatogram of the nanofiltration retentate from nitric acid oxidation of dextrose.

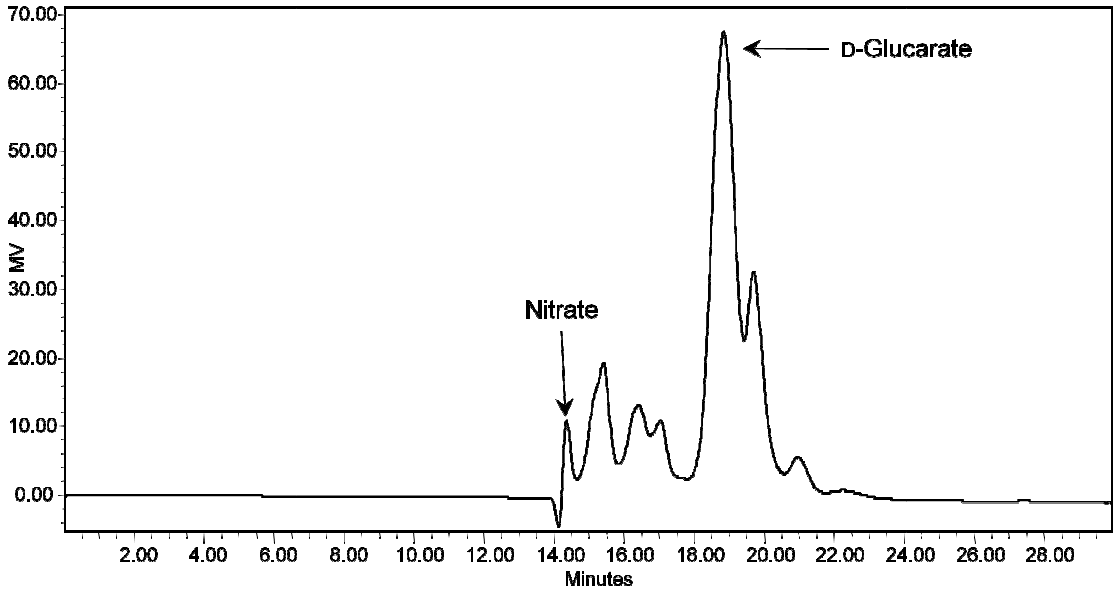
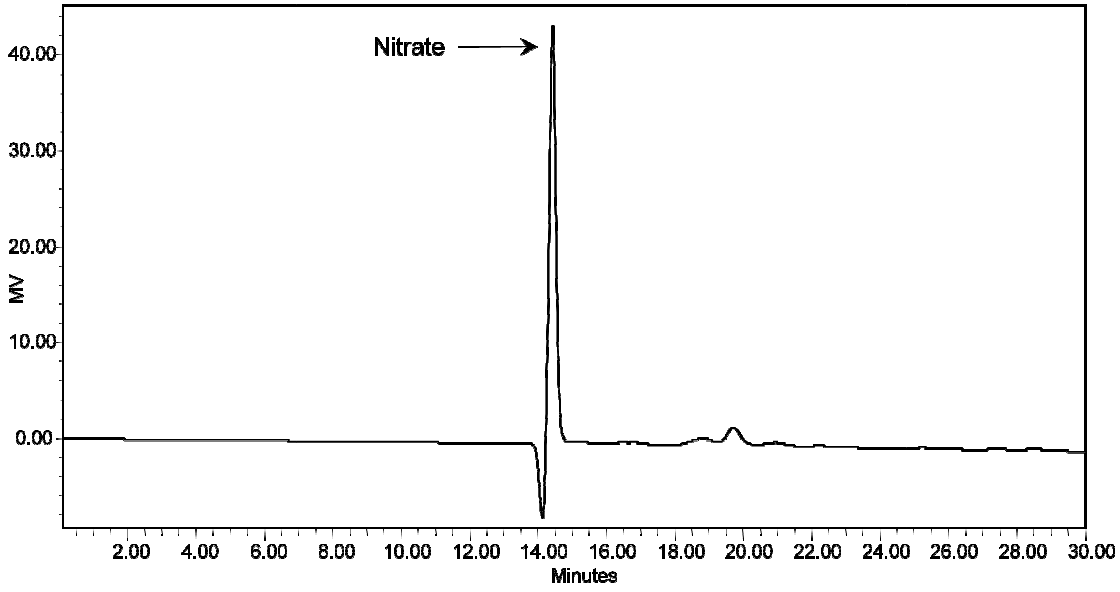


Figure 1-5. HPLC chromatogram of the nanofiltration permeate from the nitric acid oxidation of dextrose.



the starting feedstock solution (**Figure 1-3**) show high selectivity for nitrate removal; however, some monovalent and low molecular weight organic acid salts, such as D-gluconate and oxalate, also passed through the filter. The major drawback of the nanofiltration unit was that it required a dilute feedstock solution to avoid high back-pressure in the system. Additional water was also required during the filtration process to avoid low flow rates. Consequently, a very dilute product stream was produced which required vacuum distillation to remove water prior to MKG isolation. On a commercial scale, distillation of such large volumes of water is energy intensive and ultimately may render the nanofiltration method impractical.

1.2.2.4 Diffusion Dialysis

In addition to nanofiltration, diffusion dialysis (DD) was evaluated as way to separate nitric acid from the organic acid products. Diffusion dialysis is a technique for recovering strong acids from aqueous mixtures containing multivalent metal ions and is commonly used in metal processing applications such as anodizing and pickling. The DD system relies upon a cationic membrane stack which partitions the solution to be separated from a counter flow of pure water. The strong acid disassociates in solution to form an anion/hydronium ion pair. The anion passes through the positively charged

membrane into the counter flowing water along with an equal amount of hydronium ion while the larger metal cations are retained. DD had not previously been applied to the separation of strong inorganic acids from organic acids such as those generated in the nitric acid oxidation of D-glucose. However, DD proved to be an effective separation method when applied to nitric acid/organic acid product mixtures, as will be described. However, as of present, there is no clear mechanism as to how the product acids are separated from the inorganic acids using this process. Like nanofiltration, DD produces two streams, one rich in nitric acid and one rich in organic acids, but, in contrast to nanofiltration, the DD system can accept a feedstock solution with high concentration and low pH. Thus DD does not require removal of large amounts of water and facilitates recycling of the reclaimed nitric acid stream for use in subsequent oxidation reactions. In addition, the DD system operates near atmospheric pressure and requires relatively little energy input. IC was used to evaluate the separation efficiency of DD in nitric acid removal from the oxidation reaction mixture. The concentrated reaction solution (**Figure 1-2**) was diluted with an amount of water equal to distillate removed then used as the DD feedstock. IC chromatograms for the organic product stream (**Figure 1-6**) and the reclaimed nitric acid stream (**Figure 1-7**) show efficient separation of nitric acid although significant bleed through of the organic acids, primarily D-glucaric acid, was also observed.

1.2.3 Product Isolation

1.2.3.1 Monopotassium D-Glucarate

Two different isolation methods for monopotassium D-glucarate (MKG) were applied to two different oxidation methods and three different D-glucose starting materials. To establish a benchmark yield for MKG, the traditional isolation method, labeled Method 1, involving basification of the oxidation reaction mixture with potassium hydroxide followed by acidification to MKG was employed. For optimal MKG yield, isolation Method 1 was applied to an extended reaction time dextrose oxidation using 4 equivalents of nitric acid followed by concentration of the reaction to remove some residual nitric acid. An MKG yield of 45% of theoretical was obtained by this procedure,

Figure 1-6. IC chromatogram of the diffusion dialysis organic product stream from the nitric acid oxidation of D-glucose syrup (95-99 DE).

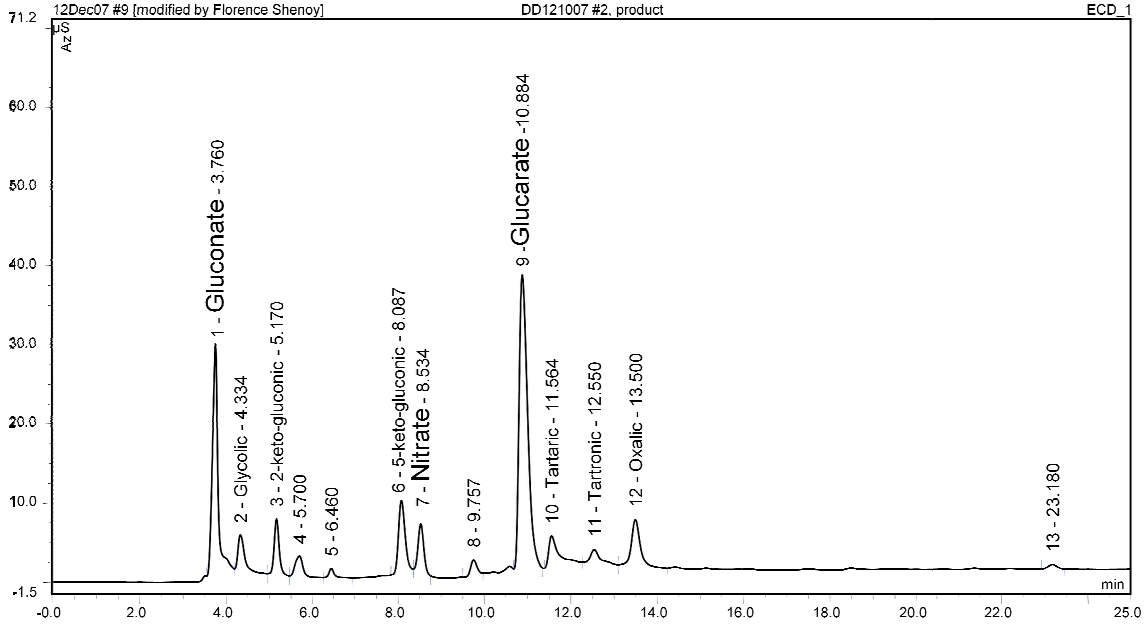
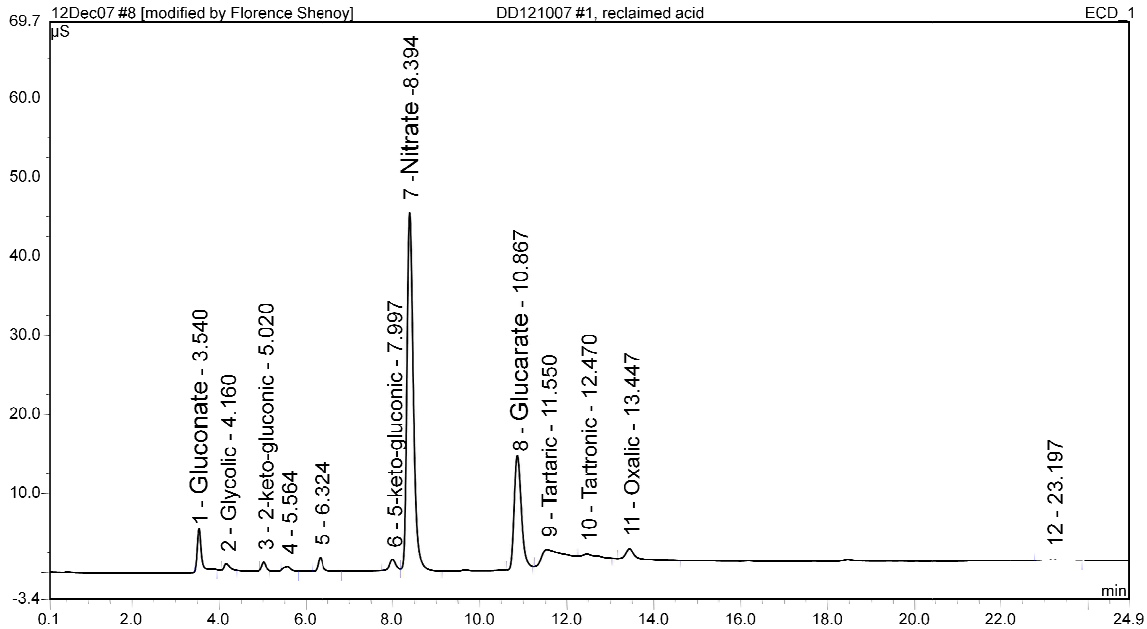


Figure 1-7. IC chromatogram of the diffusion dialysis reclaimed nitric acid stream from the nitric acid oxidation of D-glucose syrup (95-99 DE).



comparable to that previously reported (41%).[6] Isolation Method 1 was also applied to a matching dextrose oxidation mixture passed through the nanofiltration unit prior to MKG precipitation. Nanofiltration appeared to reduce the MKG yield slightly (43%), probably due to bleed through of D-glucarate into the nitrate stream.

Isolation Method 1 is advantageous for isolating the majority of D-glucaric acid present in a reaction mixture, but it requires a large amount of KOH for basification and reintroduces inorganic salts back into the organic acid side products. To avoid these problems, a second MKG isolation method (Method 2) was developed in which MKG was isolated from the acidic reaction mixture by adjusting the pH to 3.5 without complete basification. As before, a benchmark MKG yield was established for isolation Method 2 using an oxidation reaction of dextrose with 4 molar equivalents of nitric acid. The reaction mixture was concentrated, redissolved in water, and cooled to 5 °C for 36 h prior to precipitation of MKG (23% yield). The lower isolated yield of MKG underscores the significant presence of D-glucaro-1,4 and 6,3 lactones, which do not form insoluble salts, present at pH 3.5. Without complete basification to promote lactone hydrolysis, isolation Method 2 yields less MKG. However, the MKG yields from Method 2 can be maximized by shifting the equilibrium of the D-glucaric acid present in the oxidation solution to the diacid form (**2**), which is favored at lower temperatures.[25] Thus, by cooling the solution prior to pH adjustment a larger yield of MKG is obtained. For demonstration, the experiment was repeated but with heating (55 °C) of the solution prior to pH adjustment and isolation of MKG to give only 9% yield.

MKG isolation Method 2 was also applied to mixtures from oxidation reactions using 3 equivalents of nitric acid. The MKG yields from oxidation of dextrose and two D-glucose syrups after concentration and diffusion dialysis of the reaction mixture are given in **Table 1-1**. The yields of MKG were lower than the benchmark yields established with four equivalents of nitric acid due to lower conversion of D-glucose to D-glucaric acid during the oxidation reaction. Oxidation of D-glucose syrup with 95-99 DE yielded half the amount of MKG as that from dextrose oxidation while the 41-45 DE syrup yielded no MKG precipitate. The IC chromatogram of the residual organic acid mixture after isolation of MKG (**Figure 1-8**) shows a slight reduction in the amount of

Figure 1-8. IC chromatogram of residual organic acid products from the nitric acid oxidation of D-glucose syrup (DE 95-99) after MKG isolation (Method 2).

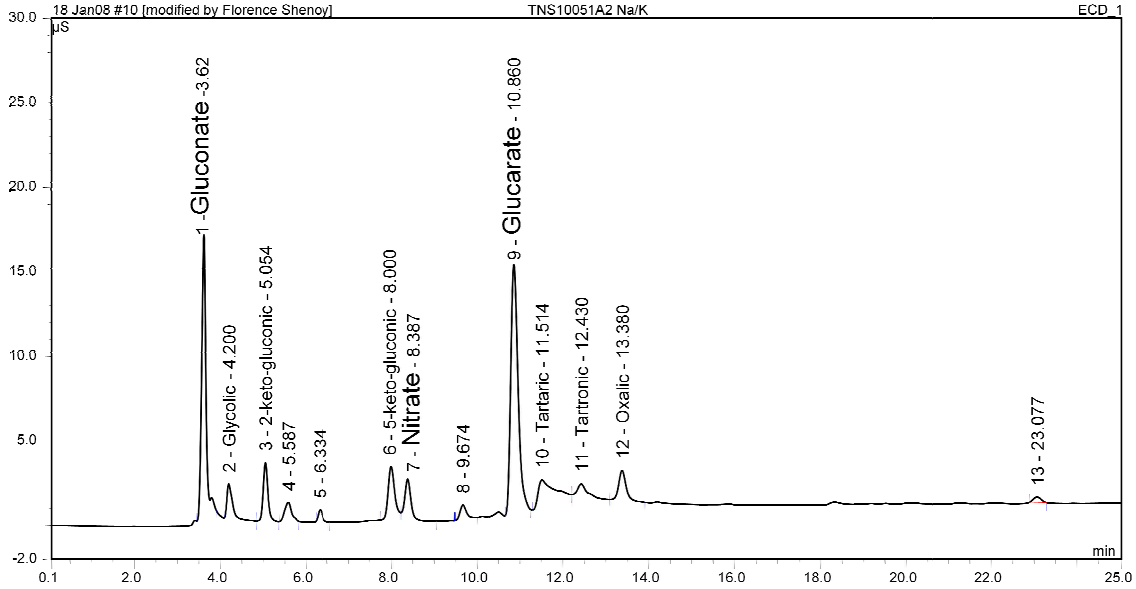


Table 1-1. Monopotassium D-glucarate yields from various D-glucose starting materials, nitric acid oxidation conditions, and isolation methods.

Starting Material	Oxidation Method	Filtration Method	MKG Isolation	MKG Yield (%)
Dextrose	4:1[a]	None	Method 1	45
Dextrose	4:1	NF	Method 1	43
Dextrose	4:1	None	Method 2	23
Dextrose	4:1	None	Method 2, heat[b]	9.3
Dextrose	3:1[c]	DD	Method 2, PS[d]	8.5
Dextrose	3:1	DD	Method 2, RAS[e]	11.2
95-99 DE [f]	3:1	DD	Method 2, PS	6.5
95-99 DE	3:1	DD	Method 2, RAS	8.2
41-45 DE [g]	3:1	DD	Method 2, PS	None

[a]Four to one molar ratio of nitric acid to D-glucose.
[b]Solution was warmed to 55 °C prior to precipitation of MKG.
[c]Three to one molar ratio of nitric acid to D-glucose.
[d]Organic product stream from diffusion dialysis.
[e] Reclaimed acid stream from diffusion dialysis.
[f] D-Glucose syrup (95-99 DE).
[g]D-Glucose syrup (41-45 DE).

D-glucarate present when compared to the organic acid product stream from diffusion dialysis (**Figure 1-6**).

During diffusion dialysis, a portion of the D-glucaric acid present in the oxidation mixture passes through the membrane into the reclaimed nitric acid stream as evidenced by IC (**Figure 1-7**). The D-glucaric acid in the reclaimed acid stream was successfully recovered as MKG using isolation Method 1 for oxidation reactions of dextrose and 95-99 DE syrup, producing 11.2% and 8.2% yields of MKG, respectively (**Table 1-1**).

1.2.3.2 Side Products

The filtration techniques described above provide for the first time a method for separating most of the nitric acid from the organic acids produced in the oxidation reaction and give the opportunity for use of the organic acid side products free from nitrate. For quantification of the organic acids, salts were made of the mixture from nanofiltration or diffusion dialysis then the salt mixtures were dried and weighed. For the total amount of organic acids, sodium salts were made using sodium hydroxide from the product stream of DD and the retentate stream of NF. The organic acid sodium salt mixtures from dextrose and D-glucose syrups using the two different oxidation reaction conditions were prepared. Also, MKG was isolated by Method 2 from the various oxidation mixtures, and the residual organic acids were made basic with sodium hydroxide to produce a mixture of sodium and potassium salt products. The amounts of the organic acid salt mixtures in comparison to the amount of starting material are given in **Table 1-2**. NF gives larger amounts of organic acid salts than DD, due to the larger amount of organic material lost through the DD membrane. The amounts of sodium/potassium salts recovered are less due to the removal of MKG.

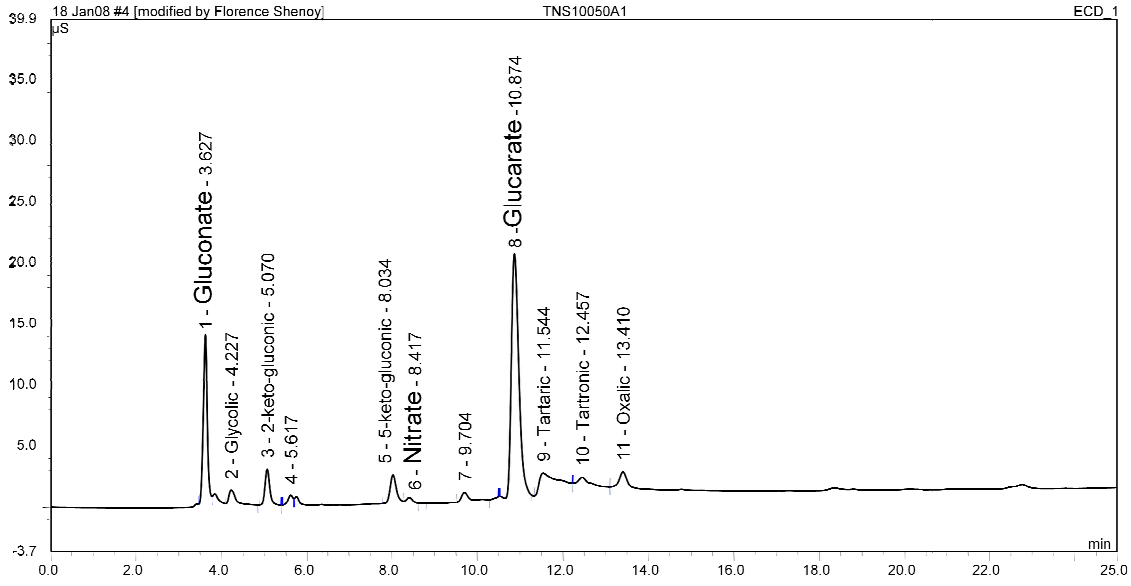
As an alternative to extensive drying of the organic acid salt mixtures under reduced pressure, the mixtures were precipitated from concentrated solutions (50% by wt) with methanol. The amounts of precipitated salts were only slightly less (<10%) than the amounts isolated by drying, but, fortuitously, the precipitated salts showed lower amounts of nitrate by IC (**Figure 1-9**) in comparison to the salts which were dried only (**Figure 1-6**).

Table 1-2. Recovery of organic acid salt mixtures from nitric acid oxidation of D-glucose and D-glucose syrups.

D-Glucose Starting Material	Starting Material Dry Weight (g)	Oxidation Method	Organic Acid Salt Mixture	Filtration Method	Salt Dry Weight (g)	Salt Yield (wt %)[a]
Dextrose	270.2	3:1	Na Salts[b]	DD	259.1	95.9
Dextrose	135.1	4:1	Na Salts	NF	186.5	138
Dextrose	270.2	3:1	Na/K Salts[c]	DD	211.8	78.4
Dextrose	135.1	4:1	Na/K Salts	NF	115.3	85.3
95-99 DE [d]	810.7	3:1	Na Salts	DD	730.4	90.1
95-99 DE	810.7	3:1	Na/K Salts	DD	653.4	80.6
41-45 DE [e]	810.7	3:1	Na Salts	DD	772.6	95.3
41-45 DE	135.1	4:1	Na Salts	NF	180.9	134

[a]Percent of product weight to starting material weight.
[b]Sodium salts of organic acid mixture.
[c]Sodium/potassium salts of organic acid mixture after isolation of MKG using Method 2.
[d]D-Glucose syrup (DE 95-99).
[e]D-Glucose syrup (DE 41-45).

Figure 1-9. IC chromatogram of the precipitated sodium salts from diffusion dialysis organic product stream and the nitric acid oxidation of D-glucose syrup (DE 95-99).



1.3 Conclusions

The work-up of nitric acid oxidations of D-glucose and D-glucose syrups were examined with focus on separation of nitric acid from the organic acid products and isolation of monopotassium D-glucarate. Vacuum distillation of the oxidation reaction mixture recaptures at least 60% of the starting amount of nitric acid for recycling in subsequent oxidation reactions. Both diffusion dialysis and nanofiltration are effective for separating residual nitric acid/nitrate from the organic acid products. Because diffusion dialysis operates at acidic pH, it also offers the opportunity to recycle nitric acid. Nanofiltration requires dilute feedstock solutions and higher applied pressure than diffusion dialysis but shows higher selectivity for nitrate removal, resulting in higher recovery of organic acid products.

1.4 Experimental

General Methods

Anhydrous D-glucose and aqueous nitric acid (15.7 M) were purchased from EMD (EMD Chemicals, Inc, Gibbstown, NJ, USA). Liquid dextrose syrup (StaleyDex® 95, 95-99 dextrose equivalent) and dextrose corn syrup (Staley® 1300, 41-45 dextrose equivalent) were obtained from Tate and Lyle (Tate and Lyle PLC, Decatur, IL, USA). All other chemicals were purchased from Sigma-Aldrich (St. Louis, MO, USA) or J.T. Baker (Philipsburg, NJ, USA) and used without further purification. Aqueous sodium hydroxide and potassium hydroxide solutions were standardized against oven dried potassium hydrogen phthalate using phenolphthalein indicator. Solutions were concentrated *in vacuo* (15-20 mbar) using a rotary evaporator and water bath at 45˚C. Drying of samples was carried out at room temperature (unless otherwise noted) using a mechanical pump. pH measurements were made with a Thermo Orion 310 pH meter (Thermo Fisher Scientific, Inc., Waltham, MA, USA) which was calibrated using standard buffer solutions prior to use.

Analytical Methods

High performance liquid chromatography (HPLC) system was used as previously described.[22] Ion chromatography (IC) was performed using a method previously described.[23] The IC system consisted of a Dionex ICS2000 (Dionex Corporation, Sunnyvale, CA, USA) equipped with a 25μL sampling loop, an AS11-HC 4mm anion separation column fitted with an AG11-HC 4mm guard column, and a Dionex autosampler. The column was maintained at 38 °C. The suppressor was an ASRS ULTRA II auto-suppressor system. The eluent was a water/NaOH mixture varying between 1 mM and 60 mM NaOH, created and controlled with the use of an EG40 eluent generator. The water component of the eluent was purified by a Millipore Simplicity 185 (Millipore Corporation, Billerica, MA, USA) water purifier and was degassed with nitrogen prior to use. Aqueous samples were prepared in a concentration range between 0.1 and 0.5 mg/mL. Samples containing calcium salts were treated with acid form ion exchange resin followed by sodium hydroxide prior to injection. The columns were equilibrated with 1 mM NaOH for 4 min, and upon injection, the eluent concentration was ramped to 30 mM over 25 min followed by a ramp to 50mM over 2 min. The eluent concentration was then held constant for 10 min before returning to 30 mM over 2 min.

Nitric Acid Oxidation Reaction

Nitric Acid Oxidation Reactor. All oxidation reactions were carried out using a LabMax automatic lab reactor (Mettler-Toledo, Columbus, OH, USA). The Labmax was designed to operate as a computer controlled closed-system reactor and was fitted with a top-loading balance, a liquid feed pump, an oxygen Sierra flow valve, a mechanically driven stirring rod, a thermometer, a 2 L thermal jacketed flask, an FTS recirculating chiller, a pressure manifold fitted with pressure relief valves and pressure gauge, and a personal computer with CamileTG v1.2 software. The software installed allows the operator to program experiments based on specific parameters and conditions.

Preparation of D-Glucose, StaleyDex® 95, and Staley® 1300 Oxidation Solutions. D-Glucose and dextrose equivalent syrups were added to the nitric acid as 62.3% solutions (w/w). D-glucose solution was prepared by dissolving anhydrous D -glucose (270.2 g, 1.50 mol) and dry sodium nitrite (1.20 g) in deionized water (162.3 g) at 60 °C with stirring. Once the D -glucose was dissolved, the solution (433.7 g) was allowed to cool to room temperature prior to addition into the reactor. StaleyDex® 95 solution was prepared by dissolving StaleyDex® 95 Liquid Dextrose (380.6 g, 71.0% solids, 95-99 DE) and dry sodium nitrite (1.20 g) in deionized water (51.8 g) at 60 °C with stirring. Once the liquid dextrose was dissolved, the solution (433.6 g) was allowed to cool to room temperature prior to addition into the reactor. Staley®1300 solution was prepared by dissolving Staley®1300 Corn Syrup (336.5 g, 80.3% solids, 41-45 DE) and dry sodium nitrite (1.20 g) in deionized water (95.8 g) at 60 °C with stirring. Once the corn syrup was dissolved, the solution (433.6 g) was allowed to cool to room temperature prior to addition into the reactor.

Oxidation of D-Glucose, 4:1 Molar Ratio of Nitric Acid to D-Glucose. The procedure for the oxidation reaction was divided into nine separate stages in the Recipe Menu of the Labmax Camille software. Stage 1 - the temperature of the reactor jacket was set at 25 °C, the stirring rod speed set at 200 rpm (and held constant throughout the remaining stages), and time set for 1 min. Stage 2 - the reactor jacket temperature was set at 25 °C, the pressure was set at 0.25 bar above atmospheric, and the time set for 3 min. Stage 3 - the temperature and pressure were held constant, and 43.3 g of 62.3% (w/w) D -glucose solution described above was set to be added over 30 min. Stage 4 - the temperature and pressure were held constant, and the time set for 10 min. Stage 5 - the temperature and pressure were held constant, and 172.9 g of D -glucose solution was set to be added over 90 min. Stage 6 - the temperature and pressure were held constant for 5 min. Stage 7 - the temperature was increased to 30 °C, the pressure was increased to 0.50 bar above atmospheric, and the time was set for 60 min. Stage 8 - the temperature and pressure were held constant, and time was set for 90 min. Stage 9 - the reactor temperature was set to cool to 25 °C over 10 min. Once the software was programmed, aqueous nitric acid (187 mL, 3 mol) was added to the reactor, the reaction recipe was initiated, and the reactor was closed to the atmosphere.

Oxidation of StaleyDex® 95 Liquid Dextrose, 4:1 Molar Ratio of Nitric Acid to StaleyDex® 95. StaleyDex® 95 liquid dextrose as an aqueous solution (216.2 g, 62.3% as described above) was oxidized with aqueous nitric acid (187 mL, 3 mol) using the LabMax reactor and the 4:1 oxidation protocol described for D-glucose.

Oxidation of Staley® 1300 Corn Syrup, 4:1 Molar Ratio of Nitric Acid to Staley® 1300. Staley® 1300 corn syrup as an aqueous solution (216.2 g, 62.3% as described above) was oxidized with aqueous nitric acid (187 mL, 3 mol) using the LabMax reactor and the 4:1 oxidation protocol described for D-glucose.

Oxidation of D-Glucose, Method 2. 3:1 Molar Ratio of Nitric Acid to D-Glucose. The procedure for the oxidation reaction was divided into six separate stages in the Recipe Menu of the Labmax Camille software. Stage 1 - the temperature was set for 25 °C (and held constant throughout all remaining stages) and the stirring rod speed set at 200 rpm (and held constant throughout all remaining stages), time was set for 1 min. Stage 2 - the pressure was set at 0.25 bar above atmospheric (and held constant throughout all remaining stages), and the time was set for 3 min. Stage 3 - 86.6 g of 62.3% D -glucose solution was set to be added over 30 min. Stage 4 - 10 min. hold. Stage 5 - 345.8 g of D -glucose solution was set to be added over 90 min. Stage 6 - 20 min. hold. Once the software was programmed, aqueous nitric acid (287 mL, 4.5 mol) was added to the reactor, the reaction recipe was initiated, and the reactor was closed to the atmosphere.

Oxidation of StaleyDex® 95 Liquid Dextrose, 3:1 Molar Ratio of Nitric Acid to StaleyDex® 95. StaleyDex® 95 liquid dextrose as an aqueous solution (432.5 g, 62.3% as described above) was oxidized with aqueous nitric acid (287 mL, 4.5 mol) using the LabMax reactor and the 3:1 oxidation protocol described for D-glucose.

Oxidation of Staley® 1300 Corn Syrup, 3:1 Molar Ratio of Nitric Acid to Staley® 1300. Staley® 1300 corn syrup as an aqueous solution (432.5 g, 62.3% as described above) was oxidized with aqueous nitric acid (287 mL, 4.5 mol) using the LabMax reactor and the 3:1 oxidation protocol described for D-glucose.

Nitric Acid and Nitrate Removal

Vacuum Distillation. The reaction solution from the oxidation of D-glucose or D-glucose syrup was distilled under vacuum (15-20 mbar) using a rotary evaporator and water bath at 55 °C until a thick syrup remained. Unless otherwise stated, the syrup was reconstituted with an amount of water equal to the weight of the distillate.

Ether Extraction. Methyl *t*-butyl ether (300mL) was added to the concentrated reaction mixture (no added water) from the distillation of the oxidation reaction solution. The precipitate, which formed over 24 h stirring, was isolation by vacuum filtration and dried to give a hygroscopic white solid (137.8 g). Water (50mL) was added to the filtrate, and the solution was concentrated until a large change in the vapor temperature was observed. The resulting aqueous solution was diluted with water (100 mL) and titrated with standardized aqueous NaOH (4.66 M, 38.5 mL, 0.179 mol) until basic by phenolphthalein indicator.

Nanofiltration. The nanofiltration unit was built in-house and comprised of valves, pump, lines, a pressure gauge and a GE DL2540F membrane. D-Glucose oxidation reaction mixture was concentrated and redissolved in with water then made basic with aqueous solutions of either sodium or potassium hydroxide. The basic solution was diluted to give a volume of 4 L and used as a feedstock solution for the nanofiltration unit. The nanofiltration system produced two streams: one passing through the filter (permeate) and one which does not (retentate). The permeate was collected in a separate container, while the retentate was fed back into the feedstock. When the permeate volume reached 1L, 1L of reverse osmosis (RO) purified water was added to the feedstock. The typical rate of the permeate flow when reducing the volume by 1L was 48 mL/min. When 2 L of permeate was removed, another 1 L of RO water was added to the feedstock. The typical rate of permeate flow when removing the second 1L was 45 mL/min. This procedure was repeated until a total of 4 L of permeate was collected and 4 L of RO water had been added to the feedstock. The typical permeate flow rate when removing the last 1L was 43 mL/min. The filtration process was continued after the last 1L of RO water was added to the feedstock until the permeate flow slowed to a trickle at

which time the filtration was stopped. The final volumes of the retentate and permeate were 2.8 L and 5.2 L, respectively.

Diffusion Dialysis. The diffusion dialysis system was a Mech-Chem laboratory scale acid purification unit (Model AP-L05, Mech-Chem Associates, Inc., Norfolk, MA, USA). The Mech-Chem unit contains two metering pumps, an acid reclaim pump, and an acid reject pump. The acid reject pump was set at 30% (pump length) and 30% (pump speed), and the acid reclaim pump was set at 40% (pump length) and 40% (pump speed), giving a flow through rate of 120 mL/h for the acid reclaim and 112 mL/h for the acid reject. The system was first primed with RO water according to a standard setup procedure and then the water was removed from the acid tank in the unit. The concentrated reaction mixture from the oxidation of D-glucose or D-glucose syrup reconstituted with water was added to the acid feedstock tank. The water tank was filled with RO water. Two output streams, an inorganic acid recovery stream (reclaimed acid stream) and a product recovery stream (product stream) were collected from the diffusion dialysis unit.

Product Isolation

Monopotassium D-Glucarate Isolation from Basic pH, Method 1. The pH of the concentrated reaction mixture from the oxidation of D-glucose or a D-glucose syrup reconstituted with water was adjusted to a constant pH of 9.5 with 45% KOH. The solution was cooled in an ice bath then back-titrated to pH 3.4 with concentrated hydrochloric acid. A precipitate was observed when the solution pH dropped below 5. After cooling the mixture at 5 °C for 4 h, the precipitate was isolated by filtration. The off-white solid cake was returned to a beaker and triturated in water at 50 °C for 30 min then cooled to 5 °C for 1 h before again isolating the solid by filtration. The solid cake was washed with cold water and dried at reduced pressure for 18 h to monopotassium D-glucarate.

Monopotassium D-Glucarate Isolation from Basic pH and Nanofiltration. The retentate stream from the nanofiltration system was concentrated to an approximate

volume of 300 mL. The pH of the concentrated solution was adjusted to a constant 9.5 with 45% KOH, then back-titrated to pH 3.4 with concentrated hydrochloric acid in an ice bath. The resulting solid monopotassium D-glucarate was isolated as described in Method 1.

Monopotassium D-glucarate Isolation from Acidic pH, Method 2. The concentrated reaction mixture from the oxidation of D-glucose or a D-glucose syrup reconstituted was chilled at 5 °C for 36 h, and then the pH of the solution adjusted to 3.4 with 45% KOH while cooled in an ice bath. After cooling the mixture to 5 °C for 4 h, the solid monopotassium D-glucarate was isolated as described in isolation Method 1.

Monopotassium D-glucarate Isolation from Diffusion Dialysis Product Stream, Method 2. The product stream from the diffusion dialysis unit was concentrated to an approximate volume of 300 mL then chilled at 5 °C for 36 h. Monopotassium D-glucarate was isolated from this solution as described in isolation Method 2.

Monopotassium D-glucarate Isolation from Diffusion Dialysis Reclaimed Acid Stream. The reclaimed acid stream from the diffusion dialysis unit was concentrated to an approximate volume of 300 mL before solid monopotassium D-glucarate was isolated as described in isolation Method 1.

Isolation of Organic Acid Sodium Salt Mixture. The organic product solution from diffusion dialysis was chilled in an ice bath and titrated to a constant pH of 9.5 with 45% NaOH. The basic solution was concentrated and dried under reduced pressure for 48 h to give a tan, amorphous solid.

Isolation of Organic Acid Sodium/Potassium Salt Mixture. The combined filtrate and washings from the isolation of monopotassium D-glucarate Method 2 was chilled in an ice bath and titrated to a constant pH of 9.5 with 45% NaOH. The basic solution was concentrated and dried under reduced pressure for 48 h to give a tan, amorphous solid.

Precipitation of Organic Acid Salt Mixture. Dried organic acid sodium salt mixture or sodium/potassium mixture (5.00 g) was dissolved in water (5 mL) to form a viscous solution. Methanol (50 mL) was added to the solution which rapidly produced a fine

precipitate followed by the slow formation of a darker tacky solid. The mixture was stirred overnight during which the appearance of the composition did not change. The precipitate mixture was isolated by filtration, washed with methanol (3 x 10 mL), and dried under reduced pressure to give an amorphous tan solid. The combined filtrate and washings were concentrated by flash evaporator and dried under reduced pressure to an amorphous solid.

1.5 References

[1] Bailey, R. B.; Joshi, D. K.; Michaels, S. L.; Wisdom, R. A. Production of Lactic Acid from Whey by Continuous Fermentation and Lactic Acid Purification by Solvent Extraction. *U.S. Patent 4,698,303,* March 27, 1986.

[2] Clark, James H. Green Chemistry and Environmentally Friendly Technologies. In *Green Separation Processes*; Afonso, C. A. M.; Crespo J. P., Eds.; Wiley-VCH: Weinheim, 2005.

[3] Fischer, E. *Ber. Dtsch. Chem. Ges.* **1891**, *24*, 1836.

[4] Fischer, E. *Ber. Dtsch. Chem. Ges.* **1891**, *24*, 2683.

[5] Mehltretter, C. L. Process of Making D-Saccharic Acid. U.S. Patent 2,436,659, Feb. 24, 1946.

[6] Mehltretter, C. L.; Rist, C. E. Sugar Oxidation, Saccharic and Oxalic Acids by the Nitric Acid Oxidation of Dextrose. *J. Agr. Food Chem.* **1953**, *1*, 779-783.

[7] Mustakas, G. C.; Slotter, R. L.; Zipf, R. L. Potassium Acid Saccharate by Nitric Acid Oxidation of Dextrose. *Ind. Eng. Chem.* **1954**, *46*, 427-434.

[8] Mehltretter, C. L.; Alexander, B. H.; Rist, C. E. Sequestration by Sugar Acids. *Ind. Eng. Chem.* **1953**, *45*, 2782-2784.

[9] Abbadi, A.; Gotlieb, K. F.; Meiberg, J. B. M.; Peters, J. A.; van Bekkum, H. New Ca-sequestering Materials Based on the Oxidation of the Hydrolysis Products of Lactose. *Green Chem.* **1999**, *1*, 231-235.

[10] Levvy, G. A. Preparation and Properties of *β*-Glucuronidase. IV. Inhibition by Sugar Acids and Their Lactones. *Biochem. J.* **1952**, *52*, 464-472.

[11] Walaszek, Zbigniew. Potential Use of D-Glucaric Acid Derivatives in Cancer Prevention. *Cancer Lett*. **1990**, *54*, 1-8.

[12] Kiely, Donald E.; Chen, Liang.; Lin, Tsu-Hsing. Hydroxylated Nylons Based on Unprotected Esterified D-Glucaric Acid by Simple Condensation Reactions. *J. Am. Chem. Soc.* **1994**, *116*, 571-578.

[13] Werpy, T.; Peterson, G., eds. Top Value Added Chemicals From Biomass, Volume 1-Results of Screening for Potential Candidates from Sugars and Synthesis Gas (U.S. Department of Energy, Oak Ridge, TN, August 2004; available at www.eere.energy.gov/biomass/pdfs/35523.pdf

[14] Mehltretter, Charles L.; Rist, Carl E.; Alexander, Benjamin H. Process for the Preparation of D-Glucosaccharic Acid. *U.S. Patent 2,472,168*, June 7, 1949.

[15] Thaburet, Jean-François; Merbouh, Nabyl; Ibert, Mathias; Marsais, Francis; Queguiner, Guy. TEMPO-Mediated Oxidation of Maltodextrins and D-Glucose: Effect of pH on the Selectivity and Sequestering Ability of the Resulting Polycarboxylates. *Carb. Res.* **2001**, *330*, 21-29.

[16] Merbouh, Nabyl; Thaburet, Jean-François; Ibert, Mathias; Marsais, Francis; Bobbitt, James M. Facile Nitroxide-Mediated Oxidation of D-Glucose to D-Glucaric Acid. *Carb. Res.* **2001**, *336*, 75-78.

[17] Merbouh, Nabyl; Bobbitt, James M.; Brückner, Christian. 4-AcNH-TEMPO-Catalyzed Oxidation of Aldoses to Aldaric Acids Using Chlorine or Bromine as Terminal Oxidants. *J. Carbohydr. Chem.* **2002**, *21*, 65-77.

[18] Coward-Kelly, Guillermo; Chen, Rachel Ruizhen. A Window into Biocatalysis and Biotransformations. *Biotechnol. Prog.* **2007**, *23*, 52-54.

[19] Kiely, Donald. E.; Carter, Andy; Shrout, David P. Oxidation Process. *U.S. Patent 5,599,977*, Feb. 4, 1997.

[20] McIssac, Gregory F.; David, Mark B.; Gertner, George Z. Goolsby, Donald A. Eutrophication: Nitrate Flux in the Mississippi River. *Nature* **2001**, *414*, 166-167.

[21] Greer, Frank R.; Shannon, Michael. Infant Methemoglobinemia: The Role of Dietary Nitrate in Food and Water. *Pediatrics*, **2005**, *116*, 784-786.

[22] Mills, Heidi Clare Maria. Development of a Method of Analysis by High Performance Liquid Chromatography for Products of the Nitric Acid Oxidation of D-Glucose. *M. Sc. Thesis*, The University of Waikato, 2007.

[23] Davey, Cara-Lee. Development of an Ion Chromatography Method for the Analysis of Nitric Acid Oxidation Reactions of Common Sugars. *M. Sc. Thesis*, The University of Waikato, 2008.

[24] Kiely, Donald. E.; Ponder, Glenn. Nitric Acid Removal from Oxidation Products. *U.S. Patent 6,049,004*, Apr 11, 2000.

[25] Hirasaka, Yoshinobu; Umemoto, Kenji; Sukegawa, Mitsuo; Matsunaga, Isao. On Equilibrium Among D-Glucosaccharic Acid and its Lactones in Aqueous Solution. *Chem. Pharm. Bull.* **1965**, *13*, 677-680.

[26] Hirasaka, Yoshinobu; Umemoto, Kenji. Structure of D-Glucosaccharodilactone. *Chem. Pharm. Bull.* **1965**, *13*, 325-329.

Chapter 2. Synthesis of Higher Molecular Weight Poly(alkylene D-glucaramides) through Alkylenediammonium D-Glucarate Salts

2.1 Introduction

Polyamides containing one or more pendant hydroxyl groups on the polymer chain are termed polyhydroxypolyamides (PHPAs). These polyamides are typically produced from derivatives of naturally occurring carbohydrates or amino acids and are therefore of interest as renewable alternatives to petroleum-based polymers. PHPAs derived from carbohydrates are of particular interest due to the natural abundance and structural variety of carbohydrate feedstocks. D-Glucose from hydrolyzed grain starches is the most abundant and least expensive carbohydrate monosaccharide to isolate and is therefore the first choice as a feedstock for commercial development of renewable chemicals including PHPAs. A number of different diamines, diacids, and amino acids suitable for condensation polymerization can be produced from D-glucose.[1] However, only the diacid, D-glucaric acid (**6**), can be synthesized directly from D-glucose in a single step without hydroxyl group protection. Historically, **6** has been prepared by oxidizing D-glucose with nitric acid and isolated as the water insoluble monopotassium salt (**1**). Nitric acid oxidation of aldoses represents a simple yet versatile and cost effective reaction that can be used to prepare any aldaric acid.[2]

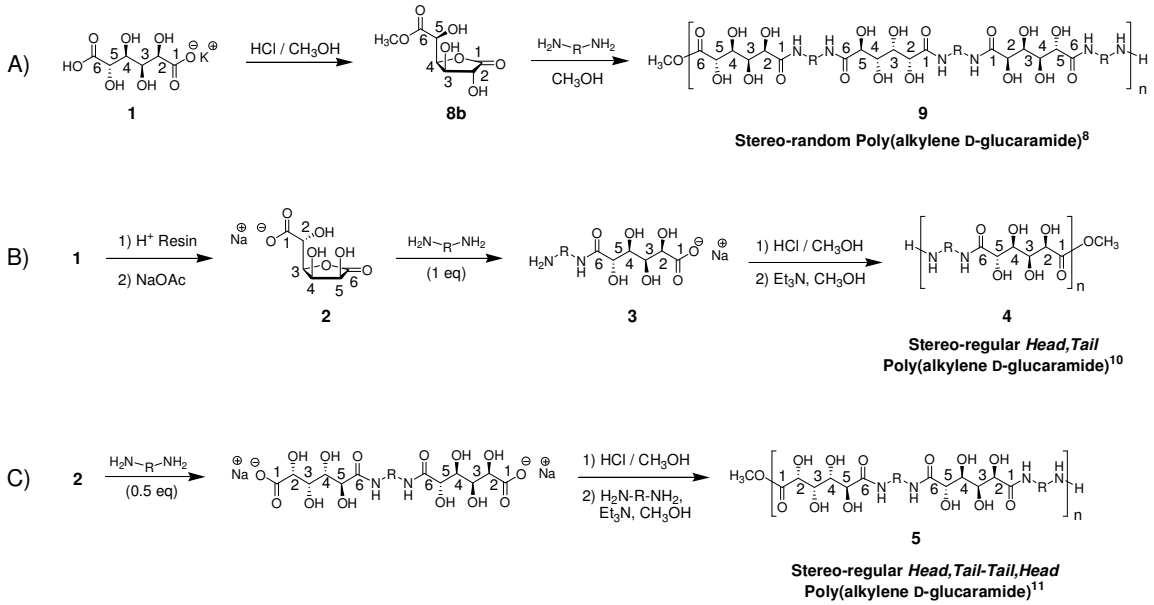
PHPAs produced from the condensation of aldaric acids and diamines were first reported by Ogata *et al.* using the diethyl esters of tartaric[3] and galactaric acids.[4] These diesters undergo aminolysis reactions under mild conditions compared to the corresponding aliphatic diesters. The first D-glucaric acid-based PHPAs were reported by Kiely *et al.* and were prepared from methyl esters of **6** prepared under Fischer esterification conditions in methanol.[5] Esterification of **6** yields not only an acyclic diester, as found with galactaric and tartaric acid but also two ester/γ-lactone structures. Key to the successful synthesis of the PHPAs was the observation by Hoagland *et al.* that

five membered (γ) lactone structures are significantly more susceptible to aminolysis than the acyclic methyl esters, as demonstrated using xylaro-1,4-lactone[6] and, later by Kiely *et al.* employing D-glucaro-1,4- and 6,3-lactones.[7] Since the lactones are formed in solution under acidic or basic equilibrium conditions from their acyclic alkyl diesters, polymerization reactions can be carried out at ambient temperature in polar solvents without the need for exotic acyl activating groups or high energy input, making D-glucaric acid based PHPAs quite attractive. Later reports of D-glucaric acid-based PHPAs utilized purified lactone forms of **6**, namely methyl D-glucaro-1,4 lactone (**10b**), ethyl D-glucaro-6,3 lactone,[8] and D-glucaro-1,4:6,3-dilactone (**10d**),[9] as reactive diacid monomers (**Scheme 2-1**, **method A**). The poly(D-glucaramides) produced by these methods are termed stereo-random because the orientation of the asymmetric glucaryl units in the polymer is not controlled. Stereo-regular poly(D-glucaramides) with *head, tail*[10] (**4**) and *head, tail-tail, head*[11] (**5**) repeating glucaryl units have also been reported. The syntheses of stereo-regular poly(D-glucaramides) take advantage of the isolable sodium D-glucarate 6,3-lactone (**2**) to set glucaryl orientation prior to polymerization (**Scheme 2-1**, **methods B and C**).

One advantage of the synthetic method for preparing stereo-regular *head, tail* poly(D-glucaramides) is the use of an AB type amino acid salt (**3**) which sets a precise 1:1 stoichiometry between the glucarate and diamine units, an essential criterion for achieving high molecular weight polymers. In general, condensation polymerizations involving two difunctional monomers of the AA and BB type require equivalent stoichiometry between the reactants to prevent chain termination through end-capping. The original methods for synthesizing stereo-random poly(D-glucaramides) relied on gravimetric measurements for stoichiometric balance and yielded low number average molecular weight (M_n) polymers, typically below 2000. Through the use of the AB amino acid salts, stereo-regular poly(D-glucaramides) with higher molecular weights than the stereo-random ones have been achieved.[12] These results suggest that the molecular weights of stereo-random poly(D-glucaramides) may be increased if the stoichiometry of the starting monomers is strictly controlled.

In the production of Nylon-6,6, a common polyamide of the AA/BB type, stoichiometric control of monomers is accomplished by first forming a 1:1 salt, hexamethylenediammonium adipate, between adipic acid and hexamethylenediamine. A similar process was envisioned for preparing stereo-random poly(D-glucaramides) in which stoichiometrically equivalent salts from D-glucaric acid and primary diamine of choice could be used as the starting material.[16] Polymerization of the 1:1 diammonium D-glucarate salts (**7**) could then be accomplished by first activating the glucarate portion through esterification followed by deprotonating the diammonium salt with an appropriate base. The primary goal of this project was to determine if the molecular weights of stereo-random poly(D-glucaramides) could be increased through the use of stoichiometrically balanced salts.

Scheme 2-1. Reported synthetic methodologies for the preparation of stereo-random and stereo-regular poly(alkylene D-glucaramides).



Previously, the molecular weights of poly(D-glucaramides) synthesized in methanol (pre-polymers, **9**) were increased through a second post-polymerization step in a different solvent system which allowed the polymers to react further in solution.[12,15,16] With these ideas in mind and the goal of increasing the molecular weights of stereo-random poly(D-glucaramides), a synthetic methodology comprising four distinct steps was devised and targeted for development and optimization: 1) synthesis of 1:1 disalts

from D-glucaric acid and different primary diamines, 2) activation of the D-glucarate portion through esterification, 3) deprotonation of the diammonium salt to initiate polymerization, and 4) further polymerization (post-polymerization) of the initial polymers (pre-polymers) in a different solvent system (**Scheme 2-2**).

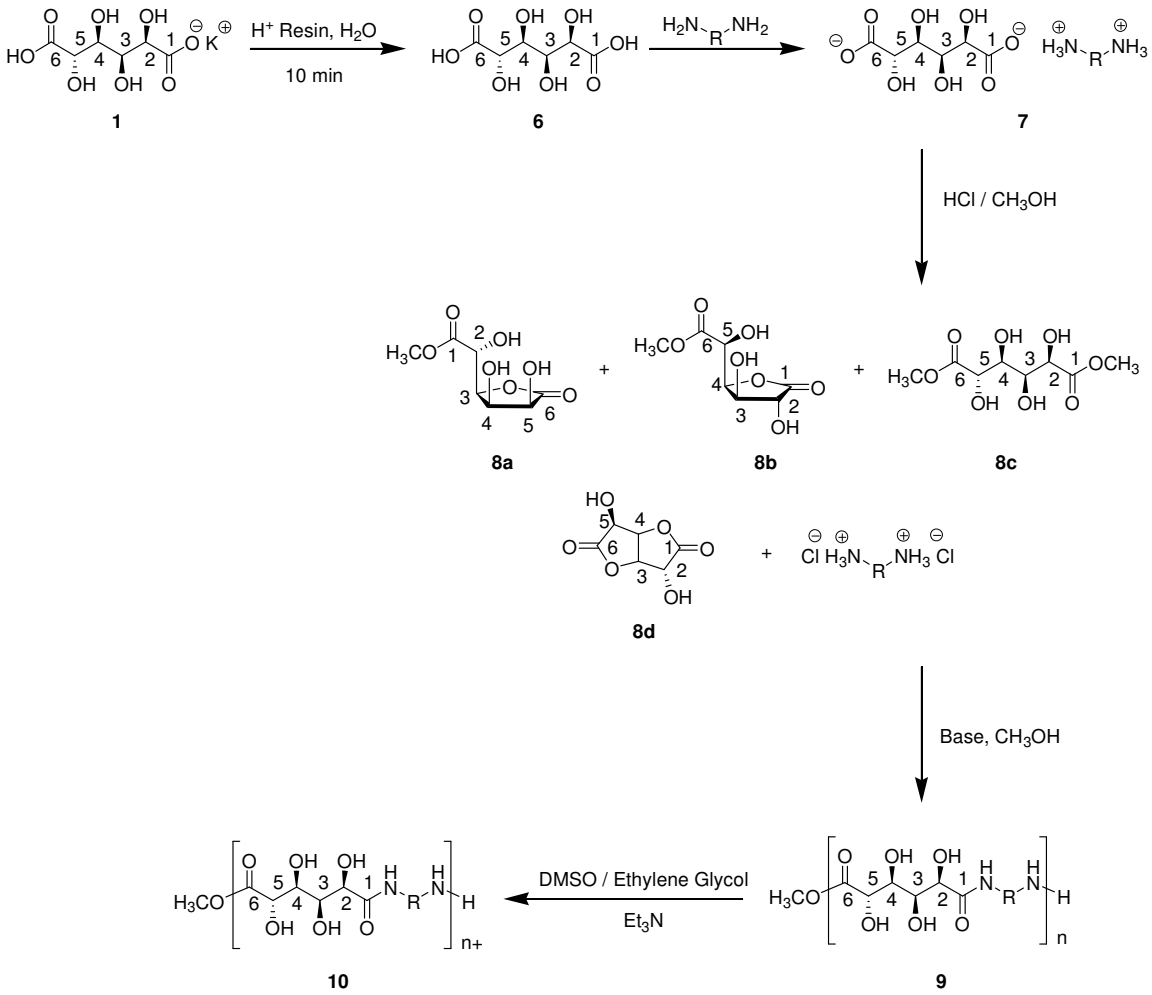
2.2 Results and Discussion

2.2.1 Synthesis

2.2.1.1 Alkylenediammonium D-Glucarate Salts

While the preparation of 1:1 diammonium adipate salts is straightforward, preparation of similar salts from D-glucaric acid was complicated by the propensity of the diacid to form lactone species in solution. Lactone formation is accelerated by the acid source required for converting **1** to **6**. Initial attempts to protonate **1** with H^+ form ion exchange resin resulted in a mixture of diacid and acid lactones species. Subsequent reaction of the aqueous mixture with a diamine resulted in a formation of not only the desired disalt but also amide salts formed by aminolysis of the lactones. Analysis of the mixture by ^{1}H NMR showed only an approximate 1:1 stoichiometry between the diammonium and glucarate units. Furthermore, the mixture was difficult to isolate as a solid and ultimately did not produce polymers with higher molecular weight than those previously described.[8,13,14] Complete hydrolysis of the amide groups to yield the pure disalt was difficult and required long reaction times at elevated temperatures.[15,16] Recently, Denton demonstrated that **6** can be selectively formed in aqueous solution by a short (< 10 min) treatment of **1** with ion exchange resin.[17] Once the resin is removed from the solution of **6**, the formation of lactones is slow without the acid catalyst. Addition of a diamine to the aqueous solution produced the target disalt which was precipitated from solution with an alcohol. This versatile method was used to produce a number of alkylenediammonium D-glucarate salts (**7a-7j)** and was scaled up to 100 g for hexamethylenediammonium D-glucarate (**7c**) without complications. With the exception of 2-methylpentamethylenediammonium D-glucarate (**7g**) and 3',6'-dioxaoctamethylenediammonium D-glucarate (**7h**), which are hygroscopic and

Scheme 2-2. Synthesis of poly(alkylene D-glucaramides) through 1:1 alkylenediammonium D-glucarate salts.



7a, 9a, 10a: R = $(CH_2)_2$

7b, 9b, 10b: R = $(CH_2)_4$

7c, 9c, 10c: R = $(CH_2)_6$

7d, 9d, 10d: R = $(CH_2)_8$

7e, 9e, 10e: R = $(CH_2)_{10}$

7f, 9f, 10f: R = $(CH_2)_{12}$

7g, 9g, 10g: R = $CH_2CHCH_2CH_2CH_2$ (CH$_3$ branch)

7h, 9h, 10h: R = $CH_2CH_2OCH_2CH_2OCH_2CH_2$

7i, 9i, 10i: R = $CHCH_2CH_2NCH_2CH_2CH_3$ (CH$_3$ branch)

7j, 9j, 10j: R = H_2C–C$_6$H$_4$–CH_2

difficult to precipitate, the resulting salts appear to have long shelf-lives, showing no degradation or water adsorption. Elemental analyses of the disalts confirmed a 1:1 ratio of diammonium to D-glucarate units, and ^{1}H NMR showed no peaks corresponding to amide functionalities. Pure 1:1 disalt was also prepared in high yield from the triamine, 4'-aza-*N*-methylheptamethylenediammonium D-glucarate (**7i**). Several of the disalts formed crystals, and X-ray crystal structures were obtained for **7c** and *m*-xylylenediammonium D-glucarate (**7j**). The melting points of the salts were typically above 125 °C, again with the exception of **7g** and **7h** which showed no melting endotherm by DSC. With a Fisher-Johns melting point apparatus, these two salts showed broad melting ranges below 60 °C.

2.2.1.2 Esterification and Polymerization

With a convenient method for the preparation of a number of diammonium D-glucarate salts available, we began developing a general polymerization method for them. As a starting point, the polymerization method used in the preparation of stereo-regular *head,tail* poly(D-glucaramides) was employed.[10] This procedure involved activation of the glucarate units through Fischer esterification of the carboxylate groups. Anhydrous HCl, generated *in situ* through the reaction of acetyl chloride and methanol, served as an acid for protonating the D-glucarate portion and catalyzing the esterification reaction. Following esterification, deprotonation of the ammonium chloride salts was necessary to initiate polymerization. Previous studies showed triethylamine (TEA) to be sufficiently basic for deprotonating the ammonium salts and superior to other non-nucleophilic amine bases, such 1,4-diazabicyclo[2.2.2]octane (DABCO) or 1,5-diazabicyclo[4.3.0]non-5-ene (DBN), for initiating polymerization.[16] However, the diammonium D-glucarate salts with the established esterification and basification procedures resulted in poly(alkylene D-glucaramides) with molecular weights lower than the stereo-random ones produced by the original method (**Scheme 2-1**, **method A**). With the goal of producing higher molecular weight polymers, the individual steps of the polymerization procedure were optimized using **7c** as a representative salt.

The first challenge was to gain a better understanding of the esterification reaction. The reaction proved difficult to monitor directly due to the complexity of the

^{1}H NMR spectrum arising from overlapping peaks corresponding to carboxylic acid, methyl ester and lactone structures. Therefore, the efficacy of a given esterification procedure was judged by the size of the resulting polymer as estimated by ^{1}H NMR end-group analysis.[8] This analytical technique gives polymer size in the form of degree of polymerization (DP) which is the average number of repeating units for a polymer sample. DP can then be related to the number average molecular weight (M_n) by multiplying the DP value by the molecular weight of the repeating unit.

The advantage of the Fischer esterification lies in the simplicity of the reaction conditions and reagents involved; however, the water by-product makes complete conversion to the ester problematic due to competing ester hydrolysis. Ester formation can be driven by removal of water during the reaction, typically through azeotropic water removal or through water scavenging agents such as molecular sieves or acetone dimethyl acetal. The latter reacts with water to form methanol and acetone under Fischer esterification conditions.[18] Both of these water scavenging techniques failed to increase the DP of the polymer compared to the benchmark procedure. Large excess of acid catalyst has also been reported to serve as a water scavenger presumably by tying water up as the hydronium ion and preventing it from acting as a nucleophile.[19] Several experiments were then carried out with varying amounts of anhydrous HCl. It was observed that smaller amounts of anhydrous HCl produced larger polymers, the opposite outcome expected if the acid served as a water scavenger. Finally, both toluene and absolute ethanol were employed to azeotropically remove water during concentration of the reaction mixture on a rotary evaporator. After concentration, the resulting mixture was treated a second time with methanolic HCl prior to basification. An increase in DP was observed, but concentrating the esterification reaction without ethanol or toluene also showed similar improvement. Ultimately, further drying of the concentrate using a vacuum pump was found to increase the DP even more, suggesting that the concentration step and not the solvent azeotrope was the important factor.

In summary, only modest DP increases were observed by altering esterification reaction conditions. The best results were obtained when the reaction mixture was concentrated and dried under reduced pressure and when minimal amounts of hydrogen chloride were used. Drying the final esterification reaction mixture is thought to

accomplish several objectives. First, it removes water from the product mixture. This is probably insignificant to the esterification since other water removal techniques failed to increase the DP of the polymer product. Second, drying induces lactonization of any unreacted carboxylic acid groups of D-glucaric acid making the lactones available for condensation with an amine function. In fact, dilactone **8d** can be prepared directly from **6** by *in vacuo* dehydration.[9] Finally, drying removes excess hydrogen chloride from the reaction mixture, corollary to the improvement observed from using smaller amounts of anhydrous HCl. The results suggest that the water by-product in the esterification procedure is not the cause for low molecular weight polymer formation but rather that the problem lies in the details of the polymerization step.

To begin investigations of the polymerization itself, experiments that varied the amount of TEA used in the basification were carried out. It was observed that when larger amounts of TEA were employed, polymers with larger DP values were generated, analogous to the results from reduced amounts of anhydrous HCl. This result led to the conclusion that TEA leaves a significant number of the primary amines protonated and therefore unable to react with esterified D-glucaric acid. Consequently, a stronger base was deemed necessary to efficiently deprotonate the diammonium groups and generate nucleophilic primary amine functions. Potassium carbonate and sodium methoxide were tested as potential base substitutes for TEA. Potassium carbonate proved unsatisfactory in this capacity as it had limited solubility in methanol and reacted slowly to give a product heavily contaminated with inorganic salts. In contrast, initial trials with sodium methoxide immediately produced higher DP polymer than seen with the use of TEA alone. Further investigations using varying amounts of sodium methoxide provided polymers with similar, higher molecular weights, but polymer yields decreased with increasing methoxide amounts. An interesting outcome from using an excess of sodium methoxide was isolation of a small amount of polymer **9c** with significantly larger DP. Approximately 1h after the addition of 1.15 eq of sodium methoxide to mixture **8** from salt **7c**, an oily precipitate which adhered to the sides of the glass reaction flask was observed. This initial precipitate was easily isolated by decanting the remainder of the reaction mixture. Analysis of **9c** prepared in this manner showed high DP (~75) by ^{1}H NMR, although the yield was low (40%).

Ultimately, a standard method was established based upon optimal yield and DP value for polymer **9c**. The established method involved concentrating and drying the esterification reaction prior to basification with sodium methoxide (0.9 equivalents) and TEA. This procedure was generally applied to all of the alkylenediammonium D-glucarate salts and was modified as needed. With salts **7a**, **7b**, and **7i**, the standard amount of sodium methoxide did not make the reaction solution basic. DP values were low for all three polymers and, in the case of **7b** and **7j**, the reactions also gave low polymer yields. Increasing the amount of sodium methoxide improved the DP values and yields for all three.

In most cases, the polymer products precipitated from the reaction mixture and were isolated by filtration. However, with polymers **9g**, **9h**, and **9i**, the yields of the precipitates were particularly low due to their higher solubility in methanol. Increased yields for polymers **9h** and **9i** were obtained by concentrating the polymerization reaction and triturating the resulting solid with a 1:1 methanol/ethanol mixture to remove residual TEA/TEA·HCl.

The results of the new polymerization method for stereo-random poly(D-glucaramides) in comparison to the original polymerization method[8,13,14] (**Scheme 2-1, Method A**) are given in **Table 2-1**. The polymers are labeled pre-polymers to distinguish them from the post-polymers discussed in the next section. In all cases, the DP values of the pre-polymers from the new method were comparable or better to those produced by Method A and were significantly higher than those derived from the disalt and TEA alone.

The first poly(alkylene D-glucaramides) given in **Table 2-1** (**9a**-**9f**) are derived from non-branched alkylenediamines. With Method A, similar yields and DP values were obtained regardless of the starting diamine's alkyl chain length. With the new polymerization method, DP differences are observed depending upon the type of diamine used. For pre-polymers containing short (C_2, **9a** and C_4, **9b**) and long (C_{10}, **9e** and C_{12}, **9f**) alkylene chains in the diamino unit, the results are comparable. This suggests that these pre-polymers have similar low solubility in methanol and that their low solubility is the governing factor limiting their molecular weight. With polymers of intermediate diamino chain length (C_6, **9c** and C_8, **9d**), higher DP values with the new method

Table 2-1. Comparison of poly(alkylene D-glucaramides) synthesized from the original method and from alkylenediammonium D-glucarate salts using sodium methoxide basification.

	Method A[8,13,14]			Disalt/Methoxide Method		
Pre-Polymer	**Yield (%)**	**DP[a]**	**M_n**	**Yield (%)**	**DP[a]**	**M_n[a]**
9a	93	9	2036	80	7	1639
9b	88	10	2725	75	9	2360
9c	89	9	2552	75	18	5226
9d	87	8	2562	80	11	3502
9e	90	9	3218	76	8	2771
9f	94	7	2730	85	6	2247
9g	74	NR[b]	NR[b]	46	52	15096
9h	62	NR[b]	NR[b]	29 (74[c])	31 (12[c])	9992 (3868[c])
9i	79	23	7300	20 (68[c])	67 (32[c])	21396 (10219[c])
9j	97	NR[b]	NR[b]	88	5	1552

[a]Degree of polymerization estimated by ^{1}H NMR end group analysis.
[b]Not reported.
[c]Polymerization reaction concentrated then triturated with 1:1 methanol/ethanol mixture

over Method A were observed. Polymers **9c** and **9d** also appear to have the highest solubility in methanol as they typically precipitate from methanol more slowly than the other four alkylene polymers. Higher polymer solubility allows longer reaction times in solution and therefore should lead to an increased DP. With **9c** and **9d**, stoichiometric control of the monomers appears to have improved the DP of the pre-polymers.

The remaining poly(D-glucaramides) are derived from a branched diamine (**9g**), two diamines containing hetero atoms (**9h** and **9i**), and an aryl diamine (**9j**). The first three polymers have higher methanol solubility as evidenced by their lower yields and higher DP values. Yield and DP for polymers **9h** and **9i** isolated by triturating the reaction concentrate are given in parentheses. Again, higher yields and corresponding lower DP values were observed in the triturated samples. Polymer **9j** appears to have very low solubility in methanol based upon rapid precipitation, high yield, and low molecular weight.

2.2.1.3 Post-polymerization

Methanol was chosen as the standard polymerization solvent because it allows the aminolysis reaction to proceed rapidly at ambient temperature. However, low polymer solubility in methanol appears to be a dominant factor limiting polymer growth. Therefore, a second polymerization, or post-polymerization, step was evaluated as a way to increase the molecular weights of the polymers. Because chain terminated polymers would fail to react in the post-polymerization step, this reaction would be facilitated by pre-polymers with on average molar equivalent amounts of terminal amine and ester functions. Essentially, the pre-polymer was dissolved in an alternate solvent system chosen to increase solubility and allow further polymerization to occur. A challenge to a post-polymerization arises from limited solubility of poly(aldaramides) in solvents compatible with aminolysis reactions. Dimethyl sulfoxide (DMSO) was capable of dissolving all poly(D-glucaramides) included in this study, but only moderate molecular weight increase was observed when DMSO was used alone as the post-polymerization solvent. This observation is consistent with earlier reports that underscore slow polymerization rates for activated aldaric acids and diamines in this solvent.[4,7]

To balance polymer solubility with reactivity, a mixture of DMSO and methanol was shown to be effective.[12] Other solvent systems in which PHPAs are known to be soluble[9] were also tested in this study (**Table 2-2**). These include alcohol/DMSO mixtures, polar aprotic solvent solutions of lithium chloride, and fluorinated solvents. Methanol and ethylene glycol in conjunction with DMSO both gave substantial increases in the DP of polymers **9b** and **9c**. Polymer **9f**, which is derived from the more hydrophobic dodecamethylenediamine, gave better results with *t*-butanol, a more hydrophobic alcohol. Lithium chloride solutions with DMSO, dimethylacetamide (DMA), and dimethylformamide (DMF) also gave large increases in DP with **9c**. Trifluoroethanol (TFE) and hexafluoroisopropanol (HFIPA) are common solvents for aliphatic polyamides such as nylon-6,6; however, most of the poly(D-glucaramides) were soluble only in HFIPA. Despite the solubility of **9c** in HFIPA, post-polymerization reaction in this solvent failed to increase the DP of the polymer. The poor results using HFIPA may be explained by the relatively low pK_a of HFIPA (9.3),[20] suggesting that this alcohol could protonate the terminal amine groups to some extent and prevent further

polycondensation. The low solubility of **9c** in TFE accounts for the moderate increase in DP.

Table 2-2. Comparison of different solvent systems for post-polymerization of various poly(alkylene D-glucaramides).

Post-Polymer	Solvent System[a]	Yield (%)	DP[b]	M_n[b]	DP Increase (DP Post / DP Pre)
10a	MeOH/DMSO	67	11	2576	1.6
10a	EG	49	12	2810	1.7
10a	EG/DMSO	70	14	3279	2.0
10b	MeOH/DMSO	72	21	5507	2.3
10b	EG	71	17	4458	1.9
10b	EG/DMSO	63	21	5507	2.3
10c	DMSO	84	18	5226	1.0
10c	MeOH/DMSO	87	31	9000	1.7
10c	EG/DMSO	86	34	9870	1.9
10c	LiCl/DMSO[c]	88	29	8419	1.6
10c	LiCl/DMA[c]	86	27	7838	1.5
10c	LiCl/DMF[c]	91	31	9000	1.7
10c	Trifluoroethanol	91	19	5516	1.0
10c	HFIPA	79	14	4064	0.8
10f	MeOH/DMSO	91	12	4494	2.0
10f	EG/DMSO	90	16	5992	2.7
10f	*t*-Butanol/DMSO	88	18	6740	3

[a]All post-polymerizations carried out at 60 °C for 16 h.
[b]Estimated by ^{1}H NMR end group analysis.
[c]5% LiCl by weight.

In general, a mixture of ethylene glycol and DMSO gave the best post-polymerization results for the pre-polymers. A standard post-polymerization method was developed using a 1:1 mixture of ethylene glycol and DMSO as solvent with TEA to promote lactonization of the terminal glucarate units. Results from post-polymerization reactions carried out at 60 °C in this solvent system are summarized in **Table 2-3**. Post-

polymerization reactions with polymers **9g**, **9h**, and **9i** were excluded due to their low yields and high DPs obtained from the first polymerization reaction. In all cases, the DP values approximately double from the pre-polymers during the post-polymerization reaction. The original reports for the synthesis of poly(D-glucaramides) did not include post-polymerization reactions, so direct comparison of post-polymers from the two methods was not possible. To see the effects of post-polymerization on poly(D-glucaramides) prepared by the Method A, **9c** was prepared from **8b** and hexamethylenediamine. Post-polymerization of the resulting polymer using the ethylene glycol/DMSO procedure gave a modest increase in DP from 6 to 10 in comparison to the increase in DP from 18 to 34 (**Tables 2-1** and **2-3**) for the same polymer (**10c**) derived from hexamethylenediammonium D-glucarate (**7c**). This suggests that a substantial amount of end-capping occurs in polymers prepared by the original method and impedes further reaction in the post-polymerization step. In contrast, polymer samples from alkylenediammonium D-glucarate salts appear to have closer to equal amounts of glucarate and amine end-groups, and thus have a better chance for increasing the molecular weight through the post-polymerization reaction.

Table 2-3. Poly(alkylene D-glucaramide) post-polymers from ethylene glycol/DMSO.

Post-Polymer[a]	Yield (%)	DP	M_n	DP Increase (DP Post / DP Pre)
10a	70	14	3279	2.0
10b	63	21	5507	2.3
10c	82	34	9870	1.9
10d	96	40	12735	3.6
10e	93	18	6236	2.2
10f	90	16	5992	2.7
10j	70	NO[b]	NO[b]	-

[a]All post-polymerizations carried out at 60 °C for 16 h.
[b]No terminal peak observed by ^{1}H NMR for end-group analysis.

2.2.1.4 Mechanism for Aminolysis of Hydroxy Lactones

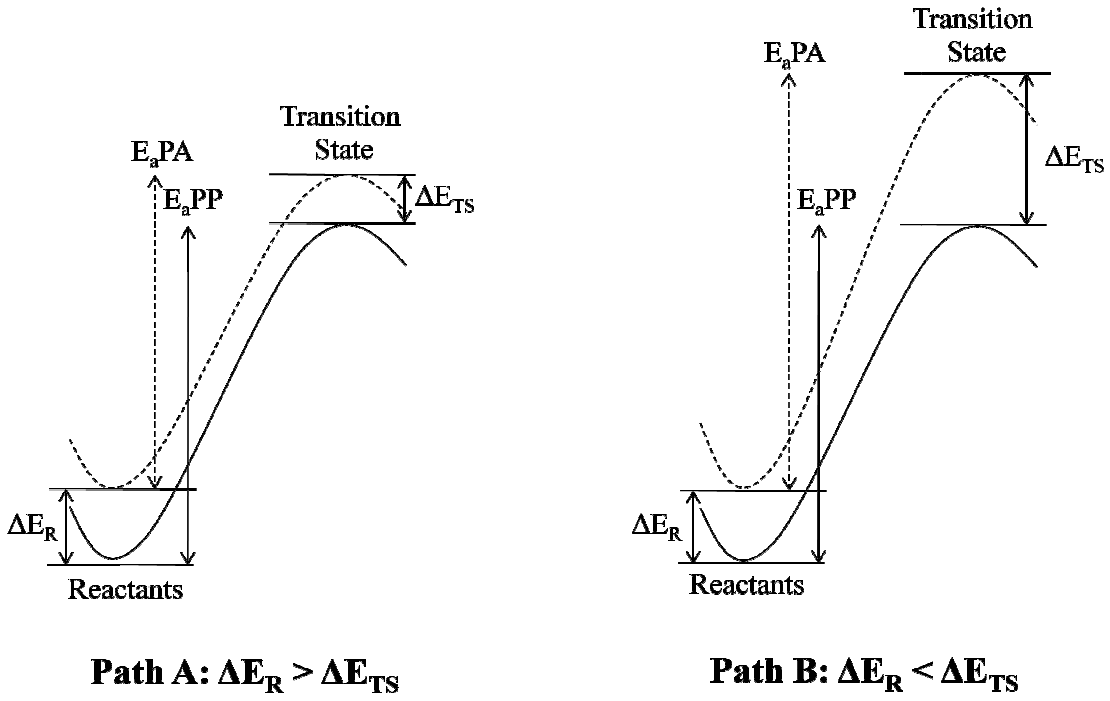
Although slow reaction rates for aminolysis of D-glucarate esters in DMSO have been reported,[7] no explanation for this observation has been given. The results in **Table 2-2** for post-polymerization reactions in DMSO and DMSO mixtures have led us to propose a mechanism which accounts for solvent effects on aminolysis of D-glucarate esters. Typically, the rates of reactions involving nucleophilic attack at carbonyl groups are enhanced in dipolar aprotic solvents such as DMSO when compared to polar protic solvents,[21] opposite of what is observed for D-glucarate aminolysis. This relative rate enhancement in dipolar aprotic solvents has been attributed to the absence of a hydrogen bonded solvation shell around the nucleophile which increases reactivity through destabilization of the nucleophile.[22] A similar destabilization of the transition state leading to the tetrahedral intermediate formed from nucleophilic addition to the ester carbonyl carbon can also occur in a dipolar aprotic solvent. Although the two destabilizing effects are related, they influence the reaction rate in opposite ways. Destabilization of the reactants, in this case the nucleophile, raises the energy of the reactants, thereby lowering the activation energy of the reaction transition state leading to an increase in the reaction rate. On the other hand, destabilization of the reaction transition state raises the activation energy and slows the reaction rate (**Figure 2-1**). Given the typical rate enhancement in polar aprotic solvents, as noted, the gain in energy from destabilizing the nucleophile must be greater than the increase in activation energy from destabilization of the transition state.

In the special case of aminolysis of aldonic and aldaric esters/lactones, hydroxyl groups near the ester/lactone can stabilize the transition state leading to the tetrahedral intermediate by delocalizing the developing negative charge of the incipient oxygen anion through intramolecular hydrogen bonding (**Figure 2-2**). DMSO can disrupt those hydrogen bonds by acting as a competitive hydrogen bond acceptor for the vicinal hydroxyl group, thereby negating the stabilizing effect of the hydroxyl group. Destabilizing the transition state, in this case, may outweigh the destabilization of the nucleophile, leading to higher activation energy and slower reaction rate. This destabilization would affect both the lactonization and aminolysis reactions since both go through tetrahedral addition intermediates. Since lactonization precedes aminolysis in

the case of glucarate esters,[7] slowing the rates of both reactions could have profound effects on the overall polymerization rate.

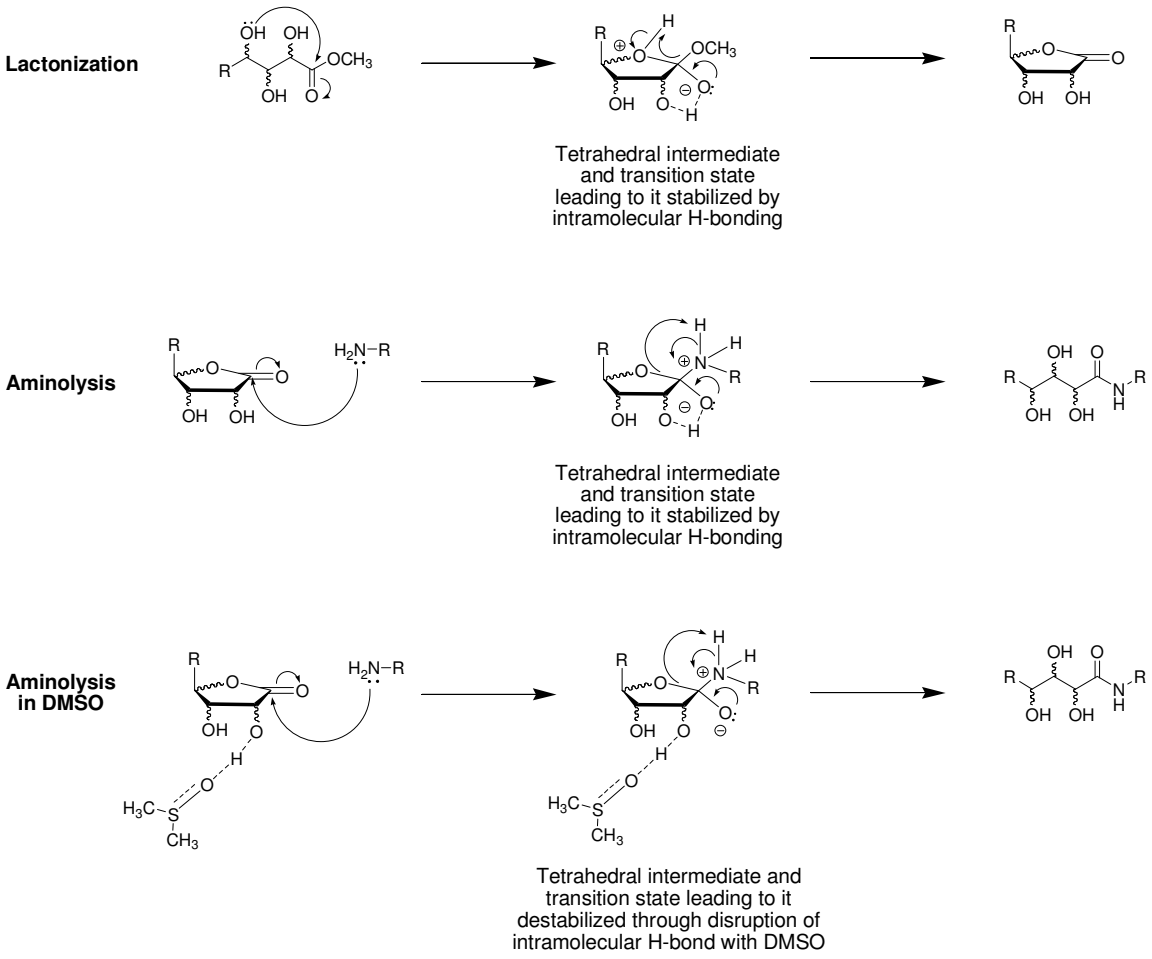
Figure 2-1. Differences in reaction activation energy (E_a) from destabilization of reactants (R) and transition states (TS) in polar aprotic solvent (dashed lines) versus polar protic solvent (solid lines).

Path A: Increased reaction rate due to greater destabilization of reactants over transition state.
Path B: Decreased reaction rate due to greater destabilization of transition state over reactants.



With regard to the results in **Table 2-2**, DMSO in combination with an alcohol or lithium chloride gave a larger increase in DP over the same time period as compared to DMSO alone. Alcohols and LiCl both provide a positive center, either as a hydroxyl group proton or a cation, capable of directly stabilizing the transition state at the incipient oxygen anion or disrupting the DMSO-glucarate hydrogen bonding system.

Figure 2-2. Proposed mechanism for lactonization and aminolysis of aldaric acid esters and the destabilizing effect of DMSO on these reactions.



2.2.1.5 Conclusions

A novel method for the synthesis of poly(D-glucaramides) was developed in effort to increase the molecular weights of the polymer products through strict control of monomer stoichiometry. To this end, a standard procedure for the preparation of 1:1 alkylenediammonium D-glucarate salts was established. From the 1:1 salts, the glucarate portion was activated using a simple Fischer esterification, followed by polymerization through basification of the diammonium salt. Sodium methoxide was shown to be an effective base for rapid deprotonation of the diammonium groups, whereas triethylamine

proved insufficient and resulted in lower molecular weight polymers. For poly(alkylene D-glucaramides) with higher methanol solubility, the use of 1:1 salts produced higher molecular weights than the previous reports which relied on gravimetric methods for stoichiometric control. Poly(hexamethylene D-glucaramide), a structural analog of nylon-6,6, had the highest molecular weight, almost twice that of previous methods. The remaining poly(alkylene D-glucaramides) produced by this new method had comparable molecular weights to those previously reported. In these cases, the polymeric size appears to be limited by low solubility in methanol. An additional polymerization (post-polymerization) step was used to increase the molecular weights of the methanol precipitated polymers. A mixture of dimethyl sulfoxide and an alcohol or inorganic salt provided a balance between polymer solubility and end-group reactivity. Using a mixture of ethylene glycol and dimethyl sulfoxide, the molecular weights of the initial polymers were doubled on average. For poly(hexamethylene D-glucaramide) and poly(octamethylene D-glucaramide), the molecular weights of the post-polymers are in the 10,000 range, close to those of commercially produced polyamides (~15,000).[30]

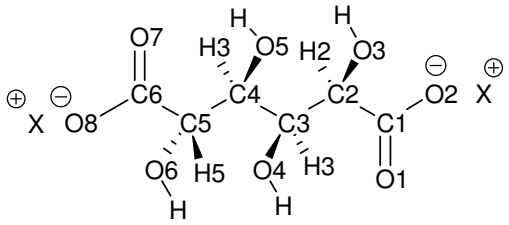
2.2.2 Characterization

2.2.2.1 X-ray Crystallography

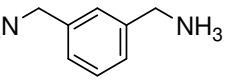
The crystal structures for two new salts of D-glucaric acid, hexamethylenediammonium D-glucarate (**7c)** and *m*-xylylenediammonium D-glucarate (**7j**) are reported here. The structures of **7c** and **7j** are compared to crystalline D-glucaric acid (**19**)[17] and other acyclic D-glucarate derivatives, including monopotassium D-glucarate (**1**),[23] dipotassium D-glucarate monohydrate (**11**),[24] sodium potassium D-glucarate dihydrate (**12**),[24] ammonium D-glucarate (**13**),[25] and *N*,*N*'-dimethyl-D-glucaramide (**14**).[24] The atom numbering scheme used in the crystal structures is shown **Figure 2-3** and select torsion angles for the crystalline compounds are listed in **Table 2-4**. Crystal structures of D-glucarate derivatives are of interest because they provide insight into the conformation of the glucaryl units in poly(D-glucaramides). Previously, *N*,*N*'-dimethyl-D-glucaramide (**14**) was of particular interest because it contains the amide functionalities of the polymers.[24] Similarly, the new salts **7c** and **7j**, while lacking

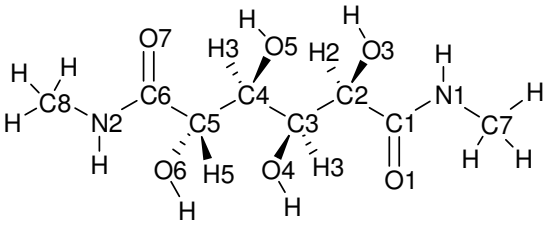
amide groups, contain both the glucaryl and diamino portions of the corresponding polyamides.

Figure 2-3. Atom numbering for x-ray crystal structures of D-glucaric acid and D-glucarate derivatives.



1) X = H, K
6) X = H, H
7c) X = $H_3N(CH_2)_6NH_3$
11) X = K, K
12) X = Na, K
13) X = H, NH_3

7j) X = 



14

Crystalline forms of D-glucaric acid and acyclic derivatives exist in two predominant conformations, either extended with 180° torsion angles among carbon atoms (*anti* relationship) or double-sickle with two 60° torsion angles among carbon atoms (*gauche* relationship). The double-sickle conformation arises from rotating the C3-C4 and C4-C5 bonds 120° clockwise (G^-) or counter-clockwise (G^+) from the starting extended conformation. The C3-C4 rotation is important because it alleviates unfavorable 1,3 parallel steric interactions between the hydroxyl groups on C2 and C4.[26] These steric interactions are comparable to the 1,3 diaxial interactions observed with substituted cyclohexanes in their chair conformations. The 1,3 parallel interactions occur in acyclic molecules between alternating substituents of the same configuration.

Most of the D-glucarate compounds listed in **Table 2-4** (**1**, **6**, **7c**, and **13**) have very similar double-sickle (*S* shaped) conformations consisting of an *anti* relationship between C1 and C4 and *gauche* relations between C2 and C5 and C3 and C6. Using the nomenclature established by Horton *et al*.,[27] these compounds have the conformation $_3G^-,_4G^-$. Compound **12** has a double-sickle conformation with a torsion angle of opposite sign between C3 and C6 relative to the C4-C5 and therefore is of the form $_3G^-,_4G^+$.

Table 2-4. Select torsion angles (°) for D-glucaric acid and D-glucarate derivatives.

Torsion Angle	1	6	7c	7j	11	12	13[b]	14
C1-C2-C3-C4	179.3	169.2	170.9	-172.0	-170.8	-161.4	-179.2, -179.5[c]	-177.9
C2-C3-C4-C5	67.4	57.8	63.1	-176.2	165.7	67.9	62.4, 64.3[c]	179.3
C3-C4-C5-C6	68.7	67.9	55.9	91.4	174.2	-73.0	75.8, 71.0[c]	-179.4
O3-C2-C3-O4	NR[a]	-70.4	-71.3	-64.8	-57.7	-50.0	-59.4, -60.4[c]	-61.6
O4-C3-C4-O5	NR[a]	-62.8	-63.1	71.0	51.1	-49.8	-53.3, 51.2[c]	61.0
O5-C4-C5-O6	NR[a]	74.1	62.0	85.3	173.3	-65.8	73.5, 69.4[c]	-179.8
H2-C2-C3-H3	57.6	45.9	51.5	63.2	70.8	26.7	65.1, 59.0[c]	-60.4
H3-C3-C4-H4	-168.2	177.6	177.3	-52.0	-79.1	30.8	179.2, 179.8[c]	-60.9
H4-C4-C5-H5	68.3	72.3	60.2	89.9	-167.7	57.6	75.4, 77.4[c]	-177.4

[a]Not reported.
[b]Torsion angles not reported in original publication. Angles measured from crystal structure 268035 obtained from the Cambridge Crystallographic Data Centre.
[c]Two torsion angle values corresponding to two different glucarate moieties in the unit cell.

The $_3G^-,_4G^-$ double sickle conformation was also seen in the crystal structure of **7c** (**Figure 2-4**). Of the other D-glucarate derivatives in **Table 2-4**, only **11** and **14** have a true extended conformation as evidenced by their 180 ° carbon atom torsion angles. Compound **7j** exhibits a semi-extended conformation in which all carbons are *anti* except C3 and C6 which are 90 ° to one another relative to the C4-C5 bond.

Figure 2-4. X-ray crystal structure of hexamethylenediammonium D-glucarate (**7c**).

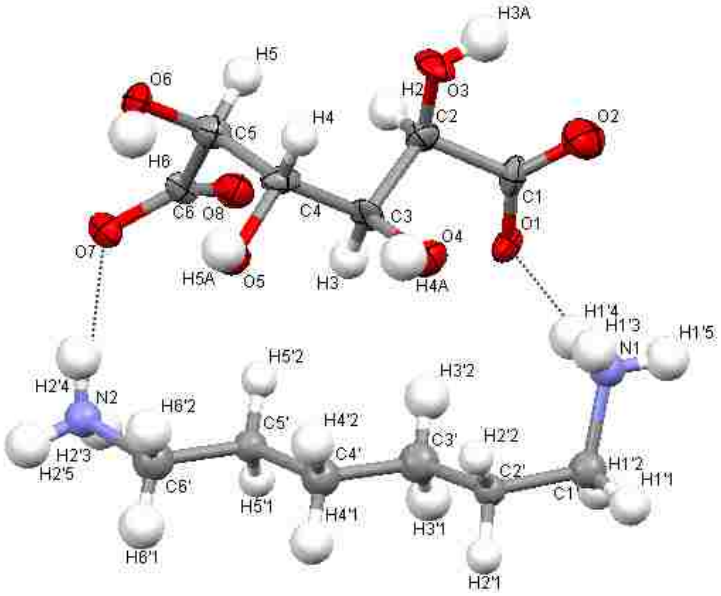


Figure 2-5. X-ray crystal structure of *m*-xylylenediammonium D-glucarate (**7j**).

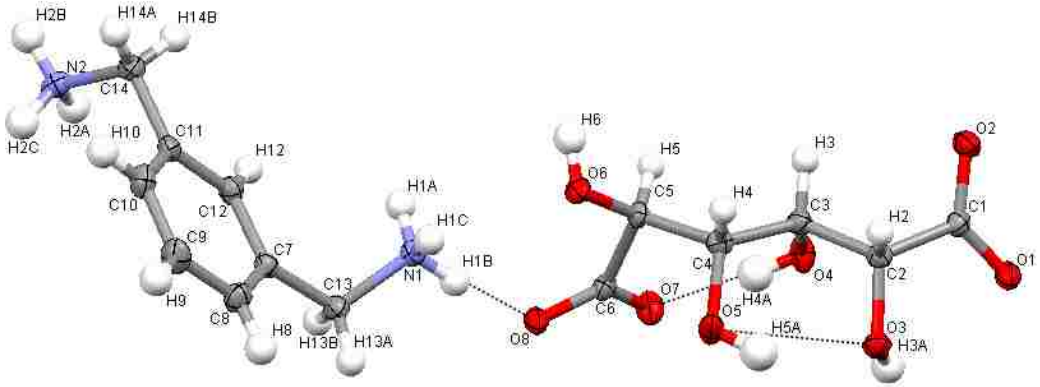
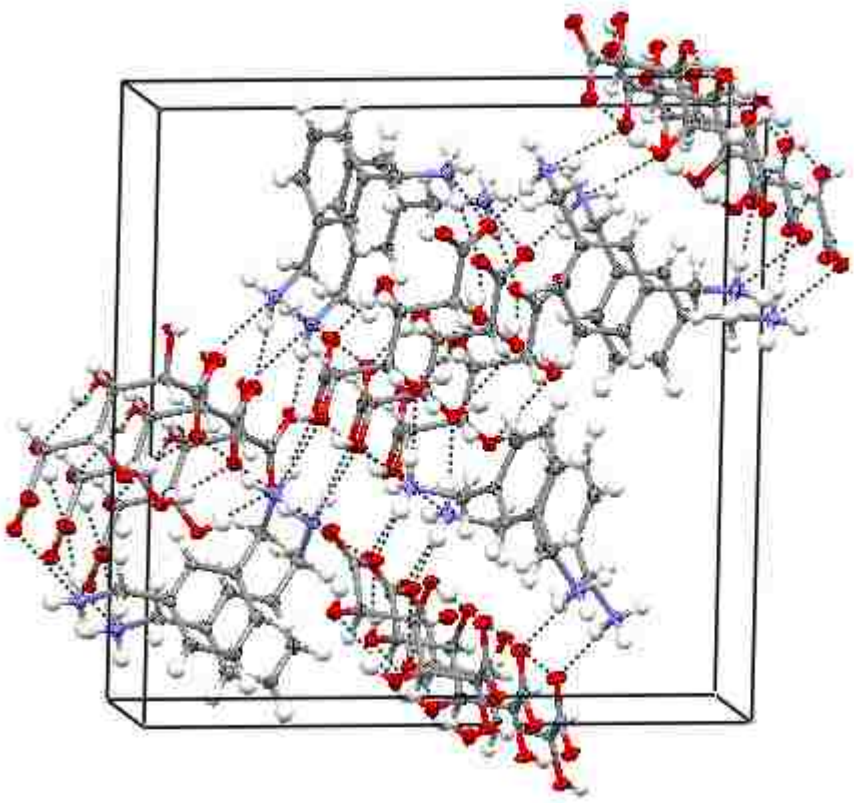


Figure 2-5 shows the 1,3 parallel relationship between the C2 and C4 hydroxyl groups (O3-H and O5-H) in **7j**. The steric repulsion of the parallel C2 and C4 hydroxyl groups in **7j** is stabilized by an intramolecular hydrogen bond (1.920 Å) between O5-H and O3. Intramolecular hydrogen bonds between hydroxyl groups of acyclic polyhydroxy compounds are rare. One of the few examples is potassium D-gluconate, the C1 monocarboxylic acid from D-glucose. This compound has an extended conformation and shows the same hydrogen bond between O3 and O5 hydroxyl groups.[28] Intramolecular hydrogen bonds between hydroxyl groups are not found in the extended compounds **11** and **14**. Compound **7j** has another intramolecular hydrogen bond (1.784 Å) between O4-H and O7 of the C6 carboxylate group. This hydrogen bond stabilizes the bend at the C6 end of the glucaryl unit and accounts for the unusual 90 ° torsion angle between C3 and C6. Conversely, **7c** shows no intramolecular hydrogen bonds in the D-glucarate portion. The shape of the D-glucarate in **7j** is dictated at least in part by the rigid phenyl ring of the diammonium segment. The phenyl rings show π-stacking in the

Figure 2-6. Extended structure and unit cell of *m*-xylylenediammonium D-glucarate with hydrogen bonding network (dashed lines).



extended crystal structure (**Figure 2-6**). The diammonium segment of **7c** is more flexible than **7j** and, therefore, should exert less influence over the conformation of the D-glucarate portion. In fact, the D-glucarate portion of **7c** causes a contortion of one of the ammonium groups. The torsion angle between C3' and N1 relative to C2'-C1' is 76 ° in contrast to the more stable trans (180 °) relationship found with the other carbon atoms. The bend of the N1 ammonium group allows hydrogen bonding and close proximity to the C1 carboxylate group.

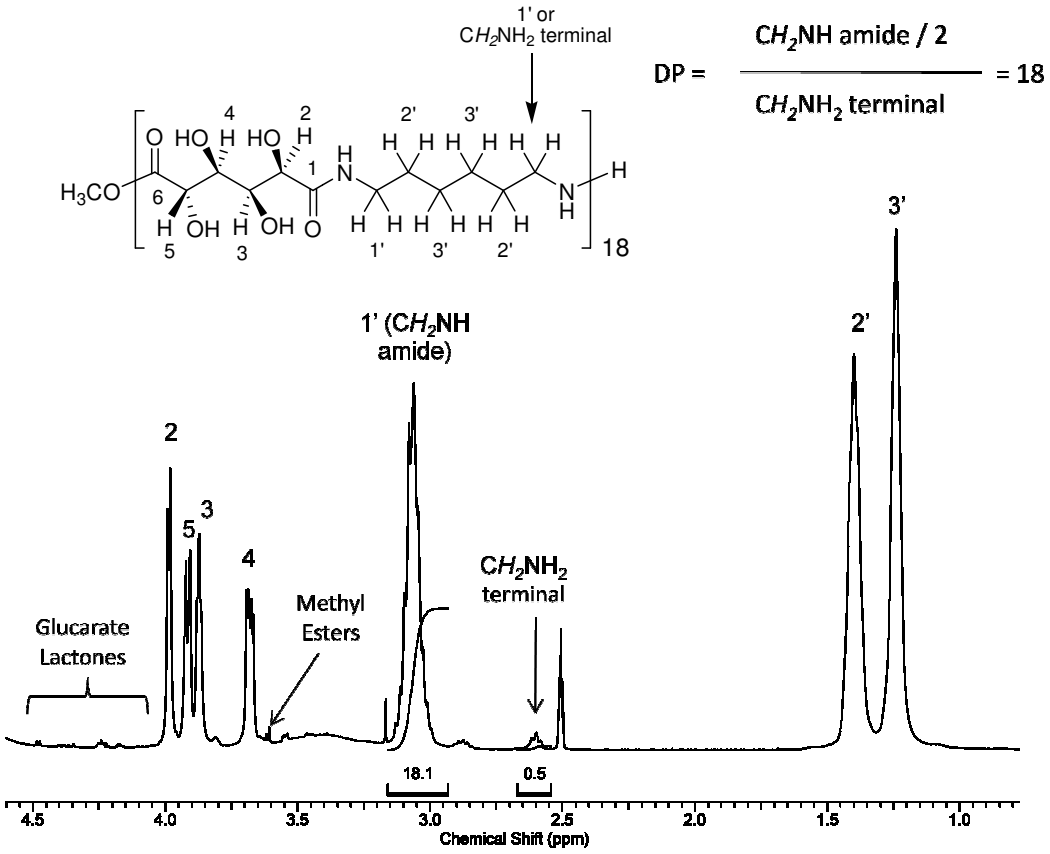
2.2.2.2 Ion Chromatography

A potential problem associated with the use of sodium methoxide in the basification step of the polymerization process is contamination of the resulting poly(D-glucaramides) with sodium chloride by-product. To get an estimate of the residual sodium chloride in the polymer samples, **9b** and **9c** were hydrolyzed with aqueous sodium hydroxide and then analyzed for glucarate and chloride using ion chromatography (IC). The hydrolysis reaction was monitored by ^{1}H NMR, and no peaks corresponding to amide groups remained after 48 h. Concentrations of chloride and glucarate were then determined using the areas of the IC peaks and calibration curves generated from standard solutions. Polymer **9b** showed 5% sodium chloride contaminant by weight while polymer **9c** contained 1% sodium chloride. Washing **9c** with water showed a reduction of the sodium chloride contaminant to less than 0.2% by weight. Potentially, a washing step could cause hydrolysis of the amides or ester end-groups in the polymer. However, no amide degradation was observed as the DP of the washed polymer did not change (^{1}H NMR analysis), and no ester degradation was observed as post-polymerization gave a similar increase in DP relative to the unwashed polymer.

2.2.2.3 Nuclear Magnetic Resonance

^{1}H NMR has proven to be the most convenient tool for analyzing both starting salts and polymer products. The most telling features of the ^{1}H NMR spectra are the distinct peaks relating to the diamino methylene protons adjacent to an amide nitrogen compared to the corresponding protons adjacent to an amine nitrogen. The diammonium

Figure 2-7. Partial ^{1}H NMR spectrum of poly(hexamethylene D-glucaramide) (**9c**) with peak assignments and DP calculation.



D-glucarate salts lack signals arising from amide groups, indicating no aminolysis of lactone forms occurred during salt preparation. In the polymers, the integrals of the two distinct sets of peaks can be compared to estimate the degree of polymerization (DP) as a form of end-group analysis.[8] The ratio of half the internal methylene protons adjacent to the amides to the number of methylene protons adjacent to terminal amines gives the average number of repeating units for the polymer sample. **Figure 2-7** shows the partial spectrum for **9c** along with the DP calculation method. The glucaryl units of the polymers show four distinct peaks corresponding to the four protons on carbons 2-5. Unfortunately, peaks correlating to terminal D-glucarate moieties are difficult to integrate due to the multiple ester and lactone forms present. This prevents an accurate DP calculation based upon the D-glucarate ends of the polymers. False DP values are possible if the polymers are capped by one of the co-monomers or if a significant amount

of cyclic oligomers are present. These inaccuracies are undetectable without a second independent DP value. In an effort to get a DP value from the D-glucarate end, terminal D-glucarate units were converted into a single entity with a unique NMR signal. Pre-polymer **9c** was treated with an excess of benzyl amine in a DMSO/methanol solvent system. The ^{1}H NMR spectrum of the resulting polymer contained a new, distinct peak corresponding to the benzyl methylene protons next to amide nitrogens. Comparison of the integrals of terminal amine to terminal D-glucarate showed 1.6:1 ratio. Further work is necessary to clarify the discrepancy between the ratio of the glucarate and amine ends of the polymer, but the results suggest that extensive end-capping with one co-monomer does not occur. If the polymers do have more amine ends then our method of calculating DP errs on the side of lower DP. At this point, the DP calculation serves only as an estimate until the NMR results are fully correlated to a second method for molecular weight determination.

2.2.2.4 Gel Permeation Chromatography

We are continuing to develop a standard method for determining molecular weights and distributions by size exclusion chromatography. Progress has been hindered by the limited solubility of poly(D-glucaramides) in solvents suitable for gel permeation chromatography (GPC). Efforts have been made to develop a standard GPC procedure using tetrahydrofuran eluent and derivatized poly(D-glucaramides) for increased solubility. Both acetate ester and trimethylsilyl ether derivatives of the hydroxyl groups have been evaluated, the per *O*-TMS derivatives are more THF soluble. At this point, the GPC results have been inconsistent and further study is required to develop a reliable methodology. In search of an alternate method, representative samples of **9c** and **10c** were sent to Viscotek for GPC analysis using HFIPA eluent. Triplicate injections were carried out and the results are given in **Table 2-5**. Pre-polymer **9c1** was synthesized using the standard diammonium D-glucarate procedure with sodium methoxide basification while **9c2** was prepared from the disalt with an excess amount of sodium methoxide and shorter reaction time as described in **Section 2.2.1.2**. Sample **10c** is the post-polymer product from **9c1**. Pre-polymer **9c1** has a higher DP by GPC than the

Table 2-5. GPC data from poly(hexamethylene D-glucaramides) using HFIPA eluent.

Polymer	M_z	M_w	M_n	DP[a]	M_w/M_n	[η] (dL/g)	Rh (nm)	dn/dc	Recovery (%)
9c1	15,822	11,266	7,301	25	1.54	0.092	2.45	0.217	98.3
9c1	16,095	11,472	7,994	28	1.44	0.092	2.47	0.217	97.7
9c1	15,960	11,243	7,130	25	1.58	0.091	2.44	0.217	97.5
Average	**15,959**	**11,327**	**7,475**	**26**	**1.52**	**0.092**	**2.45**	**0.217**	**97.8**
9c2[b]	19,399	13,940	10,464	36	1.33	0.117	2.86	0.217	82.1
9c2[b]	18,679	13,392	9,324	32	1.44	0.115	2.80	0.217	83.6
9c2[b]	19,011	13,567	9,523	33	1.42	0.115	2.81	0.217	82.1
Average	**19,030**	**13,633**	**9,770**	**34**	**1.40**	**0.116**	**2.82**	**0.217**	**82.6**
10c	27,040	16,032	8,788	30	1.82	0.121	2.97	0.217	101.9
10c	27,436	16,348	9,842	34	1.66	0.122	3.01	0.217	103.3
10c	26,989	16,075	9,071	31	1.77	0.121	2.98	0.217	103.8
Average	**27,155**	**16,152**	**9,234**	**32**	**1.75**	**0.121**	**2.99**	**0.217**	**103.0**

[a]Degree of polymerization calculated from M_n
[b]Pre-polymer first precipitate fraction from excess sodium methoxide procedure.

one calculated by ^{1}H NMR end-group analysis (DP = 18, **Table 2-1**) while **10c** matches the NMR calculation closely (DP = 34, **Table 2-3**). The lower DP value of **9c1** from the ^{1}H NMR calculation suggests that the polymer contains a portion of N-capped polymers. This result is in agreement with the ^{1}H NMR results from the D-glucarate capping experiment using benzyl amine. Amine end-capping can also be supported by comparing the polydispersity (M_w/M_n) of **9c1** and **10c**. Polydispersity is a measure of the breadth of molecular weight distribution for a given polymer sample. Polymer samples containing molecules of multiple molecular weights are termed polydisperse and have M_w/M_n values greater than one. Polymer samples consisting of one molecular weight have an M_w/M_n equal to one. Polydispersity increased during the post-polymerization reaction of **9c1** to **10c**. Amine end-capped pre-polymer would not react during the post-polymerization step, leaving a percentage of the sample with unchanged molecular weights. The

remainder of the polymers in the sample would react and increase in size, thus leading to an increase in polydispersity. Sample **9c2** showed the highest molecular weight by both GPC and ^{1}H NMR. However, the DP obtained from GPC was much lower than the ^{1}H NMR calculated value (~75). This discrepancy is most likely due to incomplete solubility of the higher molecular weight portion of **9c2** in HFIPA and from inaccuracy of integrating the small NMR peak for the terminal methylene. Evidence of the incomplete solubility is shown by the percent recovery for the GPC sample (**Table 2-5**, last column) which is calculated from the refractive index measurement. Only 82% of **9c2** was recovered in contrast to the near 100% recovery for **9c1** and **10c**.

2.2.2.5 Thermal Analysis

Although all of the poly(alkylene D-glucaramides) synthesized here have been previously reported, a unified study of their thermal characteristics suitable for comparison has not been carried out. To this end, differential scanning calorimetry (DSC) was used to measure both the melting point (MP) and glass transition temperatures (T_g) for all pre- and post-polymers (**9a-10j**, **Table 2-6**). The observed melting points for pre-polymers **9c**-**9f** match closely, typically within several degrees, to the reported values measured using a Fisher-Johns melting point apparatus;[5] however, the DSC thermograms reveal multiple melting endotherms for these polymers (**Figure 2-8**). This is a common feature of polyamides and has been reported for tartaric acid-based PHPAs.[29] For polymers **9a**, **9b**, **9g** and **9i**, the DSC thermograms showed no sharp melting endotherms. Polymer **9a** was reported to melt at 185 °C as measured by Fisher-Johns melting apparatus,[8] but no sharp melting point was observed, in our hands, with this polymer using the same technique. Pre-polymer **9b** showed no melting endotherm, but the post-polymer **10b** showed a melting temperature of 192 °C in accordance with the reported value (192-195 °C).[8] The results for **9g** and **9i** are consistent with previous reports in which no sharp melting points were observed by Fisher-Johns melting apparatus.

From the values given in **Table 2-6**, we see similar melting temperatures, near 200 °C, for polymers **9c**-**9f** and **10b-10f**. This suggests that the common glucaryl unit, and not the diamino unit, dictates the melting temperature by providing the strongest intermolecular forces. Polymer **9h** which has two oxygen atoms in the diamino unit does

Table 2-6. Melting points and glass transition temperatures for poly(alkylene D-glucaramide) pre- and post-polymers.

	Pre-Polymer (9)		Post-Polymer (10)	
Polymer	**MP (°C)[a]**	**T_g (°C)**	**MP (°C)**	**T_g (°C)**
a	NO[a]	90	NO[a]	88
b	NO[b]	96	192	110
c	185	90	188	90
d	192	76	197	75
e	197	60	197	69
f	197	NO[c]	197	NO[c]
g	NO[b]	88	-	-
h	109	66	-	-
i	NO[b]	60	-	-
j	NO[b]	132	225	136

[a]Melting point taken as peak of the highest temperature endotherm.
[b]No melting endotherm observed by DSC.
[c]No glass transition observed by DSC.

not follow this trend. The molecular weight and chain length of the repeat unit in **9h** is similar to that of **9d**, yet the melting point is almost 100 degrees lower, suggesting that the two ether oxygens have disrupted the intermolecular hydrogen bonds of the glucaryl unit by serving as hydrogen bond acceptors. Pre-polymer **9j** showed no melting endotherm by DSC, but the post-polymer **10j** produced a single peak at 225 °C. The higher melting point of **10j** compared to the other poly(alkylene D-glucaramides) is presumably due to stabilizing intermolecular interactions by the phenyl rings.

Glass transition is a unique phenomenon of amorphous materials like polymers and is associated with an increase in heat capacity of a sample due to increased freedom in long range molecular motion. Physically, the polymer undergoes a change from a brittle, glass-like state to an elastic, rubber-like state during the glass transition. The temperature at which this transition takes influences how a given polymer will be processed and used. The glass transition temperature (T_g) is influenced by many factors. Among different types of polymers, molecular structure plays a large role in determining

Figure 2-8. DSC thermogram for the first heating of poly(hexamethylene D-glucaramide) pre-polymer (**9c**).

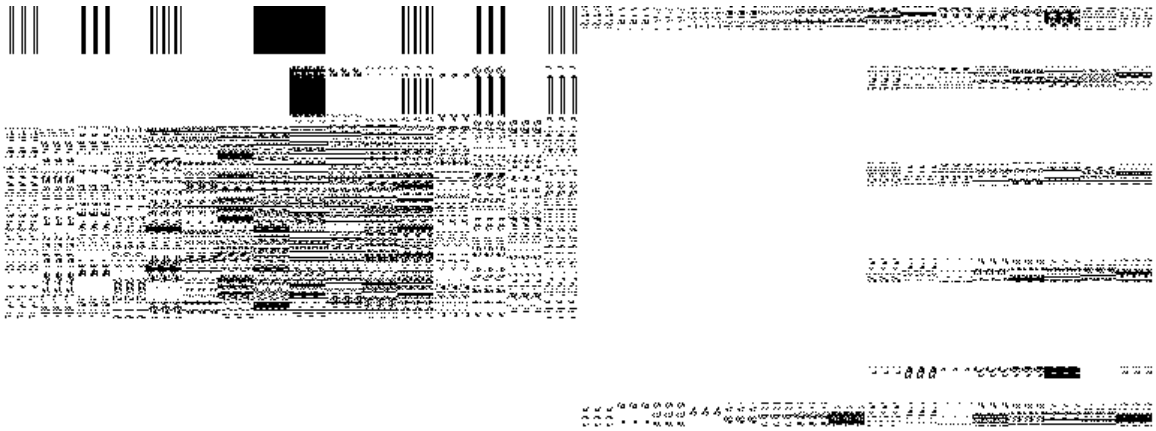
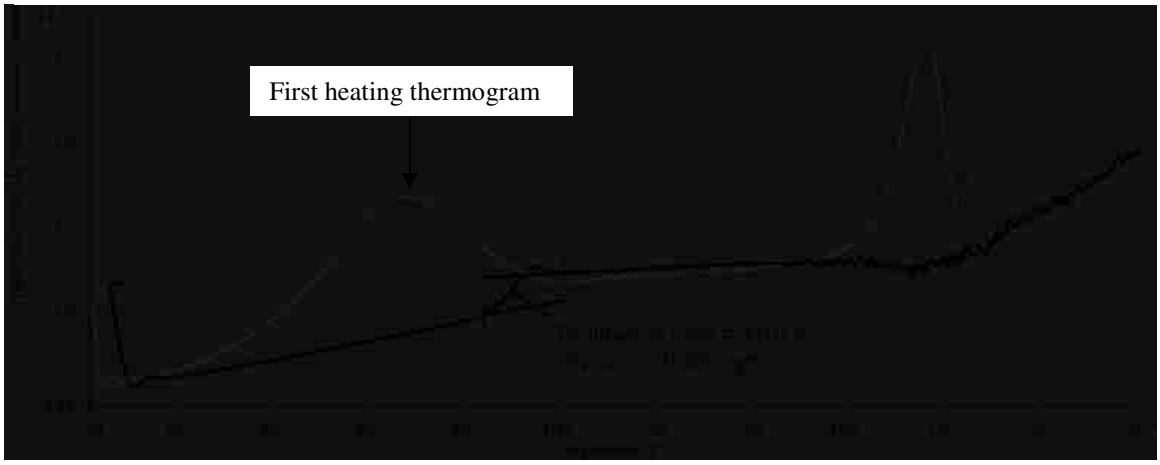


Figure 2-9. DSC thermogram of the second heating (black line) of poly(hexamethylene D-glucaramide) pre-polymer (**9c**).



T_g. However, different T_g values are also observed among different samples of the same type of polymer. The sample dependence of T_g can occur from differences in molecular weight or thermal history of the polymer. Method of measurement can also give rise to variations in T_g.[30] In order to minimize the effects of thermal history and measurement method, all polymer samples were first heated to their melting point, cooled back to room temperature, then reheated. The T_g value was obtained from the second heating (**Figure**

2-9). The influence of a samples molecular weight on T_g can be observed by comparing the values for polymers **9b** and **10b** as T_g increased almost 15 °C from the pre- to post-polymer. No other dramatic changes are seen between pre- and post-polymers; however, the T_g for pre-polymer **9i** was 11 °C higher than previously reported.[14] Comparing the molecular weights of the two samples, **9i** used in this study was more than double that of the original report.

Overall, the T_g values for poly(alkylene D-glucaramides) are higher than the comparable aliphatic polyamides[30] due to the bulky and polar hydroxyl of the glucaryl unit. Comparing the values among the different poly(alkylene D-glucaramides), we see some interesting trends. Unlike the melting point, T_g appears to be influenced by chemical structure of the diamino unit. With pre-polymers **9b**-**9e** and post-polymers **10b**-**10e**, T_g decreases as the length of the carbon chain in the diamino unit increases. The lowering of T_g results from an increase in polymer chain flexibility due to the additional methylene groups. In aliphatic polyamides, T_g also decreases with increasing number of methylene groups for repeat unit (nylon-4,6: T_g = 57 °C versus nylon-4,10: T_g = 50 °C). Polymers **10b**-**10e** follow this trend, although from this assessment, polymers **9a** and **10a** should have the highest T_g. This is not the case, perhaps due to the relatively low molecular weights of these two polymers. Polymers with branching groups and hetero atoms in the diamino unit of the backbone chain (**9g-9i**) have lower T_g values than **10c** and **10d** which have repeating units of comparable molecular weight and length. Polymers **9j** and **10j** have the highest T_g due to the rigid aryl diamino unit.

2.2.2.6 Conclusions

A new method for synthesizing poly(alkylene D-glucaramides) utilizing alkylenediammonium D-glucarate salts for stoichiometric control of the monomers produced a variety of polyamides that were characterized by ^{1}H NMR and DSC. The x-ray crystal structures for two new salts of D-glucaric acid are reported. The structure of hexamethylenediammonium D-glucarate shows the glucaryl unit in a double-sickle conformation similar to that of D-glucaric acid, while crystalline *m*-xylylenediammonium D-glucarate, exhibits an extended conformation with a rare intramolecular hydrogen bond between two alternate hydroxyl groups.

^{1}H NMR gives an estimate of the polymer's molecular weight expressed in terms of degree of polymerization. Although the DP values from ^{1}H NMR are not absolute, they showed similar trends to the molecular weights measured by gel permeation chromatography for poly(hexamethylene D-glucaramide) using hexafluoroisopropanol as the eluent.

Thermal properties of poly(alkylene D-glucaramides) were analyzed using differential scanning calorimetry. Most of the polymers show high melting points near 200 °C. The glass transition temperatures are higher than those of corresponding aliphatic polyamides due to intermolecular hydrogen bonding contributions from pendant hydroxyl groups. Unlike the melting points, the glass transition temperatures are strongly affected by the chemical structure of diamino group.

2.3 Experimental

General Methods

Materials. Monopotassium D-glucarate was purchased from Applied Foods Sciences, LLC, (Austin, TX, USA). Sodium methoxide was purchased as a 0.5 M solution in methanol from Sigma-Aldrich (St. Louis, MO, USA). All other chemicals and solvents were purchased from Sigma-Aldrich (St. Louis, MO, USA) or J.T. Baker (Philipsburg, NJ, USA) and used without further purification. Solutions were concentrated *in vacuo* (15-20 mbar) using a rotary evaporator and water bath at 30 °C**.** Drying of samples was carried out at room temperature for 16 h (unless otherwise noted) using a mechanical pump.

Differential scanning calorimetry (DSC). DSC was carried out using a Perkin Elmer Jade differential scanning calorimeter calibrated with an indium standard and purged with N_2 at (20 mL/min). Samples (2-4 mg) were heated and cooled at 10 °C/min in sealed aluminum pans in reference to an empty aluminum pan. Melting points (mp) are reported as the onset temperature of the endotherm from the first heating. When multiple melting

peaks were observed, the mp is reported as the onset of the highest temperature endotherm. Glass transition temperatures (T_g) were determined by heating the sample to melting, holding for 2 min followed by rapidly cooling back to room temperature. T_g is reported as the inflection point derived from the second heating.

Nuclear Magnetic Resonance (NMR). All ^{1}H and ^{13}C NMR spectra were recorded on a Varian 400 MHz spectrometer. Chemical shifts (δ) are reported in parts per million (ppm) downfield from 1% tetramethylsilane in dimethyl sulfoxide-d_6 (DMSO-d_6, 0 ppm for ^{1}H and ^{13}C), 1% *t*-butyl alcohol in D_2O (1.20 ppm for ^{1}H and 30.70 for ^{13}C), or the residual solvent peak in trifluoroacetic acid-d (TFA-d, 11.50 ppm for ^{1}H).

Crystal Structure Analysis. Suitable crystals of hexamethylenediammonium D-glucarate (**7c**) and *m*-xylylenediammonium D-glucarate (**7j**) were coated with Paratone N oil, suspended in a small fiber loop and placed in a cooled nitrogen gas stream at 173 K on a Bruker D8 APEX II CCD sealed tube diffractometer with graphite monochromated CuK_α (1.54178 Å) radiation. Data were measured using a series of combinations of phi and omega scans with 10 s frame exposures and 0.5^o frame widths. Data collection, indexing and initial cell refinements were all carried out using APEX II[31] software. Frame integration and final cell refinements were done using SAINT[32] software. The structure was solved using Direct methods and difference Fourier techniques (SHELXTL, V6.12).[33] Hydrogen atoms were placed their expected chemical positions using the HFIX command and were included in the final cycles of least squares with isotropic U_{ij}'s related to the atom's ridden upon. All non-hydrogen atoms were refined anisotropically. Scattering factors and anomalous dispersion corrections are taken from the *International Tables for X-ray Crystallography*.[34] Structure solution, refinement, graphics and generation of publication materials were performed by using SHELXTL, V6.12 and Mercury 1.4.2[35] software.

Other Analytical Techniques. Optical rotations were measured using an Optical Activity Limited (Cambridgeshire, UK) polarimeter on samples at three different

concentrations in a standard 0.5 decimeter cell. Elemental analyses were carried out by Atlantic Microlab, Inc. (Norcross, GA, USA).

Alkylenediammonium D-Glucarate Salts (7)

Hexamethylenediammonium D-Glucarate (7c). Acid form cation exchange resin (70 mL, 147 mmol, Dowex 50WX8-100, 2.1 meq/mL) was washed with deionized water (3 x 150 mL). Monopotassium D-glucarate (**1**, 20.00 g, 80.57 mmol) was added to a slurry of the washed resin in water (100 mL) then mixed on an orbital shaker for 10 min. The resin was removed by filtration and washed with water (3 x 20 mL). Hexamethylenediamine (9.77 g, 84.1 mmol) was added to the combined filtrate and washings, and the resulting solution was stirred for 3 h before concentrating to a viscous syrup. Methanol (200 mL) was added to the syrup, and the mixture was stirred until all of the oil solidified to a fine, white solid (24 h). The precipitate was isolated by filtration, washed with methanol (3 x 20 mL), and dried to give hexamethylenediammonium D-glucarate (**7c**, 24.02 g, 73.60 mmol, 91.3%) as a white powder. Crystals of **7c** were obtained by dissolving the salt (10.00 g) in hot water (17 mL) and then diluting the solution with methanol (30 mL). The crystals formed from the solution over a 24 h period, were isolated by filtration, washed with cold 3:1 methanol/water (3 x 5 mL), and dried to give **7c** (7.89 g, 78.9% recovery): mp 174 °C; $[\alpha]_D^{25}$ +1.5 (*c* 1.0, H_2O). ^{1}H NMR (D_2O) δ 4.10 (d, 1H, H-2, $J_{2,3}$ = 2.9 Hz), 4.08 (d, 1H, H-5, $J_{4,5}$ = 5.1Hz), 4.03 (dd, 1H, H-3, $J_{3,4}$ = 4.4), 3.89 (m, 1H, H-4), 2.97 (t, 4H, H-1' and H-6', $J_{1',2'\text{and}5',6'}$ = 7.3), 1.63 (m, 4H, H-2' and H-5'), 1.38 (m, 4H, H-3' and H-4'); ^{13}C NMR (D_2O) δ 179.67, 179.57, 74.81, 74.77, 74.65, 72.80, 40.41, 27.59, 26.18. Anal. Calcd for $C_{12}H_{26}N_2O_8$ (326.34): C, 44.16; H, 8.03; N, 8.58. Found: C, 44.37; H, 8.04, N, 8.62.

Ethylenediammonium D-Glucarate (7a). Salt **7a** was prepared according to the method for **7c** using monopotassium D-glucarate (**1**; 20.01 g, 80.60 mmol), acid form cation exchange resin (70 mL, 147 mmol, Dowex 50WX8-100, 2.1 meq/mL), and ethylenediamine (5.6 mL, 85 mmol). Salt **7a** was solidified using methanol (200 mL), isolated by filtration, washed with methanol (3 x 20 mL), and dried to give

ethylenediammonium D-glucarate (**7a**, 15.60 g, 57.73 mmol, 71.6%) as a white powder: mp 131 °C; $[\alpha]_D^{25}$ +1.5 (*c* 1.0, H_2O); ^{1}H NMR (D_2O) δ 4.12 (d, 1H, H-2, $J_{2,3}$ = 2.9 Hz), 4.10 (d, 1H, H-5, $J_{4,5}$ = 4.4 Hz), 4.03 (dd, 1H, H-3, $J_{3,4}$ = 4.4), 3.90 (m, 1H, H-4), 3.31 (s, 4H, H-1' and H-2'); ^{13}C NMR (D_2O) δ 179.86, 179.67, 74.82, 74.76, 74.70, 72.86, 37.88. Anal. Calcd for $C_8H_{18}N_2O_8$ (270.24): C, 35.56; H, 6.71; N, 10.37. Found: C, 35.29; H, 6.74; N, 10.41.

Tetramethylenediammonium D-Glucarate (7b). Salt **7b** was prepared according to the method for **7c** using monopotassium D-glucarate (**1**, 20.07 g, 80.87 mmol), acid form cation exchange resin (70 mL, 147 mmol, Dowex 50WX8-100, 2.1 meq/mL), and tetramethylenediamine (7.52 g, 85.2 mmol). Salt **7b** was solidified using methanol (200 mL), isolated by filtration, washed with methanol (3 x 20 mL), and dried to give tetramethylenediammonium D-glucarate (**7b**, 21.45 g, 71.91 mmol, 88.9%) as a white powder: mp 168 °C; $[\alpha]_D^{25}$ +1.5 (*c* 1.0, H_2O); ^{1}H NMR (D_2O) δ 4.10 (d, 1H, H-2, $J_{2,3}$ = 2.9 Hz), 4.08 (d, 1H, H-5, $J_{4,5}$ = 5.1 Hz), 4.03 (dd, 1H, H-3, $J_{3,4}$ = 4.4), 3.89 (m, 1H, H-4), 3.00 (m, 4H, H-1' and H-4'), 1.71 (m, 4H, H-2' and H-3'); ^{13}C NMR (D_2O) δ 179.71, 179.60, 74.81, 74.77, 74.65, 72.80, 39.89, 24.96. Anal. Calcd for $C_{10}H_{22}N_2O_8$ (298.29): C, 40.27; H, 7.43; N, 9.39. Found: C, 40.15; H, 7.42; N, 9.41.

Octamethylenediammonium D-Glucarate (7d). Salt **7d** was prepared according to the method for **7c** using monopotassium D-glucarate (**1**, 20.01 g, 80.62 mmol), acid form cation exchange resin (70 mL, 147 mmol, Dowex 50WX8-100, 2.1 meq/mL), and octamethylenediamine (12.26 g, 85.00 mmol). Salt **7d** was solidified using methanol (200 mL), isolated by filtration, washed with methanol (3 x 20 mL), and dried to give octamethylenediammonium D-glucarate (**7d**, 24.45 g, 76.79 mmol, 85.6%) as a white powder: mp 149 °C; $[\alpha]_D^{25}$ +1.5 (*c* 1.0, H_2O); ^{1}H NMR (D_2O) δ 4.10 (d, 1H, H-2, $J_{2,3}$ = 2.9 Hz), 4.07 (d, 1H, H-5, $J_{4,5}$ = 4.4 Hz), 4.03 (dd, 1H, H-3, $J_{3,4}$ = 4.4), 3.89 (t, 1H, H-4), 2.94 (t, 4H, H-1’ and H-8’, $J_{1',2' \text{ and } 7',8'}$ = 7.3), 1.61 (m, 4H, H-2' and H-7'), 1.11 (m, 8H, H-3', H-4’, H-5’, and H-6'); ^{13}C NMR (D_2O) δ 179.64, 179.54, 74.82, 74.79, 74.64, 72.79, 40.56, 29.02, 27.76, 26.54. Anal. Calcd for $C_{14}H_{30}N_2O_8$ (354.40): C, 47.45; H, 8.53; N, 7.90. Found: C, 47.21; H, 8.48; N, 7.80.

Decamethylenediammonium D-Glucarate (7e). Salt **7e** was prepared according to the method for **7c** using monopotassium D-glucarate (**1**, 8.88 g, 35.8 mmol), acid form cation exchange resin (30 mL, 63 mmol, Dowex 50WX8-100, 2.1 meq/mL), and decamethylenediamine (6.47 g, 37.6 mmol). Salt **7e** was solidified using methanol (100 mL), isolated by filtration, washed with methanol (3 x 10 mL), and dried to give decamethylenediammonium D-glucarate (**7e**, 10.88 g, 28.45 mmol, 79.5%) as a white powder: mp 145 °C; $[\alpha]_D^{25}$ +1.5 (*c* 1.0, H_2O); ^{1}H NMR (D_2O) δ 4.10 (d, 1H, H-2, $J_{2,3}$ = 2.9 Hz), 4.07 (d, 1H, H-5, $J_{4,5}$ = 5.1 Hz), 4.03 (dd, 1H, H-3, $J_{3,4}$ = 4.4), 3.89 (t, 1H, H-4), 2.94 (t, 4H, H-1' and H-10', $J_{1',2' \text{ and } 9',10'}$ = 7.3), 1.61 (m, 4H, H-2' and H-9'), 1.11 (m, 12H, H-3', H-4', H-5', H-6', H-7', and H-8'); ^{13}C NMR (D_2O) δ179.63, 179.52, 74.82, 74.77, 74.62, 72.77, 40.59, 29.46, 29.21, 27.80, 26.63. Anal. Calcd for $C_{16}H_{34}N_2O_8$ (382.45): C, 50.25; H, 8.96; N, 7.32. Found: C, 50.16; H, 8.95; N, 7.31.

Dodecamethylenediammonium D-Glucarate (7f). Salt **7f** was prepared according to the method for **7c** using monopotassium D-glucarate (**1**, 18.62 g, 75.00 mmol), acid form cation exchange resin (61 mL, 130 mmol, Dowex 50WX8-100, 2.1 meq/mL), and dodecamethylenediamine (15.77 g, 78.70 mmol). Salt **7f** was solidified using methanol (200 mL), isolated by filtration, washed with methanol (3 x 20 mL), and dried to give dodecamethylenediammonium D-glucarate (**7f**, 15.70 g, 41.92mmol, 55.9%) as a white powder: mp 138 °C; $[\alpha]_D^{25}$ +1.5 (*c* 1.0, H_2O); ^{1}H NMR (D_2O) δ 4.09 (d, 1H, H-2, $J_{2,3}$ = 2.9 Hz), 4.07 (d, 1H, H-5, $J_{4,5}$ = 4.4 Hz), 4.02 (t, 1H, H-3, $J_{3,4}$ = 5.1), 3.89 (t, 1H, H-4), 2.93 (t, 4H, H-1' and H-12', $J_{1',2' \text{ and } 11',12'}$ = 7.3), 1.60 (m, 4H, H-2' and H-11'), 1.29 (m, 8H, H-3', H-4', H-9', and H-10'), 1.25 (s, 8H, H-5', H-6', H-7', and H-8'); ^{13}C NMR (D_2O) δ179.63, 179.51, 74.82, 74.77, 74.61, 72.76, 40.61, 29.70, 29.59, 29.27, 27.85, 26.66. Anal. Calcd for $C_{18}H_{38}N_2O_8$ (410.50): C, 52.67; H, 9.33; N, 6.82. Found: C, 52.67; H, 9.28; N, 6.82.

2-Methylpentamethylenediammonium D-Glucarate (7g). Salt **7g** was prepared according to the method for **7c** using monopotassium D-glucarate (**1**, 21.3 g, 85.8 mmol), acid form cation exchange resin (72 mL, 150 mmol, Dowex 50WX8-100, 2.1 meq/mL),

and 2-methylpentamethylenediamine (11 mL, 81.7 mmol). After concentrating the aqueous salt solution, methanol (100 mL) was added to the syrup and the mixture was stirred for 4 h. The clear methanol phase was decanted from the syrup, fresh methanol (100 mL) was added, and the mixture was stirred for another 4 h. The methanol phase was again decanted from the syrup, and the syrup dried to give 2-methylpentamethylenediammonium D-glucarate (**7g**, 22.7 g, 69.6 mmol, 80.9%) as a white solid: mp 57-59 °C (Fisher-Johns Melting Point Apparatus, Thermo Fisher Scientific Inc., Waltham, MA, USA); $[\alpha]_D^{25}$ +1.5 (*c* 1.0, H_2O); ^{1}H NMR (D_2O) δ 4.10 (d, 1H, H-2, $J_{2,3}$ = 2.9 Hz), 4.08 (d, 1H, H-5, $J_{4,5}$ = 4.4 Hz), 4.02 (dd, 1H, H-3, $J_{3,4}$ = 4.4), 3.89 (t, 1H, H-4), 2.94 (m, 2H, H-5'), 2.85 (dd, 2H, H-1'), 1.81 (m, 1H, H-2'), 1.66 (m, 2H, H-4'), 1.34 (dd, 2H, H-3'), 0.97 (d, 3H, methyl, $J_{2',\text{methyl}}$ = 6.6); ^{13}C NMR (D_2O) δ 179.64, 179.52, 74.77, 74.71, 74.62, 72.80, 45.83, 40.46, 31.75, 30.97, 25.04, 16.98. Anal. Calcd for $C_{16}H_{34}N_2O_8 \cdot 0.5\ H_2O$ (335.18): C, 42.98; H, 8.12; N, 8.35. Found: C, 42.61; H, 8.14; N, 8.13.

3',6'-Dioxaoctamethylenediammonium D-Glucarate (7h). Salt **7h** was prepared according to the method for **7c** using monopotassium D-glucarate (**1**, 20.1 g, 80.9 mmol), form cation exchange resin (70 mL, 147 mmol, Dowex 50WX8-100, 2.1 meq/mL), and 3',6'-dioxaoctamethylenediamine (12 mL, 84 mmol). After concentrating the aqueous salt solution, methanol (100 mL) was added to the syrup and the mixture was stirred for 4 h. The clear methanol phase was decanted from the syrup, fresh methanol (100 mL) was added, and the mixture was stirred for another 4 h. The methanol phase was again decanted from the syrup, and the syrup was dried to give 3',6'-dioxaoctamethylenediammonium D-glucarate (**7h**, 21.0 g, 58.7 mmol, 72.6%) as a white solid: 53-56 °C (Fisher-Johns Melting Point Apparatus); $[\alpha]_D^{25}$ +1.5 (*c* 1.0, H_2O); ^{1}H NMR (D_2O) δ 4.10 (d, 1H, H-2, $J_{2,3}$ = 2.9 Hz), 4.08 (d, 1H, H-5, $J_{4,5}$ = 4.4 Hz), 4.02 (dd, 1H, H-3, $J_{3,4}$ = 4.4), 3.89 (t, 1H, H-4), 3.74 (t, 4H, H-2' and H-5', $J_{1',2' \text{ and } 5',6'}$ = 5.1), 3.70 (s, 4H, H-3' and H-4'), 3.18 (t, 4H, H-1' and H-6'); ^{13}C NMR (D_2O) δ 179.58, 179.45, 74.77, 74.64, 74.56, 72.77, 70.57, 67.57, 40.03. Anal. Calcd for $C_{12}H_{26}N_2O_{10}$ (358.34): C, 40.22; H, 7.31; N, 7.82. Found: C, 39.77; H, 7.64; N, 7.38.

4'-Aza-*N*-methylheptamethylenediammonium D-Glucarate (7i). Salt **7i** was prepared according to the method for **7c** using monopotassium D-glucarate (**1**, 50.0 g, 0.201 mol), acid form cation exchange resin (140 mL, 0.266 mol, Amberlite IR 120H, 1.9 meq/mL), and 4'-aza-*N*-methylheptamethylenediamine (35 mL, 0.217 mol). Salt **7i** was solidified using absolute ethanol (400 mL), isolated by filtration, washed with ethanol (3 x 50 mL), and dried to give 4'-aza-*N*-methylheptamethylenediammonium D-glucarate (**7i**, 62.6 g, 0.176 mol, 87.5%) as a white powder: mp 141 °C; $[\alpha]_D^{25}$ +1.5 (*c* 1.0, H_2O); ^{1}H NMR (D_2O) δ 4.10 (d, 1H, H-2, $J_{2,3}$ = 2.9 Hz), 4.08 (d, 1H, H-5, $J_{4,5}$ = 4.4 Hz), 4.03 (dd, 1H, H-3, $J_{3,4}$ = 5.1), 3.89 (t, 1H, H-4), 2.97 (t, 4H, H-1' and H-7', $J_{1',2' \text{ and } 6',7'}$ = 7.3), 2.54 (t, 4H, H-3' and H-5', $J_{2',3' \text{ and } 5',6'}$ = 8.1), 2.26 (s, 3H, methyl), 1.83 (m, 4H, H-2'and H-6'); ^{13}C NMR (D_2O) δ179.67, 179.57, 74.82, 74.79, 74.67, 72.80, 54.57, 41.61, 39.00, 24.98. Anal. Calcd for $C_{13}H_{29}N_3O_8$ (355.38): C, 43.94; H,8.33; N, 11.82. Found: C, 43.37; H, 8.14; N, 11.40.

***m*-Xylylenediammonium D-Glucarate (7j).** Salt **7j** was prepared according to the method for **7c** using monopotassium D-glucarate (**1**, 20.00 g, 80.57 mmol), acid form cation exchange resin (70 mL, 147 mmol, Dowex 50WX8-100, 2.1 meq/mL), and *m*-xylylenediamine (11.5 mL, 85.3 mmol). Salt **7j** was solidified using methanol (200 mL), isolated by filtration, washed with methanol (3 x 20 mL), and dried to give *m*-xylylenediammonium D-glucarate (**7j**; 22.49 g, 64.94 mmol, 80.6%) as a white powder which was recrystallized from ethanol/water: mp 197 °C; $[\alpha]_D^{25}$ +1.5 (*c* 1.0, H_2O); ^{1}H NMR (D_2O) δ 7.54-7.45 (m, 4H, Ar), 4.18 (s, 4H, CH_2-Ar), 4.05-3.99 (m, 3H, H-2, H-5, and H-3), 3.87 (t, 1H, H-4); ^{13}C NMR (D_2O) δ179.66, 179.54, 134.81, 131.11, 130.58, 130.26, 74.82, 74.73, 74.61, 72.79, 43.88. Anal. Calcd for $C_{14}H_{22}N_2O_8$ (346.33): C, 48.55; H, 6.40; N, 8.09. Found: C, 48.68; H, 6.41; N, 8.15.

Stereo Random Poly(alkylene D-glucaramide) Pre-polymers (9)

Stereo Random Poly(hexamethylene D-glucaramide) Pre-polymer (9c). Acetyl chloride (2.0 mL, 28 mmol) was added drop wise to methanol (45 mL) at 0 °C. The methanolic HCl solution was allowed to warm to room temperature (10 min) prior to the

addition of hexamethylenediammonium D-glucarate (**7c**, 2.29 g, 7.02 mmol). The solution was stirred for 3 h at room temperature, concentrated to a solid, and dried. The solid was re-dissolved in methanol (20 mL) followed by the addition of sodium methoxide solution (26 mL, 13 mmol) and triethylamine (0.49 mL, 3.5 mmol); a precipitate was observed within 30 min. After the mixture was stirred at room temperature for 24 h, the precipitate was isolated by filtration, washed with methanol (3 x 10 mL), and dried to give stereo random poly(hexamethylene D-glucaramide) pre-polymer (**9c**; 1.52 g, 5.24 mmol, 74.6%) as a white powder: mp 185 °C; ^{1}H NMR (DMSO-d_6) δ 7.86 (t, 1H, N-H, J = 5.1 Hz), 7.62 (t, 1H, N-H, J = 5.9 Hz), 3.99 (d, 1H, H-2, $J_{2,3}$ = 3.7 Hz), 3.92 (d, 1H, H-5, $J_{4,5}$ = 6.6 Hz), 3.87 (m, 1H, H-3), 3.69 (d, 1H, H-4, $J_{3,4}$ = 2.9 Hz), 3.06 (m, 4H, H-1' and H-6'), 2.60 (m, CH_2-N terminal), 1.40 (m, 4H, H-2' and H-5'), 1.24 (m, 4H, H-3' and H-4').

Stereo Random Poly(ethylene D-glucaramide) Pre-polymer (9a).
Ethylenediammonium D-glucarate (**7a** 1.90 g, 7.02 mmol) was esterified and dried as described for **9c**. Some solid remained undissolved throughout the esterification step. Polymerization was initiated by the addition of sodium methoxide solution (26 mL, 13 mmol) and triethylamine (0.49 mL, 3.5 mmol); a precipitate was observed within 10 min. After the mixture was stirred at room temperature for 24 h, the precipitate was isolated by filtration, washed with methanol (3 x 10 mL), and dried to give stereo random poly(ethylene D-glucaramide) pre-polymer (**9a**, 1.33 g, 5.66 mmol, 80.7%) as a white powder: no melting point observed by DSC or Fisher-Johns melting point apparatus. ^{1}H NMR (D_2O) δ 4.30 (d, 1H, H-2, $J_{2,3}$ = 2.93 Hz), 4.22 (d, 1H, H-5, $J_{4,5}$ = 5.37 Hz), 4.06 (dd, 1H, H-3, $J_{3,4}$ = 4.88 Hz), 3.92 (m, 1H, H-4), 3.39 (s, 4H, H-1'), 2.85 (m, CH_2-N terminal).

Stereo Random Poly(tetramethylene D-glucaramide) Pre-polymer (9b).
Tetramethylenediammonium D-glucarate (**7b**, 2.10 g, 7.02 mmol) was esterified and dried as described for **9c**. Some solid remained undissolved throughout the esterification step. Polymerization was initiated by the addition of sodium methoxide solution (29.5 mL, 14.8 mmol) and triethylamine (0.49 mL, 3.5 mmol); a precipitate was observed

within 20 min. After the mixture was stirred at room temperature for 24 h, the precipitate was isolated by filtration, washed with methanol (3 x 10 mL), and dried to give stereo random poly(tetramethylene D-glucaramide) pre-polymer (**9b**, 1.38 g, 5.26 mmol, 74.9%) as a white powder: mp 179-183 °C Fisher-Johns melting point apparatus (lit. 192-195 °C);[8] $[\alpha]_D^{25}$ +10.0 (*c* 1.0, H_2O). ^{1}H NMR (DMSO-d_6) δ 7.87 (t, 1H, N-H, J = 5.9 Hz), 7.64 (t, 1H, N-H, J = 5.1 Hz), 4.00 (d, 1H, H-2, $J_{2,3}$ = 2.9 Hz), 3.93 (d, 1H, H-5, $J_{4,5}$ = 6.6 Hz), 3.88 (m, 1H, H-3), 3.69 (m, 1H, H-4), 3.08 (m, 4H, H-1' and H-4'), 2.74 (m, CH_2-N terminal), 1.41 (br s, 4H, H-2' and H-3').

Stereo Random Poly(octamethylene D-glucaramide) Pre-polymer (9d). Octamethylenediammonium D-glucarate (**7d**, 2.49 g, 7.03 mmol) was esterified and dried as described for **9c**. Polymerization was initiated by the addition of sodium methoxide solution (26 mL, 13 mmol) and triethylamine (0.49 mL, 3.5 mmol); a precipitate was observed within 10 min. After the mixture was stirred at room temperature for 24 h, the precipitate was isolated by filtration, washed with methanol (3 x 10 mL), and dried to give stereo random poly(octamethylene D-glucaramide) pre-polymer (**9d**, 1.78 g, 5.59 mmol, 79.5%) as a white powder: mp 192 °C (lit. 190-200 °C).[8] ^{1}H NMR (DMSO-d_6) δ 7.85 (t, 1H, N-H, J = 5.1 Hz), 7.60 (t, 1H, N-H, J = 5.9 Hz), 3.98 (d, 1H, H-2, $J_{2,3}$ = 3.7 Hz), 3.92 (d, 1H, H-5, $J_{4,5}$ = 5.9 Hz), 3.87 (t, 1H, H-3), 3.68 (dd, 1H, H-4, $J_{3,4}$ = 2.9 Hz), 3.06 (m, 4H, H-1' and H-8'), 2.66 (m, CH_2-N terminal), 1.40 (m, 4H, H-2' and H-7'), 1.24 (m, 1.24 (m, 8H, H-3', H-4', H-5', and H-6').

Stereo Random Poly(decamethylene D-glucaramide) Pre-polymer (9e). Decamethylenediammonium D-glucarate (**7e**, 2.69 g, 7.03 mmol) was esterified and dried as described for **9c**. Polymerization was initiated by the addition of sodium methoxide solution (26 mL, 13 mmol) and triethylamine (0.49 mL, 3.5 mmol); a precipitate was observed within 10 min. After the mixture was stirred at room temperature for 24 h, the precipitate was isolated by filtration, washed with methanol (3 x 10 mL), and dried to give stereo random poly(decamethylene D-glucaramide) pre-polymer (**9e**, 1.86 g, 5.37 mmol, 76.4%) as a white powder: mp 197 °C (lit. 200-205 °C).[8] ^{1}H NMR (DMSO-d_6) δ 7.85 (t, 1H, N-H, J = 5.1 Hz), 7.60 (t, 1H, N-H, J = 5.9 Hz), 3.98 (d, 1H, H-2, $J_{2,3}$ = 2.9

Hz), 3.92 (d, 1H, H-5, $J_{4,5}$ = 5.9 Hz), 3.87 (t, 1H, H-3), 3.68 (dd, 1H, H-4, $J_{3,4}$ = 2.2 Hz), 3.06 (m, 4H, H-1' and H-10'), 2.64 (t, CH_2-N terminal), 1.40 (m, 4H, H-2' and H-9'), 1.24 (m, 12H, H-3', H-4', H-5', H-6', H-7', and H-8').

Stereo Random Poly(dodecamethylene D-glucaramide) Pre-polymer (9f). Dodecamethylenediammonium D-glucarate (**7f**, 2.88 g, 7.02 mmol) was esterified and dried as described for **9c**. Polymerization was initiated by the addition of sodium methoxide solution (26 mL, 13 mmol) and triethylamine (0.49 mL, 3.5 mmol); a precipitate was observed within 25 min. After the mixture was stirred at room temperature for 24 h, the precipitate was isolated by filtration, washed with methanol (3 x 10 mL), and dried to give stereo random poly(dodecamethylene D-glucaramide) pre-polymer (**9f**, 2.25 g, 6.00 mmol, 85.4%) as a white powder: mp 197 °C (lit. 200-205 °C).[8] ^{1}H NMR (DMSO-d_6) δ 7.84 (t, 1H, N-H, J = 5.1 Hz), 7.59 (t, 1H, N-H, J = 5.9 Hz), 3.97 (d, 1H, H-2, $J_{2,3}$ = 6.6 Hz), 3.92 (d, 1H, H-5, $J_{4,5}$ = 6.6 Hz), 3.86 (m, 1H, H-3), 3.68 (m, 1H, H-4), 3.05 (m, 4H, H-1' and H-12'), 2.62 (m, CH_2-N terminal), 1.39 (m, 4H, H-2' and H-11'), 1.23 (m, 16H, H-3', H-4', H-5', H-6', H-7', H-8', H-9', and H10').

Stereo Random Poly(2-methylpentamethylene D-glucaramide) Pre-polymer (9g). 2-Methylpentamethylenediammonium D-glucarate (**7g**, 2.29 g, 7.02 mmol) was esterified and dried as described for **9c**. Polymerization was initiated by the addition of sodium methoxide solution (26 mL, 13 mmol) and triethylamine (0.49 mL, 3.5 mmol); an oily solid formed gradually. After the mixture was stirred at room temperature for 24 h, the methanol layer was decanted from the oil, and the oil was washed with methanol (3 x 5 mL), and dried to give stereo random poly(2-methylpentamethylene D-glucaramide) pre-polymer (**9g**, 0.94 g, 3.2 mmol, 46%) as an amorphous yellow solid: no melting point observed by DSC or Fisher-Johns melting point apparatus. ^{1}H NMR (D_2O) δ 4.27 (d, 1H, H-2, $J_{2,3}$ = 2.93 Hz), 4.19 (d, 1H, H-5, $J_{4,5}$ = 4.88 Hz), 4.05 (m, 1H, H-3), 3.92 (m, 1H, H-4), 3.19 (m, 2H, H-5'), 3.08 (m, 2H, H-1'), 2.73 (m, CH_2-N terminal), 2.60 (m, CH_2-N terminal), 1.67 (m, 1H, H-2'), 1.52 (m, 1H, H-4'), 1.34 (m, 1H, H-3'), 1.12 (m, 1H, H-3'), 0.85 (d, 3H, methyl, $J_{2',CH3}$ = 6.35).

Stereo Random Poly(3',6'-dioxaoctamethylene D-glucaramide) Pre-polymer (9h). 3',6'-Dioxaoctamethylenediammonium D-glucarate (**7h**, 2.52 g, 7.04 mmol) was esterified and dried as described for **9c**. Polymerization was initiated by the addition of sodium methoxide solution (26 mL, 13 mmol) and triethylamine (0.49 mL, 3.5 mmol); an oily solid formed gradually. After the mixture was stirred at room temperature for 24 h, the methanol layer was decanted from the oil, and the oil was washed with methanol (3 x 5 mL), and dried to give stereo random poly(3',6'-dioxaoctamethylene D-glucaramide) pre-polymer (**9h**, 0.65 g, 2.0 mmol, 30%) as an amorphous white solid: mp 109 °C. ^{1}H NMR (D_2O) δ 4.32 (d, 1H, H-2, $J_{2,3}$ = 2.93 Hz), 4.23 (d, 1H, H-5, $J_{4,5}$ = 5.13 Hz), 4.07 (t, 1H, H-3, $J_{3,4}$ = 4.40 Hz), 3.91 (t, 1H, H-4), 3.65 (s, 4H, H-3' and H-4'), 3.62 (t, 4H, H-2' and H-5', $J_{1',2' \text{ and } 5',6'}$ = 5.13), 3.43 (m, 4H, H-1' and H-6'), 3.01(m, CH_2-N terminal).

Stereo Random Poly(4'-aza-*N*-methylheptamethylene D-glucaramide) Pre-polymer (9i). 4'-Aza-*N*-methylheptamethylenediammonium D-glucarate (**7i**, 1.25 g, 3.52 mmol) was esterified and dried as described for **9c**. Polymerization was initiated by the addition of sodium methoxide solution (20 mL, 10 mmol) and triethylamine (0.4 mL, 3 mmol); an oily solid formed gradually. After the mixture was stirred at room temperature for 24 h the methanol layer was decanted from the oil, and the oil was washed with methanol (3 x 5 mL), and dried to give stereo random poly(4'-aza-*N*-methylheptamethylene D-glucaramide) pre-polymer (**9i**, 0.23 g, 0.70 mmol, 20%) as an amorphous, white solid: no melting point observed by DSC or Fisher-Johns melting point apparatus. ^{1}H NMR (D_2O) δ 4.27 (d, 1H, H-2, $J_{2,3}$ = 2.9 Hz), 4.20 (d, 1H, H-5, $J_{4,5}$ = 5.4 Hz), 4.04 (t, 1H, H-3, $J_{3,4}$ = 4.4 Hz), 3.91 (t, 1H, H-4), 3.22 (m, 4H, H-1' and H-6'), 2.75 (m, CH_2-N terminal), 2.42 (t, 4H, H-3' and H-4', $J_{3',4'}$ = 7.32 Hz), 2.19 (s, 3H, methyl), 1.69 (m, 4H, H-2' and H-5').

Stereo Random Poly(*m*-xylylene D-glucaramide) Pre-polymer (9j). *m*-Xylylenediammonium D-glucarate (**7j,** 2.43 g, 7.02 mmol) was esterified and dried as described for **6c**. Polymerization was initiated by the addition of sodium methoxide solution (26 mL, 13 mmol) and triethylamine (0.49 mL, 3.5 mmol); a precipitate was observed within 25 min. After the mixture was stirred at room temperature for 24 h, the precipitate was isolated by filtration, washed with methanol (3 x 10 mL), and dried to

give stereo random poly(*m*-xylylene D-glucaramide) pre-polymer (**9j**, 1.92 g, 6.20 mmol, 88.3%) as a white powder: (no melting point observed by DSC or Fisher-Johns melting point apparatus, lit. 210-215 °C).[8] ^{1}H NMR (DMSO-d_6) δ 8.37 (t, 1H, N-H, J = 5.86 Hz), 8.15 (t, 1H, N-H, J = 5.86 Hz), 7.31-7.0 (m, 4H, aryl), 4.30 (m, 4H, CH_2-aryl), 4.12 (d, 1H, H-2, $J_{2,3}$ = 2.93 Hz), 4,04 (d, 1H, H-5, $J_{4,5}$ = 5.86 Hz), 3.99 (m, 1H, H-3), 3.88 (m, N-CH_2-terminal), 3.80 (dd, 1H, H-4, $J_{3,4}$ = 3.66 Hz).

Stereo Random Poly(alkylene D-glucaramide) Post-polymers (10)

Stereo Random Poly(hexamethylene D-glucaramide) Post-polymer (10c). Ethylene glycol (4.5mL) and triethylamine (0.75 mL) were added to a 60 °C solution of stereo random poly(hexamethylene D-glucaramide) pre-polymer (**9c**; 0.50 g) in DMSO (4.5 mL). The solution became cloudy within 15 min. The mixture was stirred at 60 °C for 18 h before diluting with methanol (15 mL) and allowing to cool to room temperature. The resulting precipitate was isolated by filtration, washed with methanol (3 x 5 mL), and dried to give stereo random poly(hexamethylene D-glucaramide) post-polymer (**10c**; 0.41 g, 82%) as an off-white powder: mp 188 °C; ^{1}H NMR (DMSO-d_6) δ 7.85 (t, 1H, N-H, J = 5.1 Hz), 7.61 (t, 1H, N-H, J = 5.9 Hz), 5.53 (d, 1H, O-H, J = 5.9), 5.39 (d, 1H, O-H, J = 4.4), 4.76 (d, 1H, O-H, J = 4.4), 4.63 (d, 1H, O-H, J = 6.6), 3.99 (br s, 1H, H-2), 3.91 (t, 1H, H-5), 3.87 (br s, 1H, H-3), 3.69 br s, 1H, H-4), 3.06 (m, 4H, H-1' and H-6'), 2.77 (m, N-CH_2 terminal), 1.40 (br s, 4H, H-2' and H-5'), 1.24 (br s, 4H, H-3' and H-4').

Stereo Random Poly(ethylene D-glucaramide) Post-polymer (10a). Post polymerization of stereo random poly(ethylene D-glucaramide) pre-polymer (**9a**) (0.50 g) was carried out as described for stereo random poly(hexamethylene D-glucaramide) post-polymer (**10c**) with the exception of methanol used in place of ethylene glycol, giving stereo random poly(ethylene D-glucaramide) post-polymer (**10a**; 0.34 g, 68%) as an off-white powder: no melting point observed by DSC or Fisher-Johns melting point apparatus. ^{1}H NMR (D_2O) δ 4.30 (d, 1H, H-2, $J_{2,3}$ = 2.93 Hz), 4.22 (d, 1H, H-5, $J_{4,5}$ = 5.37 Hz), 4.06 (dd, 1H, H-3, $J_{3,4}$ = 4.88 Hz), 3.92 (m, 1H, H-4), 3.39 (s, 4H, H-1'), 2.85 (m, CH_2-N terminal).

Stereo Random Poly(tetramethylene D-glucaramide) Post-polymer (10b). Post polymerization of stereo random poly(tetramethylene D-glucaramide) pre-polymer (**9b**; 0.50 g) was carried out as described for stereo random poly(hexamethylene D-glucaramide) post-polymer (**10c**) with the exception of methanol used in place of ethylene glycol, giving stereo random poly(tetramethylene D-glucaramide) post-polymer (**10b**; 0.36 g, 72%) as an off-white powder: mp 192 °C; ^{1}H NMR (DMSO-d_6) δ 7.87 (br t, 1H, N-H, J = 5.9 Hz), 7.63 (br t, 1H, N-H, J = 5.1 Hz), 4.00 (d, 1H, H-2, $J_{2,3}$ = 2.9 Hz), 3.93 (d, 1H, H-5, $J_{4,5}$ = 5.9 Hz), 3.88 (br t, 1H, H-3), 3.70 (m, 1H, H-4), 3.08 (br s, 4H, H-1' and H-4'), 2.74 (m, 2H, N-CH_2 terminal), 1.40 (br s, 4H, H-2' and H-3').

Stereo Random Poly(octamethylene D-glucaramide) Post-polymer (10d). Post polymerization of stereo random poly(octamethylene D-glucaramide) pre-polymer (**9d**; 0.50 g) was carried out as described for stereo random poly(hexamethylene D-glucaramide) post-polymer (**10c**) to give stereo random poly(octamethylene D-glucaramide) post-polymer (**10d**; 0.48 g, 96%) as an off-white powder: mp 197 °C. ^{1}H NMR (DMSO-d_6) δ 7.84 (t, 1H, N-H, J = 5.13 Hz), 7.59 (t, 1H, N-H, J = 5.86 Hz), 5.52 (br s, 1H, O-H), 5.36 (br s, 1H, O-H), 4.76 (br s, 1H, O-H), 4.62 (br s, 1H, O-H), 3.98 (d, 1H, H-2, $J_{2,3}$ = 2.93), 3.92 (d, 1H, H-5, $J_{4,5}$ = 5.86), 3.87 (br s, 1H, H-3), 3.68 (br s, 1H, H-4), 3.06 (m, 4H, H-1' and H-8'), 2.71 (m, N-CH_2 terminal), 1.40 (br s, 4H, H-2' and H-7'), 1.24 (br s, 8H, H-3', H-4', H-5', and H-6').

Stereo Random Poly(decamethylene D-glucaramide) Post-polymer (10e). Post polymerization of stereo random poly(decamethylene D-glucaramide) pre-polymer (**9e**; 0.50 g) was carried out as described for stereo random poly(hexamethylene D-glucaramide) post-polymer (**10c**) to give stereo random poly(decamethylene D-glucaramide) post-polymer (**10e**; 0.46 g, 93%) as an off-white powder: mp 197 °C; ^{1}H NMR (DMSO-d_6) δ 7.84 (t, 1H, N-H, J = 5.13 Hz), 7.59 (t, 1H, N-H, J = 5.86 Hz), 3.98 (d, 1H, H-2, $J_{2,3}$ = 3.66 Hz), 3.92 (d, 1H, H-5, $J_{4,5}$ = 6.59 Hz), 3.86 (br s, 1H, H-3), 3.68 (dd, 1H, H-4, $J_{3,4}$ = 5.86 Hz), 3.05 (m, 4H, H-1' and H-10'), 2.69 (t, N-CH_2 terminal), 1.40 (m, 4H, H-2' and H-9'), 1.24 (br s, 12H, H-3', H-4', H-5', H-6', H-7', and H-8')

Stereo Random Poly(dodecamethylene D-glucaramide) Post-polymer (10f). Post polymerization of stereo random poly(dodecamethylene D-glucaramide) pre-polymer (**9f**; 0.50 g) was carried out as described for stereo random poly(hexamethylene D-glucaramide) post-polymer (**10c**) to give stereo random poly(dodecamethylene D-glucaramide) post-polymer (**10f**; 0.45 g, 90%) as an off-white powder: mp 197 °C; ^{1}H NMR (DMSO-d_6) δ 7.84 (t, 1H, N-H, J = 5.13 Hz), 7.59 (t, 1H, N-H, J = 5.86 Hz), 3.97 (d, 1H, H-2, $J_{2,3}$ = 3.66 Hz), 3.92 (d, 1H, H-5, $J_{4,5}$ = 6.59 Hz), 3.86 (t, 1H, H-3), 3.68 (dd, 1H, H-4, $J_{3,4}$ = 2.93 Hz), 3.05 (m, 4H, H-1' and H-12'), 2.72 (m, CH_2-N terminal), 1.39 (m, 4H, H-2' and H-11'), 1.24 (m, 16H, H-3', H-4', H-5', H-6', H-7', H-8', H-9', and H10').

Stereo Random Poly(*m*-xylylene D-glucaramide) Post-polymer (10j). Post polymerization of stereo random poly(*m*-xylylene D-glucaramide) pre-polymer (**9j**; 0.50 g) was carried out as described for stereo random poly(hexamethylene D-glucaramide) post-polymer (**10c**) to give stereo random poly(*m*-xylylene D-glucaramide) post-polymer as an off-white powder (**10j**; 0.35 g, 70%): mp 225 °C; ^{1}H NMR (DMSO-d_6) δ 8.35 (br t, 1H, N-H), 8.13 (t, 1H, N-H), 7.20 (br s, 2H, aryl), 7.15 (br s, 2H, aryl), 4.30 (m, 4H, CH_2-aryl), 4.12 (br s, 1H, H-2), 4.02 (d, 1H, H-5, $J_{4,5}$ = 5.9 Hz), 3.98 (br s, 1H, H-3), 3.79 (br s, 1H, H-4).

2.4 References

[1] Thiem, Joachim; Bachmann, Frank. Carbohydrate-derived Polyamides. *Trends Polym. Sci.* **1994**, *2*, 425-432.

[2] Stick, Robert V. *Carbohydrates: The Sweet Molecules of Life*; Academic: San Diego, 2001; p 5.

[3] Ogata, Naoya; Hosoda, Yoshikazu. Synthesis of Hydrophilic Polyamide by Active Polycondensation. *J. Polym. Sci., Polym. Lett. Ed.* **1974**, *12*, 355-358.

[4] Ogata, Naoya; Sanui, Kohei; Hosoda, Yoshikazu; Nakamura, Hiroyuki. Active Polycondensation of Diethyl 2,3,4,5-Tetrahydroxyadipate with Diamines. *J. Polym. Sci., Polym. Chem. Ed.* **1976**, *14*, 783-792.

[5] Kiely, D. E.; Lin, Tsu-Hsing. Polyhydroxypolyamides and Process for Making Same. *U.S. Patent 4,833,230*, May 23, 1989.

[6] Hoagland, Peter D.; Pessen, Helmut; McDonald, George G. The Formation of Intermediate Lactones During Aminolysis of Diethyl Xylarate. *J. Carbohydr. Chem.* **1987**, *6*, 495-499.

[7] Viswanathan, Arvind; Kiely, Donald E. Mechanisms for the Formation of Diamides and Polyamides by Aminolysis of D-Glucaric Acid Esters. *J. Carbohydr. Chem.* **2003**, *22*, 903-918.

[8] Kiely, Donald E.; Chen, Liang.; Lin, Tsu-Hsing. Hydroxylated Nylons Based on Unprotected Esterified D-Glucaric Acid by Simple Condensation Reactions. *J. Am. Chem. Soc.* **1994**, *116*, 571-578.

[9] Hashimoto, Kazuhiko; Wibullucksanakul, Sirinat; Matsuura, Mitsuyasu; Okada, Masahiko. Macromolecular Synthesis from Saccharic Lactones. Ring-Opening Polyaddition of D-Glucaro- and D-Mannaro-1,4;6,3-dilactones with Alkyldiamines. *J. Polym. Sci., Polym. Chem. Ed.* **1993**, *31*, 3141-3149.

[10] Chen, Liang.; Kiely, Donald E. Synthesis of Stereoregular *Head,Tail* Hydroxylated Nylons Derived from D-Glucose. *J. Org. Chem.* **1996**, *61*, 5847-5851.

[11] Styron, Susan D.; Kiely, Donald E.; Ponder, Glenn. Alternating Stereoregular *Head, Tail-Tail,Head*-Poly(alkylene D-glucaramides) Derived from a Homologous Series of

Symmetrical Diamido-Di-D-Glucaric Acid Monomers. *J. Carbohydr. Chem.* **2003**, *22*, 123-142.

[12] Kiely, Donald. E.; Kramer, Kylie. High Molecular Weight Stereoregular Head-Tail Poly(Glucaramides). *U.S. Patent 7,314,906*, January 1, 2008.

[13] Kiely, Donald E.; Chen, Liang.; Lin, Tsu-Hsing. Synthetic Polyhydroxypolyamides from Galactaric, Xylaric, D-Glucaric and D-Mannaric Acids and Alkylenediamine Monomers-Some Comparisons. *J. Polym. Sci., Polym. Chem. Ed.* **2000**, 38, 594-603.

[14] Morton, David W.; Kiely, Donald E. Synthesis of Poly(azaalkylene aldaramides) and Poly(oxaalkylene aldaramides) Derived from D-Glucaric and D-Galactaric Acids. *J. Polym. Sci., Polym. Chem. Ed.* **2000**, *38*, 604-613.

[15] Kiely, Donald. E.; Kramer, Kylie; Zhang, Jinsong. Method for Preparing High Molecular Weight Random Polyhydroxypolyamides. *U.S. Patent 6,894,135*, May 17, 2005.

[16] Zhang, Jinsong. Poly(alkylene D-aldaramides) and their Corresponding Esters – Synthesis and Conformational Studies. *Ph.D. Dissertation*, The University of Montana, 2003.

[17] Denton, Travis T. unpublished results.

[18] Lorette, N. B.; Brown, J. H., Jr. Use of Acetone Dimethyl Acetal in Preparation of Methyl Esters. *J. Am. Chem. Soc.* **1959**, *24*, 261-262.

[19] Bowden, Everett. Methyl Oxalate. *Org. Syntheses, Coll. Vol. II* **1943**, 414.

[20] Kesavan, Venkitasamy; Bonnet-Delpon, Danièle; Bégué, Jean-Pierre. Fluoro Alcohol as Reaction Medium: One-pot Synthesis of β-Hydroxy Sulfoxides from Epoxides. *Tetrahedron Lett.* **2000**, *41*, 2895-2898.

[21] Carey, Francis A.; Sundberg, Richard J. *Advanced Organic Chemistry Part A: Structure and Mechanism*, 4th ed.; Kluwer Academic/Plenum: New York, 2000; pp 242-243.

[22] Parker, Alan J. Protic-Dipolar Aprotic Solvent Effects on Rates of Bimolecular Reactions. *Chem. Rev.* **1969**, *69*, 1-32.

[23] Taga, Tooru; Kuroda, Yoshihiro; Osaki, Kenji. Interactions of Calcium Ions with Carbohydrates: X-Ray Diffraction and NMR Spectroscopic Studies of the Potassium Salt and the Calcium Salt of D-Glucaric Acid. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 3079-3083.

[24] Styron, Susan D.; French, Alfred D.; Friedrich, Joyce D.; Lake, Charles H.; Kiely, Donald E. MM3(96) Conformational Analysis of D-Glucaramide and X-Ray Crystal Structures of Three D-Glucaric Acid Derivatives- Models for Synthetic Poly(alkylene D-glucaramides). *J. Carbohydr. Chem.* **2002**, *21*, 27-51.

[25] Bontchev, Ranko P.; Moore, Robert C. Crystal Structure and Aqueous Solubility of Ammonium D-Glucarate. *Carbohydr. Res.* **2005**, *340*, 2195-2200.

[26] Jeffrey, G. A.; Kim, H. S. Conformations of the Alditols. *Carbohydr. Res.* **1970**, *14*, 207-216.

[27] Horton, Derek; Wander, Joseph D. Conformation of Acyclic Derivatives of Sugars. XI. Conformations of the D-Aldopentose Diethyl and Diphenyl Dithioacetals in Solution. *J. Org. Chem.* **1974**, *39*, 1859-1863.

[28] Jeffrey, G. A.; Fasiska, E. J. Conformation and Intramolecular Hydrogen-Bonding in the Crystal Structure of Potassium D-Gluconate Monohydrate. *Carbohydr. Res.* **1972**, *21*, 187-199.

[29] Bou, J. J.; Rodríguez-Galán, A.; Muñoz-Guerra, S. Optically Active Polyamides Derived from L-Tartaric Acid. *Macromolecules* **1993**, *26*, 5664-5670.

[30] Stevens, Malcolm P. *Polymer Chemistry: An Introduction*, 3rd ed.; Oxford University: New York, 1999; 70-74.

[31] APEX II, **2005**, Bruker AXS, Inc., Analytical X-ray Systems, 5465 East Cheryl Parkway, Madison WI 53711-5373.

[32] SAINT Version 6.45A, **2003**, Bruker AXS, Inc., Analytical X-ray Systems, 5465 East Cheryl Parkway, Madison WI 53711-5373.

[33] SHELXTL V6.12, **2002**, Bruker AXS, Inc., Analytical X-ray Systems, 5465 East Cheryl Parkway, Madison WI 53711-5373.

[34] Wilson, A. J. C., Ed.; In *International Tables for X-ray Crystallography, Volume C.* Kynoch Academic, Dordrecht, 1992; pp 219-222 and 500-502.

[35] Macrae, C. F.; Edgington, P. R.; McCabe, P.; Pidcock, E.; Shields, G. P.; Taylor, R.; Towler M.; van de Streek J. Mercury: Visualization and Analysis of Crystal Structures. *J. Appl. Cryst.* **2006**, *39*, 453-457.

Chapter 3. Poly(aldaramide) Gel Forming Agents

3.1 Introduction

Gelators are defined as chemical substances which, at low concentrations (typically < 2%), are capable of immobilizing a liquid into a deformable, semi-solid material known as a gel. Gelators encompass a structurally diverse group of materials that range from polymers and dendrimers to small organic molecules and organo-metallic complexes. These gel forming agents can be divided into two classes: polymeric gelators and low molecular weight gelators (LMWG). Polymeric gelators in the form of superabsorbent polymers (SAPs) are capable of absorbing up to 1000 grams of a fluid per gram of polymer. SAPs are the most commercially important gelators and are primarily used in the absorption of water and aqueous solutions in personal hygiene and agricultural applications. SAPs can be either polyelectrolytes (polyionic) or neutral (non-ionic) polymers depending upon the molecular structure of the hydrophilic groups found on the polymer. Polyanionic SAPs in the form of cross-linked polyacrylates are the most common with approximately 75% of world production being used in baby diapers for urine absorption.[1] Polycationic SAPs include poly(vinyl amine)[2] and chitosan,[3] while neutral SAPs are typically cross-linked derivatives of poly(vinyl alcohol)[4] and polyacrylamide.[5] SAPs with ionic hydrophilic groups typically absorb water faster and require less material for gelation than the neutral SAPs. In addition to hydrophilic groups, SAPs generally contain some degree of cross-links. While the hydrophilic groups promote water affinity, the cross links prevent complete dissolution of the material. Covalent cross-links are formed by introducing a small amount of a branching monomer into the polymerization reaction.

Although a number of LMWGs have been reported,[6,7] these molecules have not reached commercial significance. The wide variety of structural motifs found in LMWGs offers some advantages over SAPs which are mostly limited to polymers from vinyl monomers. Structural variety allows for fine tuning of the molecules for specific applications such as drug delivery where biocompatibility is critical.[8] Primarily, LMWGs are organic molecules composed of both hydrophilic and hydrophobic groups,

and, as with SAPs, the hydrophilic groups can be either charged or neutral. The amphiphilic nature gives some LMWGs the ability to form gels in both aqueous and organic liquids.[9]

Unlike SAPs, cross-links are not present in the molecular structure of LMWGs; however, cross-linking of the molecules through physical interactions rather than covalent bonds does occur during gel formation. The physical cross-links arise from intermolecular attractive forces such as ionic interactions, hydrogen bonding, π-π interactions, and van der Waals attractive interactions and lead to the formation of supramolecular polymers.[10] Because the cross-links lack the strength of covalent bonds, gels formed through physical interactions are thermally reversible.

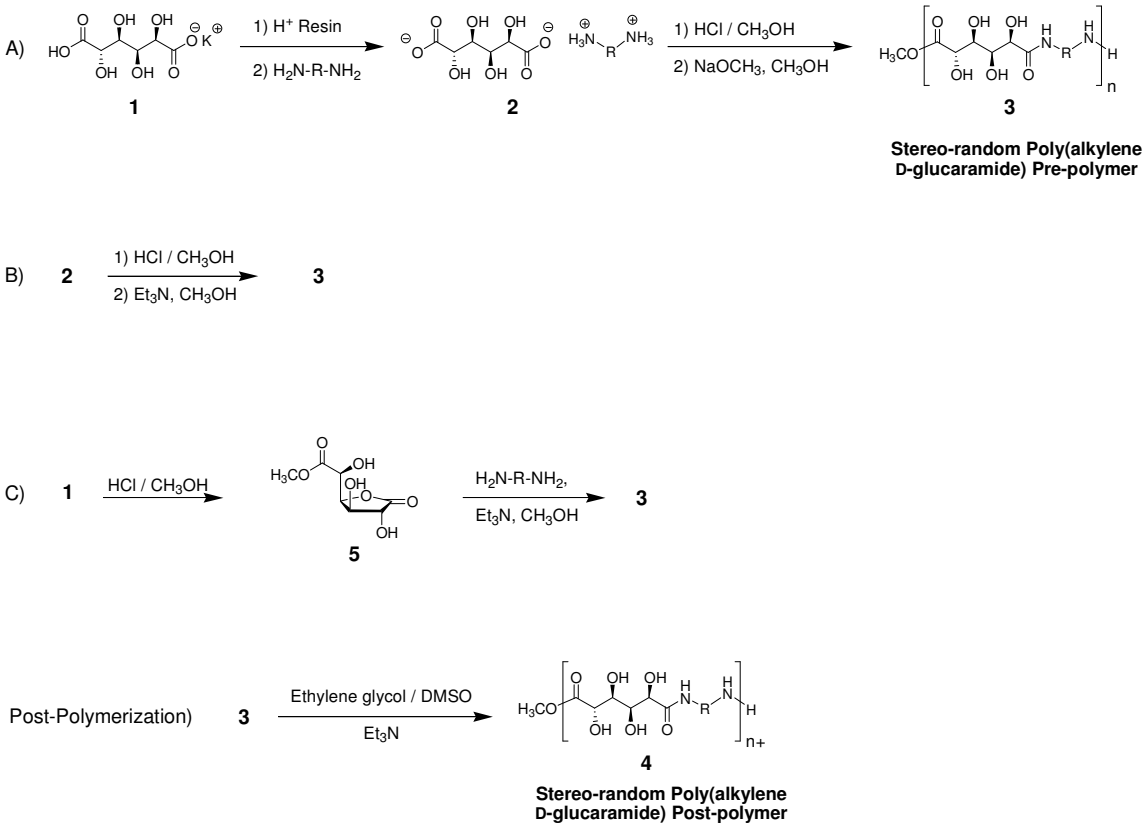
The mechanism of gel formation is related to the nature of the cross-links found in the gelator. In SAPs, covalent cross-links increase the molecular weights of the polymers and provide a three dimensional, insoluble network capable of absorbing water through a diffusive mechanism. The absorption capacity is proportional to the swelling pressure which is the difference between osmotic pressure and deformation pressure of the system. Osmotic pressure manifests from the tendency of the hydrophilic portion of the polymer to hydrate and uncoil. Osmotic pressure is resisted by deformation pressure arising from the covalently bonded cross-links.[11] Swelling pressure can be determined by measuring the force required to remove the water from a swollen hydrogel mixture. Swelling pressure is enhanced when ionized groups are present in the polymer. When polyelectrolyte SAPs are placed in pure water, the counter ions not attached to the polymeric chain diffuse into the water, and swelling pressure is increased by Coulombic repulsion of the charged groups attached to the polymer chain. When polyelectrolyte SAPs are allowed to swell in salt solutions, diffusion of the counter ions occurs to a lesser extent, resulting in less Coulombic repulsion and lower swelling pressure.[12] As a result, the water absorbing capability of polyelectrolyte SAPs decreases with increasing concentrations of salt. In some cases, a decrease by a factor of ten is observed.

In the case of LMWGs, gels are formed by first dissolving the gelators in the liquid medium followed by changing the conditions of the medium to promote gel formation. A typical procedure involves dissolving the LMWG in hot liquid then allowing the solution to cool during which time gel formation occurs. Gel formation from solution is similar to

crystallization except that only parts of the molecules (the hydrophobic parts in the case of hydrogels) form intermolecular attachments while the hydrophilic groups remain solvated with large amounts of water. A recent study demonstrated that solubility is a dominant factor governing gelation of small molecules, and that gelation can be controlled by tuning the solubility.[13] A number of LMWGs are chiral molecules and structural asymmetry seems to be important for gel formation with small molecules. Work by Fuhrhop *et al.* showed the ability of octyl D-gluconamide to form gels from hot water while the corresponding racemic (D and L) mixture crystallized from solution rather than gelling.[14] Further investigations on the influence of chirality found the diastereomer octyl D-mannonamide to be capable of gel formation while another diastereomer, octyl D-gulonamide, formed crystals.[15]

In this report, we describe the first examples of a new class of gelators from polyamides with one or more pendant hydroxyl groups on the main polymer chain, also known as polyhydroxypolyamides (PHPAs). The gel forming PHPAs were prepared by several polycondensation methods from diamines and hydroxylated diacids derived from carbohydrate sources. PHPAs are of general interest as renewable alternatives to petrochemical-based polymers and show high rates of environmental degradation to benign products.[16] Poly(alkylene D-glucaramides) are PHPAs derived from D-glucaric acid and are particularly attractive because the starting material, D-glucaric acid, is prepared in one step by chemical oxidation of D-glucose, a widely available and inexpensive feedstock. Also, poly(alkylene D-glucaramides) are prepared from polycondensation reactions under mild conditions in methanol using methyl or ethyl esters of D-glucaric acid and any bis primary amine (diamine). The simplicity of this procedure was demonstrated by the condensation of methyl D-glucaro-1,4-lactone (**5**) and a variety of diamines to produce a number of poly(alkylene D-glucaramides) (**Scheme 3-1**, **Method C**).[17] An alternate synthetic strategy using stoichiometrically equivalent diammonium D-glucarate salts as starting material yielded poly(alkylene D-glucaramides) with higher number average molecular weights (M_n) (**Scheme 3-1**, **Method A**) as described in Chapter 2. Additional increase in M_n can be achieved by a subsequent

Scheme 3-1. Synthetic methods for the preparation of stereo-random poly(alkylene D-glucaramides).



2a, 3a, 4a: R = $(CH_2)_2$

2b, 3b, 4b: R = $(CH_2)_4$

2c, 3c, 4c: R = $(CH_2)_5$

2d, 3d, 4d: R = $(CH_2)_6$

2e, 3e, 4e: R = $(CH_2)_7$

2f, 3f, 4f: R = $(CH_2)_8$

2g, 3g, 4g: R = $(CH_2)_{12}$

2h, 3h, 4h: R = $CH_2CH(CH_3)CH_2CH_2CH_2$

2i, 3i, 4i: R = $CH_2CH_2OCH_2CH_2OCH_2CH_2$

2j, 3j, 4j: R = $CH(CH_3)CH_2NCH_2CH_2CH_3$

polymerization reaction (post-polymerization) of the initially formed polymers (pre-polymers) in a different solvent system, preferably dimethylsulfoxide (DMSO) and ethylene glycol (EG). The gel forming ability of poly(alkylene D-glucaramides) was first observed in post-polymerization reactions when poly(hexamethylene D-glucaramide) (**4d**) formed an immobilized mixture from a solution of 1:1 DMSO/EG. Substituting water for ethylene glycol **3d** produced hydrogels in 5% DMSO/water with as little as

0.75% polymer by weight; however, without DMSO, gel formation did not occur. The goals of this research were to elucidate the basic factors governing poly(alkylene D-glucaramide) hydrogel formation, to investigate the role of DMSO, to test other poly(alkylene aldaramides) as gel forming agents, and to try to improve the gelling efficiency of the polymers.

3.2 Results and Discussion

3.2.1 Hydrogels from Poly(alkylene D-glucaramide) Homopolymers

To investigate the factors governing gel formation of poly(hexamethylene D-glucaramide), samples of **3d** and **4d** were prepared from different synthetic methods to give a range of molecular weights and compositions. Polymer **3d** was prepared from hexamethylenediammonium D-glucarate (**2d**) using both sodium methoxide/triethylamine (Method A) and triethylamine only (Method B)[18] in the basification step and from **5** and hexamethylenediamine (Method C) (**Scheme 3-1**). Post-polymerization of the pre-polymers from the different methods was also carried out in a 1:1 mixture of DMSO and EG. The minimum gelling concentrations (MGC) of the resulting polymers were determined by dissolving the polymers in DMSO followed by the addition of water. After brief mixing, gels formed over several minutes from undisturbed solutions. A gel was defined as mixture which resisted flow under its own weight (stable to inversion of the gel container),[19] and MGC was determined as the minimum amount of each polymer sample required to produce a gel. From the MGC values in **Table 3-1**, pre-polymers generally out perform their corresponding post-polymers, and the best performing pre-polymer was prepared using Method A.

In addition to higher molecular weights, the pre-polymer product from Method A, as opposed to Methods B and C, contains sodium chloride by-product (ca. 1%) from neutralization with sodium methoxide as evidenced by ion chromatography (Chapter 2). To determine the effect of sodium chloride on gel formation, aqueous sodium chloride solutions (0.5% and 0.25%) were used instead of deionized water. Additional sodium

Table 3-1. Gel forming ability of poly(hexamethylene D-glucaramides) from different preparation methods.

Poly(hexamethylene D-glucaramide)	Pre-polymer Synthesis Method[a]	DP[b]	M_n[b]	Gel Medium	MGC[c] (% w/v)
Pre-polymer	A	18	5226	5% DMSO / H_2O	0.75
Pre-polymer	A	18	5226	10% DMSO / H_2O	0.75
Pre-polymer	A	18	5226	15% DMSO / H_2O	0.75
Pre-polymer	A	18	5226	20% DMSO / H_2O	0.75
Pre-polymer	A	18	5226	25% DMSO / H_2O	0.75
Pre-polymer	B	7	2032	5% DMSO / H_2O	1.00
Pre-polymer	C	6	1742	5% DMSO / H_2O	1.25
Post-polymer	A	34	9870	5% DMSO / H_2O	1.00
Post-polymer	B	13	3774	5% DMSO / H_2O	1.00
Post-polymer	C	10	2903	5% DMSO / H_2O	1.25

[a]Synthetic methods depicted in Scheme 1.
[b]Determined by ^{1}H NMR end group analysis.
[c]Minimum gelation concentration in weight to volume determined at room temperature.

chloride lowers MGC values for **3d** pre-polymers from Method C and post-polymers from Methods A and C (**Table 3-2**) while the MGC of the other polymers remained the same. Sodium chloride appears to have a slight positive effect but, perhaps more importantly, no negative effect on gelation of **3d** and **4d**. This is highlighted by pre-polymer **3d** from Method A which showed no decrease in MGC in 1% sodium chloride solution.

Since solubility is a key factor governing gelation of low molecular weight gelators and because poly(hexamethylene D-glucaramide) forms gels from solution analogous to LMWGs, an investigation of the relationship between solubility and gelation with poly(alkylene D-glucaramides) was deemed necessary. Previously, the solubility of poly(alkylene D-glucaramides) was shown to be affected by the molecular structure of the diamino portion of the polymer.[20] Diamines with short alkylene chains (two and four methylene groups), branched alkylene chains, and with one or more chain methylene units replaced by heteroatoms confer water solubility to the resulting

Table 3-2. Gel forming ability of poly(hexamethylene D-glucaramides) from different preparation methods in aqueous salt solutions.

Poly(hexamethylene D-glucaramide)	Pre-polymer Synthesis Method[a]	DP[b]	M_n[b]	NaCl (%) in 5% DMSO/ Water	MGC[c] (% w/v)
Pre-polymer	A	18	5226	0.25	0.75
Pre-polymer	A	18	5226	0.50	0.75
Pre-polymer	A	18	5226	1.00	0.75
Pre-polymer	B	7	2032	0.25	1.00
Pre-polymer	B	7	2032	0.50	1.00
Pre-polymer	C	6	1742	0.25	1.00
Pre-polymer	C	6	1742	0.50	1.00
Post-polymer	A	34	9870	0.25	0.75
Post-polymer	A	34	9870	0.50	0.75
Post-polymer	B	13	3774	0.25	1.00
Post-polymer	B	13	3774	0.50	1.00
Post-polymer	C	10	2903	0.25	1.00
Post-polymer	C	10	2903	0.50	1.00

[a]Synthetic methods depicted in Scheme 1.
[b]Determined by ^{1}H NMR end group analysis.
[c]Minimum gelation concentration in weight to volume determined at room temperature.

polymers, while diamines with six or more methylene groups in the alkylene chain give water insoluble polymers. Poly(pentamethylene D-glucaramide) (**3c**) was synthesized using method A in hopes of striking a balance between the water solubility of poly(tetramethylene D-glucaramide) (**3b**) and the insolubility of **3d**. Pre-polymer **3c** was capable of gel formation from water without DMSO but only at high polymer concentrations (>10%). Despite the high MGC of **3c**, these results suggest that DMSO only contributes to the solubility of **3d** and does not contribute directly to gel formation. To further probe the effect of the diamino group on hydrogel formation, poly(heptamethylene D-glucaramide) (**3e**) and poly(octamethylene D-glucaramide) (**3f**) were also tested as gelators. Under the gelling conditions for **3d**, these more hydrophobic polymers precipitated rapidly from solution. These results suggest that water solubility is

important in gel formation with poly(alkylene D-glucaramides) and that a polymer with a water solubility profile between **3c** and **3d** would be optimal.

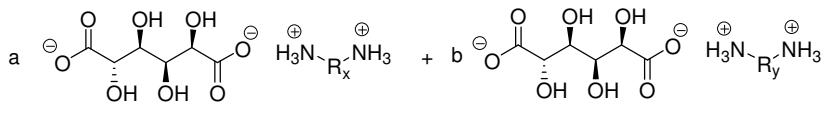
3.2.2 Hydrogels from Mixed Polyhydroxypolyamides

3.2.2.1 Neutral Polymers

To fine tune the water solubility profile of poly(alkylene D-glucaramides), polymers from multiple diamines were prepared. Mixed PHPAs from multiple diamines and from multiple aldaric acids have been prepared through Method C[21] as a way of tailoring the physical properties of the polymers; however, the aldaric acid and diamine combinations were chosen to yield PHPAs with higher water solubility for aqueous adhesive application. A polymerization process using Method A was developed in which two or more alkylene D-glucarate salts in the desired molar ratio were added together into the esterification reaction (**Scheme 3-2**). After concentrating and drying the esterification mixture, polymerization was initiated through neutralization of the esterification mixture with sodium methoxide and triethylamine. Using this method, a number of mixed diamine PHPAs, labeled poly(R_x/R_y D-glucaramide) mixed polymers, were prepared containing both water soluble (hydrophilic, R_x) and water insoluble (hydrophobic, R_y) diamino units. The hydrophilic diamino units were derived from D-glucarate salts of ethylenediamine (**2a**) and tetramethylenediamine (**2b**), 2-methylpentamethylenediamine (**2h**), 3',6'-dioxaoctamethylenediamine (**2i**), and 4'-aza-*N*-methylheptamethylenediamine (**2j**). Due to the success of **3d** as a gelator, hexamethylenediamine was chosen as the preferred hydrophobic diamino unit; although mixed polymers from D-glucarate salts of octamethylenediamine (**2f**) and dodecamethylenediamine (**2g**) were also investigated.

Using ^{1}H NMR, the R_x to R_y ratio of the mixed polymer products could be estimated by comparing the integrals of distinct peaks for each diamino group. Also from the ^{1}H spectra, the average number of repeat units per polymer molecule (degree of polymerization, DP) could be estimated using end-group analysis.[17] These values along

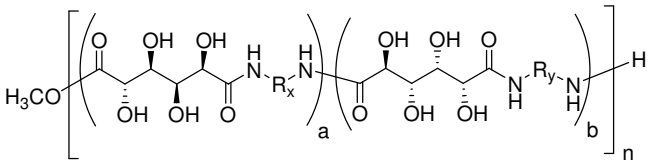
Scheme 3-2. Preparation of poly(R_x / R_y D-glucaramide) mixed polymers.



2

1) HCl / CH_3OH

2)$NaOCH_3$, Et_3N, CH_3OH



6

6a: $R_x = (CH_2)_2$

$R_y = (CH_2)_6$

6b: $R_x = (CH_2)_4$

$R_y = (CH_2)_6$

6c: $R_x = (CH_2)_4$

$R_y = (CH_2)_8$

6d: $R_x = (CH_2)_4$

$R_y = (CH_2)_{12}$

6e: $R_x = CHCH_2CH_2NCH_2CH_2CH_3$ (with CH_3 branch)

$R_y = (CH_2)_6$

6f: $R_x = CH_2CH_2OCH_2CH_2OCH_2CH_2$

$R_y = (CH_2)_6$

6g: $R_x = CH_2CH(CH_3)CH_2CH_2CH_2$

$R_y = (CH_2)_6$

with the yields of the various mixed polymers are given in **Table 3-3**. The DP values for the mixed polymers generally fall in between the DP values for the corresponding homopolymers.

In all cases, the observed R_x to R_y ratio was lower than the theoretical ratio based on the starting amount of salt which means that in all cases the more hydrophobic diamine [$R_y = (CH_2)_6$, $(CH_2)_8$, $(CH_2)_{12}$] was incorporated into the polymer product to a greater extent than the more hydrophilic diamine [$R_x = (CH_2)_2$, $(CH_2)_4$,]. This may result from increased methanol solubility of mixed polymers with higher R_x content or could be a sign of decreased nucleophilicity of the primary amine groups in the shorter

Table 3-3. Characterization and hydrogel forming ability of poly(R_x / R_y D-glucaramide) mixed polymers.

Poly(R_x/R_y D-glucaramide) Mixed Polymer	R_x:R_y Salt Ratio	R_x:R_y Observed Ratio[a]	DP[a]	Yield (%)	MGC[b] (% w/v)
6a	1:5	NR[c]	NR[c]	43	1.5
6a	1:4	1:5.5	11	71	0.3
6a	1:3	1:4.2	12	73	1.0
6a	1:2	1:2.5	15	76	1.0
6b	1:4	1:5.0	26	51	0.75
6b	1:3	1:4.0	14	69	0.5
6b	1:2	1:2.5	15	74	0.5
6b	1:1	1:1.0	25	74	1.5
6c	1:1	1:1.4	14	78	5.0
6c	2:1	1.8:1	20	75	2.0
6c	3:1	2.7:1	11	67	4.0
6d	4:1	3.5:1	16	62	2.0
6e	1:4	1:4.5	NR[c]	66	0.75
6e	1:3	1:3.6	14	62	0.5
6e	1:2	1:2.4	13	50	1.0
6e	2:3	1:1.7	30	49	1.0
6e	1:1	1:1.2	18	22	1.5
6f	1:2	1:3.5	23	54	0.75
6g	1:1	1:2.5	63	68	0.5

[a]Determined by ^{1}H NMR.
[b]Minimum gelation concentration in weight to volume determined at room temperature.
[c]R_x component not resolved in ^{1}H NMR spectrum.

alkylenediamines and heteroatom containing diamines. Previous studies have shown decreased nucleophilicity in alkylenediamines with shorter alkylene chains. For example, 1,2-diaminoethane (ethylenediamine) showed lower reactivity compared to 1,3-diaminopropane.[22] Also, amines with adjacent electronegative heteroatoms, such ethanolamine, are less reactive than the corresponding alkylamines.[22] Correlating these

trends to the diamines in this work, one would predict hexamethylenediamine to be more reactive than the shorter alkylene chain diamine, ethylenediamine, and the heteroatom containing diamines, 3',6'-dioxaoctamethylenediamine and 4'-aza-*N*-methylheptamethylenediamine. Because these polycondensations involving more than one diamine are essentially competitive reactions, a diamine with higher reactivity should incorporate into polymers to a greater extent and should be concentrated in the middle region of the polymer molecules. Less reactive diamines should therefore be incorporated into the polymers less and should have a higher concentration at the ends of the polymer molecules.

All poly(R_x/R_y D-glucaramide) mixed polymers shown in **Scheme 3-2** were capable of forming hydrogels from hot aqueous solutions of the polymer without DMSO. From the MGC values given in **Table 3-3**, mixed polymers **6a**, **6b**, and **6e**-**6g**, all containing the hexamethylene diamino unit [$R_y = (CH_2)_6$], showed superior gel forming ability to polymers **6c** and **6d** which contain other hydrophobic diamino units [$R_y = (CH_2)_8$ and $(CH_2)_{12}$]. Mixed polymers with the hexamethylene diamino unit showed comparable gel forming ability, regardless of the chemical nature of the R_x hydrophilic diamino unit, and these polymers were capable of forming hydrogels at lower concentrations than the poly(hexamethylene D-glucaramide) homopolymer. These results suggest that solubility of a given poly(D-glucaramide) is a major controlling factor for gel formation and that the R_x portion is important primarily for increasing solubility of the polymers.

Physical properties of PHPAs are influenced not only by the diamino portions of the polymers but also by the aldaryl portion. Changing the number of carbon atoms or the stereochemistry of the hydroxyl groups in the aldaric acid starting material can lead to significant changes in the resulting polymers.[20] To investigate the influence of the aldaryl unit in gel formation, polyamides from alkylenediammonium xylarate salts[23] and alkylenediammonium galactarate[24] were prepared using synthetic methods A and B respectively. As with poly(tetramethylene D-glucaramide) (**3b**), poly(tetramethylene xylaramide) was water soluble. On the other hand, poly(hexamethylene xylaramide) precipitated rapidly from DMSO solution upon addition of water and was not capable of gel formation unlike poly(hexamethylene D-glucaramide) (**3d**). Mixed PHPAs using

alkylenediammonium xylarate salts were also prepared, including the mixed diamine polymer, poly(tetramethylene / hexamethylene xylaramide), the mixed diacid polymer, poly(hexamethylene D-glucaramide / xylaramide), and the mixed diacid / mixed diamine polymer, poly(tetramethylene / hexamethylene D-glucaramide / xylaramide). Of the three, only the two polymers containing glucaryl units were capable of gel formation.

The water solubility of poly(alkylene galactaramides) is generally lower than that of the corresponding poly(alkylene D-glucaramides), and as previously reported, poly(ethylene galactaramide), poly(tetramethylene galactaramide), and poly(hexamethylene galactaramide) all showed low water solubility[20] and no significant swelling in water. These results suggest that the glucaryl unit is important for gel formation perhaps due to the structural conformation which it adapts. Because the aldaryl units are not always found in an extended conformation as evidenced by x-ray crystal structures (Chapter 2), it is likely that the conformational diversity of these units influence the polymer's overall three dimensional structure, and, as a result, the polymers gelling properties. The polymeric structure(s) dictated by glucaryl unit, as opposed to those arising from other aldaryl units, may be more favorable for the formation of supramolecular networks required for gel formation.

3.2.2.2 Charged Polymers

While a number of the mixed poly(alkylene D-glucaramides) were capable of forming hydrogels at low concentration and without DMSO, the time required for gel formation was typically over an hour. In SAPs, the time required for gel formation is reduced when ionized groups are present on the polymer chain. In attempt to improve the efficiency of gel formation of poly(alkylene D-glucaramides), several mixed polymers with ionized groups, both polycationic and polyanionic, in the repeating unit were synthesized. A polycationic PHPA was prepared by treating the gel forming polymer, poly(4'-aza-*N*-methylheptamethylene / hexamethylene D-glucaramide) (**6e**) with aqueous HCl to form hydrochloride salts of the tertiary amine groups. The resulting hydrochloride salts of **6e** (R_x / R_y ratio of 1:1 and 2:3) were more water soluble and did not form gels from solution even at double the MGC of the neutral polymers. However, neutralization of an aqueous solution of the polymer hydrochloride salt with base resulted

in gel formation. Despite the basic pH of the gel medium, which typically results in hydrolysis of poly(alkylene D-glucaramides), the gel mixtures remained stable for months. While these polymers do not show fast gelation times as other polyelectrolyte gelators, gels could be formed from the hydrochloride salts without heating the mixture, thus providing the opportunity for controlled gel formation through pH manipulation of the aqueous medium.

A polyanionic poly(alkylene D-glucaramide) was prepared with pendant carboxylate functionalities using a 3:1 mixture of lysine and hexamethylenediamine and activated glucarate derivative **5** through a modification of polymerization Method C. L-Lysine monohydrochloride was neutralized with 2 equivalents of sodium methoxide then allowed to react with **5** and in the presence of hexamethylenediamine. The resulting polymer was capable of gel formation but required heat and extended time similar to the neutral mixed polymers. In contrast to the cationic PHPA described above, pH controlled gel formation was not possible with this polymer.

3.2.2.3 Cross-linked Polymers

Cross-links are key structural features of SAPs which allow efficient absorption and retention of water. To investigate the effect of cross-linking on PHPA gel formation, branched poly(D-glucaramides) were prepared using modifications of polymerization Methods A and C and the tri functional monomer, tris(2-aminoethyl)amine (TREN). For Method A, a salt between TREN and D-glucaric acid (2:3 ratio) was first formed to give stoichiometric equivalence between the primary amine and carboxylate functionalities. Polymerizations of this salt at 10 and 20% concentration relative to hexamethylenediammonium D-glucarate were carried out by the established sodium methoxide procedure. Similar polymers were also prepared by direct condensation of the amines with activated D-glucarate derivative **5** using Method C. All of the resulting polymers showed limited solubility in DMSO and swelled slightly in water at room temperature. Upon heating in water, the polymers mostly dissolved, and the resulting solutions formed gel upon cooling. As observed with the charged poly(D-glucaramides), the gel forming ability of the branched poly(D-glucaramides) was not improved over the mixed poly(R_x / R_y D-glucaramides).

3.3 Conclusions

A number of novel polyhydroxypolyamide gelators capable of forming hydrogels at very low concentrations (0.3 - 1%) were described. Gels were formed from aqueous solutions of these molecules in similar fashion to many low molecular weight gelators, and as with LMWGs, the resulting gels are thermally reversible. Poly(hexamethylene D-glucaramide) was found to form hydrogels from concentrated solutions of DMSO. The synthetic method used for preparing the poly(hexamethylene D-glucaramide) affected the gel forming ability, and polymers from stoichiometrically equivalent salts using a modified basification procedure (Chapter 2) were found to form gels at lower concentrations than those prepared by previously described methods.[17,18] By tuning the water solubility of poly(alkylene D-glucaramides), the need for DMSO in gel formation was eliminated. Solubility was tuned by synthesizing mixed polymers from combinations of multiple diamines and diacids. Mixed diamino poly(D-glucaramides) proved to be the most efficient gel forming polymers. The use of charged or branched diamino units in mixed poly(D-glucaramides) did not improve their gel forming ability. Polyhydroxypolyamides from xylaric acid and galactaric acid proved to be inferior gelators in comparison to poly(alkylene D-glucaramide) mixed polymers, suggesting that the glucaryl unit plays a key role in promoting gel formation.

3.4 Experimental

General Methods and Materials. Monopotassium D-glucarate was purchased from Applied Foods Sciences, LLC, (Austin, TX, USA). Sodium methoxide was purchased as a 0.5 M solution in methanol from Sigma-Aldrich (St. Louis, MO, USA). All other chemicals and solvents were purchased from Sigma-Aldrich (St. Louis, MO, USA) or J.T. Baker (Philipsburg, NJ, USA) and used without further purification. Solutions were concentrated *in vacuo* (15-20 mbar) using a rotary evaporator and water bath at 30 °C**.** Drying of samples was carried out at room temperature for 16 h (unless otherwise noted) using a mechanical pump. Methyl-D-glucarate-1,4-lactone (**5**),[17] poly(ethylene galactaramide),[24] poly(tetramethylene galactaramide),[24] poly(hexamethylene

galactaramide),[24] and alkylenediammonium xylarate salts[23] were prepared as previously described. All ^{1}H NMR spectra were recorded on a Varian 400 MHz spectrometer.

Alkylenediammonium D-glucarate Salt (2). Acid form cation exchange resin (70 mL, 147 mmol, Dowex 50WX8-100, 2.1 meq/mL) was washed with deionized water (3 x 150 mL). Monopotassium D-glucarate (**1**, 20.00 g, 80.57 mmol) was added to a slurry of the washed resin in water (100 mL) then mixed on an orbital shaker for 10 min. The resin was removed by filtration and washed with water (3 x 20 mL). An alkylenediamine (84.1 mmol) was added to the combined filtrate and washings, and the resulting solution was stirred for 3 h and then concentrated to a viscous syrup. Methanol (200 mL) was added to the syrup, and the mixture was stirred until all of the oil solidified to a solid. The precipitate was isolated by filtration, washed with methanol (3 x 20 mL), and dried to give alkylenediammonium D-glucarate (**2**).

Stereo Random Poly(alkylene D-glucaramide) Pre-polymer (3), Method A. Acetyl chloride (2.0 mL, 28 mmol) was added drop wise to methanol (45 mL) at 0 °C. The methanolic HCl solution was allowed to warm to room temperature (10 min) prior to the addition of alkylenediammonium D-glucarate (**2**, 7.02 mmol). The solution was stirred for 3 h at room temperature, concentrated to a solid, and dried. The solid was re-dissolved in methanol (20 mL) followed by the addition of sodium methoxide solution (26 mL, 13 mmol) and triethylamine (0.49 mL, 3.5 mmol). After the mixture was stirred at room temperature for 24 h, the precipitate was isolated by filtration, washed with methanol (3 x 10 mL), and dried to give stereo random poly(alkylene D-glucaramide) pre-polymer (**3**).

Stereo Random Poly(alkylene D-glucaramide) Pre-polymer (3), Method B. Alkylenediammonium D-glucarate (**2**, 7.02 mmol) was esterified and dried as described in Method A. Polymerization was initiated by the addition of triethylamine (10 mL, 72 mmol). After the mixture was stirred at room temperature for 24 h, the precipitate was isolated by filtration, washed with methanol (3 x 10 mL), and dried to give stereo random poly(alkylene D-glucaramide) pre-polymer (**3**).

Stereo Random Poly(alkylene D-glucaramide) Pre-polymer (3), Method C. Poly(alkylene D-glucaramide) pre-polymer (**3**) was prepared from methyl-D-glucarate-1,4-lactone (**5**) and alkylenediamine as previously described.[17] Briefly, equal volumes of solutions of alkylenediamine (0.142 M) and **5** (0.136 M) both in methanol were mixed along with triethylamine (0.7 eq). After the mixture was stirred at room temperature for 24 h, the precipitate was isolated by filtration, washed with methanol, and dried to give stereo random poly(alkylene D-glucaramide) pre-polymer (**3**).

Stereo Random Poly(alkylene D-glucaramide) Post-polymer (4). Ethylene glycol (4.5mL) and triethylamine (0.75 mL) were added to a 60 °C solution of stereo random poly(alkylene D-glucaramide) pre-polymer (**3**; 0.50 g) in DMSO (4.5 mL). The mixture was stirred at 60 °C for 18 h, the mixture was diluted with methanol (15 mL) and allowed to cool to room temperature. The resulting precipitate was isolated by filtration, washed with methanol (3 x 5 mL), and dried to give stereo random poly(hexamethylene D-glucaramide) post-polymer (**4**).

Stereo Random Poly(R_x/R_y D-glucaramide) Mixed Pre-polymers (6). Two alkylenediammonium D-glucarate salts in the desired ratio (3.5 mmol total) were esterified together and dried as described in Method A for **3**. Polymerization was initiated by the addition of sodium methoxide solution (13 mL, 6.5 mmol) and triethylamine (0.25 mL, 1.8 mmol). After stirring the mixture at room temperature for 24 h, the resulting precipitate was isolated by filtration, washed with methanol (3 x 5 mL), and dried at reduced pressure for 18 h to give poly(R_x/R_y D-glucaramide) mixed pre-polymer (**6**).

Poly(R_x/R_y xylaramide) Mixed Pre-polymers. Poly(R_x/R_y xylaramide) mixed pre-polymers were prepared from alkylenediammonium xylarate salts as described for poly(R_x/R_y D-glucaramide) mixed pre-polymers.

Poly(4'-aza-4'-methylheptamethylene /hexamethylene D-glucaramide) Pre-polymer Hydrochloride Salt. Poly(4'-aza-4'-methylheptamethylene / hexamethylene D-

glucaramide) pre-polymer (**6e**, 0.11 g) was dissolved in H_2O (2 mL). The pH of the resulting solution was adjusted from pH 9 to pH 2 with aqueous HCl (0.14 mL, 1.0 M). After stirring briefly, the solution was concentrated to a clear film. The film was triturated with methanol and dried at reduced pressure for 18 h to give poly(4'-aza-4'-methylheptamethylene /hexamethylene D-glucaramide) pre-polymer hydrochloride salt (0.094 g) as a white, amorphous solid.

Representative Examples of Gel Preparation with PHPAs

Hydrogel Preparation with DMSO. Water or an aqueous solution was added to poly(alkylene D-glucaramide) (**3** or **4**) dissolved in dimethyl sulfoxide. After brief mixing, the solution was allowed to sit undisturbed. Cloudiness developed rapidly, and an opaque gel formed, typically, within 10 min.

Hydrogel Preparation in Water and Aqueous Solutions. PHPA was dissolved in water or an aqueous solution with heat (70-80 °C). The solution was allowed to sit undisturbed, and a clear gel formed over several hours.

pH Dependent Hydrogel Preparation, Method 1. Aqueous HCl (0.28 mL, 0.1 M) was added to poly(4'-aza-4'-methylheptamethylene /hexamethylene D-glucaramide) (1:1) pre-polymer (25 mg) suspended in H_2O (0.16 mL). To the resulting solution (pH 2) was added aqueous NaOH (0.42 mL, 0.1 M). After brief mixing, the solution (pH 8) was allowed to sit undisturbed, and a clear gel formed over several hours.

pH Dependent Hydrogel Preparation, Method 2. Poly(4'-aza-4'-methylheptamethylene /hexamethylene D-glucaramide) pre-polymer hydrochloride salt (10 mg) was dissolved in water (0.25 mL) at room temperature. To the resulting solution (pH 4), aqueous sodium carbonate (0.75 mL, 1%) was added. After brief mixing, the resulting solution (pH 10) was allowed to sit undisturbed, and a clear gel formed over several hours.

3.5 References

[1] Buchholz, Fredric L.; Graham, Andrew T. *Modern Superabsorbent Polymer Technology*; John Wiley and Sons: New York, 1998.

[2] Mitchell M; Beihoffer T; Trzupek L; Darlington Jr, J; Anderson M. Poly(vinylamine)-Based Superabsorbent Gels and Method of Manufacturing the Same. U.S. Patent No. 6,194,631 B1, 2001.

[3] Dutkiewicz, Jacek K. Superabsorbent Materials from Shellfish Waste – A Review. J. Biomed. Mater. Res. **2002**, 63, 373-381.

[4] Peppas, Nikolaos A.; Merrill, Edward W. Crosslinked Poly(vinyl alcohol) Hydrogels as Swollen Elastic Networks. *J. Appl. Polym. Sci.* **1977**, *21*, 1763-1770.

[5] Bashaw, R. N.; Harper, B. G. Method for Controlling the Spread of Fire. *U.S. Patent 3,229,769*, Jan. 18, 1966.

[6] Estroff, Lara A.; Hamilton, Andrew D. Water Gelation by Small Organic Molecules. *Chem. Rev.* **2004**, *104*, 1201-1217.

[7] Terech, Pierre; Weiss, Richard G. Low Molecular Mass Gelators of Organic Liquids and the Properties of Their Gels. *Chem. Rev.* **1997**, *97*, 3133-3159.

[8] Xing, Bengang; Yu, Chun-Wing; Chow, Kin-Hung; Ho, Pak-Leung; Fu, Degang; Xu, Bing. Hydrophobic Interaction and Hydrogen Bonding Cooperatively Confer a Vancomycin Hydrogel: A Potential Candidate for Biomaterials. *J. Am. Chem. Soc.* **2002**, *124*, 12846-14847.

[9] Makarević, Janja; Jokić, Milan; Perić, Berislav; Tomišić, Vladislav; Kojić-Prodić, Biserka; Žinić, Mladen. Bis(AminoAcid) Oxalyl Amides as Ambidextrous Gelators of Water and Organic Solvents: Supramolecular Gels with Temperature Dependent Assembly/Dissolution Equilibrium. *Chem.-Eur. J.* **2001**, *7*, 3328-3341.

[10] Sangeetha, Neralagatta M.; Maitra, Uday. Supramolecular Gels: Functions and Uses. *Chem. Soc. Rev.* **2005**, *34*, 821-836.

[11] Swarbrick, James; Boylan, James C. *Encyclopedia of Pharmaceutical Technology: Volume 18 - Supplement 1 - Absorption Enhancers to WHO and Harmonization of Regulatory Requirements for Medicinal Products*. Informa Health Care: New York, 1998.

[12] Flory, Paul J. *Principles of Polymer Chemistry*. Cornell University: Ithaca, NY, 1953.

[13] Hirst, Andrew R.; Coates, Ian A.; Boucheteau, Thomas R.; Miravet, Jaun F.; Escuder, Beatriu; Castelletto, Valeria; Hamley, Ian W.; Smith David K. Low-Molecular-Weight Gelators: Elucidating the Principles of Gelation Based on Gelator Solubility and a Cooperative Self-Assembly Model. *J. Am. Chem. Soc.* **2008**, *130*, 9113-9121.

[14] Fuhrhop, Jürgen-Hinrich; Schnieder, Peter; Rosenberg, Jörg; Boekema, Egbert. The Chiral Bilayer Effect Stabilizes Micellar Fibers. *J. Am. Chem. Soc.* **1987**, *109*, 3387-3390.

[15] Fuhrhop, Jürgen-Hinrich; Svenson, Sönke; Boettcher, Christoph; Rössler, Ernst; Vieth, Hans-Martin. Long-Lived Micellar *N*-Alkylaldonamide Fiber Gels. Solid-State NMR and Electron Microscopic Studies. *J. Am. Chem. Soc.* **1990**, *112*, 4307-4312.

[16] Jahns, Thomas; Kiely, Donald E. Abiotic Hydrolysis of Some Poly-d-Glucaramides and Subsequent Microbial Utilization/Degradation. *J. Polym. Environ.* **2006**, 14, 165-169.

[17] Kiely, Donald E.; Chen, Liang.; Lin, Tsu-Hsing. Hydroxylated Nylons Based on Unprotected Esterified D-Glucaric Acid by Simple Condensation Reactions. *J. Am. Chem. Soc.* **1994**, *116*, 571-578.

[18] Zhang, Jinsong. Poly(alkylene D-aldaramides) and their Corresponding Esters – Synthesis and Conformational Studies. *Ph.D. Dissertation*, The University of Montana, 2003.

[19] Raghavan, S. R.; Cipriano, B. H. Gel Formation: Phase Diagrams Using Tabletop Rheology and Calorimetry. In *Molecular Gels*; Weiss, R. G.; Terech P., Eds.; Springer: Amsterdam, 2005; Chapter 8.

[20] Kiely, Donald E.; Chen, Liang.; Lin, Tsu-Hsing. Synthetic Polyhydroxypolyamides from Galactaric, Xylaric, D-Glucaric and D-Mannaric Acids and Alkylenediamine Monomers-Some Comparisons. *J. Polym. Sci., Polym. Chem. Ed.* **2000**, 38, 594-603.

[21] Morton, David W.; Kiely, Donald E. Evaluation of the Film and Adhesive Properties of Some Block Copolymer Polyhydroxypolyamides from Esterified Aldaric Acids and Diamines. *J. Appl. Polym. Sci.* **2000**, 77, 3085-3092.

[22] Brotzel, Frank; Chu Ying Cheung; Mayr, Herbert. Nucleophilicities of Primary and Secondary Amines in Water. *J. Org. Chem.* **2007**, *72*, 3679-3688.

[23] Hinton, Michael R. Xylaric Acid, D-Arabinaric Acid (D-Lyxaric Acid), L-Arabinaric Acid (L-Lyxaric Acid), and Ribaric Acid-1,4-Lactone; Synthesis and Isolation-Synthesis of Polyhydroxypolyamides Therefrom. *Ph.D. Dissertation*, The University of Montana, 2008.

[24] Jarman, Bevan. Synthesis of Polyhydroxypolyamides Based on Galactaric Acid and X-Ray Crystal Analysis of Their Precursors. *M. Sc. Thesis*, The University of Waikato, 2006.

Appendix A. X-Ray Crystal Structure Data

Table 1. Crystal data and structure refinement for hexamethylenediammonium D-glucarate.

Empirical formula	$C_{12}H_{26}N_2O_8$	
Formula weight	326.35	
Temperature	173(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 10.042(3) Å	α= 90°.
	b = 5.9151(19) Å	β= 93.811(16)°.
	c = 13.252(4) Å	γ = 90°.
Volume	785.4(4) $Å^3$	
Z	2	
Density (calculated)	1.380 Mg/m^3	
Absorption coefficient	0.986 mm^{-1}	
F(000)	352	
Crystal size	0.61 x 0.61 x 0.11 mm^3	
Theta range for data collection	3.34 to 65.99°.	
Index ranges	-11<=h<=11, -6<=k<=6, -15<=l<=15	
Reflections collected	3741	
Independent reflections	1764 [R(int) = 0.0518]	
Completeness to theta = 65.99°	85.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8992 and 0.5844	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1764 / 1 / 207	
Goodness-of-fit on F^2	1.057	
Final R indices [I>2sigma(I)]	R1 = 0.0781, wR2 = 0.2199	
R indices (all data)	R1 = 0.1923, wR2 = 0.3164	
Absolute structure parameter	0.1(11)	
Extinction coefficient	0.026(6)	
Largest diff. peak and hole	0.862 and -1.134 $e.Å^{-3}$	

Table 2. Atomic co-ordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for hexamethylenediammonium D-glucarate. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	2824(10)	6250(20)	9603(8)	28(3)
C(2)	1700(9)	7930(20)	9358(7)	32(3)
C(3)	2102(10)	9430(20)	8485(8)	32(3)
C(4)	1129(10)	11430(20)	8281(8)	29(3)
C(5)	-297(11)	10720(20)	7945(8)	32(3)
C(6)	-361(9)	9280(20)	7053(7)	24(3)
C(1S)	6674(10)	6670(30)	8065(8)	40(4)
C(2S)	6028(10)	8270(20)	7283(7)	25(2)
C(3S)	4760(9)	7390(30)	6748(8)	41(4)
C(4S)	4067(11)	9050(20)	6024(9)	37(3)
C(5S)	2794(9)	8308(19)	5541(7)	25(2)
C(6S)	2135(11)	10070(30)	4840(9)	41(3)
N(1S)	5917(8)	6689(19)	9009(6)	32(3)
N(2S)	774(8)	9388(18)	4449(7)	33(2)
O(1)	3216(6)	5075(14)	8858(5)	26(2)
O(2)	3265(8)	6160(20)	10484(6)	53(3)
O(3)	1405(8)	9262(15)	10190(5)	34(2)
O(4)	3416(7)	10319(17)	8802(7)	37(2)
O(5)	1582(7)	12789(15)	7448(5)	33(2)
O(6)	-1096(7)	12707(16)	7806(6)	37(2)
O(7)	-715(7)	9965(14)	6164(5)	28(2)
O(8)	-138(7)	7106(15)	7185(6)	32(2)

Table 3. Bond lengths (Å) and angles (°) for hexamethylenediammonium D-glucarate.

C(1)-O(2)	1.222(12)	C(6S)-H(6S1)	0.9900
C(1)-O(1)	1.290(13)	C(6S)-H(6S2)	0.9900
C(1)-C(2)	1.522(16)	N(1S)-H(1S3)	0.9100
C(2)-O(3)	1.405(13)	N(1S)-H(1S4)	0.9100
C(2)-C(3)	1.535(15)	N(1S)-H(1S5)	0.9100
C(2)-H(2)	1.0000	N(2S)-H(2S3)	0.9100
C(3)-O(4)	1.456(12)	N(2S)-H(2S4)	0.9100
C(3)-C(4)	1.545(17)	N(2S)-H(2S5)	0.9100
C(3)-H(3)	1.0000	O(3)-H(3A)	0.8400
C(4)-O(5)	1.464(13)	O(4)-H(4A)	0.8400
C(4)-C(5)	1.530(15)	O(5)-H(5A)	0.8400
C(4)-H(4)	1.0000	O(6)-H(6)	0.8400
C(5)-O(6)	1.429(15)		
C(5)-C(6)	1.456(15)	O(2)-C(1)-O(1)	126.8(11)
C(5)-H(5)	1.0000	O(2)-C(1)-C(2)	116.7(11)
C(6)-O(7)	1.275(12)	O(1)-C(1)-C(2)	116.5(8)
C(6)-O(8)	1.312(15)	O(3)-C(2)-C(1)	113.0(8)
C(1S)-N(1S)	1.507(13)	O(3)-C(2)-C(3)	110.2(11)
C(1S)-C(2S)	1.516(15)	C(1)-C(2)-C(3)	108.2(8)
C(1S)-H(1S1)	0.9900	O(3)-C(2)-H(2)	108.4
C(1S)-H(1S2)	0.9900	C(1)-C(2)-H(2)	108.4
C(2S)-C(3S)	1.509(15)	C(3)-C(2)-H(2)	108.4
C(2S)-H(2S1)	0.9900	O(4)-C(3)-C(2)	105.7(8)
C(2S)-H(2S2)	0.9900	O(4)-C(3)-C(4)	109.0(10)
C(3S)-C(4S)	1.509(18)	C(2)-C(3)-C(4)	112.4(8)
C(3S)-H(3S1)	0.9900	O(4)-C(3)-H(3)	109.9
C(3S)-H(3S2)	0.9900	C(2)-C(3)-H(3)	109.9
C(4S)-C(5S)	1.458(14)	C(4)-C(3)-H(3)	109.9
C(4S)-H(4S1)	0.9900	O(5)-C(4)-C(5)	105.2(8)
C(4S)-H(4S2)	0.9900	O(5)-C(4)-C(3)	109.1(7)
C(5S)-C(6S)	1.517(16)	C(5)-C(4)-C(3)	114.2(10)
C(5S)-H(5S1)	0.9900	O(5)-C(4)-H(4)	109.4
C(5S)-H(5S2)	0.9900	C(5)-C(4)-H(4)	109.4
C(6S)-N(2S)	1.484(14)	C(3)-C(4)-H(4)	109.4

O(6)-C(5)-C(6)	112.5(9)	C(3S)-C(4S)-H(4S2)	108.3
O(6)-C(5)-C(4)	108.6(10)	H(4S1)-C(4S)-H(4S2)	107.4
C(6)-C(5)-C(4)	112.8(9)	C(4S)-C(5S)-C(6S)	113.5(10)
O(6)-C(5)-H(5)	107.6	C(4S)-C(5S)-H(5S1)	108.9
C(6)-C(5)-H(5)	107.6	C(6S)-C(5S)-H(5S1)	108.9
C(4)-C(5)-H(5)	107.6	C(4S)-C(5S)-H(5S2)	108.9
O(7)-C(6)-O(8)	118.1(10)	C(6S)-C(5S)-H(5S2)	108.9
O(7)-C(6)-C(5)	123.9(11)	H(5S1)-C(5S)-H(5S2)	107.7
O(8)-C(6)-C(5)	117.9(10)	N(2S)-C(6S)-C(5S)	112.5(11)
N(1S)-C(1S)-C(2S)	110.2(9)	N(2S)-C(6S)-H(6S1)	109.1
N(1S)-C(1S)-H(1S1)	109.6	C(5S)-C(6S)-H(6S1)	109.1
C(2S)-C(1S)-H(1S1)	109.6	N(2S)-C(6S)-H(6S2)	109.1
N(1S)-C(1S)-H(1S2)	109.6	C(5S)-C(6S)-H(6S2)	109.1
C(2S)-C(1S)-H(1S2)	109.6	H(6S1)-C(6S)-H(6S2)	107.8
H(1S1)-C(1S)-H(1S2)	108.1	C(1S)-N(1S)-H(1S3)	109.5
C(3S)-C(2S)-C(1S)	114.6(10)	C(1S)-N(1S)-H(1S4)	109.5
C(3S)-C(2S)-H(2S1)	108.6	H(1S3)-N(1S)-H(1S4)	109.5
C(1S)-C(2S)-H(2S1)	108.6	C(1S)-N(1S)-H(1S5)	109.5
C(3S)-C(2S)-H(2S2)	108.6	H(1S3)-N(1S)-H(1S5)	109.5
C(1S)-C(2S)-H(2S2)	108.6	H(1S4)-N(1S)-H(1S5)	109.5
H(2S1)-C(2S)-H(2S2)	107.6	C(6S)-N(2S)-H(2S3)	109.5
C(2S)-C(3S)-C(4S)	114.4(12)	C(6S)-N(2S)-H(2S4)	109.5
C(2S)-C(3S)-H(3S1)	108.6	H(2S3)-N(2S)-H(2S4)	109.5
C(4S)-C(3S)-H(3S1)	108.6	C(6S)-N(2S)-H(2S5)	109.5
C(2S)-C(3S)-H(3S2)	108.6	H(2S3)-N(2S)-H(2S5)	109.5
C(4S)-C(3S)-H(3S2)	108.6	H(2S4)-N(2S)-H(2S5)	109.5
H(3S1)-C(3S)-H(3S2)	107.6	C(2)-O(3)-H(3A)	109.5
C(5S)-C(4S)-C(3S)	116.0(10)	C(3)-O(4)-H(4A)	109.5
C(5S)-C(4S)-H(4S1)	108.3	C(4)-O(5)-H(5A)	109.5
C(3S)-C(4S)-H(4S1)	108.3	C(5)-O(6)-H(6)	109.5
C(5S)-C(4S)-H(4S2)	108.3		

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for hexamethylenediammonium D-glucarate. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$.

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	24(5)	21(6)	36(6)	9(6)	-7(4)	-4(5)
C(2)	21(5)	49(9)	27(5)	5(6)	4(4)	-4(6)
C(3)	24(5)	46(8)	25(5)	15(6)	1(4)	-18(5)
C(4)	25(5)	41(8)	23(5)	-11(5)	7(4)	-10(5)
C(5)	36(6)	34(8)	26(5)	-5(6)	9(4)	-3(6)
C(6)	19(5)	33(7)	19(5)	-1(5)	-3(4)	-14(5)
C(1S)	29(5)	70(11)	23(5)	20(7)	6(4)	8(7)
C(2S)	31(5)	18(6)	26(5)	-3(5)	4(4)	-4(5)
C(3S)	16(4)	81(11)	25(5)	0(7)	1(4)	0(6)
C(4S)	32(5)	44(8)	33(6)	1(6)	-5(4)	-11(6)
C(5S)	24(5)	26(6)	23(5)	11(5)	-8(4)	11(5)
C(6S)	35(6)	52(9)	35(6)	8(7)	2(5)	-9(6)
N(1S)	28(4)	40(7)	28(4)	5(5)	-4(4)	0(5)
N(2S)	32(5)	37(6)	29(5)	12(5)	6(4)	-8(5)
O(1)	18(3)	26(4)	32(4)	-5(4)	1(3)	7(3)
O(2)	43(5)	84(8)	29(4)	-10(5)	0(4)	-2(5)
O(3)	47(4)	41(5)	16(3)	-7(4)	8(3)	0(4)
O(4)	26(4)	45(6)	39(4)	-2(5)	2(3)	-3(4)
O(5)	30(4)	36(6)	34(4)	0(4)	8(3)	2(4)
O(6)	30(4)	40(6)	40(4)	14(5)	4(3)	21(4)
O(7)	37(4)	24(4)	24(3)	-2(3)	3(3)	-2(4)
O(8)	36(4)	28(5)	33(4)	3(4)	6(3)	-3(4)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for hexamethylenediammonium D-glucarate.

	x	y	z	U(eq)
H(2)	880	7063	9125	39
H(3)	2154	8507	7857	38
H(4)	1116	12385	8903	35
H(5)	-654	9832	8510	38
H(1S1)	6680	5115	7785	48
H(1S2)	7610	7131	8231	48
H(2S1)	5828	9707	7621	30
H(2S2)	6676	8596	6772	30
H(3S1)	4135	6952	7262	49
H(3S2)	4972	6005	6369	49
H(4S1)	3917	10465	6396	44
H(4S2)	4676	9401	5488	44
H(5S1)	2182	7931	6072	30
H(5S2)	2939	6914	5150	30
H(6S1)	2081	11515	5209	49
H(6S2)	2694	10312	4263	49
H(1S3)	5873	8130	9246	49
H(1S4)	6345	5799	9488	49
H(1S5)	5077	6152	8864	49
H(2S3)	764	7882	4308	49
H(2S4)	539	10179	3876	49
H(2S5)	183	9687	4924	49
H(3A)	1527	8502	10724	52
H(4A)	3389	11738	8807	55
H(5A)	1635	14151	7625	49
H(6)	-599	13831	7735	55

Table 6. Torsion angles (°) for hexamethylenediammonium D-glucarate.

O(2)-C(1)-C(2)-O(3)	4.5(15)
O(1)-C(1)-C(2)-O(3)	-175.1(9)
O(2)-C(1)-C(2)-C(3)	126.8(11)
O(1)-C(1)-C(2)-C(3)	-52.8(13)
O(3)-C(2)-C(3)-O(4)	71.4(11)
C(1)-C(2)-C(3)-O(4)	-52.6(12)
O(3)-C(2)-C(3)-C(4)	-47.3(11)
C(1)-C(2)-C(3)-C(4)	-171.3(9)
O(4)-C(3)-C(4)-O(5)	62.8(10)
C(2)-C(3)-C(4)-O(5)	179.6(9)
O(4)-C(3)-C(4)-C(5)	-179.8(8)
C(2)-C(3)-C(4)-C(5)	-63.0(12)
O(5)-C(4)-C(5)-O(6)	-61.7(10)
C(3)-C(4)-C(5)-O(6)	178.7(8)
O(5)-C(4)-C(5)-C(6)	63.8(13)
C(3)-C(4)-C(5)-C(6)	-55.9(12)
O(6)-C(5)-C(6)-O(7)	21.0(14)
C(4)-C(5)-C(6)-O(7)	-102.3(12)
O(6)-C(5)-C(6)-O(8)	-153.8(9)
C(4)-C(5)-C(6)-O(8)	83.0(13)
N(1S)-C(1S)-C(2S)-C(3S)	-76.0(13)
C(1S)-C(2S)-C(3S)-C(4S)	175.9(10)
C(2S)-C(3S)-C(4S)-C(5S)	-176.2(10)
C(3S)-C(4S)-C(5S)-C(6S)	178.8(10)
C(4S)-C(5S)-C(6S)-N(2S)	-173.4(9)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bond distances (Å) and angles (°) for hexamethylenediammonium D-glucarate.

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(6)-H(6)...O(5)	0.84	2.33	2.762(10)	112.4
N(2S)-H(2S5)...O(7)	0.91	1.93	2.822(11)	165.1
N(1S)-H(1S3)...O(2)#1	0.91	2.01	2.834(16)	149.9
N(1S)-H(1S4)...O(4)#2	0.91	2.28	3.043(12)	141.1
N(1S)-H(1S4)...O(3)#2	0.91	2.45	3.168(12)	136.4
N(2S)-H(2S3)...O(7)#3	0.91	1.83	2.739(13)	171.9
N(2S)-H(2S4)...O(8)#4	0.91	1.83	2.738(12)	172.5
O(3)-H(3A)...O(6)#5	0.84	2.08	2.847(11)	152.0
O(4)-H(4A)...O(1)#6	0.84	1.98	2.821(12)	176.4
O(5)-H(5A)...O(1)#6	0.84	2.27	2.758(11)	117.5
O(5)-H(5A)...O(8)#6	0.84	2.53	3.089(12)	124.5
O(6)-H(6)...O(8)#6	0.84	2.13	2.912(12)	154.4

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,y+1/2,-z+2 #2 -x+1,y-1/2,-z+2 #3 -x,y-1/2,-z+1

#4 -x,y+1/2,-z+1 #5 -x,y-1/2,-z+2 #6 x,y+1,z

Table 8. Crystal data and structure refinement for *m*-xylylenediammonium D-glucarate.

Empirical formula	$C_{14}H_{22}N_2O_8$	
Formula weight	346.34	
Temperature	173(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 4.98140(10) Å	α= 90°.
	b = 17.3445(4) Å	β= 90°.
	c = 17.5123(5) Å	γ = 90°.
Volume	1513.06(6) $Å^3$	
Z	4	
Density (calculated)	1.520 Mg/m^3	
Absorption coefficient	1.071 mm^{-1}	
F(000)	736	
Crystal size	0.60 x 0.12 x 0.09 mm^3	
Theta range for data collection	3.59 to 65.77°.	
Index ranges	-5<=h<=5, -20<=k<=19, -16<=l<=18	
Reflections collected	5804	
Independent reflections	2162 [R(int) = 0.0264]	
Completeness to theta = 65.77°	86.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9098 and 0.5659	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2162 / 0 / 223	
Goodness-of-fit on F^2	1.012	
Final R indices [I>2sigma(I)]	R1 = 0.0303, wR2 = 0.0802	
R indices (all data)	R1 = 0.0339, wR2 = 0.0825	
Absolute structure parameter	-0.1(2)	
Largest diff. peak and hole	0.151 and -0.164 e.$Å^{-3}$	

Table 9. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for *m*-xylylenediammonium D-glucarate. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	6746(4)	5875(1)	2913(1)	18(1)
C(2)	7721(4)	5690(1)	3720(1)	17(1)
C(3)	7516(4)	4819(1)	3875(1)	18(1)
C(4)	8085(5)	4611(1)	4701(1)	18(1)
C(5)	8083(4)	3734(1)	4869(1)	17(1)
C(6)	10910(4)	3404(1)	4781(2)	18(1)
C(7)	10418(4)	2038(1)	7950(1)	18(1)
C(8)	10858(5)	2365(1)	8665(2)	24(1)
C(9)	9506(5)	2089(1)	9303(2)	26(1)
C(10)	7671(4)	1494(1)	9230(2)	24(1)
C(11)	7253(4)	1145(1)	8520(1)	18(1)
C(12)	8638(4)	1417(1)	7884(2)	19(1)
C(13)	11784(4)	2360(1)	7252(1)	20(1)
C(14)	5305(4)	480(1)	8444(1)	21(1)
N(1)	9781(3)	2696(1)	6708(1)	17(1)
N(2)	6695(4)	-284(1)	8551(1)	21(1)
O(1)	8350(3)	6184(1)	2459(1)	22(1)
O(2)	4331(3)	5700(1)	2769(1)	24(1)
O(3)	10383(3)	5959(1)	3865(1)	21(1)
O(4)	9204(3)	4453(1)	3330(1)	24(1)
O(5)	10539(4)	4923(1)	4995(1)	27(1)
O(6)	7087(3)	3600(1)	5617(1)	20(1)
O(7)	11874(3)	3422(1)	4115(1)	25(1)
O(8)	12103(3)	3148(1)	5356(1)	22(1)

Table 10. Bond lengths (Å) and angles (°) for *m*-xylylenediammonium D-glucarate.

C(1)-O(1)	1.248(3)	C(14)-H(14B)	0.9900
C(1)-O(2)	1.266(3)	N(1)-H(1A)	0.9100
C(1)-C(2)	1.528(3)	N(1)-H(1B)	0.9100
C(2)-O(3)	1.428(3)	N(1)-H(1C)	0.9100
C(2)-C(3)	1.538(3)	N(2)-H(2A)	0.9100
C(2)-H(2)	1.0000	N(2)-H(2B)	0.9100
C(3)-O(4)	1.422(3)	N(2)-H(2C)	0.9100
C(3)-C(4)	1.518(3)	O(3)-H(3A)	0.8400
C(3)-H(3)	1.0000	O(4)-H(4A)	0.8400
C(4)-O(5)	1.433(3)	O(5)-H(5A)	0.8400
C(4)-C(5)	1.549(2)	O(6)-H(6)	0.8400
C(4)-H(4)	1.0000	O(1)-C(1)-O(2)	125.8(2)
C(5)-O(6)	1.420(3)	O(1)-C(1)-C(2)	118.37(19)
C(5)-C(6)	1.528(3)	O(2)-C(1)-C(2)	115.9(2)
C(5)-H(5)	1.0000	O(3)-C(2)-C(1)	113.03(18)
C(6)-O(8)	1.251(3)	O(3)-C(2)-C(3)	110.58(16)
C(6)-O(7)	1.261(3)	C(1)-C(2)-C(3)	110.33(18)
C(7)-C(8)	1.393(3)	O(3)-C(2)-H(2)	107.6
C(7)-C(12)	1.399(3)	C(1)-C(2)-H(2)	107.6
C(7)-C(13)	1.506(3)	C(3)-C(2)-H(2)	107.6
C(8)-C(9)	1.389(4)	O(4)-C(3)-C(4)	115.02(16)
C(8)-H(8)	0.9500	O(4)-C(3)-C(2)	106.33(18)
C(9)-C(10)	1.385(3)	C(4)-C(3)-C(2)	112.89(18)
C(9)-H(9)	0.9500	O(4)-C(3)-H(3)	107.4
C(10)-C(11)	1.399(3)	C(4)-C(3)-H(3)	107.4
C(10)-H(10)	0.9500	C(2)-C(3)-H(3)	107.4
C(11)-C(12)	1.392(3)	O(5)-C(4)-C(3)	114.34(18)
C(11)-C(14)	1.512(3)	O(5)-C(4)-C(5)	107.64(17)
C(12)-H(12)	0.9500	C(3)-C(4)-C(5)	114.51(18)
C(13)-N(1)	1.497(3)	O(5)-C(4)-H(4)	106.6
C(13)-H(13A)	0.9900	C(3)-C(4)-H(4)	106.6
C(13)-H(13B)	0.9900	C(5)-C(4)-H(4)	106.6
C(14)-N(2)	1.506(3)	O(6)-C(5)-C(6)	110.74(18)
C(14)-H(14A)	0.9900	O(6)-C(5)-C(4)	109.66(17)

C(6)-C(5)-C(4)	110.39(17)	H(14A)-C(14)-H(14B)	108.0
O(6)-C(5)-H(5)	108.7	C(13)-N(1)-H(1A)	109.5
C(6)-C(5)-H(5)	108.7	C(13)-N(1)-H(1B)	109.5
C(4)-C(5)-H(5)	108.7	H(1A)-N(1)-H(1B)	109.5
O(8)-C(6)-O(7)	124.9(2)	C(13)-N(1)-H(1C)	109.5
O(8)-C(6)-C(5)	119.3(2)	H(1A)-N(1)-H(1C)	109.5
O(7)-C(6)-C(5)	115.8(2)	H(1B)-N(1)-H(1C)	109.5
C(8)-C(7)-C(12)	119.1(2)	C(14)-N(2)-H(2A)	109.5
C(8)-C(7)-C(13)	120.50(18)	C(14)-N(2)-H(2B)	109.5
C(12)-C(7)-C(13)	120.3(2)	H(2A)-N(2)-H(2B)	109.5
C(9)-C(8)-C(7)	120.5(2)	C(14)-N(2)-H(2C)	109.5
C(9)-C(8)-H(8)	119.8	H(2A)-N(2)-H(2C)	109.5
C(7)-C(8)-H(8)	119.8	H(2B)-N(2)-H(2C)	109.5
C(10)-C(9)-C(8)	120.1(2)	C(2)-O(3)-H(3A)	109.5
C(10)-C(9)-H(9)	119.9	C(3)-O(4)-H(4A)	109.5
C(8)-C(9)-H(9)	119.9	C(4)-O(5)-H(5A)	109.5
C(9)-C(10)-C(11)	120.2(2)	C(5)-O(6)-H(6)	109.5
C(9)-C(10)-H(10)	119.9		
C(11)-C(10)-H(10)	119.9		
C(12)-C(11)-C(10)	119.33(19)		
C(12)-C(11)-C(14)	120.5(2)		
C(10)-C(11)-C(14)	120.2(2)		
C(11)-C(12)-C(7)	120.7(2)		
C(11)-C(12)-H(12)	119.7		
C(7)-C(12)-H(12)	119.7		
N(1)-C(13)-C(7)	111.07(18)		
N(1)-C(13)-H(13A)	109.4		
C(7)-C(13)-H(13A)	109.4		
N(1)-C(13)-H(13B)	109.4		
C(7)-C(13)-H(13B)	109.4		
H(13A)-C(13)-H(13B)	108.0		
N(2)-C(14)-C(11)	111.39(17)		
N(2)-C(14)-H(14A)	109.3		
C(11)-C(14)-H(14A)	109.3		
N(2)-C(14)-H(14B)	109.3		
C(11)-C(14)-H(14B)	109.3		

Symmetry transformations used to generate equivalent atoms:

Table 11. Anisotropic displacement parameters ($Å^2 x\ 10^3$)for *m*-xylylenediammonium D-glucarate. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	18(1)	15(1)	21(2)	1(1)	2(1)	2(1)
C(2)	16(1)	19(1)	16(2)	0(1)	1(1)	1(1)
C(3)	17(1)	19(1)	17(2)	0(1)	-1(1)	-2(1)
C(4)	18(1)	16(1)	22(2)	-3(1)	2(1)	1(1)
C(5)	18(1)	18(1)	14(2)	2(1)	1(1)	-1(1)
C(6)	20(1)	14(1)	18(2)	1(1)	3(1)	-1(1)
C(7)	18(1)	16(1)	19(2)	1(1)	-3(1)	3(1)
C(8)	28(1)	18(1)	25(2)	1(1)	-2(1)	-3(1)
C(9)	39(1)	23(1)	18(2)	-4(1)	-4(1)	-1(1)
C(10)	30(1)	21(1)	20(2)	3(1)	3(1)	2(1)
C(11)	17(1)	18(1)	19(2)	4(1)	-3(1)	1(1)
C(12)	23(1)	20(1)	15(2)	0(1)	-3(1)	1(1)
C(13)	18(1)	21(1)	21(2)	3(1)	0(1)	2(1)
C(14)	19(1)	22(1)	23(2)	3(1)	0(1)	1(1)
N(1)	19(1)	18(1)	15(1)	-1(1)	1(1)	-1(1)
N(2)	21(1)	20(1)	22(1)	-2(1)	2(1)	-4(1)
O(1)	20(1)	25(1)	20(1)	5(1)	1(1)	2(1)
O(2)	20(1)	33(1)	20(1)	4(1)	-3(1)	-1(1)
O(3)	21(1)	23(1)	19(1)	0(1)	-2(1)	-5(1)
O(4)	36(1)	24(1)	13(1)	0(1)	3(1)	7(1)
O(5)	37(1)	20(1)	23(1)	4(1)	-13(1)	-10(1)
O(6)	18(1)	25(1)	17(1)	4(1)	4(1)	0(1)
O(7)	26(1)	28(1)	21(1)	4(1)	7(1)	9(1)
O(8)	18(1)	27(1)	21(1)	8(1)	1(1)	2(1)

Table 12. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for *m*-xylylenediammonium D-glucarate.

	x	y	z	U(eq)
H(2)	6494	5957	4086	21
H(3)	5628	4660	3761	21
H(4)	6600	4840	5011	22
H(5)	6871	3473	4494	20
H(8)	12092	2779	8717	29
H(9)	9840	2310	9790	31
H(10)	6693	1322	9663	29
H(12)	8372	1180	7401	23
H(13A)	13074	2765	7408	24
H(13B)	12800	1945	6993	24
H(14A)	3869	535	8831	25
H(14B)	4459	495	7933	25
H(1A)	8650	2319	6544	25
H(1B)	10655	2904	6301	25
H(1C)	8819	3070	6949	25
H(2A)	7708	-390	8132	31
H(2B)	5445	-661	8615	31
H(2C)	7770	-262	8970	31
H(3A)	11395	5826	3505	31
H(4A)	10159	4121	3549	36
H(5A)	10973	5314	4740	40
H(6)	5583	3383	5590	30

Table 13. Torsion angles (°) for *m*-xylylenediammonium D-glucarate.

O(1)-C(1)-C(2)-O(3)	4.4(2)
O(2)-C(1)-C(2)-O(3)	-175.09(16)
O(1)-C(1)-C(2)-C(3)	-119.96(19)
O(2)-C(1)-C(2)-C(3)	60.5(2)
O(3)-C(2)-C(3)-O(4)	-64.8(2)
C(1)-C(2)-C(3)-O(4)	61.0(2)
O(3)-C(2)-C(3)-C(4)	62.2(2)
C(1)-C(2)-C(3)-C(4)	-172.00(18)
O(4)-C(3)-C(4)-O(5)	71.0(2)
C(2)-C(3)-C(4)-O(5)	-51.3(2)
O(4)-C(3)-C(4)-C(5)	-53.9(2)
C(2)-C(3)-C(4)-C(5)	-176.15(18)
O(5)-C(4)-C(5)-O(6)	85.3(2)
C(3)-C(4)-C(5)-O(6)	-146.37(18)
O(5)-C(4)-C(5)-C(6)	-37.0(3)
C(3)-C(4)-C(5)-C(6)	91.4(2)
O(6)-C(5)-C(6)-O(8)	-7.8(2)
C(4)-C(5)-C(6)-O(8)	113.8(2)
O(6)-C(5)-C(6)-O(7)	173.04(16)
C(4)-C(5)-C(6)-O(7)	-65.3(2)
C(12)-C(7)-C(8)-C(9)	-1.4(3)
C(13)-C(7)-C(8)-C(9)	177.08(19)
C(7)-C(8)-C(9)-C(10)	-1.0(3)
C(8)-C(9)-C(10)-C(11)	2.7(3)
C(9)-C(10)-C(11)-C(12)	-1.9(3)
C(9)-C(10)-C(11)-C(14)	178.33(19)
C(10)-C(11)-C(12)-C(7)	-0.5(3)
C(14)-C(11)-C(12)-C(7)	179.24(18)
C(8)-C(7)-C(12)-C(11)	2.1(3)
C(13)-C(7)-C(12)-C(11)	-176.32(18)
C(8)-C(7)-C(13)-N(1)	-114.7(2)
C(12)-C(7)-C(13)-N(1)	63.7(2)
C(12)-C(11)-C(14)-N(2)	88.9(2)
C(10)-C(11)-C(14)-N(2)	-91.4(2)

Symmetry transformations used to generate equivalent atoms:

Table 14. Hydrogen bond distances (Å) and angles (°) for *m*-xylylenediammonium D-glucarate.

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(1)-H(1A)...O(7)#1	0.91	1.94	2.818(2)	161.1
N(1)-H(1B)...O(8)	0.91	1.85	2.750(2)	167.4
N(1)-H(1C)...O(1)#2	0.91	1.91	2.816(2)	176.9
N(2)-H(2A)...O(2)#3	0.91	1.85	2.754(2)	171.2
N(2)-H(2B)...O(6)#4	0.91	2.25	3.069(2)	150.3
N(2)-H(2B)...O(1)#1	0.91	2.33	2.889(2)	119.1
N(2)-H(2C)...O(5)#5	0.91	2.02	2.918(2)	167.0
O(3)-H(3A)...O(2)#6	0.84	1.96	2.785(2)	166.3
O(4)-H(4A)...O(7)	0.84	1.78	2.618(2)	172.5
O(5)-H(5A)...O(3)	0.84	1.92	2.674(2)	148.8
O(6)-H(6)...O(8)#7	0.84	1.83	2.643(2)	163.5

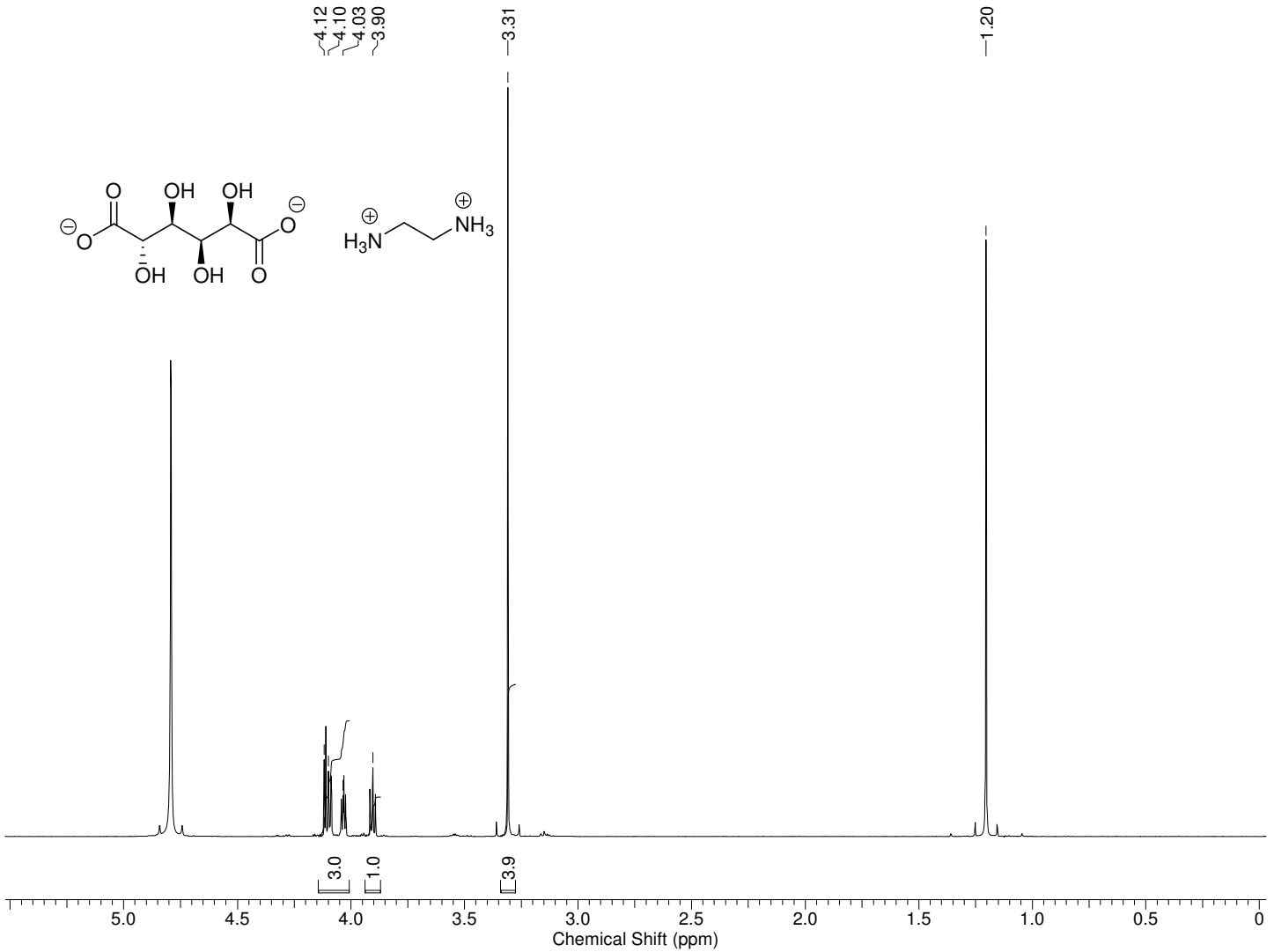
Symmetry transformations used to generate equivalent atoms:

#1 x-1/2,-y+1/2,-z+1 #2 -x+3/2,-y+1,z+1/2 #3 x+1/2,-y+1/2,-z+1

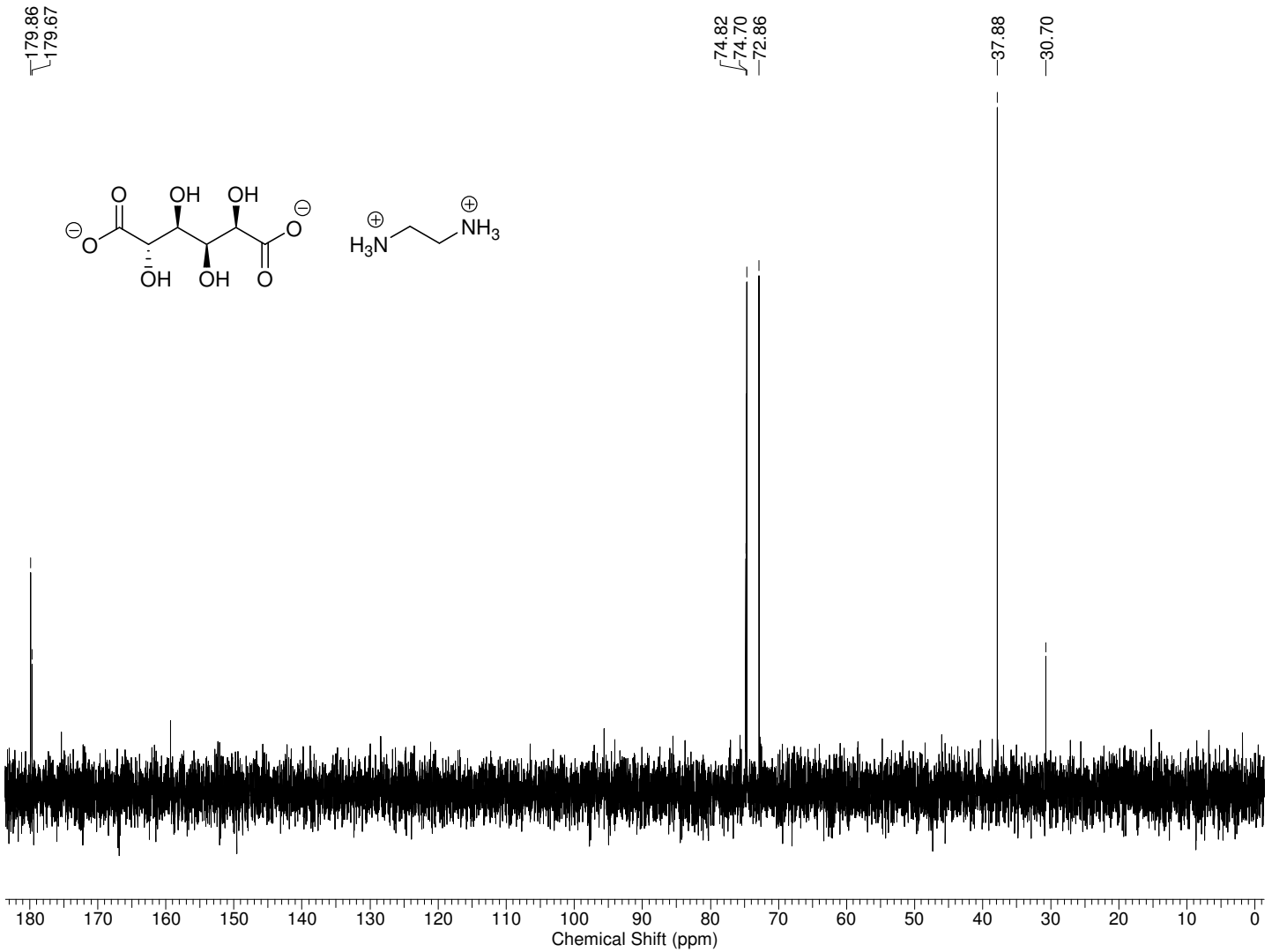
#4 -x+1,y-1/2,-z+3/2 #5 -x+2,y-1/2,-z+3/2 #6 x+1,y,z

#7 x-1,y,z

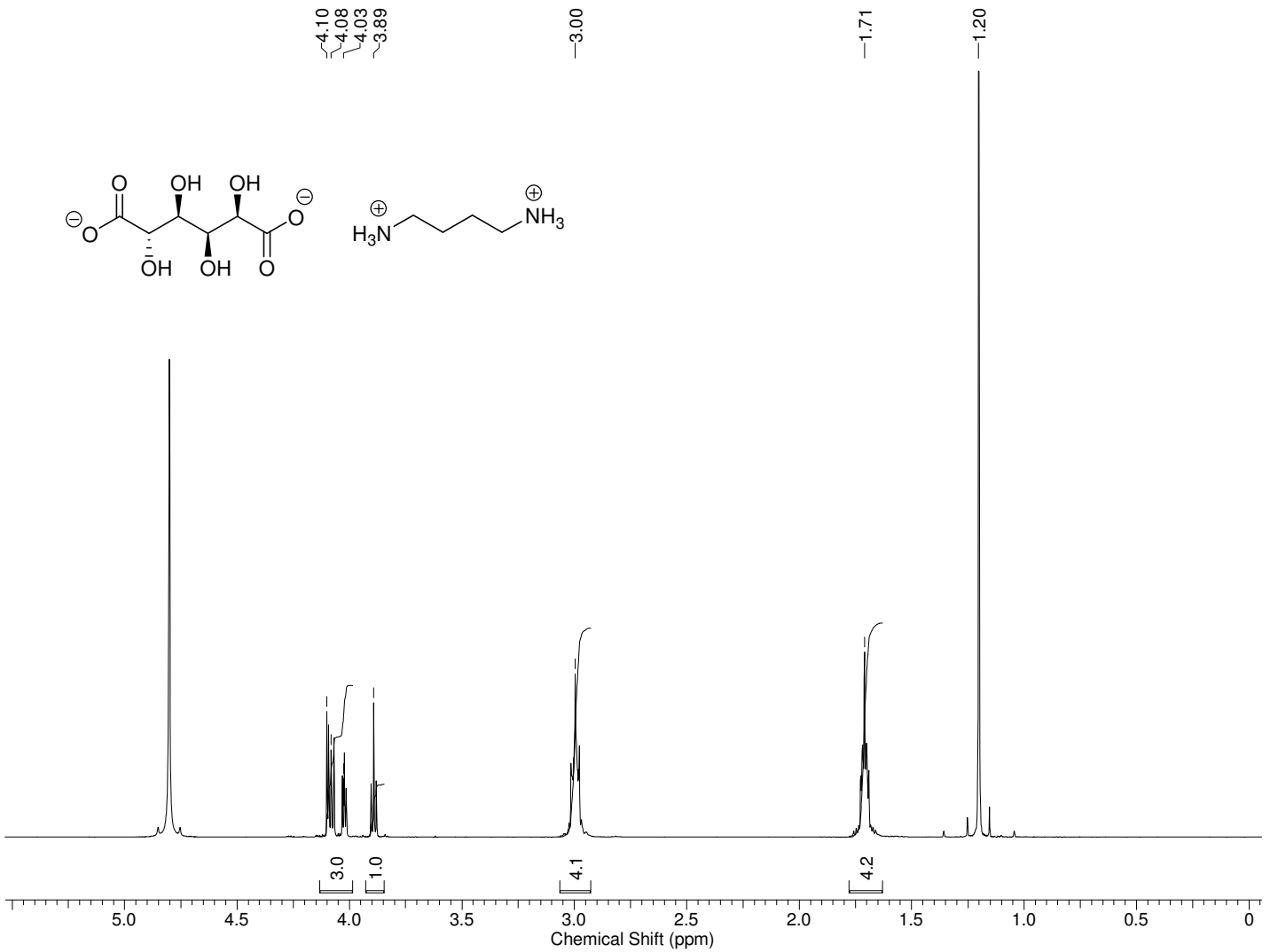
Appendix B. Nuclear Magnetic Resonance Spectra from Alkylenediammonium D-Glucarate Salts



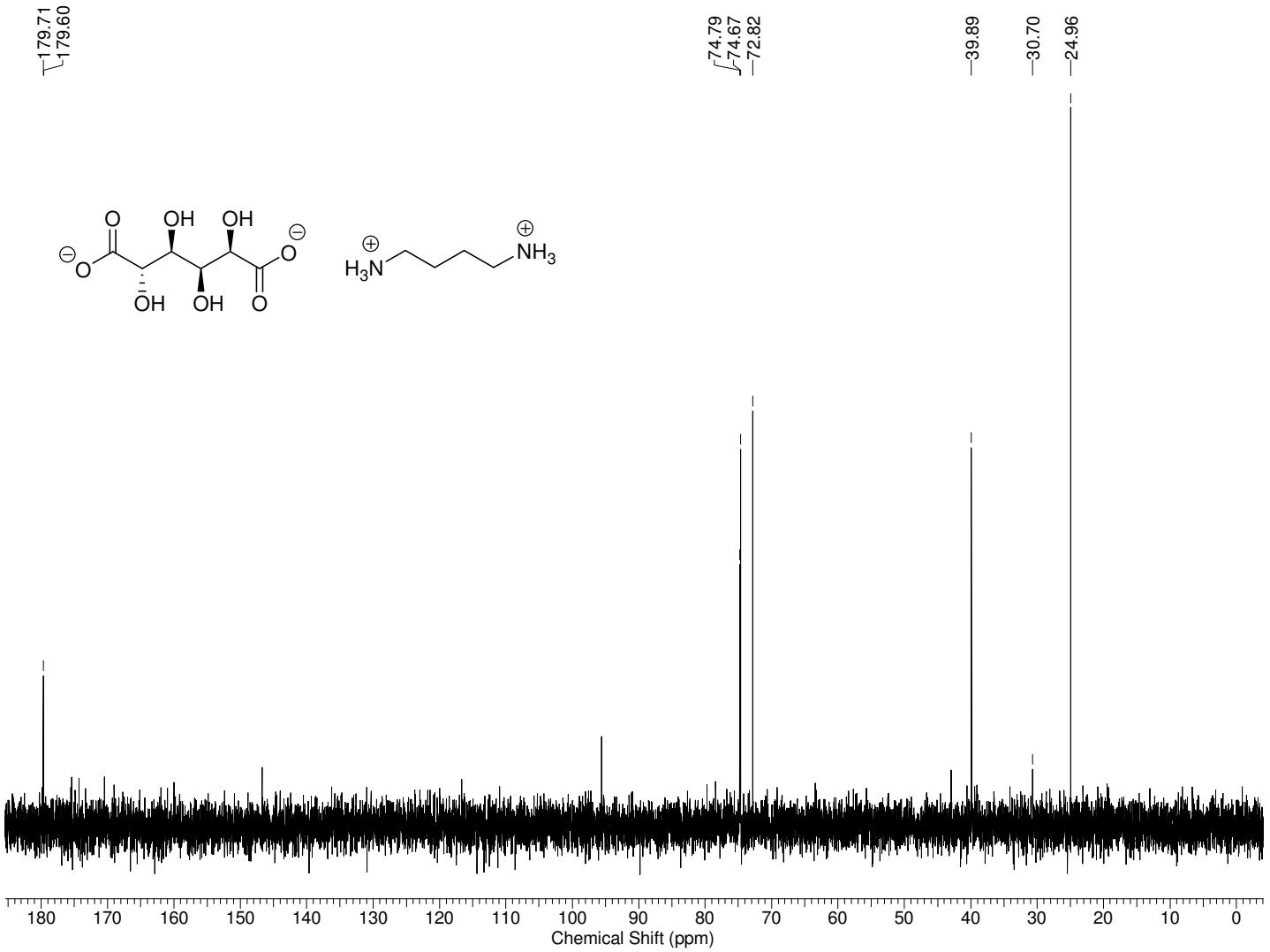
Ethylenediammonium D-glucarate ^{1}H NMR spectrum (D_2O; 1% *t*-butyl alcohol ref., 1.20 ppm)



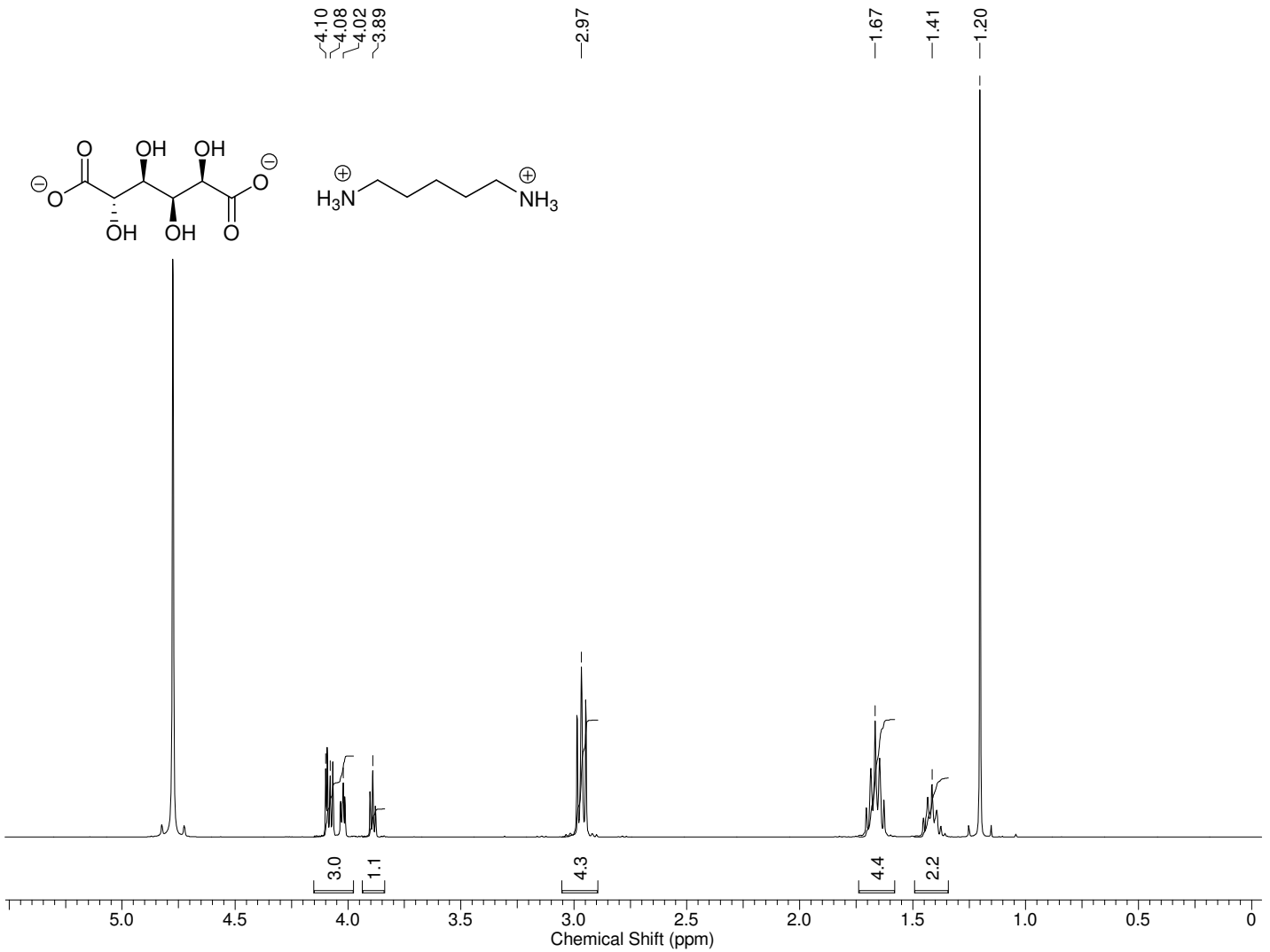
Ethylenediammonium D-glucarate ^{13}C NMR spectrum (D_2O; 1% *t*-butyl alcohol ref., 30.70 ppm)



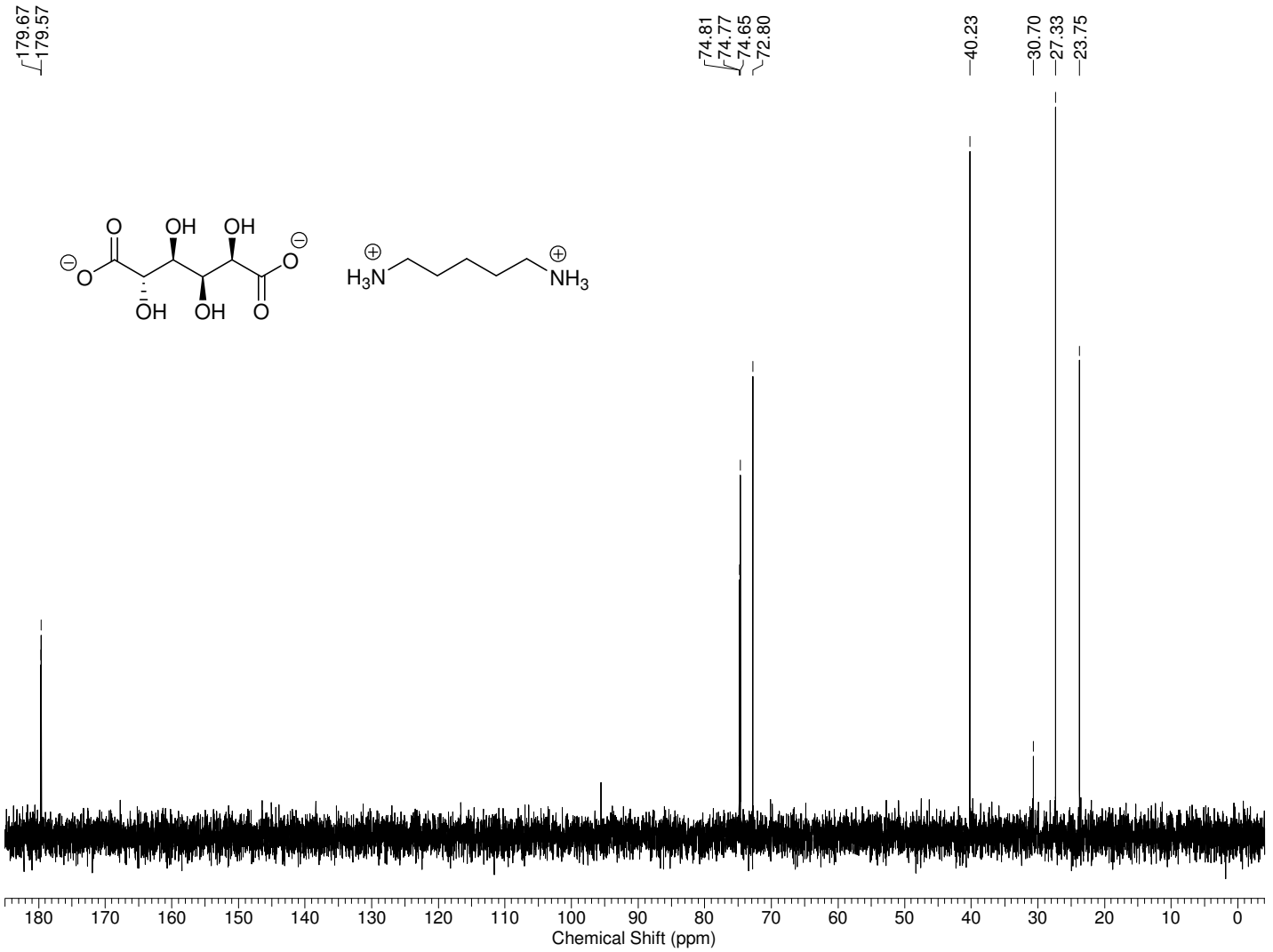
Tetramethylenediammonium D-glucarate ^{1}H NMR spectrum (D_2O; 1% *t*-butyl alcohol ref., 1.20 ppm)



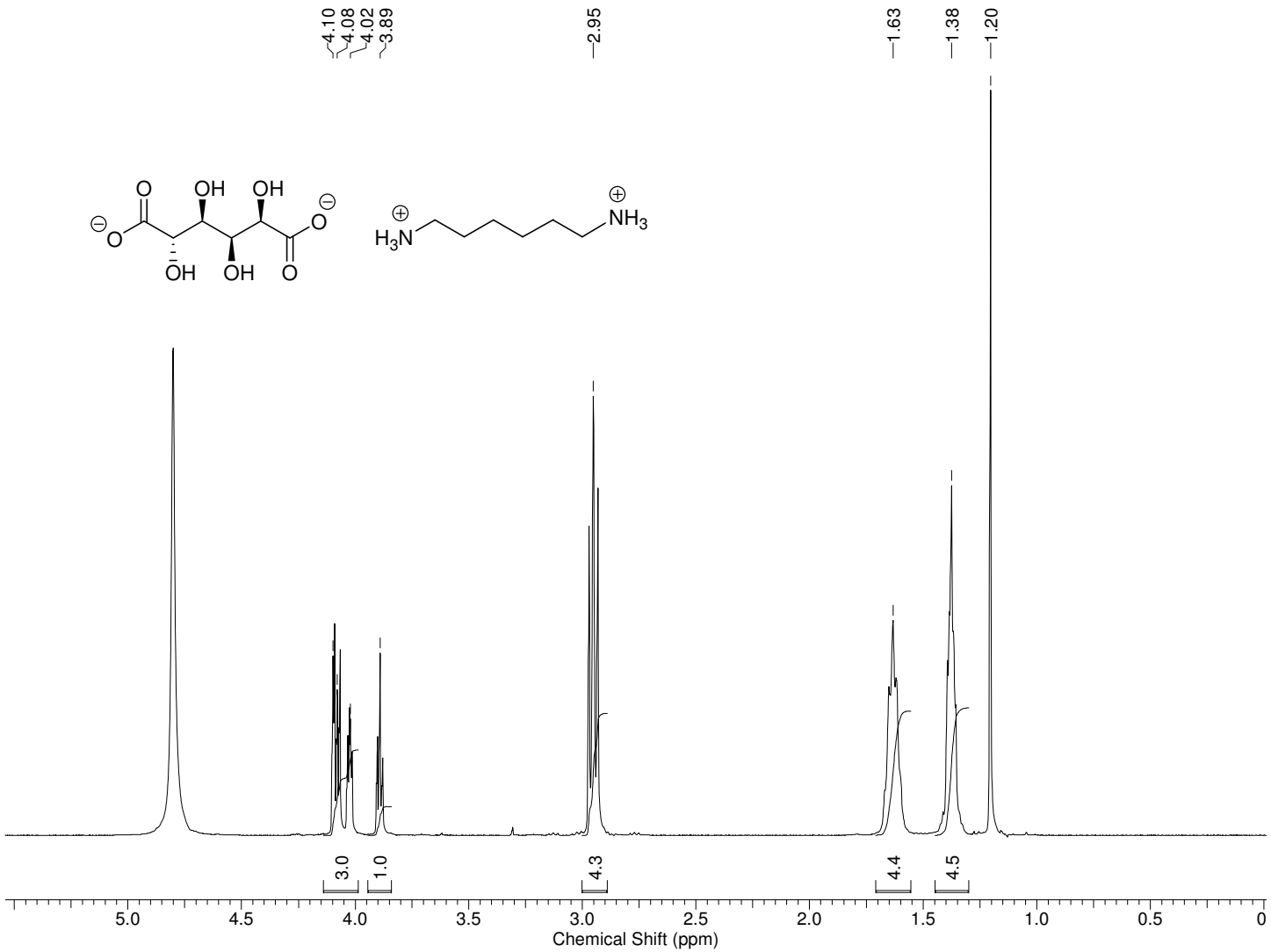
Tetramethylenediammonium D-glucarate ^{13}C NMR spectrum (D_2O; 1% *t*-butyl alcohol ref., 30.70 ppm)



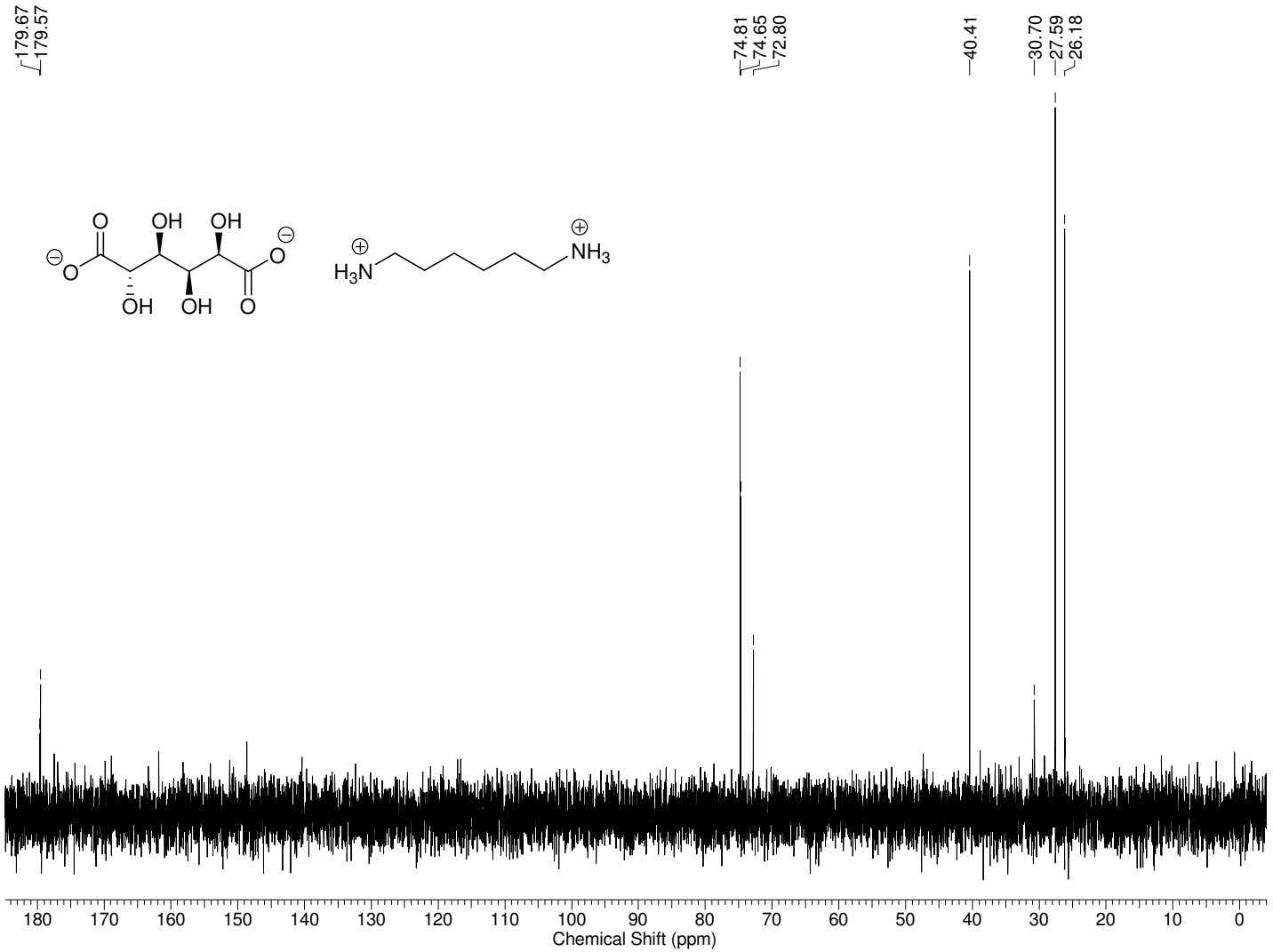
Pentamethylenediammonium D-glucarate ^{1}H NMR spectrum (D_2O; 1% *t*-butyl alcohol ref., 1.20 ppm)



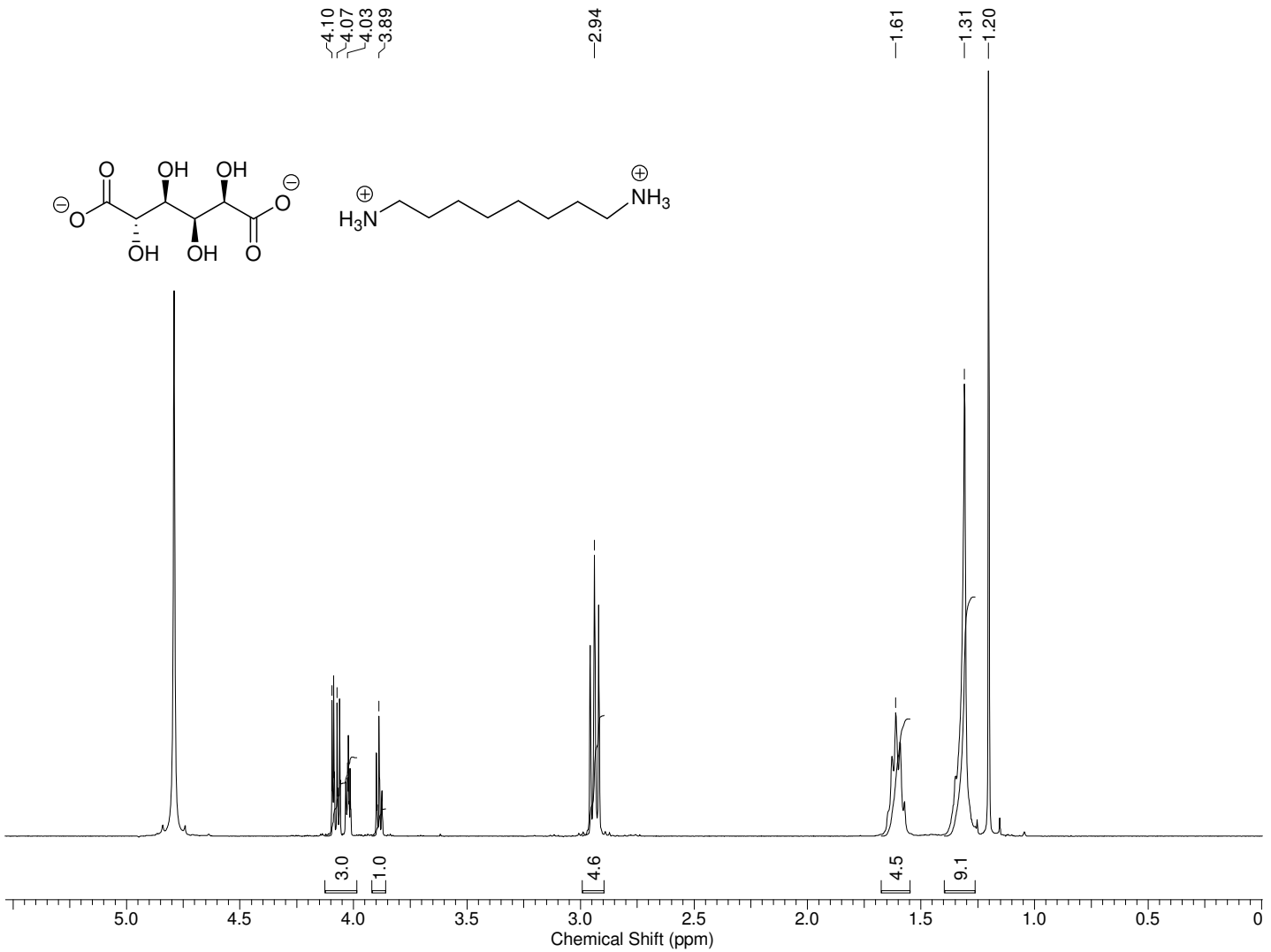
Pentamethylenediammonium D-glucarate ^{13}C NMR spectrum (D_2O; 1% *t*-butyl alcohol ref., 30.70 ppm)



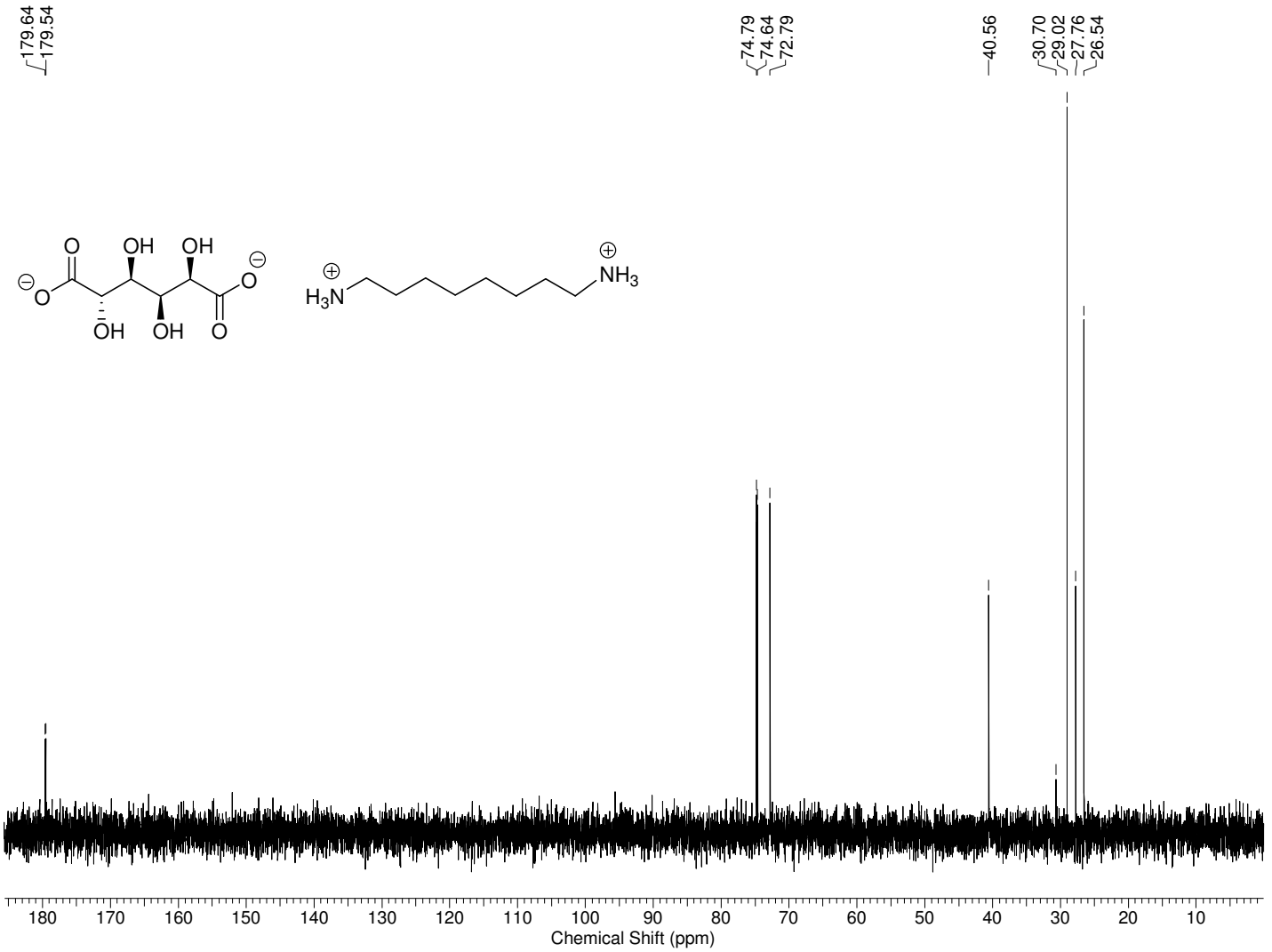
Hexamethylenediammonium D-glucarate ^{1}H NMR spectrum (D_2O; 1% *t*-butyl alcohol ref., 1.20 ppm)



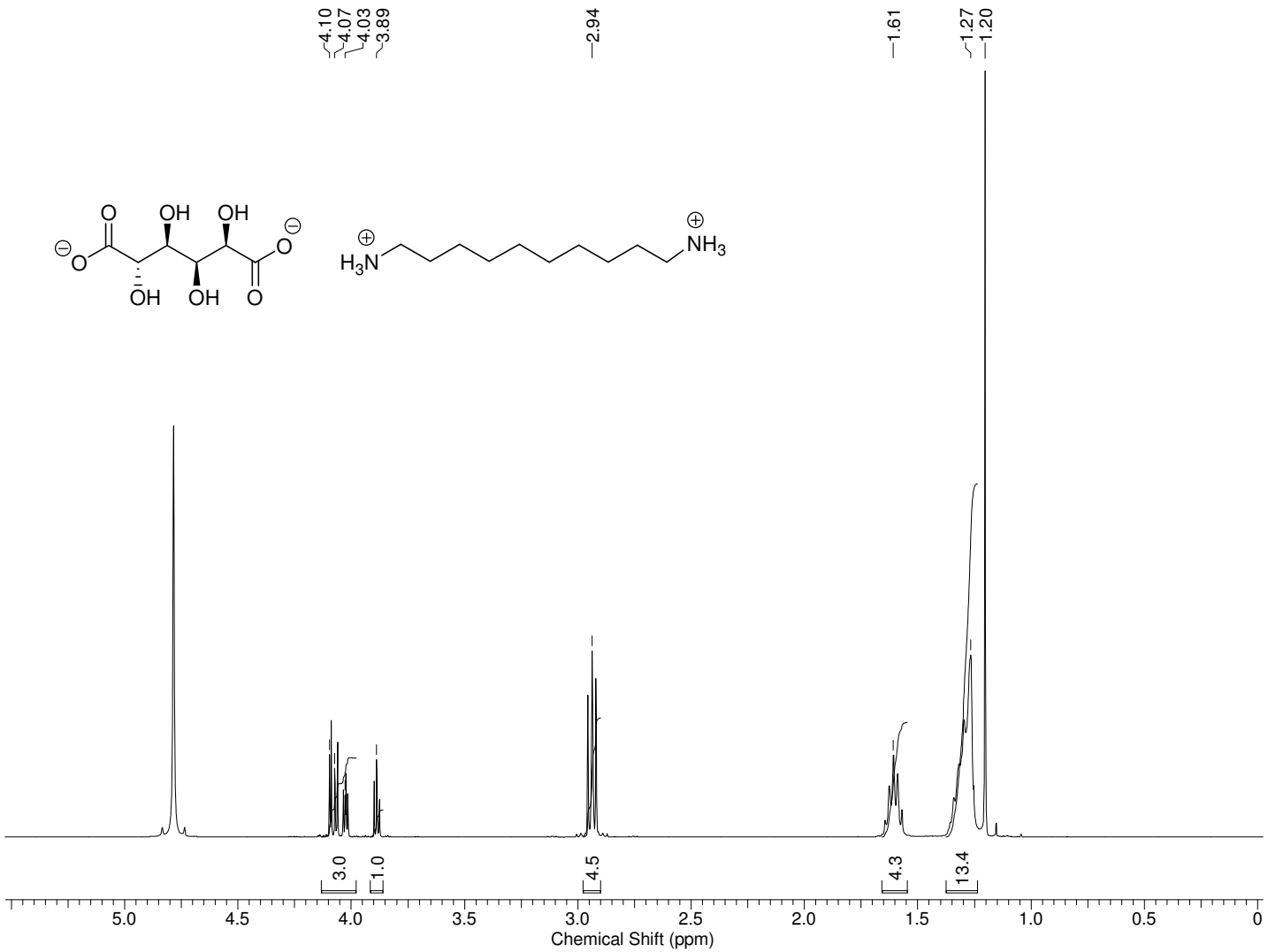
Hexamethylenediammonium D-glucarate ^{13}C NMR spectrum (D_2O; 1% *t*-butyl alcohol ref., 30.70 ppm)



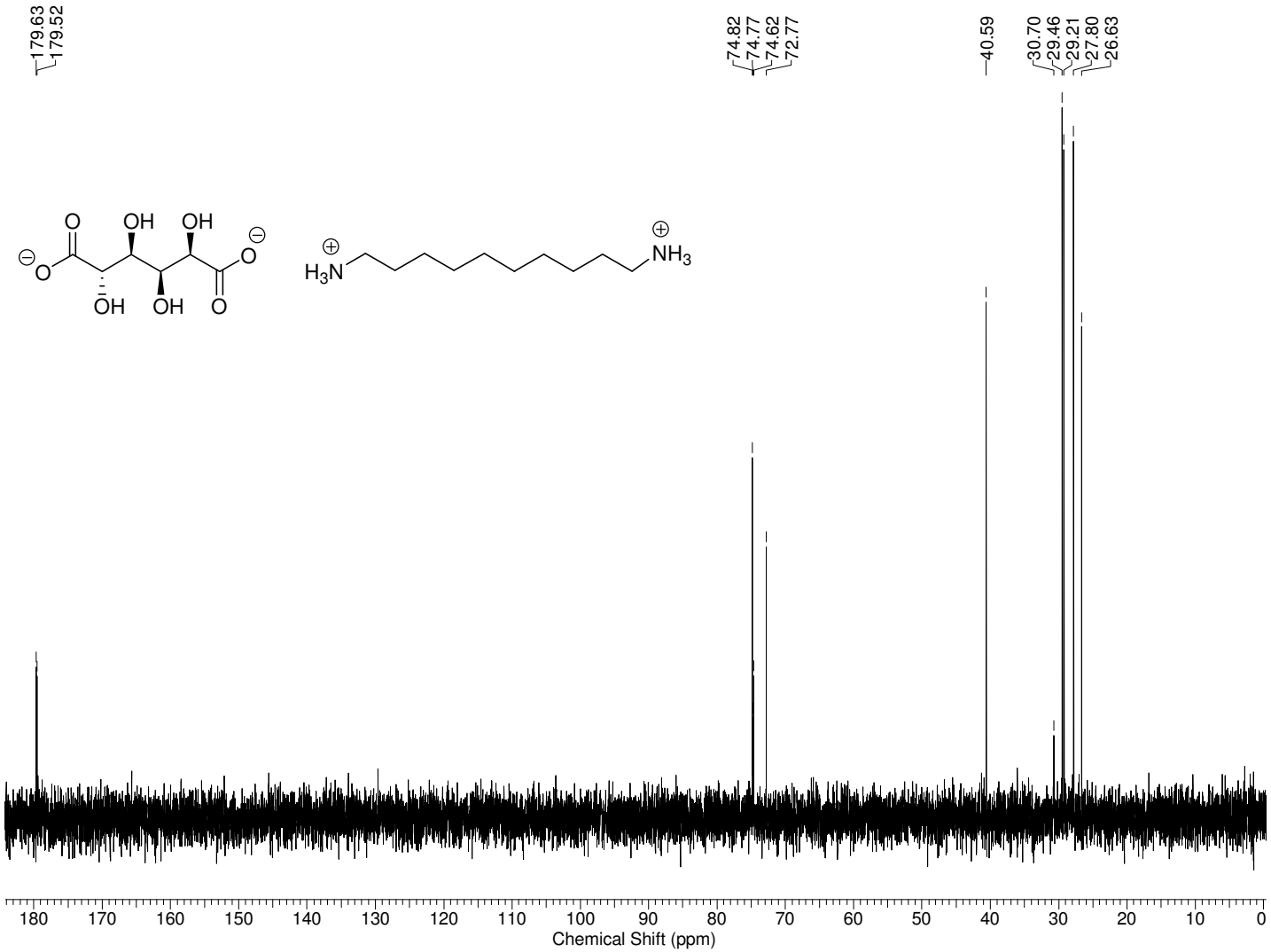
Octamethylenediammonium D-glucarate ^{1}H NMR spectrum (D_2O; 1% *t*-butyl alcohol ref., 1.20 ppm)



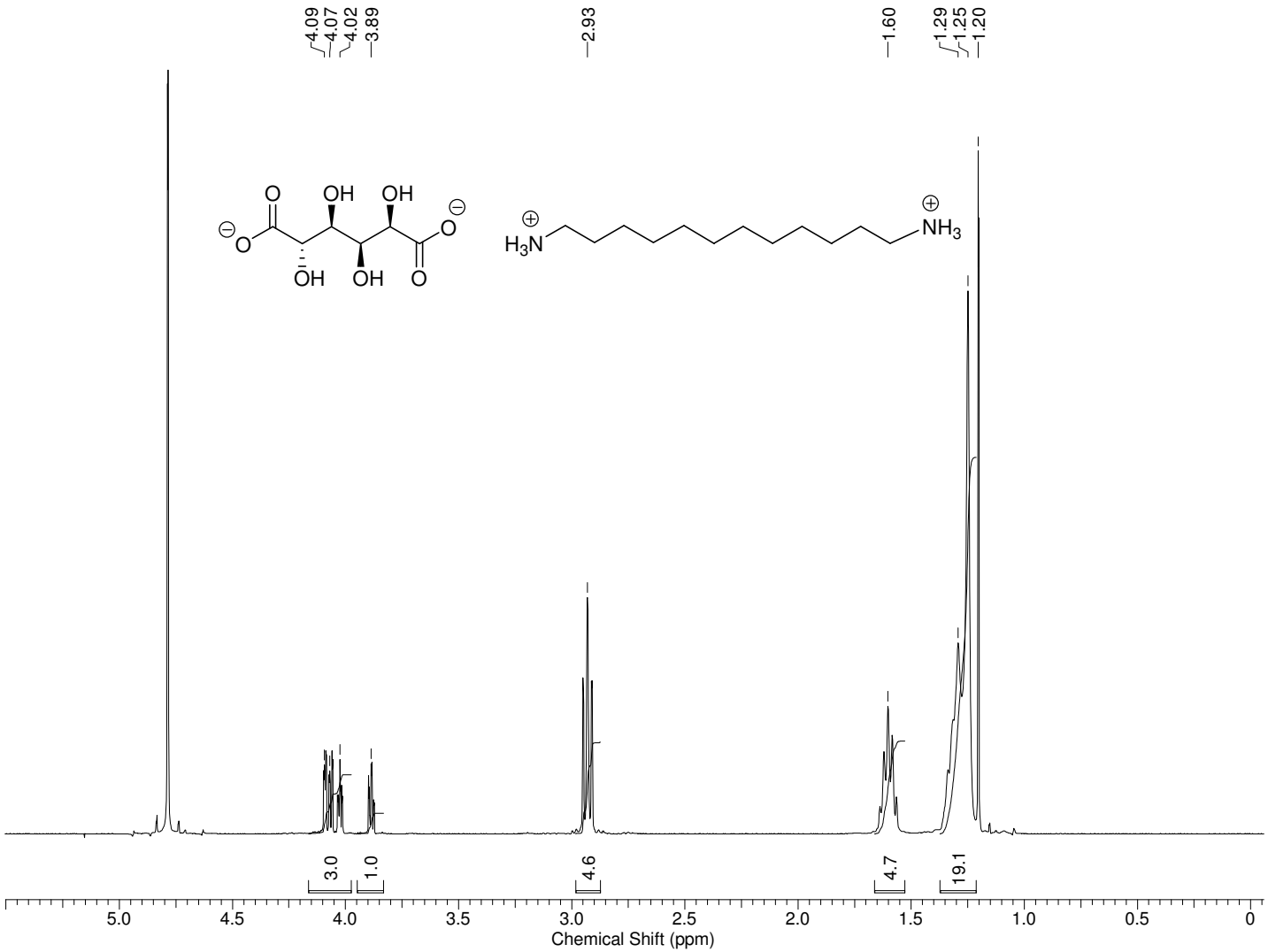
Octamethylenediammonium D-glucarate ^{13}C NMR spectrum (D_2O; 1% *t*-butyl alcohol ref., 30.70 ppm)



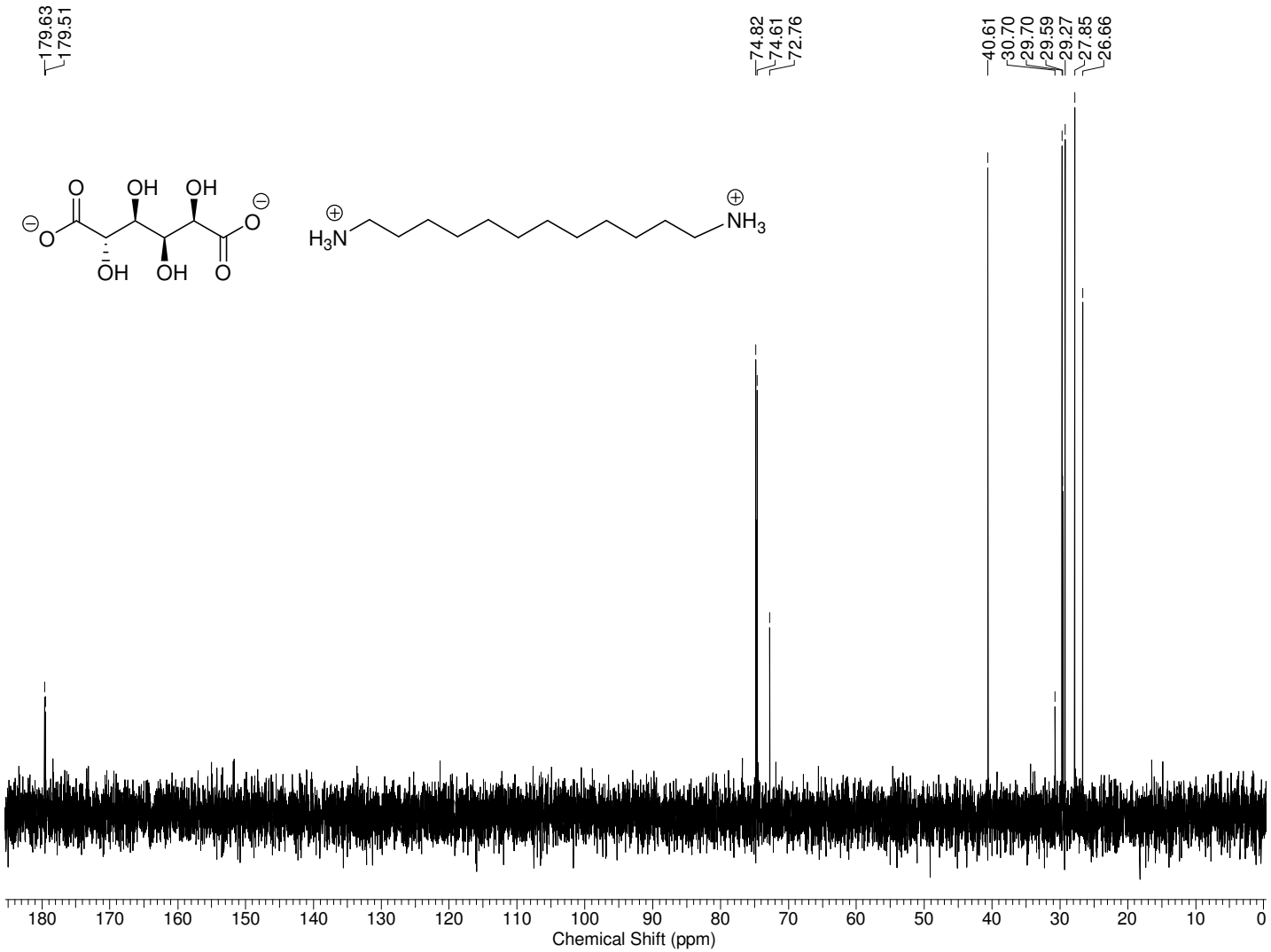
Decamethylenediammonium D-glucarate ^{1}H NMR spectrum (D_2O; 1% *t*-butyl alcohol ref., 1.20 ppm)



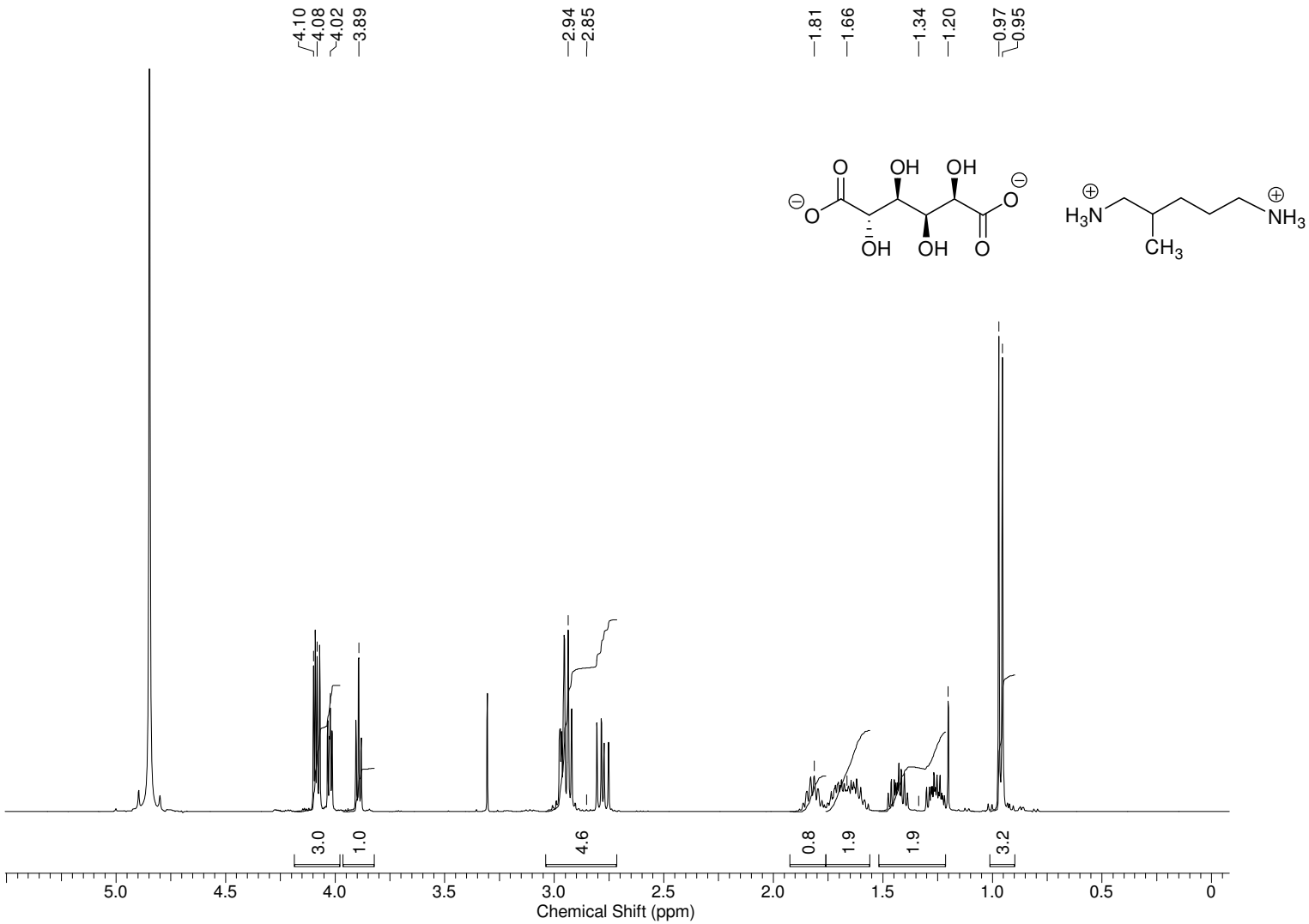
Decamethylenediammonium D-glucarate ^{13}C NMR spectrum (D_2O; 1% *t*-butyl alcohol ref., 30.70 ppm)



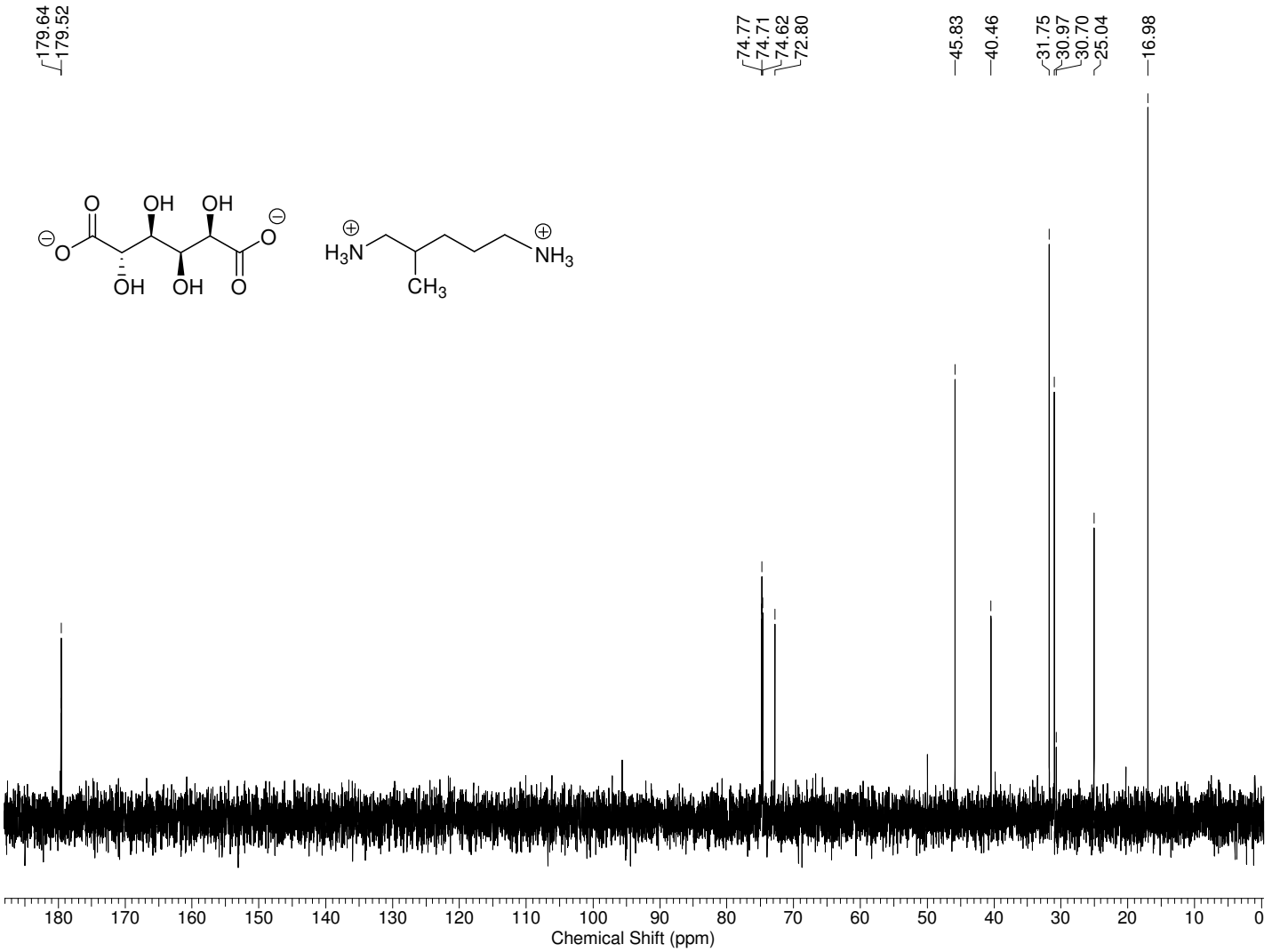
Dodecamethylenediammonium D-glucarate ^{1}H NMR spectrum (D_2O; 1% *t*-butyl alcohol ref., 1.20 ppm)



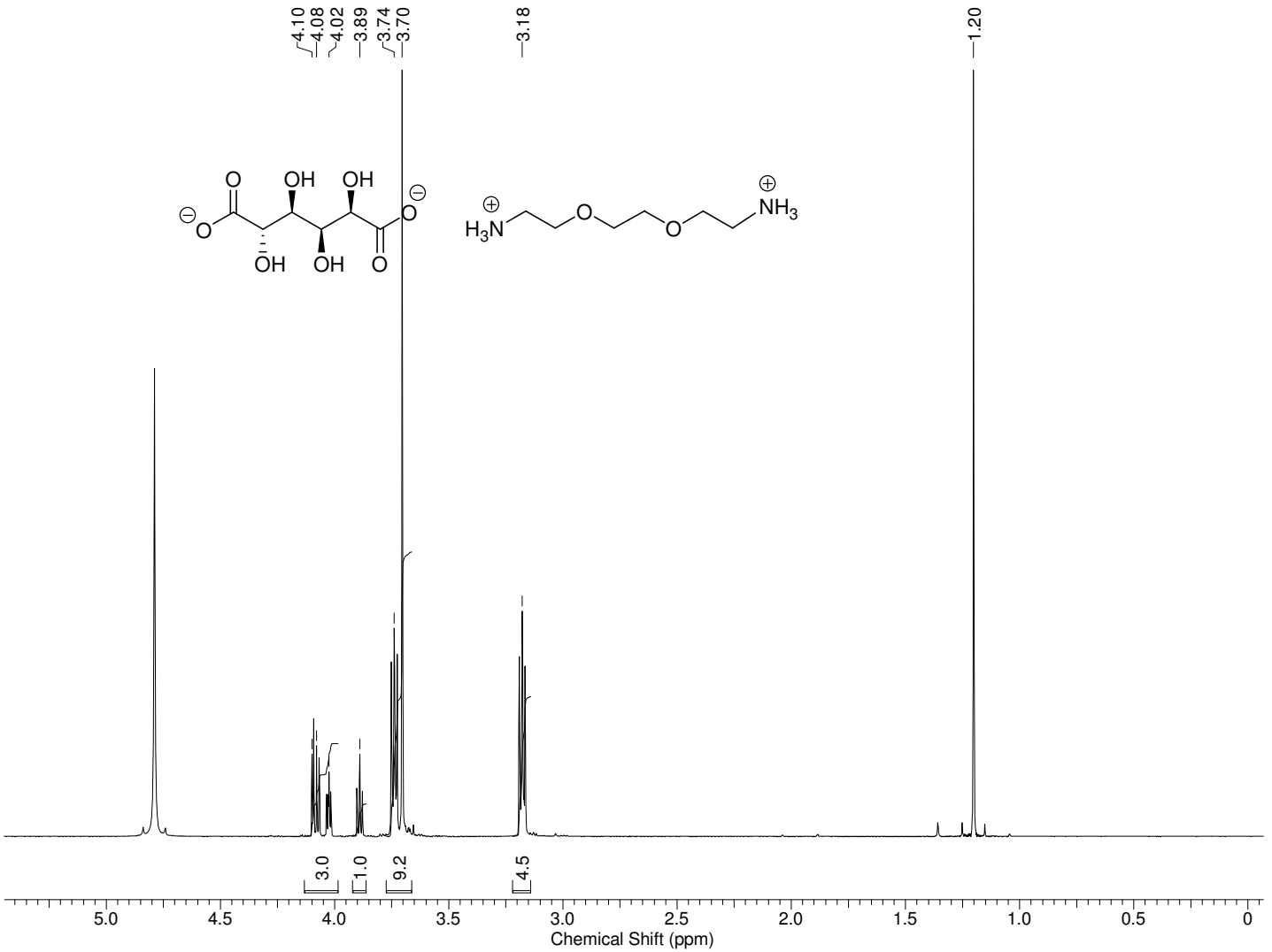
Dodecamethylenediammonium D-glucarate ^{13}C NMR spectrum (D_2O; 1% *t*-butyl alcohol ref., 30.70 ppm)



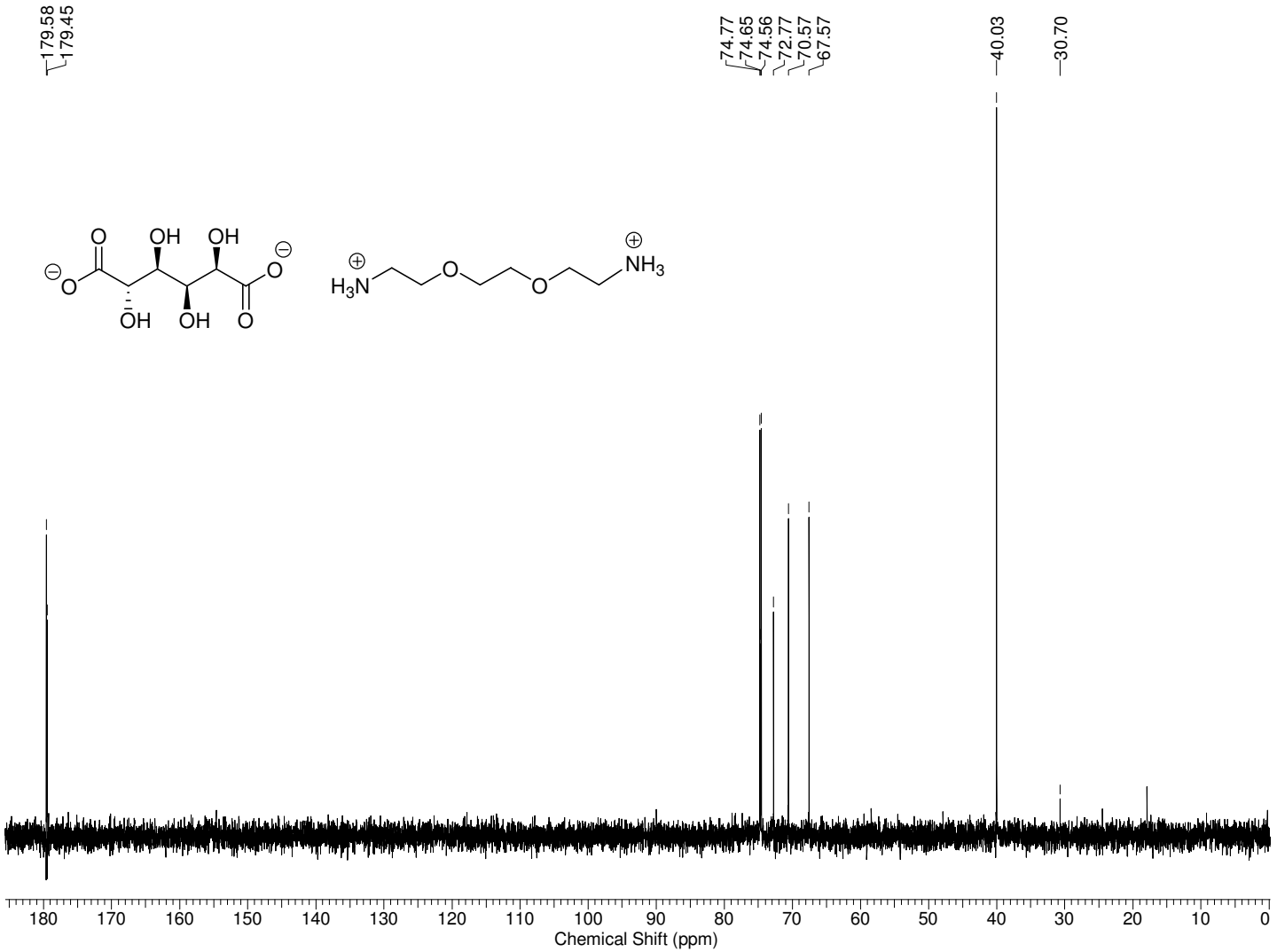
2-Methylpentamethylenediammonium D-glucarate ^{1}H NMR spectrum (D_2O; 1% *t*-butyl alcohol ref., 1.20 ppm)



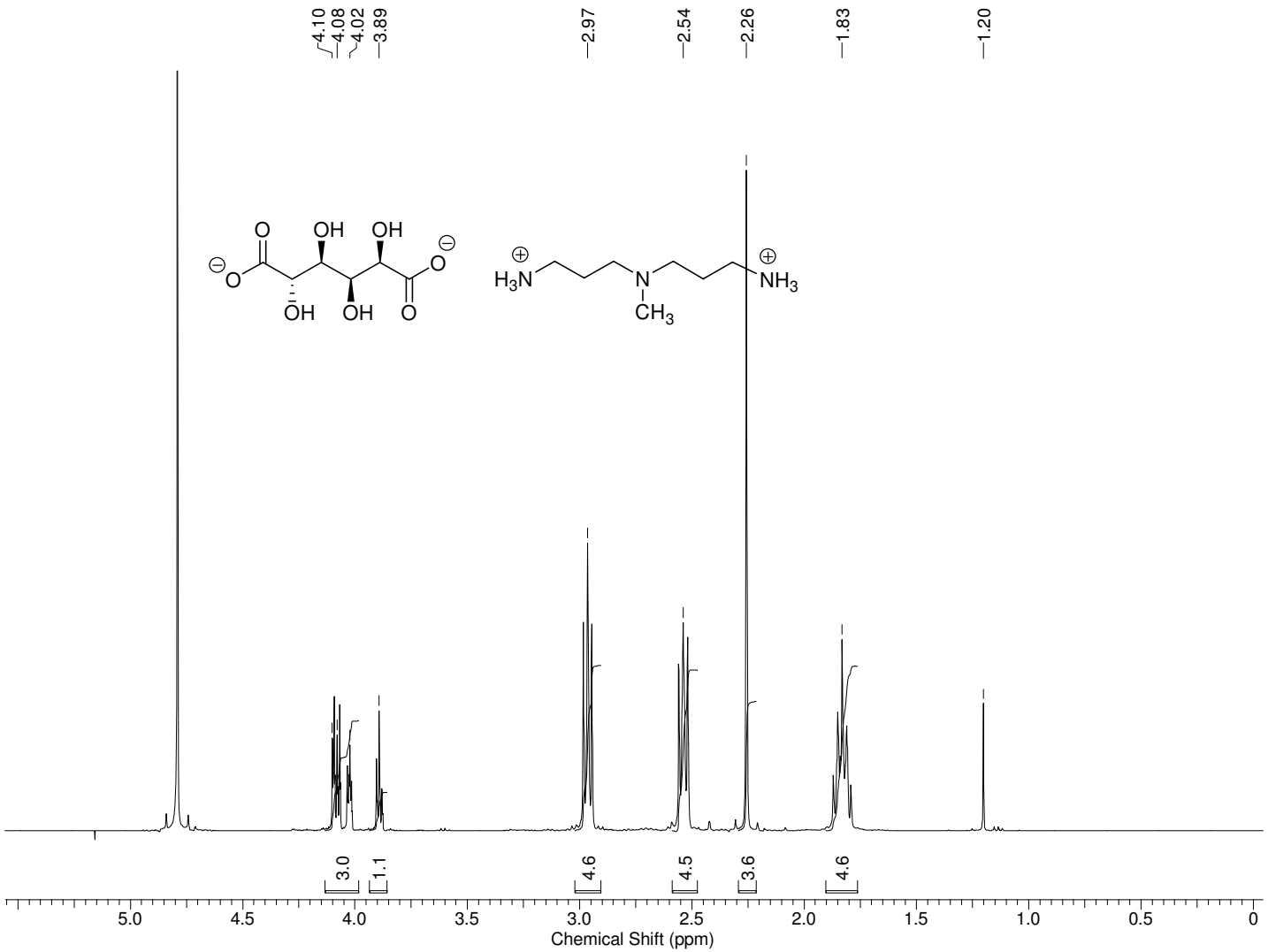
2-Methylpentamethylenediammonium D-glucarate ^{13}C NMR spectrum (D_2O; 1% *t*-butyl alcohol ref., 30.70 ppm)



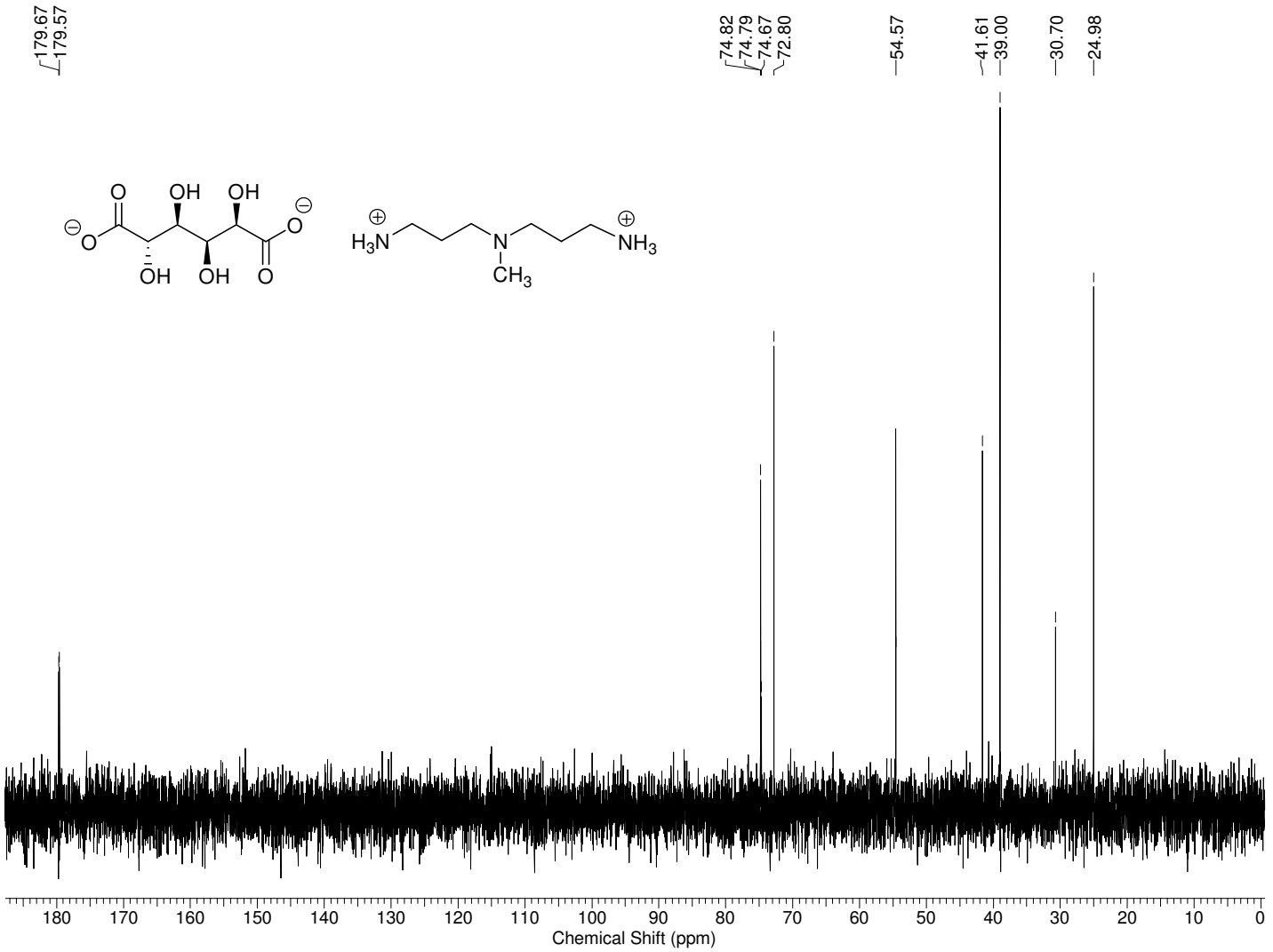
3',6'-Dioxaoctamethylenediammonium D-glucarate ^{1}H NMR spectrum (D_2O; 1% *t*-butyl alcohol ref., 1.20 ppm)



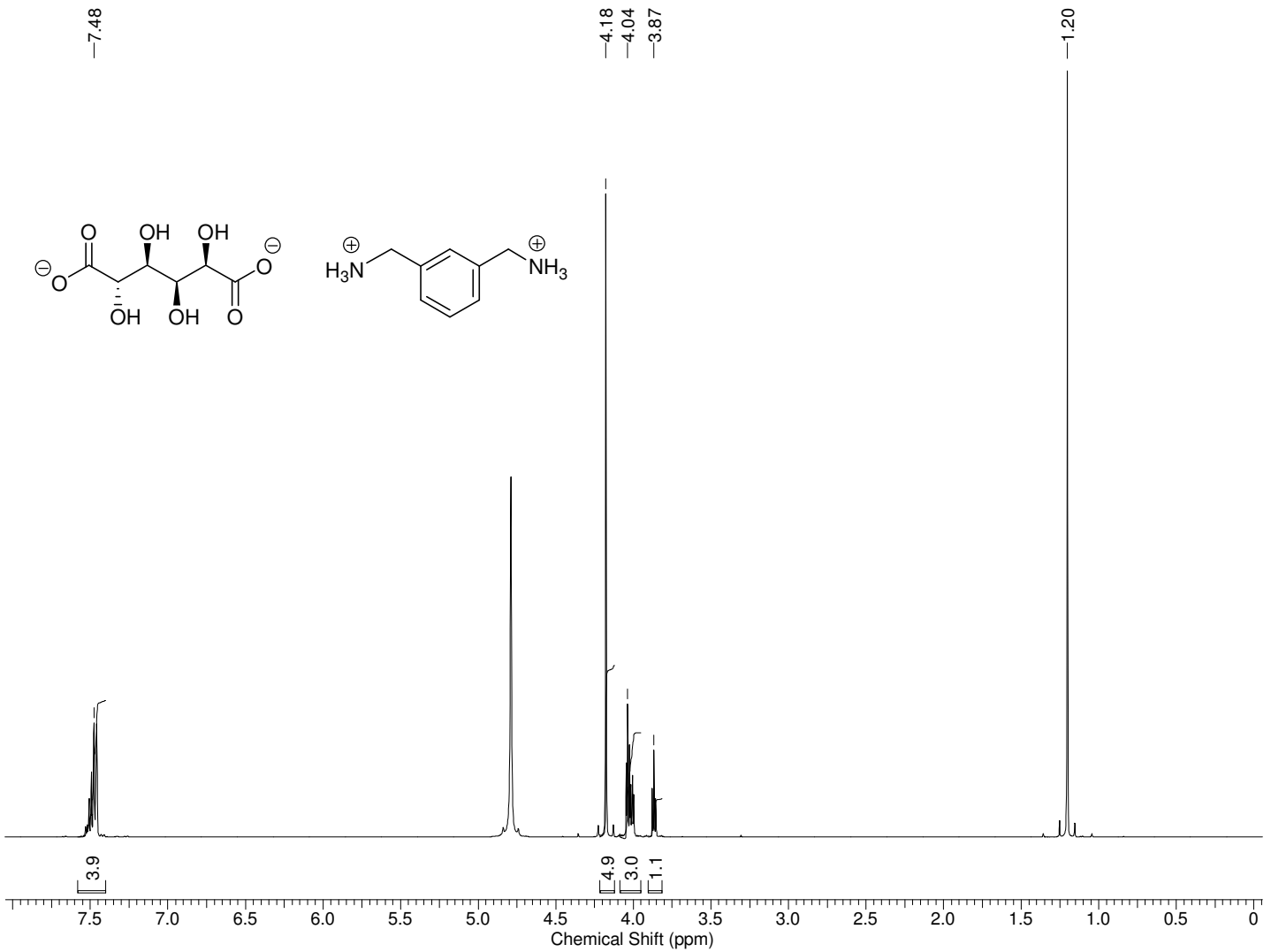
3',6'-Dioxaoctamethylenediammonium D-glucarate ^{13}C NMR spectrum (D_2O; 1% *t*-butyl alcohol ref., 30.70 ppm)



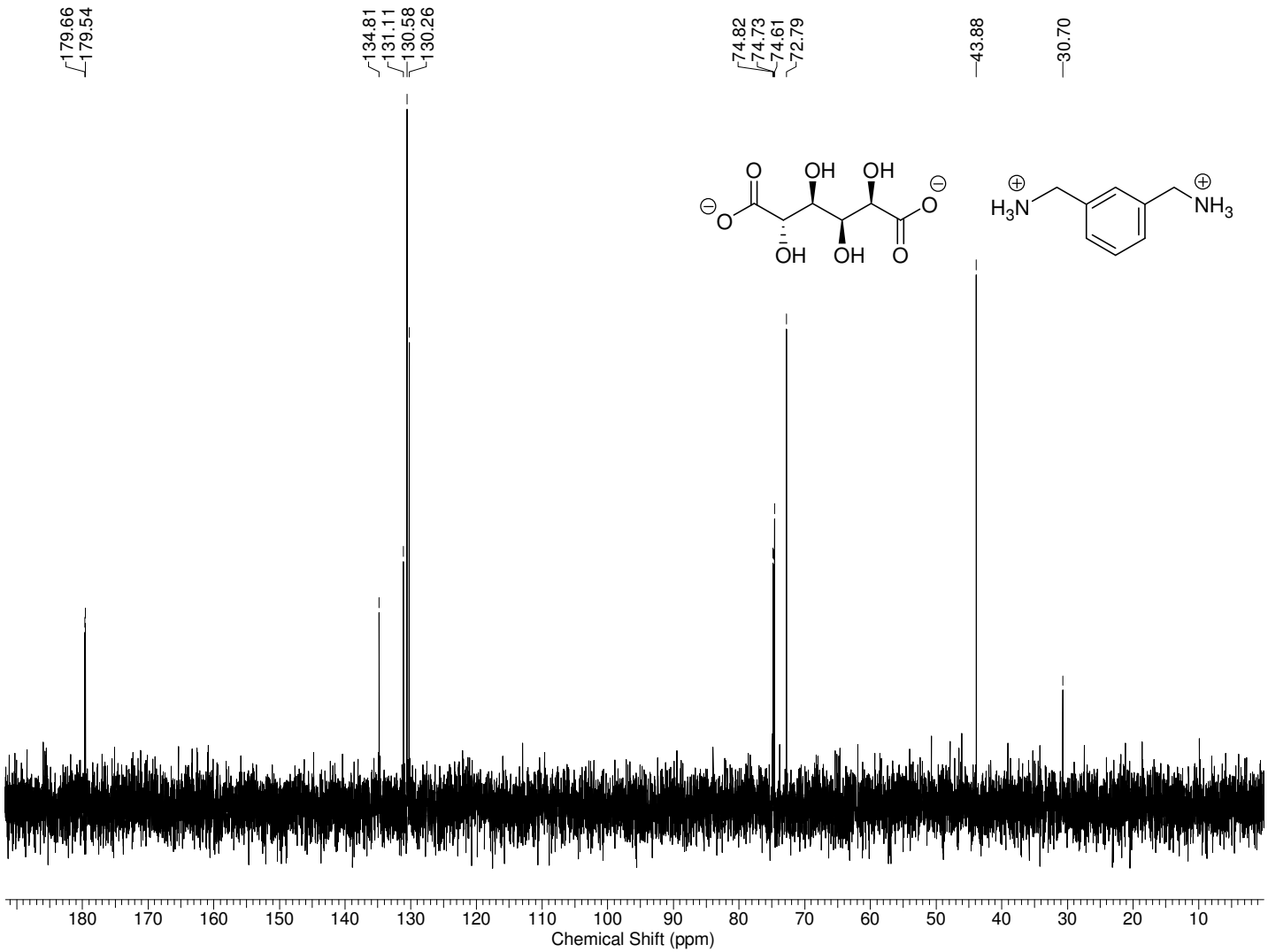
4'-Aza-*N*-methylheptamethylenediammonium D-glucarate ^{1}H NMR spectrum (D_2O; 1% *t*-butyl alcohol ref., 1.20 ppm)



4'-Aza-*N*-methylheptamethylenediammonium D-glucarate ^{13}C NMR spectrum (D_2O; 1% *t*-butyl alcohol ref., 30.70 ppm)

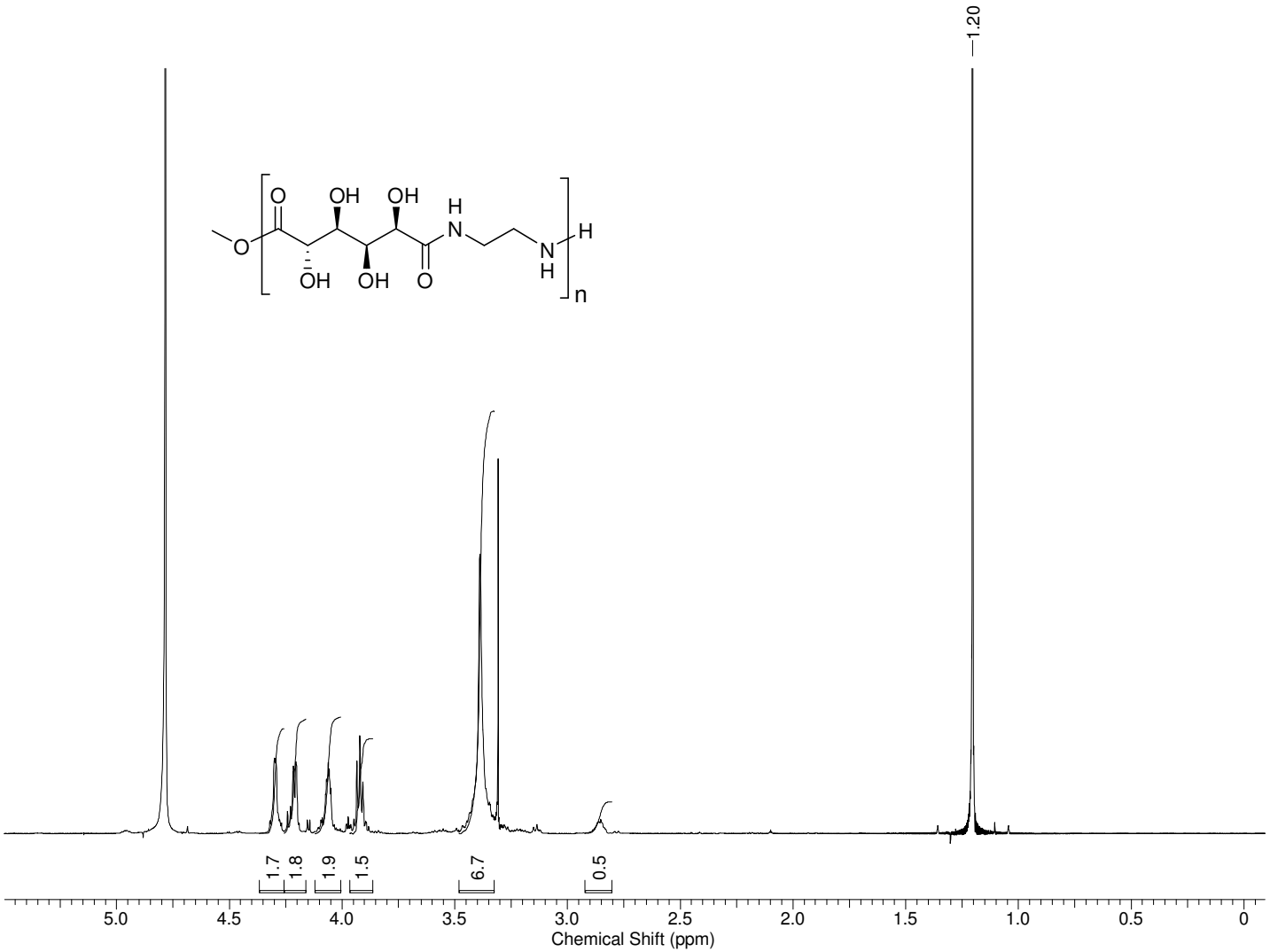


m-Xylylenediammonium D-glucarate ^{1}H NMR spectrum (D_2O; 1% *t*-butyl alcohol ref., 1.20 ppm)

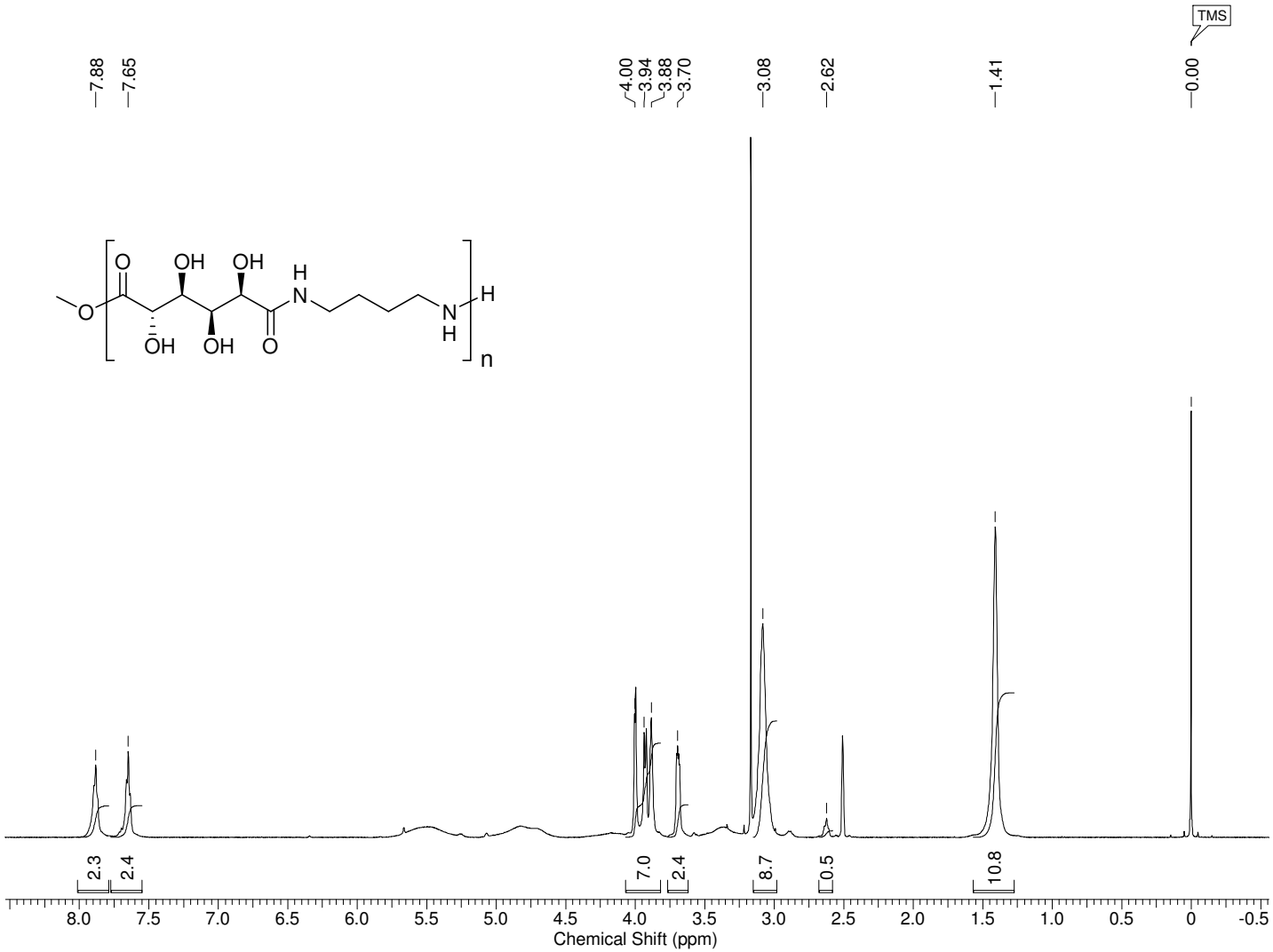


m-Xylylenediammonium D-glucarate ^{13}C NMR spectrum (D_2O; 1% *t*-butyl alcohol ref., 30.70 ppm)

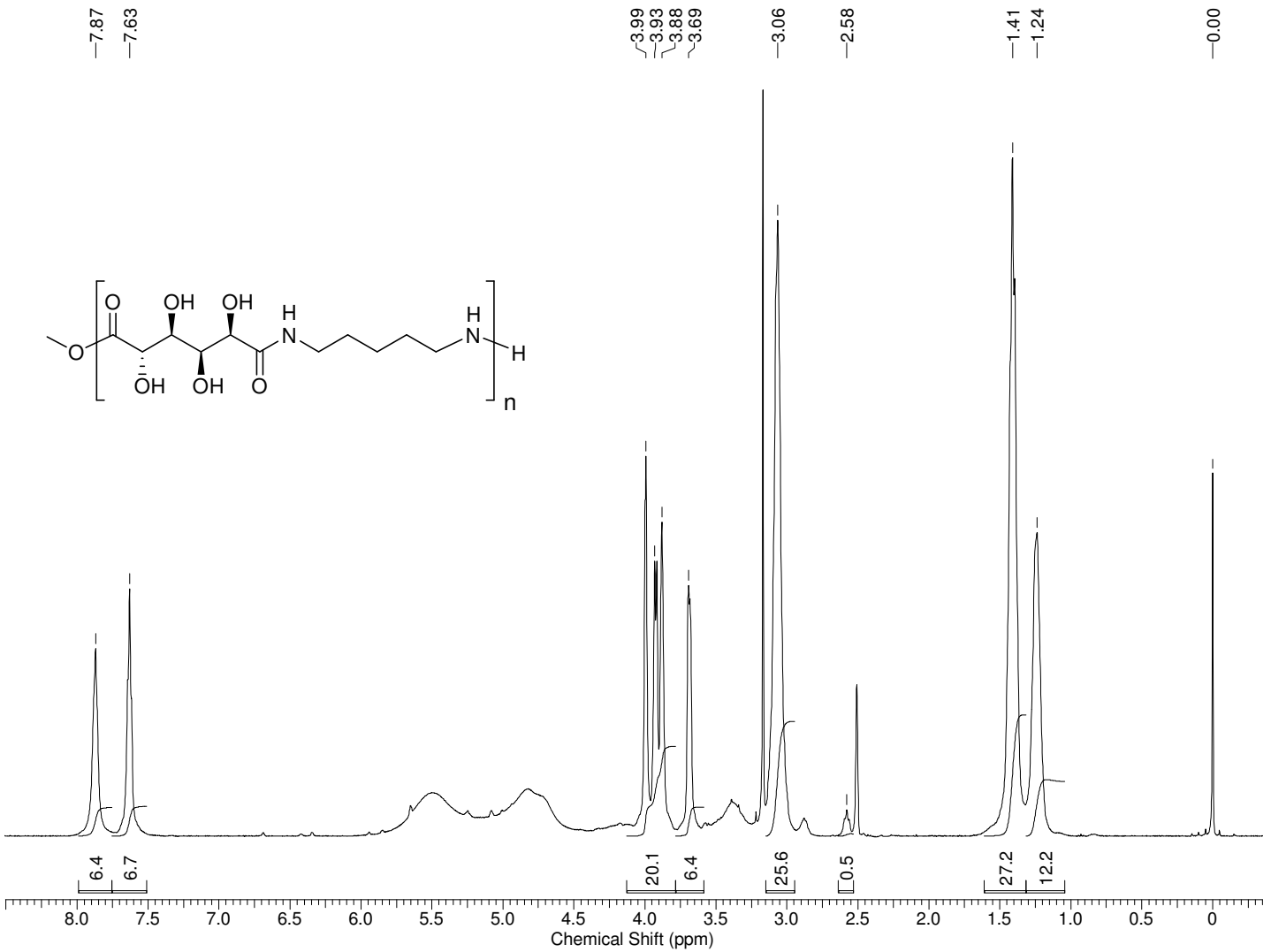
Appendix C. Nuclear Magnetic Resonance Spectra from Stereo Random Poly(alkylene D-glucaramide) Pre-polymers



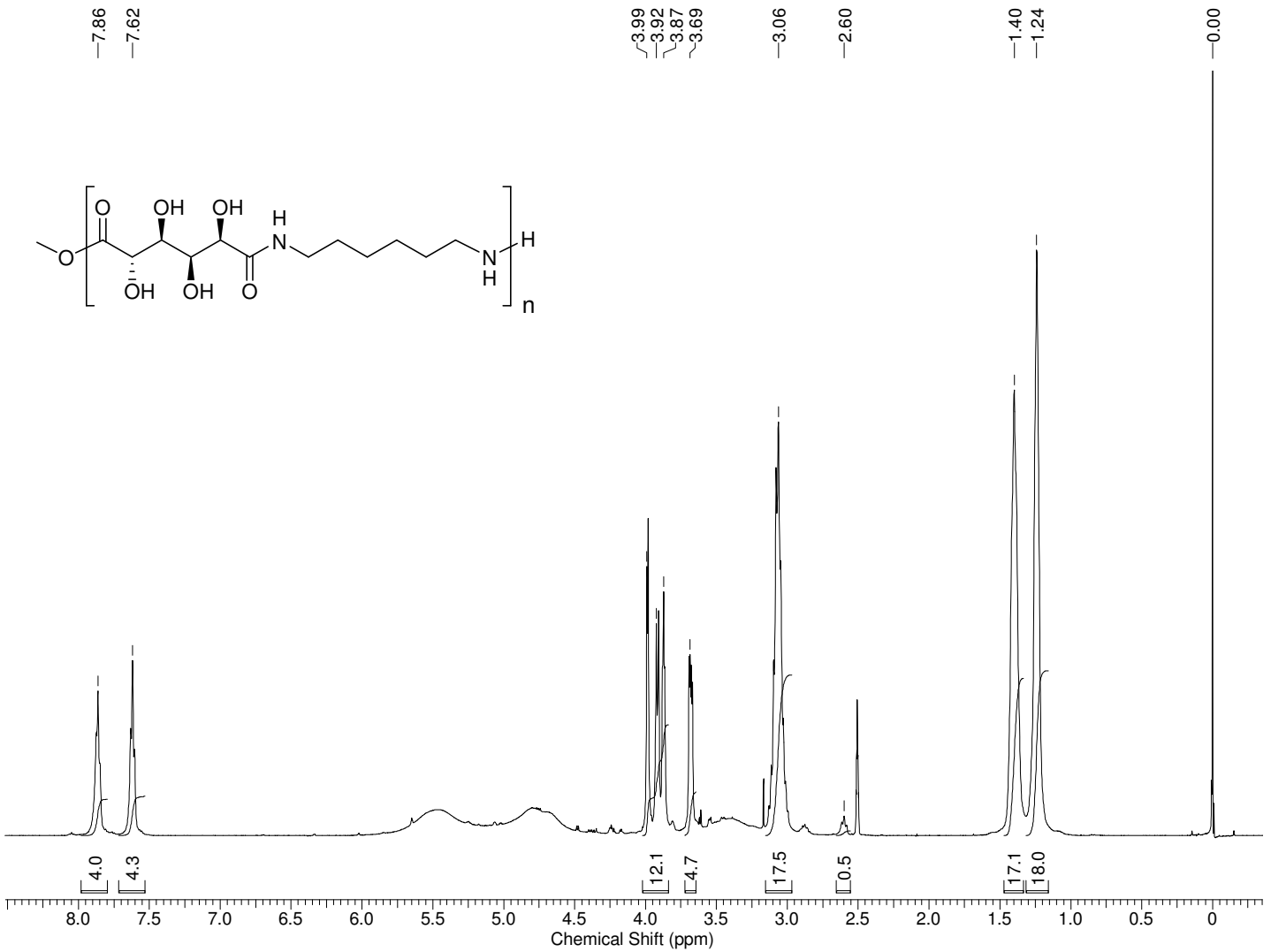
Poly(ethylene D-glucaramide) pre-polymer ^{1}H NMR spectrum (D_2O; 1% *t*-butyl alcohol ref., 1.20 ppm)



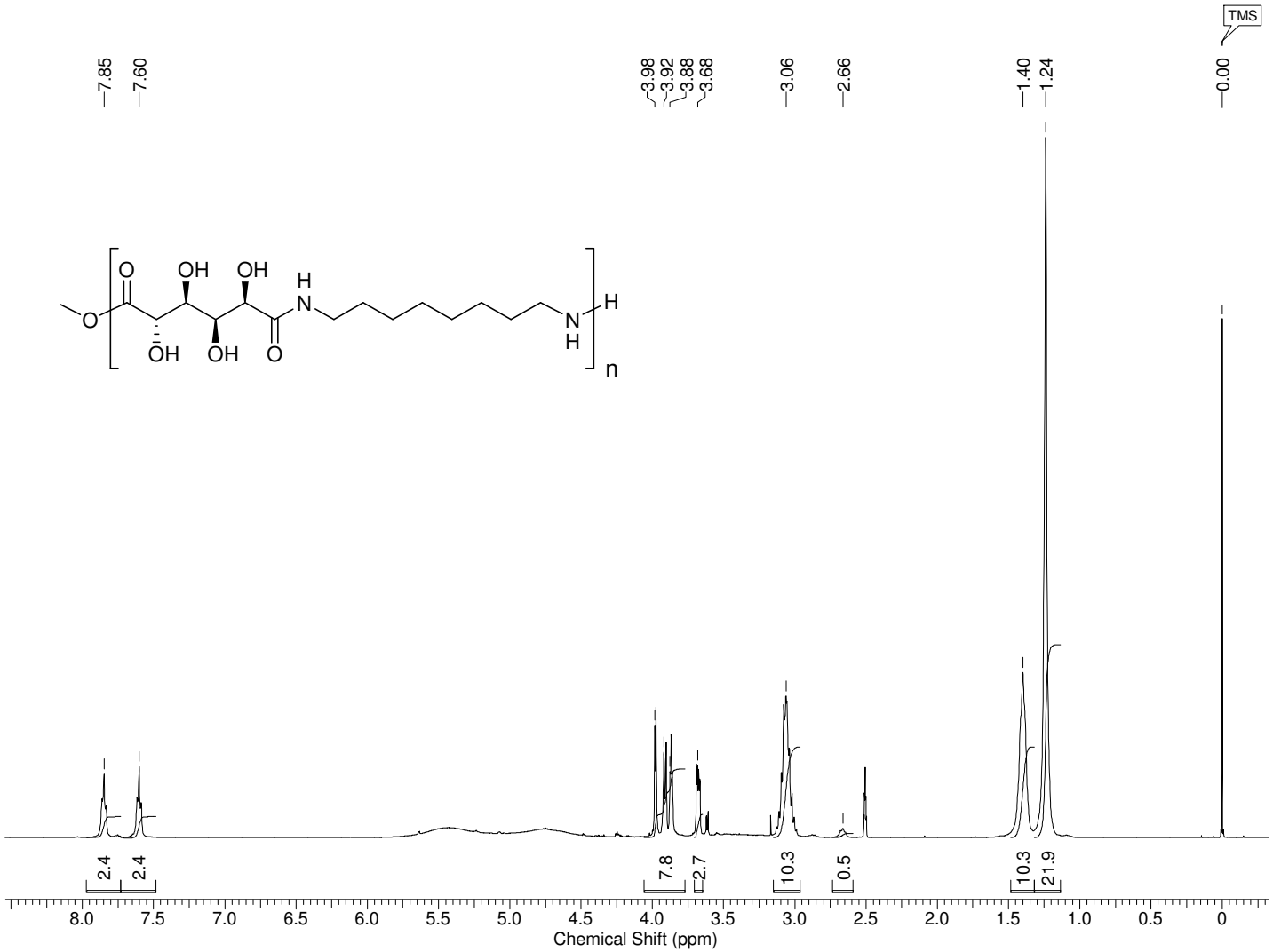
Poly(tetramethylene D-glucaramide) pre-polymer ^{1}H NMR spectrum (DMSO-d_6; TMS ref., 0.00 ppm)



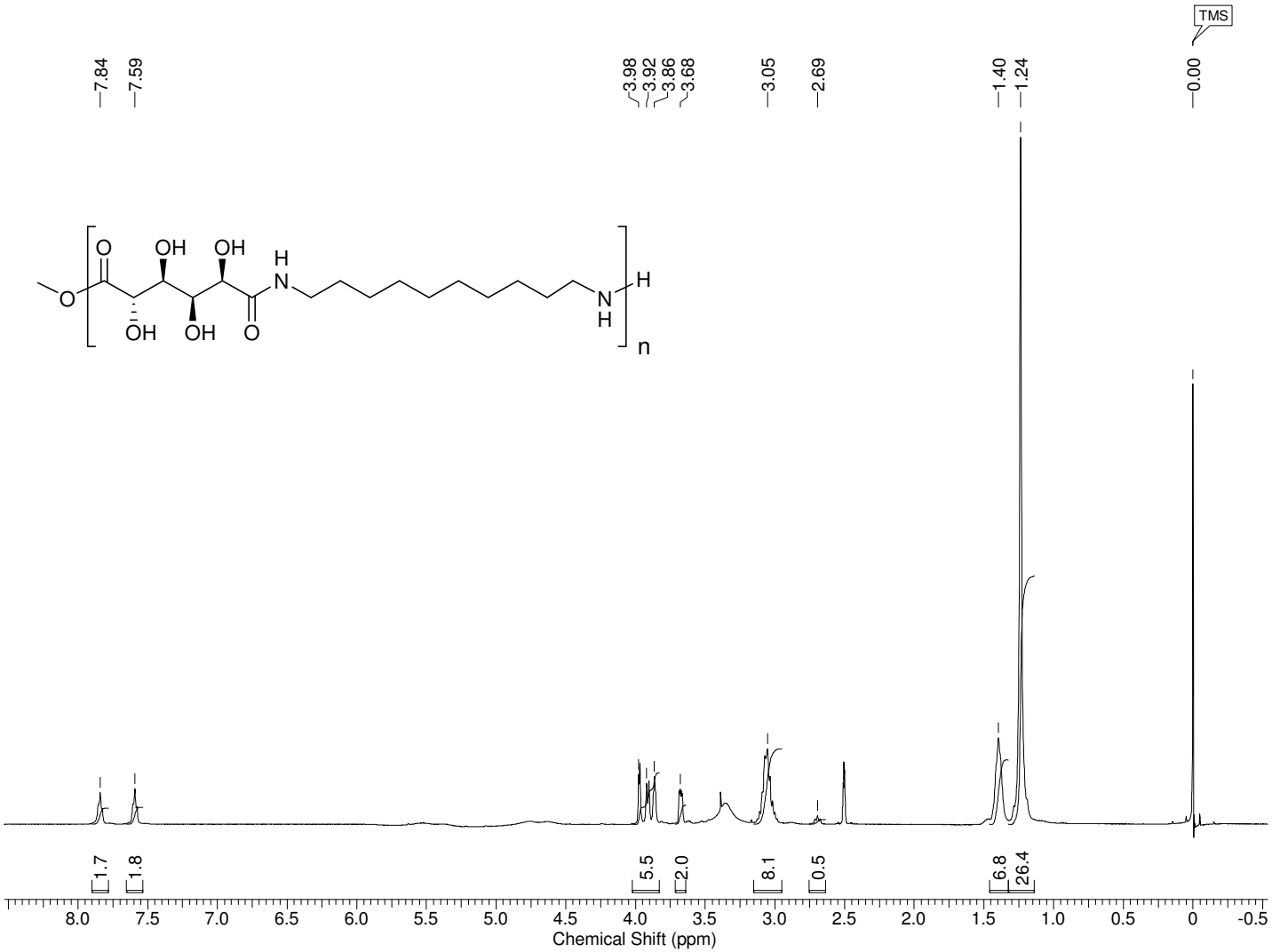
Poly(pentamethylene D-glucaramide) pre-polymer ^{1}H NMR spectrum (DMSO-d_6; TMS ref., 0.00 ppm)



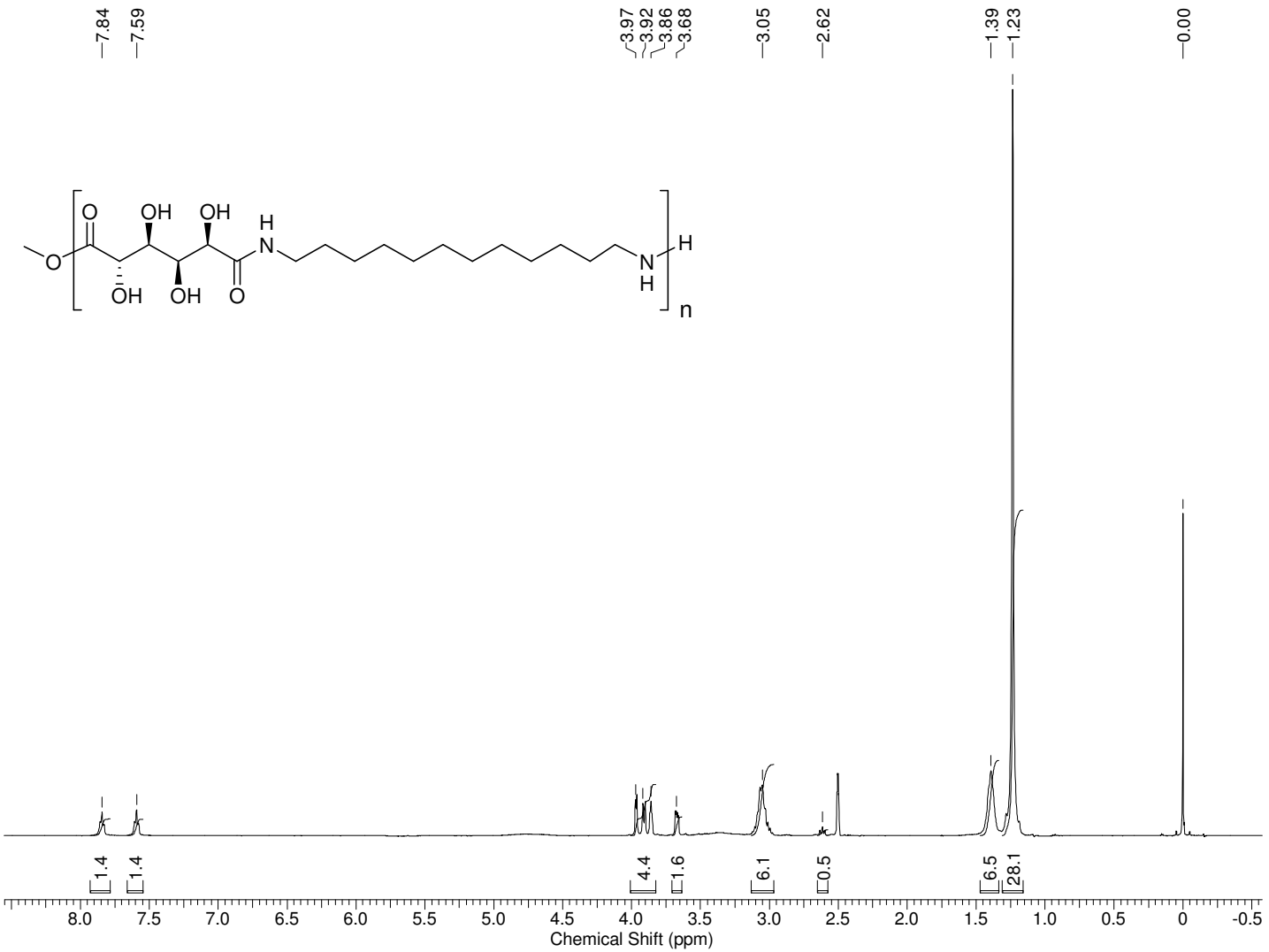
Poly(hexamethylene D-glucaramide) pre-polymer ^{1}H NMR spectrum (DMSO-d_6; TMS ref., 0.00 ppm)



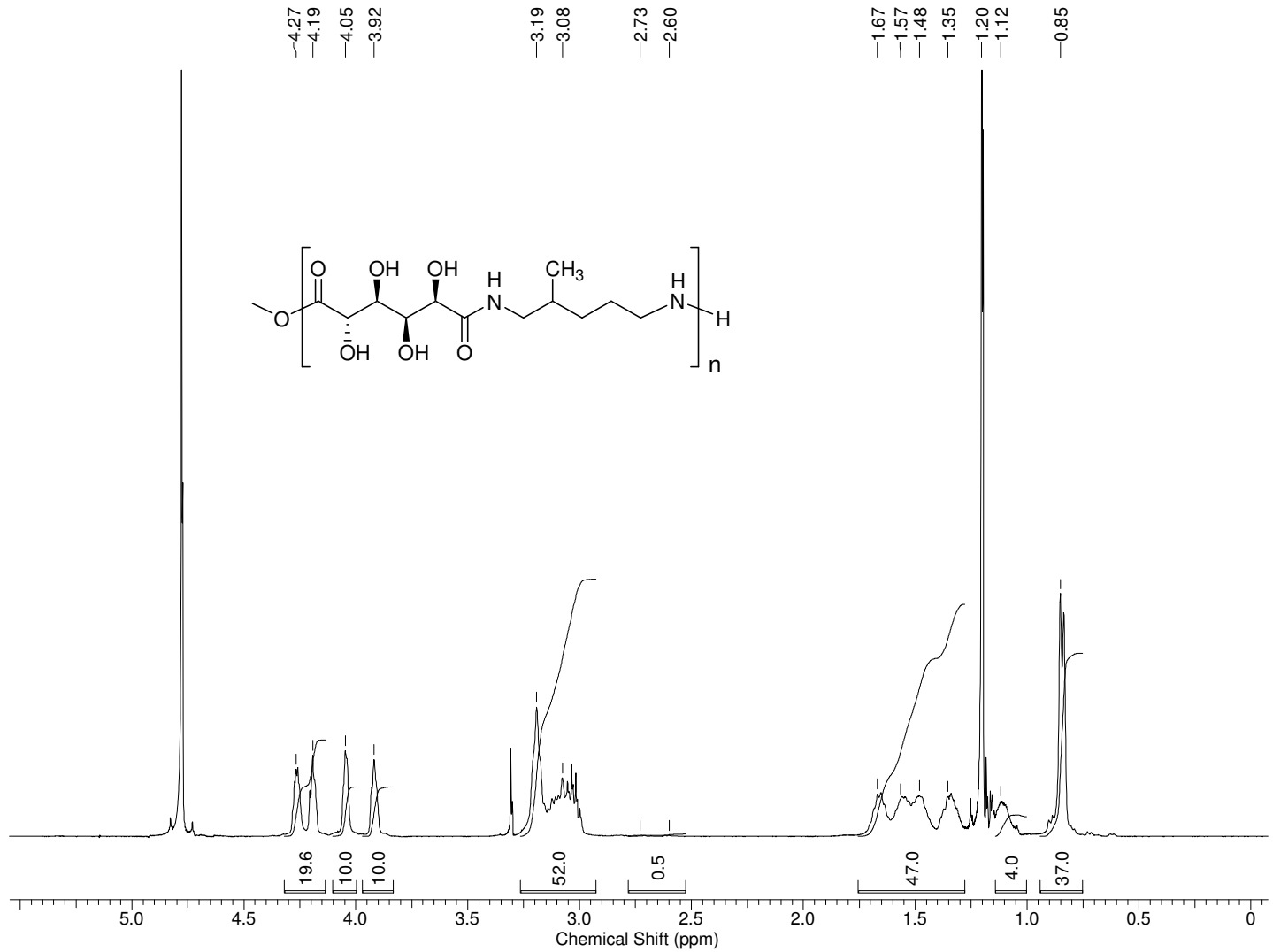
Poly(octamethylene D-glucaramide) pre-polymer ^{1}H NMR spectrum (DMSO-d_6; TMS ref., 0.00 ppm)



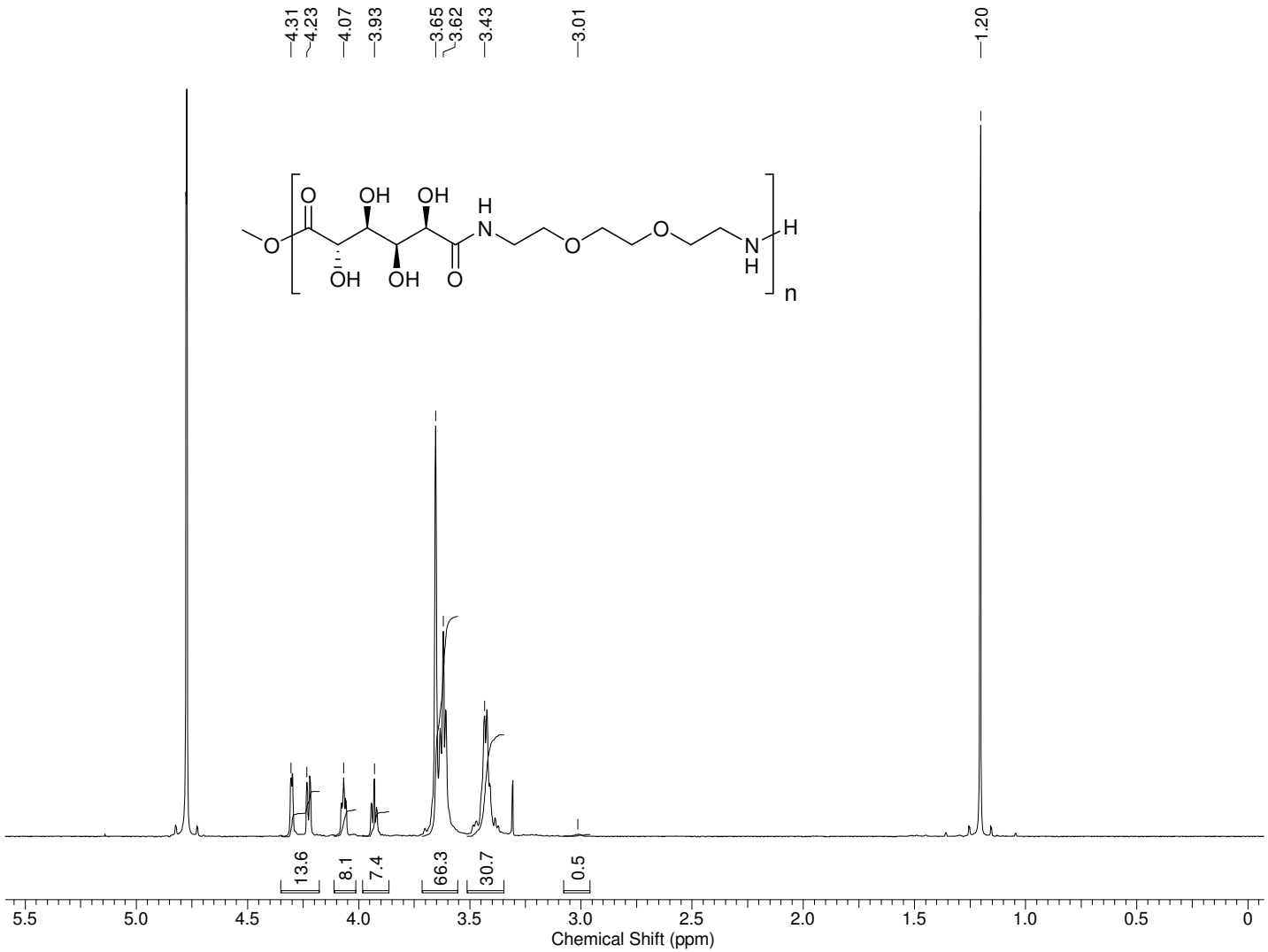
Poly(decamethylene D-glucaramide) pre-polymer ^{1}H NMR spectrum (DMSO-d_6; TMS ref., 0.00 ppm)



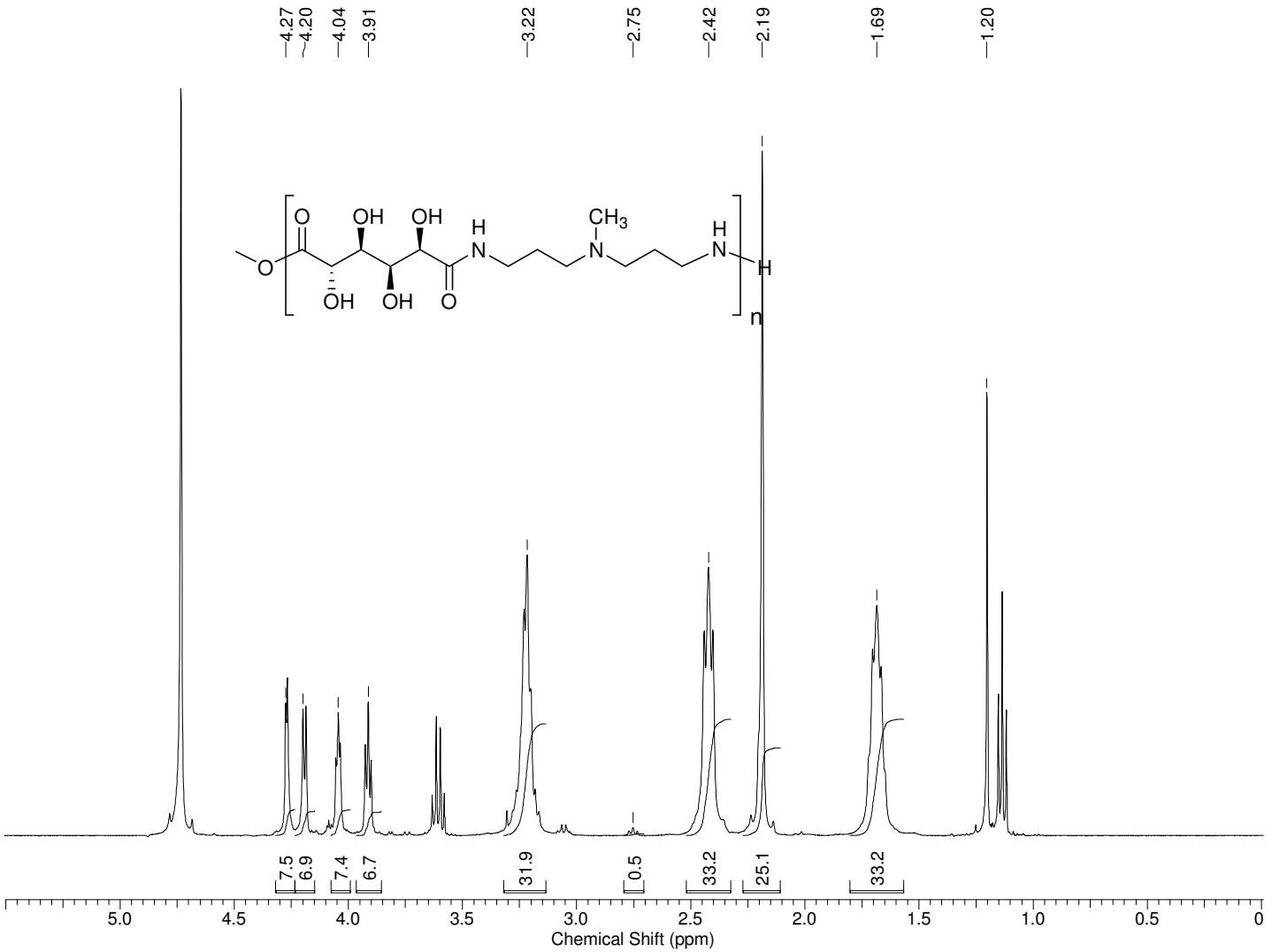
Poly(dodecamethylene D-glucaramide) pre-polymer ^{1}H NMR spectrum (DMSO-d_6; TMS ref., 0.00 ppm)



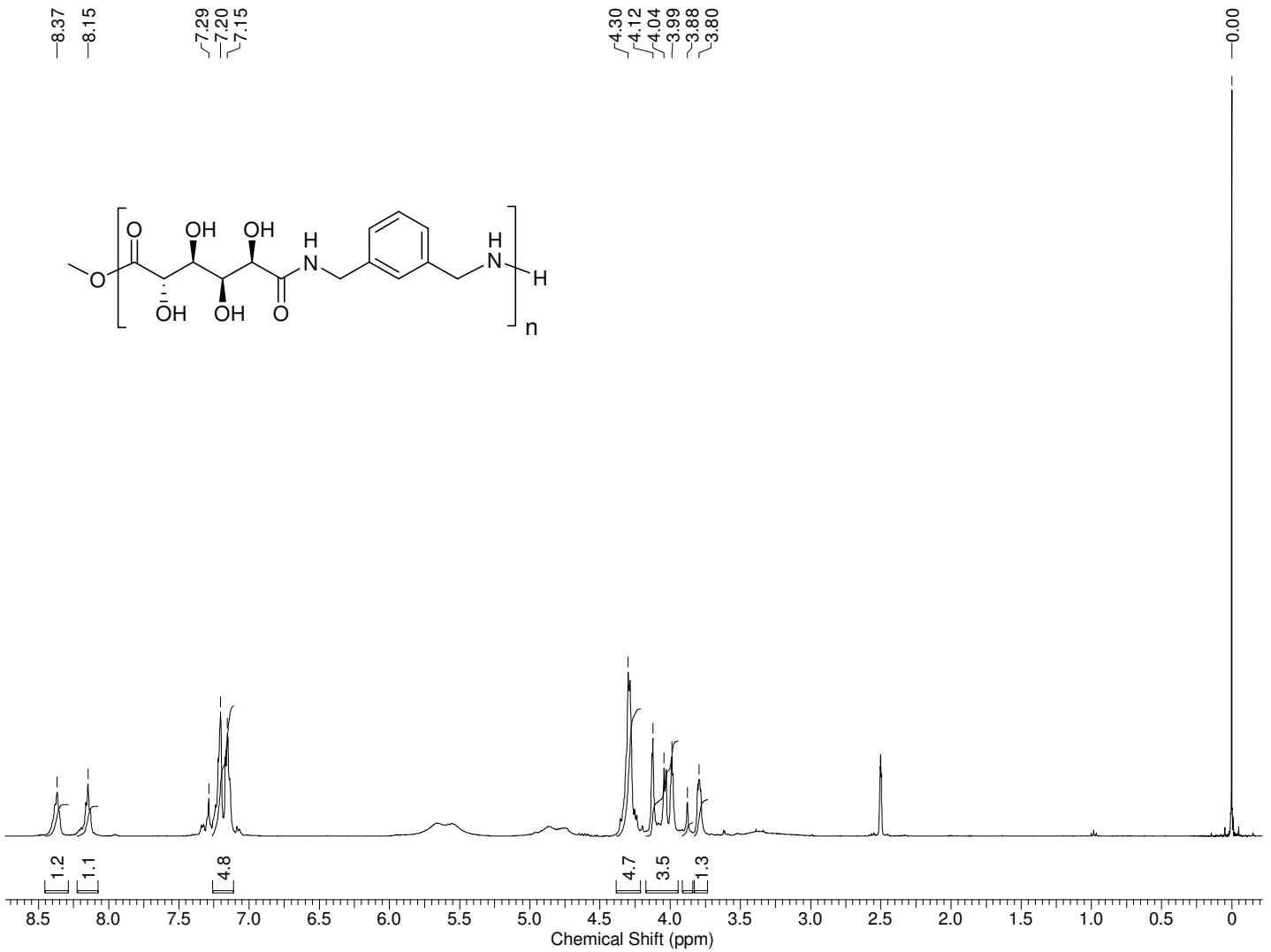
Poly(2-methylpentamethylene D-glucaramide) pre-polymer ^{1}H NMR spectrum (D_2O; 1% *t*-butyl alcohol ref., 1.20 ppm)



Poly(3',6'-dioxaoctamethylene D-glucaramide) pre-polymer ^{1}H NMR spectrum (D_2O; 1% *t*-butyl alcohol ref., 1.20 ppm)

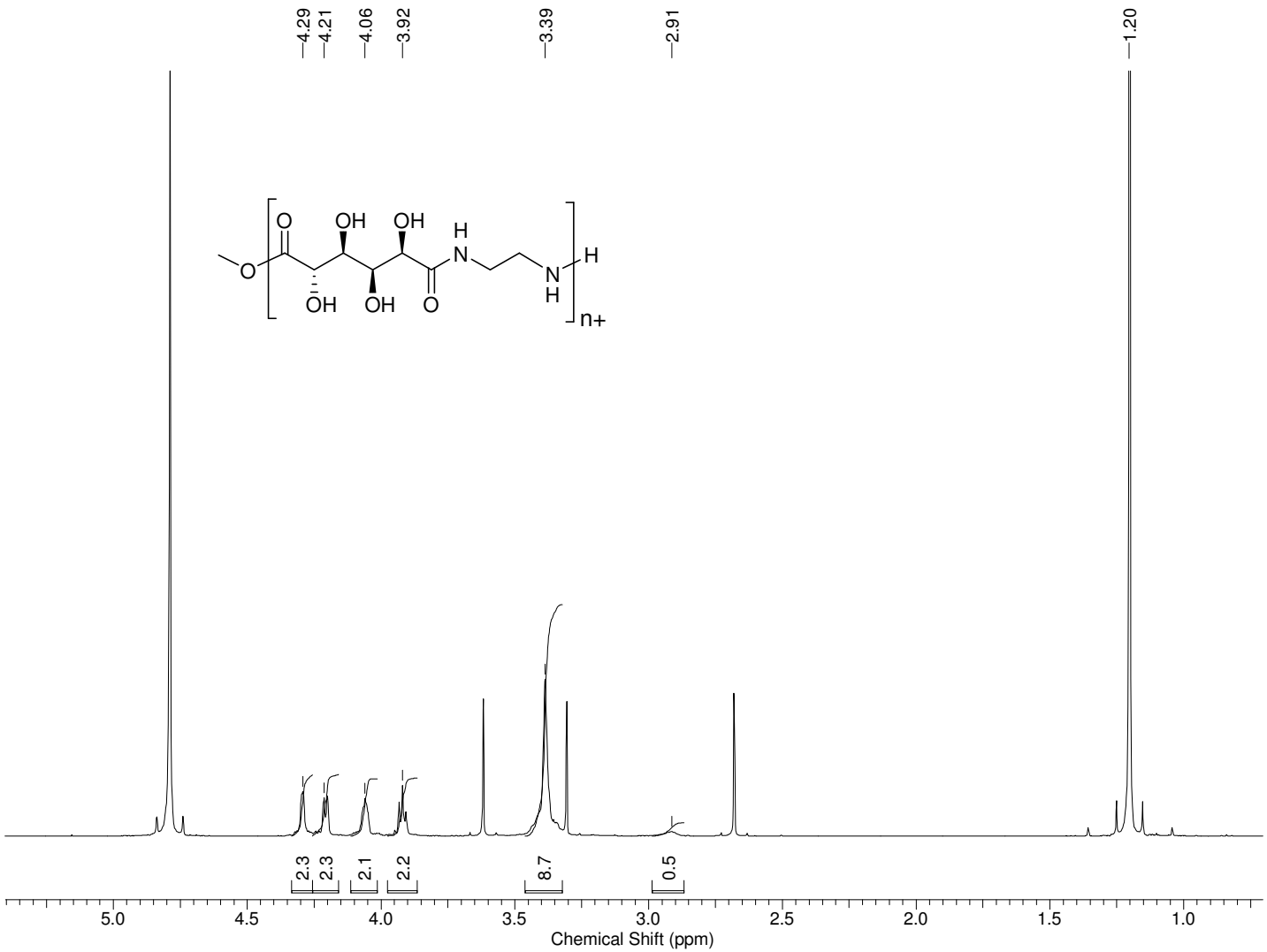


Poly(4'-aza-*N*-methylheptamethylene D-glucaramide) pre-polymer ^{1}H NMR spectrum (D_2O; 1% *t*-butyl alcohol ref., 1.20 ppm)

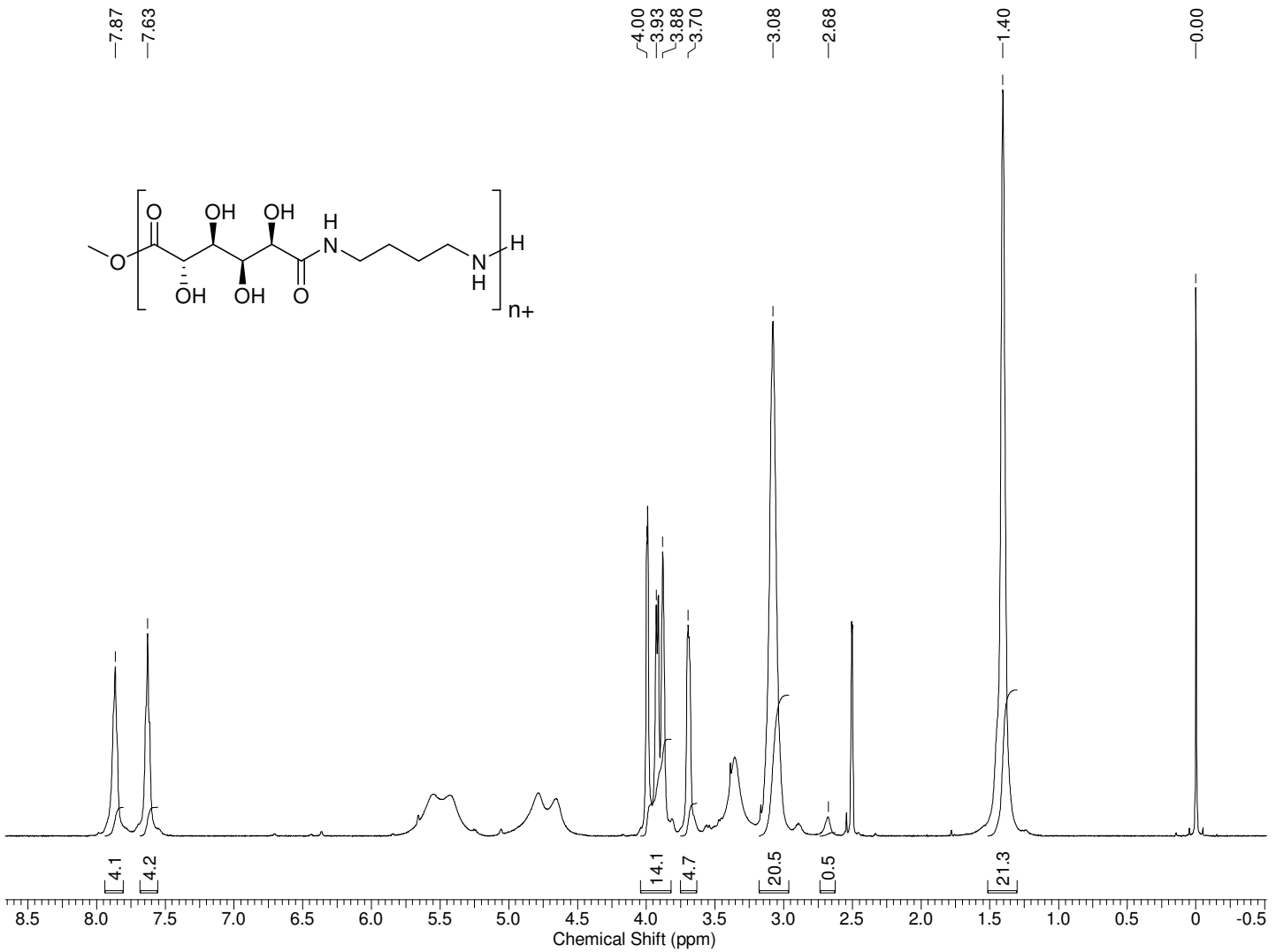


Poly(*m*-xylylene D-glucaramide) pre-polymer ^{1}H NMR spectrum (DMSO-d_6; TMS ref., 0.00 ppm)

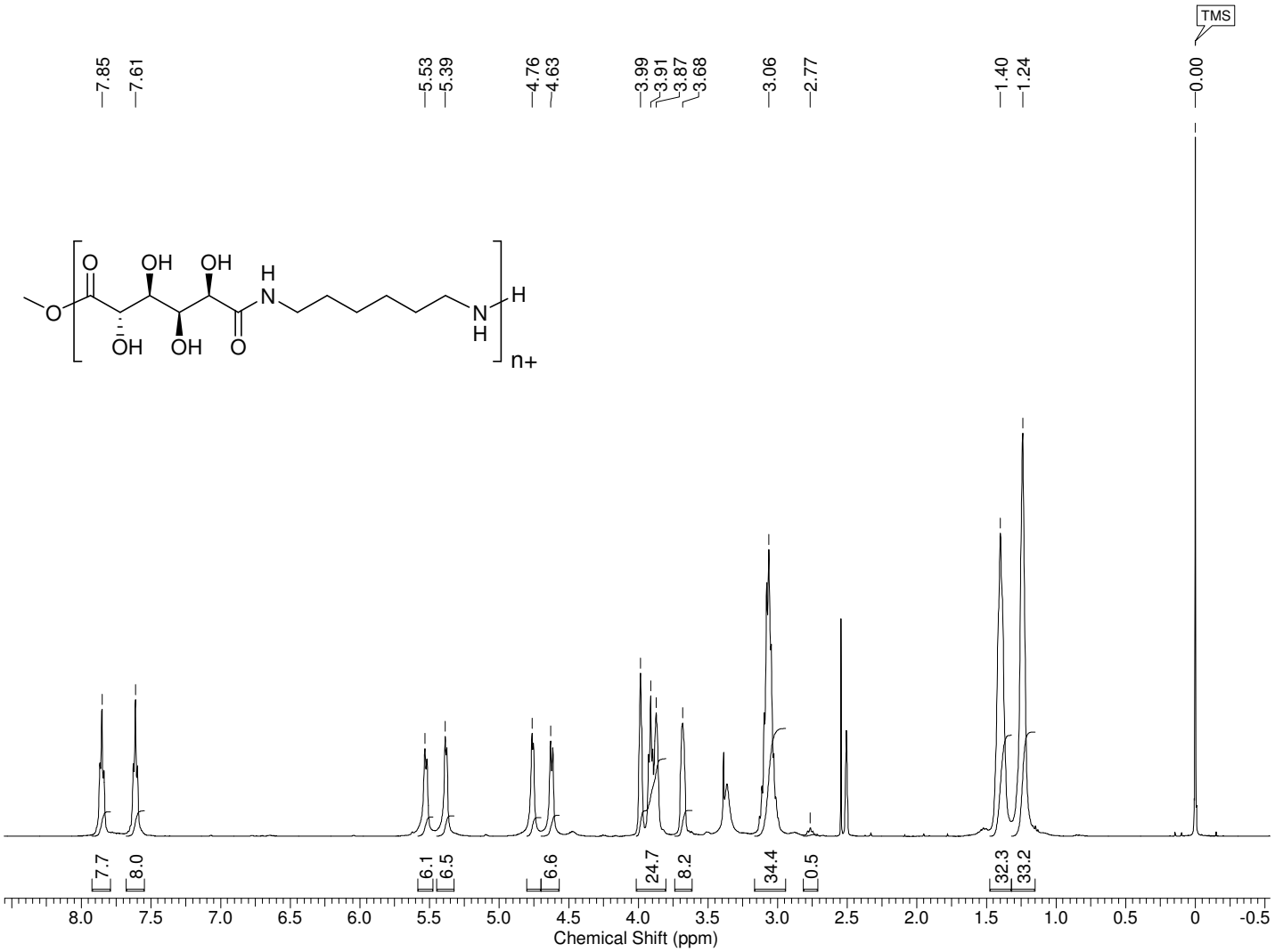
Appendix D. Nuclear Magnetic Resonance Spectra from Stereo Random Poly(alkylene D-glucaramide) Post-polymers



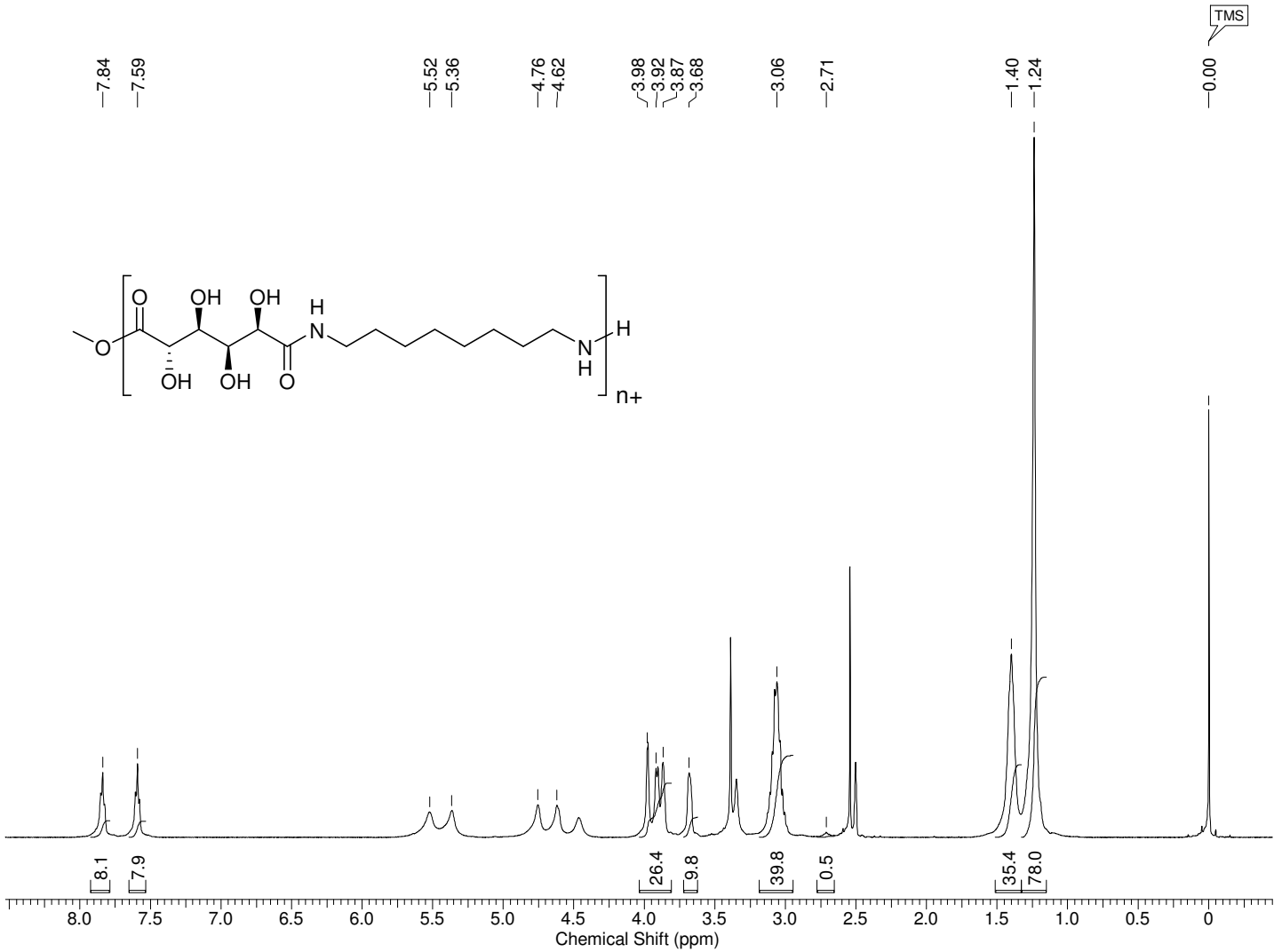
Poly(ethylene D-glucaramide) post-polymer ^{1}H NMR spectrum (D_2O; 1% *t*-butyl alcohol ref., 1.20 ppm)



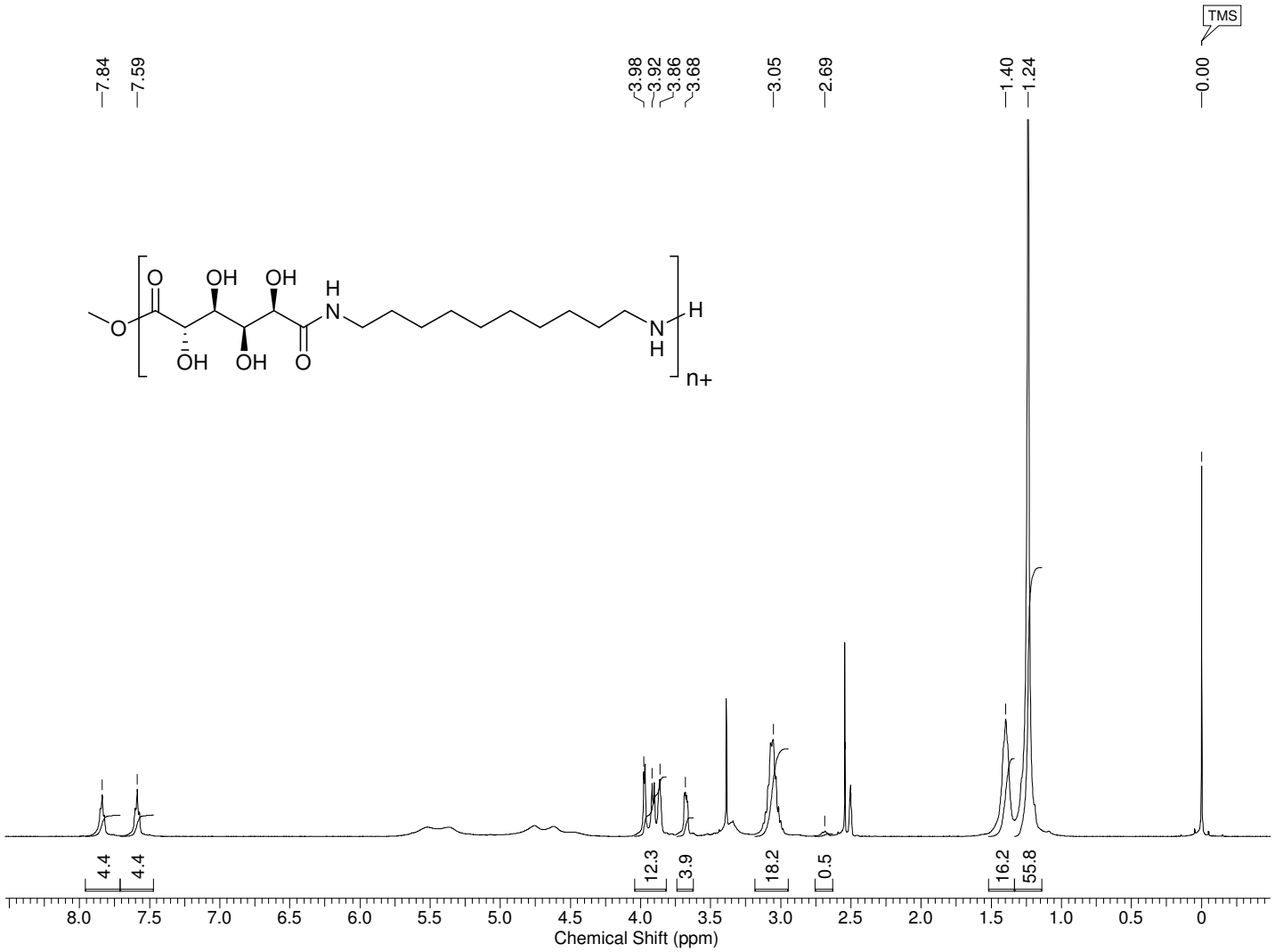
Poly(tetramethylene D-glucaramide) post-polymer ^{1}H NMR spectrum (DMSO-d_6; TMS ref., 0.00 ppm)



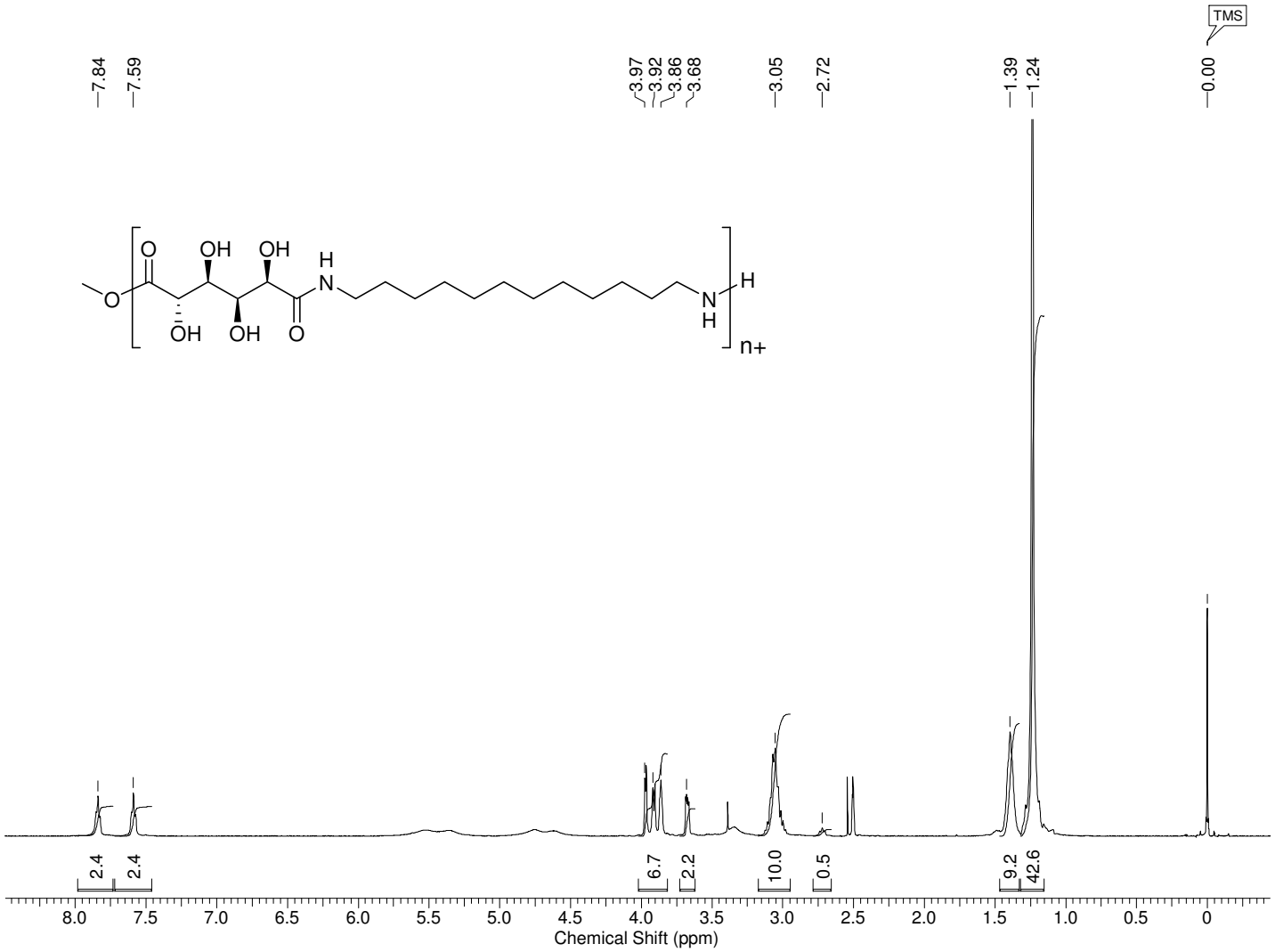
Poly(hexamethylene D-glucaramide) post-polymer ^{1}H NMR spectrum (DMSO-d_6; TMS ref., 0.00 ppm)



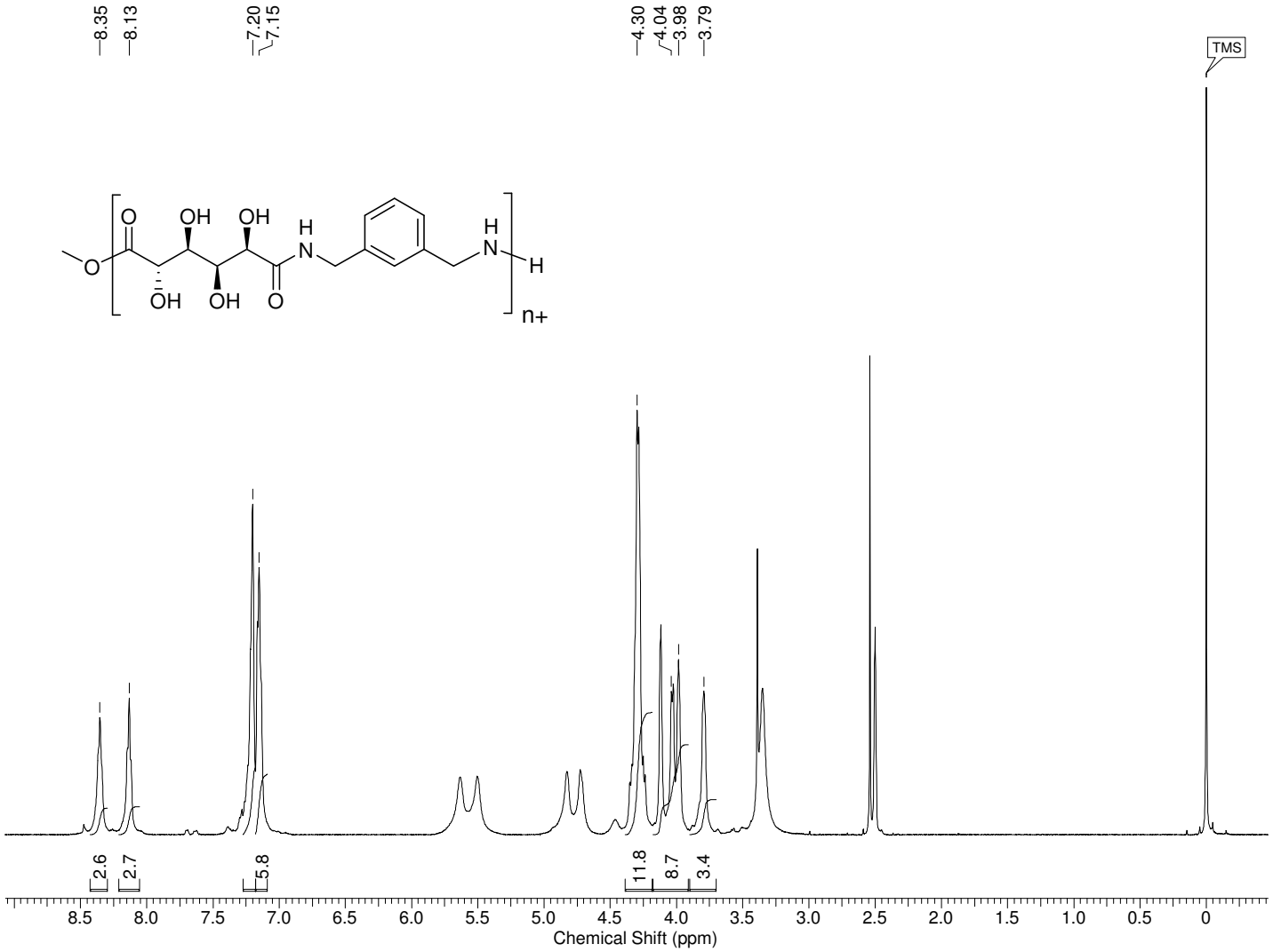
Poly(octamethylene D-glucaramide) post-polymer ^{1}H NMR spectrum (DMSO-d_6; TMS ref., 0.00 ppm)



Poly(decamethylene D-glucaramide) post-polymer ^{1}H NMR spectrum (DMSO-d_6; TMS ref., 0.00 ppm)



Poly(dodecamethylene D-glucaramide) post-polymer ^{1}H NMR spectrum (DMSO-d_6; TMS ref., 0.00 ppm)



Poly(*m*-xylylene D-glucaramide) post-polymer ^{1}H NMR spectrum (DMSO-d_6; TMS ref., 0.00 ppm)