博士論文（要約）

Synthesis and characterization of polyamides and polyesters from D-glucaric acid

（グルカル酸を原料としたポリアミドとポリエステルの合成および物性評価）

ウー　ユーシン
吴 宇鑫
WU YUXIN

TABLE OF CONTENTS

Page

LIST OF FIGURES

Page

LIST OF SCHEMES

Page

LIST OF TABLES

Page

Chapter 1

General introduction

1.1. General background

Polymer materials are widely used materials which can be easily found around us, and the daily life of us has been inseparable from the polymer materials (Namazi 2017). Most polymer materials we used today such as polyethylene, polypropylene and polyethylene terephthalate are synthesized from petroleum-based monomers. However, petroleum resources are limited (Sorrell et al. 2010), and the polymers synthesized from petroleum usually are environmentally unfriendly materials because of their low biodegradability (Harding et al. 2007). Environmental problems are getting worse with the use of petroleum polymers recently. For the sustainable development of society, degradable polymers synthesized from renewable bio-based monomers have obtained a lot of attentions (Gandini 2008).

To reduce the use of petroleum-based polymers, the research of bio-based polymer has been greatly developed in the past few decades (Mohanty, Misra and Drzal 2002). Among these renewable bio-based resources, carbohydrates and their derivatives are very important sustainable building blocks because of their large supply, rich stereochemistry and environmentally friendly (Iwata 2015, Galbis and Garcia-Martin 2010, Galbis et al. 2016). Recently, bio-based polymers like polysaccharides, polyhydroxyalkanoates, polylactide, sugar-based polymers etc. have been studied widely.

1.2. Bio-based polymers

1.2.1. Polysaccharides

Polysaccharides are a class of carbohydrate-based polymers that have received a lot attentions recent years, and these polysaccharides needs chemical modified to improved their potential of material application. (Heinze et al. 1990, Klemm et al. 2011, Iwata 2015). Cellulose, one of polysaccharides, and its derivatives have been investigated and used for a long time because it is the most abundant of all naturally occurring organic compounds (Edgar et al. 2001, Wang, Lu and Zhang 2016). Other kinds of polysaccharides derivatives with environmental friendly properties such as xylan (Ebringerova and Heinze 2000, Fundador et al. 2012), glucomannan (Danjo et al. 2014), pullulan (Enomoto-Rogers et al. 2015), paramylon

(Hongyi Gan 2017) have been synthesized and their properties were analyzed. Furthermore, polysaccharide like linear α-1,3-glucan can be produced by in vitro synthesis (Puanglek et al. 2016).

1.2.2. Polyhydroxyalkanoates (PHAs)

PHAs are also a class of biopolymers can be produced from microorganism, and the research about PHAs attracted many attentions because of its sustainability and biodegradability. (Anderson and Dawes 1990, Sudesh, Abe and Doi 2000). PHAs can be crystalline or rubbery; these properties of PHAs can be adjusted by compositions. For instance, poly(3-hydroxylbutyrate) (P(3HB)) is highly crystalline with brittle and stiff properties; the crystallinity and Tm can be lowered by introducing other medium chain length 3-hydroxyalkanoate (mcl-3HA) so that the obtained copolyester can be ductility and toughness and easier to process (Noda et al. 2005). However, the high production costs of PHAs limits its entry into the commodity market (Philip, Keshavarz and Roy 2007).

1.2.3. Polylactide (PLA)

PLA is also a class of biodegradable plastics that have been investigated and used widely recently because of its renewable, environmental friendly and biocompatibility (Nampoothiri, Nair and John 2010). PLA has many applications such as biomedical devices and packaging materials (Auras, Harte and Selke 2004, Lasprilla et al. 2012). However, PLA is a very brittle polymer material, and its degradability is slow; also with the lack of reactive side chain groups, it is difficult to modify the surface of PLA (Rasal, Janorkar and Hirt 2010). To improve physical properties of PLA-based polymer material, one way is that PLA can be used as a side chain attached to other compound with multifunction side chain groups. Recently, Y. Teramoto et. al. (Teramoto and Nishio 2003) reported a new class of graft polymers which PLA was grafted to cellulose diacetate chains; drawability of these polymers increased with increasing PLA content and the maximum elongation at rupture was be ca. 2000 %. PLA also has been used to attach the polymer chains of polymers such as polysaccharide to produce new class of bio-based block polymers with improved thermal properties (Enomoto-Rogers and Iwata 2012, Enomoto-Rogers and Iwata 2013).

1.2.4. Sugar-based monomers

Bio-based polymers synthesized from sugar-based monomers have been reported frequently in recent years. The introduce of sugar-derived units into traditional polymers such as polyamides, polyesters are considered as a potential method to prepare novel biodegradable and biocompatible materials with the physical properties related to industrial polymer materials (Yokoe, Aoi and Okada 2005, Feng et al. 2011, Gregory, Lopez-Vidal and Buchard 2017). There are many kinds of sugar-based monomers such as alditols, aldonic acids and aldaric acids (Galbis et al. 2016).

Alditols such as isomannide, isoidide and isosorbide have been used as monomers to synthesize renewable polymers (Shearouse et al. 2015, Fenouillot et al. 2010). Recently, Mitsubishi Chemical Holdings Corporation (Japan) has commoditized a new bio-based engineering plastic DURABIO^{TM}, which is a bio-based polycarbonate resin derived mainly from plant-based isosorbide, and this polymer combines the most of the advantageous properties of polycarbonate (PC) and polymethacrylate (PMMA) (Mitsubishi Chemical). Aldonic acids such as 2,4;3,5-di-*O*-methylene-D-gluconic acid was used to synthesize polyester, but the molecular weight was low (Mehltretter and Mellies 1955). Aldaric acids such as ribaric acid (Hinton et al. 2013), xylaric acid (Hinton et al. 2013), arabinaric acid (Munoz-Guerra et al. 2009), tartaric acid (Alla et al. 1997), galactaric acid (Lavilla et al. 2011), mannaric acid (Mancera et al. 2003) and D-glucaric acid (Hashimoto, Okada and Honjou 1990, Kiely, Chen and Lin 1994) are potential monomers to polymerization of polymers.

In the case of aldaric acids, because of their two carboxyl groups at ends of molecular chains, are considered to have potential to be used as dicarboxylic acid monomers to produce polyesters and polyamides. Therefore, aldarc acids can be used for synthesized carbohydrate-based nylon-type polyamides which are considered as potential novel bio-based materials and received great attention recently owing to their biocompatibility, good thermal and mechanical properties (Orgueira et al. 2001).

Because of the sugar-based monomers mostly are multifunctionalities with hydroxyl groups and carboxyl groups. In order to avoid lactone formations by reaction between these functional groups, some functional groups need protection−deprotection chemistry process to prepare available sugar-based monomers for polymerization.

1.3. D-glucaric acid (GA)

1.3.1 Introduction of GA

D-Glucaric acid (GA) is an aldaric acid based on an acyclic sugar main-chain with a carboxyl group at either end of its structure (Figure 1-1). GA occurs naturally in low concentrations in various vegetables and fruits (Walaszek et al. 1996). GA can be obtained by the oxidation of D-glucose with nitric acid, nitroxide derivatives (Merbouh et al. 2001), or microorganisms (Moon et al. 2009, Moon et al. 2010). Because of the low yield of GA production by chemical oxidation from D-glucose or D-gluconic acid, its complex stereochemical structure and easy lactones formation, the application of GA had been limited. Recently, the mass production of GA using bioengineering method have been developed rapidly (Ito, Masaki and Mikuni 2013). GA has become a sustainable resource and can be used in industry in large quantities.

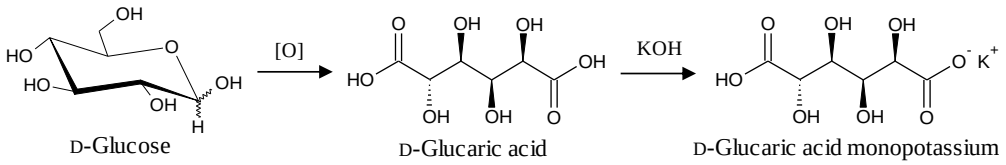


Figure 1-1. General oxidation conversion of D-glucose to D-glucaric acid, and D-glucaric acid monopotassium.

1.3.2 Application of GA

GA has been reported as a function as an anticancer agent (Walaszek 1990). Also in a report recently published by the US Department of Energy (DOE), GA was listed as one of the top twelve value-added building blocks that can be produced from sugars and subsequently converted to bio-based chemicals or materials (Werpy and Petersen 2004). Regarding environmental concerns, bio-based polymers such as poly(lactic acid)s or polysaccharides are biodegradable (Iwata 2015); unlike polymers such as nylons and poly(ethylene terephthalate), they are degraded by microorganisms in the environment. GA, which can be obtained from naturally abundant glucose, is promising as a monomer for novel sugar-based polymers with attractive properties such as biodegradability, amphiphilicity, and self-organizing properties. Since it has four hydroxyl groups in the main chain of glucaric acid, it may possibly be used as a plastic material (container, medical material, etc.), activator of detergent, adhesive and the like. Furthermore, in terms of polymer science, aldaric acids such as GA that have two carboxyl groups, one at either end, have significant potential as building blocks for the construction of polymers, including polyesters and polyamides.

Normally, GA is separated and purified as a potassium salt formation, D-glucaric acid monopotassium (GAK), because of an equilibrium state including lactonization in an aqueous solution (Brown et al. 2007).

Because GA easily forms lactones (Figure 1-2), the application of GA is limited. Therefore, protection of hydroxyls group of GA are major issues before polymerization.

In addition to GA, other kinds of aldaric acids such as tartaric acid, galactaric acid have been reported that all hydroxyl groups were protected by methyl groups, acetyl groups or aldehyde acetal group to prevent lactone formation, then polymerized as monomers to obtain novel bio-based polymers.

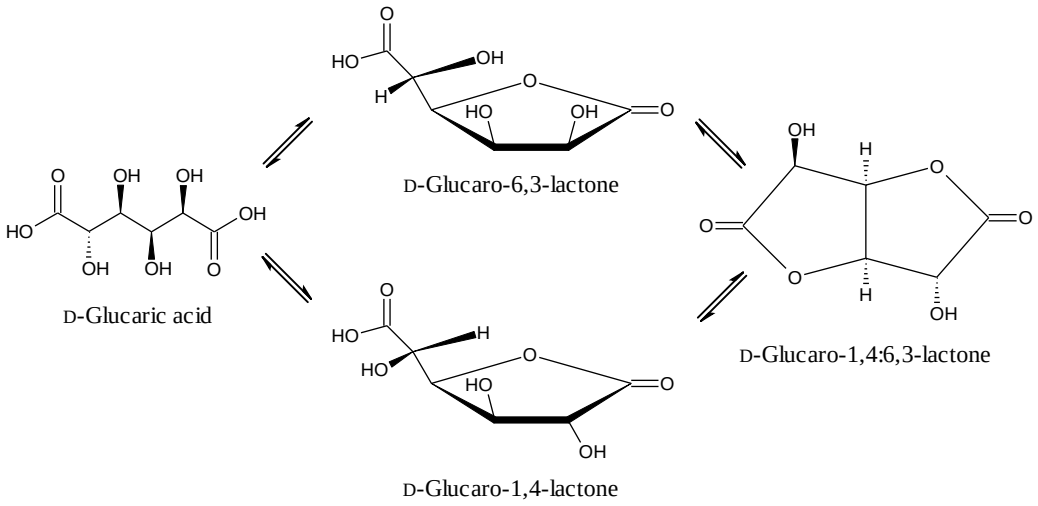


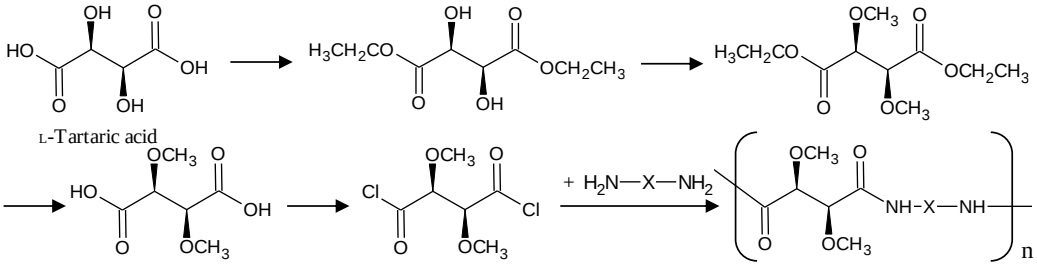
Figure 1-2. Equilibrium of D-glucaric acid and lactones。

1.4. Polymers synthesized from aldaric acids

The research of bio-based polymer has been greatly developed in the past few decades to reduce the use of petroleum-based polymers. Among these renewable bio-based resources, carbohydrates and their derivatives are very important sustainable building blocks because of their large supply, rich stereochemistry and environmentally friendly (Mohanty et al. 2002). Aldaric acids are a class of sugar acid having a carboxylic acid at both ends (Henkensmeier et al. 2004), and so far there have been examples in which synthesis of polymers was tried by polycondensation with diamines or diols using aldaric acids such as L-tartaric acid (Wu et al. 2010), galactaric acid (Lavilla et al. 2011), mannanic acid (Mancera et al. 2003).

Wu et al. (Wu et al. 2010) protected the carboxylic acid at both ends of L-tartaric acid by ethyl ester, then protected hydroxyl group by methylation with sodium hydride and methyl iodide as shown in Figure 1-3. Furthermore, the protected carboxylic acid was deprotected and

synthesized into an acid chloride. Finally, solution-polymerizes it with diamine to obtain a polyamide. The number average molecular weight of the obtained polyamide was from 1.4 × 10^4 to 3.5 × 10^4. T_g was from 106 to 191 °C, T_m was 223 °C, 10% (wt) thermal decomposition temperature $T_{d10\%}$ was from 303 to 352 °C.



Reagents: (a) C_2H_5OH, CCl_4, H_2SO_4; (b) NaH, Et_2O, CH_3I; (c) NaOH(aq), HCl; (d)PCl_5, C_6H_6

Figure 1-3. Synthesis of polyamides from L-tartaric acid (Wu et al. 2010)

Alla et al. also reported a different way to protect the hydroxyl groups of L-tartaric acid (Alla et al. 2005) by acetyl groups instead of methyl groups as shown in Figure 1-4. These polyamides were insoluble in water, chloroform, and soluble in DMSO, NMP, TFE, TFA. The M_ws of these polyamides were from 5 000 to 20 000. These polyamides were crystalline confirmed by DSC and XRD. Furthermore, the acetyl groups could be removed by alkaline solution. After deprotected, the T_g decreased, and T_m increased.

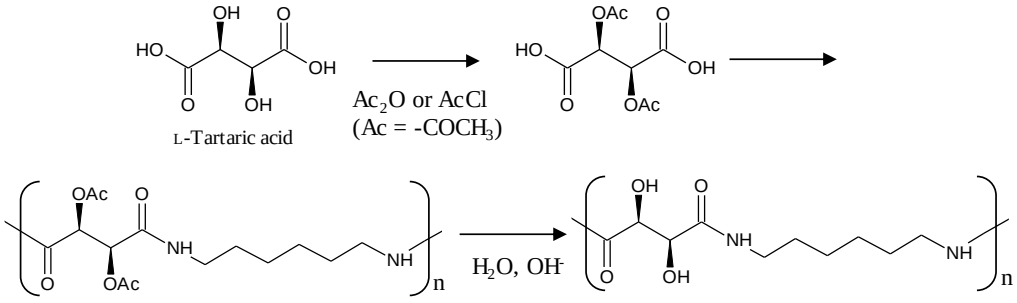


Figure 1-4. Synthetic route leading to polyamides from L-tartaric acid (Alle et al. 2005)

Mansour et al. (Mansour et al. 1990)acetylated the four hydroxyl groups of galactaric acid using acetic anhydride as a acetylation reagent and concentrated sulfuric acid as a catalyst. Then both carboxylic acid at ends were turned into acyl chloride and polymerized with diamines using DMAc as a solvent as shown in Figure 1-5. The structure was confirmed, but the molecular weights were not measured.

Thiem et al. (Bachmann and Thiem 1992) also protected the hydroxyl groups of galactaric acid with acetyl group, then polymerized with diamine by interfacial polymerization using chloroform and aqueous solution of sodium carbonate as shown in Figure 1-5. The number average molecular weights ranged from 4.2×10^3 to 5.8×10^4. T_ms ranged from 171 to 220 °C.

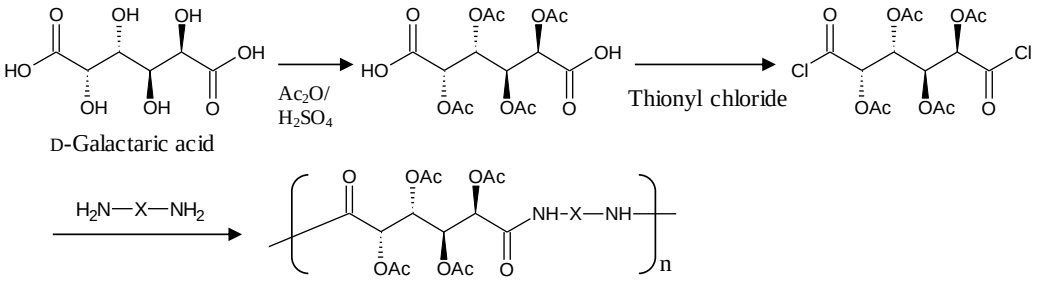


Figure 1-5 . Synthesis of polyamide from acetylated galactaric acid (Mansour et al. 1990) (Bachmann and Thiem 1992).

Mehtiö et al. (Mehtio et al. 2015) polymerized copolyanhydrides of carbohydrate-based galactaric acid and adipic acid as shown in Figure 1-6. Both ends of acetyl galactaric acid were methyl esterified with acetic anhydride using *p*-toluenesulfonic acid (PTSA) as a catalyst. copolyanhydrides were synthesized by anhydrating it and polymerition with an adipic anhydride. The weight average molecular weight of the obtained polymer was 1.1×10^4 at the maximum. T_g ranged from -28 to 60 °C, and T_m ranged from 60 to 106 °C, 10% (wt) thermal decomposition temperatures $T_{d10\%}$ ranged from 186 to 223 °C.

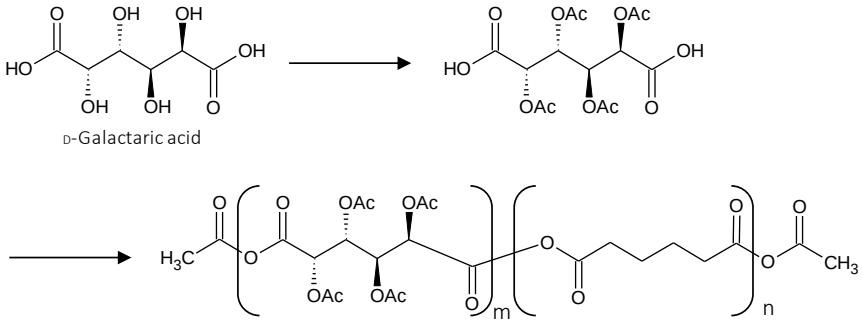


Figure 1-6. Reaction scheme from galactaric acid to poly(2,3,4,5-tetra-*O*-acetylgalactaric-*co*-adipic anhydride). （Mehtiö et al. 2015）

Lavilla et al. (Lavilla et al. 2011) acetalized the hydroxyl groups of galactaric acid at positions 2 and 3, 4 and 5, then polymerized with diol as shown in Figure 1-7. Dimethyl 2,3,4,5-di-*O*-methylene galactaric acid was synthesized from galactaric acid using concentrated sulfuric acid as a catalyst and methanol. Then, it polymerized with the diols. When titanium (IV) tetrabutoxide (TBT) was used as a catalyst, polymers having a number average molecular

weights ranged from 4.4×10^3 to 4.7×10^3 was obtained. Also, when dibutyltin oxide (DBTO) was used as a catalyst, a polymer having a number average molecular weight of 1.6×10^4 to 2.3×10^4 was obtained. T_g ranged from -61- to 6 °C, and T_m ranged from 51 to 86 °C, 5% (wt) thermal decomposition temperatures $T_{d5\%}$s ranged from 280 to 327 °C.

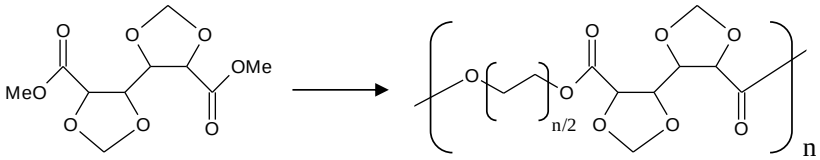
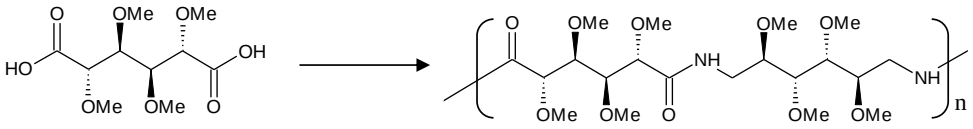


Figure 1-7. Polymerization from bicyclic acetalized galactaric acid (Lavilla et al. 2011)

Mancera et al. (Mancera et al. 2003) synthesized polymers from methylated D-mannanic acid as a monomer as shown in Figure 1-8. The weight average molecular weight of the polymer was 4.7×10^4.



2,3,4,5-Tetra-*O*-methyl-D-mannaric acid

Figure 1-8. Synthesis of polymers from 2,3,4,5-tetra-*O*-methyl-D-mannaric acid (Mancera et al. 2003).

In addition, as shown in Figure 1-9, methylated pentachlorophenyl L-arabinic acid and diol were used as monomers to synthesize polymers (Zamora et al. 2009). The number average molecular weight of the product was 6.3×10^3 to 1.7×10^4. T_g was about 67 °C and T_m ranged from 204 to 250 °C.

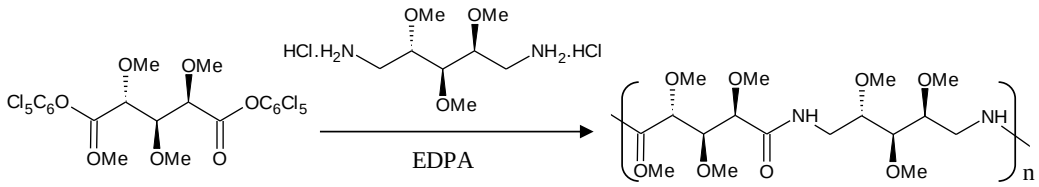


Figure 1-9. Synthesis of polymers from Pentachlorophenyl 2,3,4-tri-*O*-methyl-L-arabinarate (EDPA: *N*-ethyl-*N*,*N*-diisopropylamine) (Zamora et al. 2009).

As described above, there are several examples in which synthesis of polymers was attempted by protecting of hydroxyl groups of aldaric acids first, then polymerization with diols or diamines. However, the molecular weights of the polymers were as low as several thousand. Furthermore, the properties of these polymers are not sufficiently studied. Nevertheless, these preliminary studies provide a good reference for our research.

1.5. Polymers synthesized from D-glucaric acid

Hashimoto et al. (Hashimoto et al. 1990, Hashimoto et al. 1993, Hashimoto, Wibullcksanakul and Okada 1995) and Kiely et al. (Kiely et al. 1994, Chen and Kiely 1996, Kiely, Chen and Lin 2000, Morton and Kiely 2000) reported the synthesis of GA-based polyamides from dilactone or monolactones of GA via ring-opening polymerization as shown in Figure 1-10 and Figure 1-11, respectively. The moleculars reported for a GA-based polyamide were low. The self-organization behavior of these GA-based polyamides in strong polar organic solvent has been found (Rosu et al. 2015).

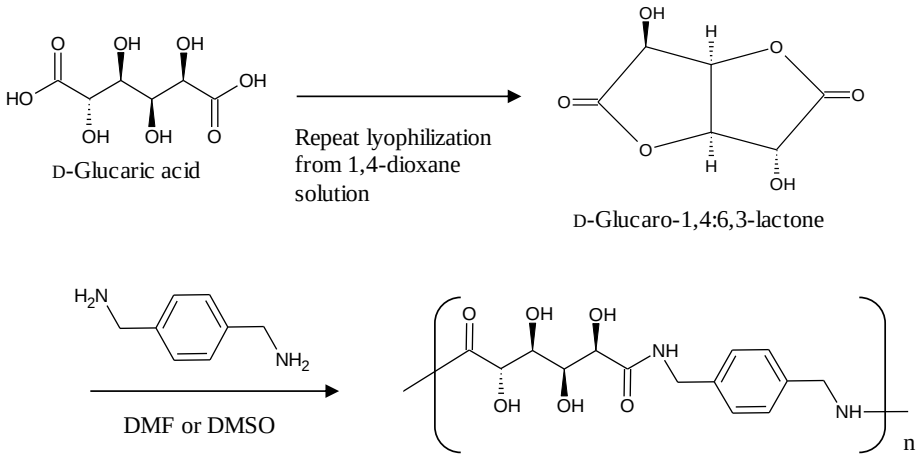


Figure 1-10 . Ring-opening polyadditon of D-gluaro-1,4:6,3-dilactone with *p*-xylylenediamine (Hashimoto, Okada and Honjo 1990).

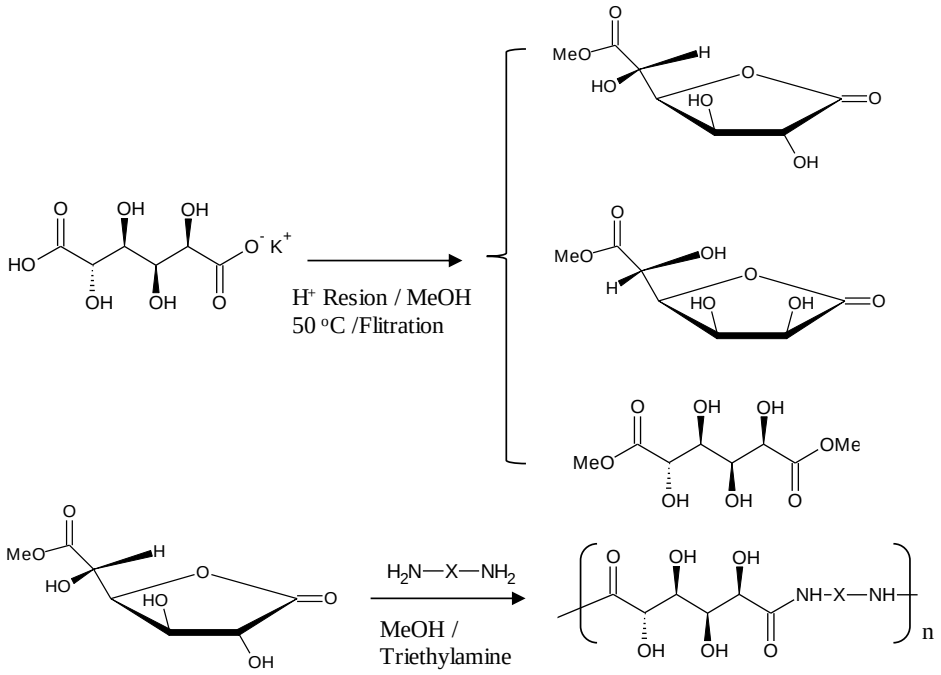


Figure 1-11. Direct method for preparation of poly(hexamethylene D-glucaramide) from monopotassium D-Glucarate (Kiely, Chen and Lin 1994).

GA also has several disadvantages in practical applications, and its use has never been commercialized. First, the yield of GA obtained by nitric acid oxidation of D-glucose is too low (<40%),5 various byproducts are formed, and GA selectivity is low. Second, GA easily forms lactones in equilibrium with the acyclic form, preventing efficient monomer or polymer synthesis; glucaric and mannaric acids do not form lactones, probably because of their stereochemical structures. In practice, GA is converted to the acyclic form as the potassium salt by neutralization. Third, protection of the hydroxyl groups of GA by acetyl or methyl groups is difficult because GA or the GA potassium salt is only soluble in water, and this prevents general reactions, which mainly proceed in organic solvents. In addition, GA derivatives are expected to be soluble in both water and organic solvents, because of their carboxyl groups, and it can be difficult to purify GA derivatives by extraction with other reagents. For these reasons, there have, as far as we know, been no reports of the direct syntheses of GA derivatives with complete acyclic structures from GA, and their polymers.

GA used in these studies was obtained by oxidation of D-glucose with nitric acid, but lactones were also produced by nitric acid oxidation. Kiely et al. And Hashimoto et al. polymerized lactones of GA with diamines by ring-opening polymerization without protecting the hydroxyl group of glucaric acid, and the molecular weight did not increase. As described above, in the synthesis of a polymer using GA, there are problems such as the fact that a large

amount of lactone is contained as an impurity, resulted in that the molecular weights were low. Therefore, in the synthesis of GA-based polymers with linear structures, four hydroxyl groups need to be protected to prevent undesired side reactions and to allow polymerization with counter monomers through carboxyl groups.

1.6. Objectives of study

In the examples of polymerization of GA so far, the hydroxyl groups of the monomer glucaric acid were not protected and used as a lactone mixture. Since GA tends to form lactones, it is isolated and purified in the form of a potassium salt, but potassium glucaramide is insoluble in solvents other than water.

In order to prevent the formation of lactones of GA and make it soluble in an organic solvent, it is necessary to synthesize a monomer which the hydroxyl groups are protected with ester or ether. The ester groups such as acetyl groups can be easily removed after polymerization. Therefore, in this research, we aim to develop a new polymer material based on GA, and developed D-glucaric acid acetate (GAA), which the hydroxyl groups of glucaric acid are fully protected by acetyl groups, with a complete acyclic structure. Then we synthesized new class of polyesters and polyamides by polymerization with diols and diamines, and analyze their properties.

In chapter 2, we describe the synthesis of acyclic GAA using acetic anhydride and sulfuric acid and the process to extract pure GAA from reaction mixture. Then the carboxyl groups of GAA were converted into acyl chloride for polymerization.

In chapter 3, we synthesized GAA with different kinds of aliphatic diols or diamines. We tried both solution polymerization and interfacial polymerization. The polyesters obtain from solution polymerization had low molecular weights. The polyamides obtained via solution polymerization had higher molecular weights than polyesters, but still not high enough to be used as polymer materials. The polyamides synthesized via interfacial polymerization had higher molecular weights and showed crystalline properties. These polyamides were mixture and need to be purified. However, because of their amphiphilicity, it is very difficult to separate pure polyamides.

References

Alla, A., J. Oxelbark, A. Rodriguez-Galan & S. Munoz-Guerra (2005) Acylated and hydroxylated polyamides derived from L-tartaric acid. *Polymer,* 46**,** 2854-2861.

Alla, A., A. RodriguezGalan, A. M. deIlarduya & S. MunozGuerra (1997) Degradable poly(ester amide)s based on L-tartaric acid. *Polymer,* 38**,** 4935-4944.

Anderson, A. J. & E. A. Dawes (1990) OCCURRENCE, METABOLISM, METABOLIC ROLE, AND INDUSTRIAL USES OF BACTERIAL POLYHYDROXYALKANOATES. *Microbiological Reviews,* 54**,** 450-472.

Auras, R., B. Harte & S. Selke (2004) An overview of polylactides as packaging materials. *Macromolecular Bioscience,* 4**,** 835-864.

Bachmann, F. & J. Thiem (1992) SYNTHESIS OF HYDROPHILIC CARBOHYDRATE-DERIVED POLYAMIDES. *Journal of Polymer Science Part a-Polymer Chemistry,* 30**,** 2059-2062.

Brown, J. M., M. Manley-Harris, R. J. Field & D. E. Kiely (2007) An NMR study of the equilibration of D-glucaric acid with lactone forms in aqueous acid solutions. *Journal of Carbohydrate Chemistry,* 26**,** 455-467.

Chen, L. & D. E. Kiely (1996) Synthesis of stereoregular head,tail hydroxylated nylons derived from D-glucose. *Journal of Organic Chemistry,* 61**,** 5847-5851.

Danjo, T., Y. Enomoto-Rogers, A. Takemura & T. Iwata (2014) Syntheses and properties of glucomannan acetate butyrate mixed esters. *Polymer Degradation and Stability,* 109**,** 373-378.

Ebringerova, A. & T. Heinze (2000) Xylan and xylan derivatives - biopolymers with valuable properties, 1 - Naturally occurring xylans structures, procedures and properties. *Macromolecular Rapid Communications,* 21**,** 542-556.

Edgar, K. J., C. M. Buchanan, J. S. Debenham, P. A. Rundquist, B. D. Seiler, M. C. Shelton & D. Tindall (2001) Advances in cellulose ester performance and application. *Progress in Polymer Science,* 26**,** 1605-1688.

Enomoto-Rogers, Y., N. Iio, A. Takemura & T. Iwata (2015) Synthesis and characterization of pullulan alkyl esters. *European Polymer Journal,* 66**,** 470-477.

Enomoto-Rogers, Y. & T. Iwata (2012) Synthesis of xylan-graft-poly(L-lactide) copolymers via click chemistry and their thermal properties. *Carbohydrate Polymers,* 87**,** 1933-1940.

--- (2013) Syntheses of poly(L-lactide)-block-xylan butyrate-block-poly(L-lactide) triblock copolymers and their properties. *Journal of Wood Science,* 59**,** 489-498.

Feng, X. H., A. J. East, W. B. Hammond, Y. Zhang & M. Jaffe (2011) Overview of advances in sugar-based polymers. *Polymers for Advanced Technologies,* 22**,** 139-150.

Fenouillot, F., A. Rousseau, G. Colomines, R. Saint-Loup & J. P. Pascault (2010) Polymers from renewable 1,4:3,6-dianhydrohexitols (isosorbide, isomannide and isoidide): A review. *Progress in Polymer Science,* 35**,** 578-622.

Fundador, N. G. V., Y. Enomoto-Rogers, A. Takemura & T. Iwata (2012) Syntheses and characterization of xylan esters. *Polymer,* 53**,** 3885-3893.

Galbis, J. A., M. D. Garcia-Martin, M. V. de Paz & E. Galbis (2016) Synthetic Polymers from Sugar-Based Monomers. *Chemical Reviews,* 116**,** 1600-1636.

Galbis, J. A. & M. G. Garcia-Martin (2010) Synthetic Polymers from Readily Available Monosaccharides. *Carbohydrates in Sustainable Development Ii: a Mine for Functional Molecules and Materials,* 295**,** 147-176.

Gandini, A. (2008) Polymers from Renewable Resources: A Challenge for the Future of Macromolecular Materials. *Macromolecules,* 41**,** 9491-9504.

Gregory, G. L., E. M. Lopez-Vidal & A. Buchard (2017) Polymers from sugars: cyclic monomer synthesis, ring-opening polymerisation, material properties and applications. *Chemical Communications*, 53**,** 2198-2217.

Harding, K. G., J. S. Dennis, H. von Blottnitz & S. T. L. Harrison (2007) Environmental analysis of plastic production processes: Comparing petroleum-based polypropylene and polyethylene with biologically-based poly-beta-hydroxybutyric acid using life cycle analysis. *Journal of Biotechnology*, 130**,** 57-66.

Hashimoto, K., M. Okada & N. Honjou (1990) RING-OPENING POLYADDITION OF D-GLUCARO-1,4-6,3-DILACTONE WITH PARA-XYLYLENEDIAMINE. *Makromolekulare Chemie-Rapid Communications*, 11**,** 393-396.

Hashimoto, K., S. Wibullcksanakul & M. Okada (1995) MACROMOLECULAR-SYNTHESIS FROM SACCHARIC LACTONES - POLYADDITION OF D-GLUCARO-1,4/6,3-DILACTONES AND D-MANNARO-1,4/6,3-DILACTONES WITH DIISOCYANATES AND HYDROLYZABILITY OF THE RESULTING POLYURETHANES HAVING DILACTONE RINGS IN THE MAIN CHAINS. *Journal of Polymer Science Part a-Polymer Chemistry*, 33**,** 1495-1503.

Hashimoto, K., S. Wibullucksanakul, M. Matsuura & M. Okada (1993) MACROMOLECULAR-SYNTHESIS FROM SACCHARIC LACTONES - RING-OPENING POLYADDITION OF D-GLUCARO-1,4/6,3-DILACTONES AND D-MANNARO-1,4/6,3-DILACTONES WITH ALKYLENEDIAMINES. *Journal of Polymer Science Part a-Polymer Chemistry*, 31**,** 3141-3149.

Heinze, T., D. Klemm, F. Loth & B. Philipp (1990) PREPARATION, STRUCTURE AND APPLICATION OF IONOTROPIC GELS OF POLYSACCHARIDES CONTAINING CARBOXY GROUPS. *Acta Polymerica*, 41**,** 259-269.

Henkensmeier, D., B. C. Abele, A. Candussio & J. Thiem (2004) Synthesis, characterisation and degradability of polyamides derived from aldaric acids and chain end functionalised polydimethylsiloxanes. *Polymer*, 45**,** 7053-7059.

Hinton, M. R., M. Manley-Harris, K. I. Hardcastle & D. E. Kiely (2013) Pentaric Acids and Derivatives from Nitric Acid-Oxidized Pentoses. *Journal of Carbohydrate Chemistry*, 32**,** 68-85.

Hongyi Gan, Y. E., Taizo Kabe, Daisuke Ishii, Takaaki Hikima, Masaki Takata, Tadahisa Iwata (2017) Synthesis, Properties and Molecular Conformation of Paramylon Ester Derivatives. *Polymer Degradation and Stability*, 145**,** 142-149.

Ito, T., H. Masaki & K. Mikuni. 2013. D-Glucaric acid-producing bacterium, and method for manufacturing D-glucaric acid.

Iwata, T. (2015) Biodegradable and Bio-Based Polymers: Future Prospects of Eco-Friendly Plastics. *Angewandte Chemie-International Edition*, 54**,** 3210-3215.

Kiely, D. E., L. Chen & T. H. Lin (1994) HYDROXYLATED NYLONS BASED ON UNPROTECTED ESTERIFIED D-GLUCARIC ACID BY SIMPLE CONDENSATION-REACTIONS. *Journal of the American Chemical Society*, 116**,** 571-578.

--- (2000) Synthetic polyhydroxypolyamides from galactaric, xylaric, D-glucaric, and D-mannaric acids and alkylenediamine monomers - Some comparisons. *Journal of Polymer Science Part a-Polymer Chemistry*, 38**,** 594-603.

Klemm, D., F. Kramer, S. Moritz, T. Lindstrom, M. Ankerfors, D. Gray & A. Dorris (2011) Nanocelluloses: A New Family of Nature-Based Materials. *Angewandte Chemie-International Edition*, 50**,** 5438-5466.

Lasprilla, A. J. R., G. A. R. Martinez, B. H. Lunelli, A. L. Jardini & R. Maciel (2012) Poly-lactic acid synthesis for application in biomedical devices - A review. *Biotechnology Advances,* 30**,** 321-328.

Lavilla, C., A. Alla, A. M. de Ilarduya, E. Benito, M. G. Garcia-Martin, J. A. Galbis & S. Munoz-Guerra (2011) Carbohydrate-Based Polyesters Made from Bicyclic Acetalized Galactaric Acid. *Biomacromolecules,* 12**,** 2642-2652.

Mancera, M., I. Roffe, M. Rivas & J. A. Galbis (2003) New derivatives of D-mannaric and galactaric acids. Synthesis of a new stereoregular Nylon 66 analog from carbohydrate-based monomers having the D-manno configuration. *Carbohydrate Research,* 338**,** 1115-1119.

Mansour, E., S. H. Kandil, H. Hassan & M. A. E. Shaban (1990) SYNTHESIS OF CARBOHYDRATE-CONTAINING POLYAMIDES AND STUDY OF THEIR PROPERTIES. *European Polymer Journal,* 26**,** 267-276.

Mehltretter, C. L. & R. L. Mellies (1955) THE POLYESTERIFICATION OF 2,4-3,5-DI-O-METHYLENE-D-GLUCONIC ACID. *Journal of the American Chemical Society,* 77**,** 427-428.

Mehtio, T., L. Nurmi, V. Ramo, H. Mikkonen & A. Harlin (2015) Synthesis and characterization of copolyanhydrides of carbohydrate-based galactaric acid and adipic acid. *Carbohydrate Research,* 402**,** 102-110.

Merbouh, N., J. F. Thaburet, M. Ibert, F. Marsais & J. M. Bobbitt (2001) Facile nitroxide-mediated oxidations of D-glucose to D-glucaric acid. *Carbohydrate Research,* 336**,** 75-78.

Mitsubishi Chemical. New Bio-based Engineering Plastic DURABIO™. https://www.m-chemical.co.jp/en/products/departments/mcc/sustainable/product/1201026_7964.html.

Mohanty, A. K., M. Misra & L. T. Drzal (2002) Sustainable bio-composites from renewable resources: Opportunities and challenges in the green materials world. *Journal of Polymers and the Environment,* 10**,** 19-26.

Moon, T. S., J. E. Dueber, E. Shiue & K. L. J. Prather (2010) Use of modular, synthetic scaffolds for improved production of glucaric acid in engineered E. coli. *Metabolic Engineering,* 12**,** 298-305.

Moon, T. S., S.-H. Yoon, A. M. Lanza, J. D. Roy-Mayhew & K. L. J. Prather (2009) Production of Glucaric Acid from a Synthetic Pathway in Recombinant Escherichia coli. *Applied and Environmental Microbiology,* 75**,** 589-595.

Morton, D. W. & D. E. Kiely (2000) Synthesis of poly(azaalkylene aldaramide)s and poly(oxaalkylene aldaramide)s derived from D-glucaric and D-galactaric acids. *Journal of Polymer Science Part a-Polymer Chemistry,* 38**,** 604-613.

Munoz-Guerra, S., C. E. Fernandez, E. Benito, R. Marin, M. G. Garcia-Martin, M. Bermudez & J. A. Galbis (2009) Crystalline structure and crystallization of stereoisomeric polyamides derived from arabinaric acid. *Polymer,* 50**,** 2048-2057.

Namazi, a. (2017) Polymers in our daily life. *BioImpacts,* 7**,** 73-74.

Nampoothiri, K. M., N. R. Nair & R. P. John (2010) An overview of the recent developments in polylactide (PLA) research. *Bioresource Technology,* 101**,** 8493-8501.

Noda, I., P. R. Green, M. M. Satkowski & L. A. Schechtman (2005) Preparation and properties of a novel class of polyhydroxyalkanoate copolymers. *Biomacromolecules,* 6**,** 580-586.

Orgueira, H. A., R. Erra-Balsells, H. Nonami & O. Varela (2001) Synthesis of chiral polyhydroxy polyamides having chains of defined regio and stereoregularity. *Macromolecules,* 34**,** 687-695.

Philip, S., T. Keshavarz & I. Roy (2007) Polyhydroxyalkanoates: biodegradable polymers with a range of applications. *Journal of Chemical Technology and Biotechnology,* 82**,** 233-247.

Puanglek, S., S. Kimura, Y. Enomoto-Rogers, T. Kabe, M. Yoshida, M. Wada & T. Iwata (2016) In vitro synthesis of linear alpha-1,3-glucan and chemical modification to ester derivatives exhibiting outstanding thermal properties. *Scientific Reports,* 6.

Rasal, R. M., A. V. Janorkar & D. E. Hirt (2010) Poly(lactic acid) modifications. *Progress in Polymer Science,* 35**,** 338-356.

Rosu, C., P. S. Russo, W. H. Daly, R. Cueto, J. A. Pople, R. A. Laine & Negulescu, II (2015) Sugar-Based Polyamides: Self-Organization in Strong Polar Organic Solvents. *Biomacromolecules,* 16**,** 3062-3072.

Shearouse, W. C., L. M. Lillie, T. M. Reineke & W. B. Tolman (2015) Sustainable Polyesters Derived from Glucose and Castor Oil: Building Block Structure Impacts Properties. *Acs Macro Letters,* 4**,** 284-288.

Sorrell, S., J. Speirs, R. Bentley, A. Brandt & R. Miller (2010) Global oil depletion: A review of the evidence. *Energy Policy,* 38**,** 5290-5295.

Sudesh, K., H. Abe & Y. Doi (2000) Synthesis, structure and properties of polyhydroxyalkanoates: biological polyesters. *Progress in Polymer Science,* 25**,** 1503-1555.

Teramoto, Y. & Y. Nishio (2003) Cellulose diacetate-graft-poly(lactic acid)s: synthesis of wide-ranging compositions and their thermal and mechanical properties. *Polymer,* 44**,** 2701-2709.

Walaszek, Z. (1990) POTENTIAL USE OF D-GLUCARIC ACID-DERIVATIVES IN CANCER PREVENTION. *Cancer Letters,* 54**,** 1-8.

Walaszek, Z., J. Szemraj, M. Hanausek, A. K. Adams & U. Sherman (1996) D-glucaric acid content of various fruits and vegetables and cholesterol-lowering effects of dietary D-glucarate in the rat. *Nutrition Research,* 16**,** 673-681.

Wang, S., A. Lu & L. N. Zhang (2016) Recent advances in regenerated cellulose materials. *Progress in Polymer Science,* 53**,** 169-206.

Werpy, T. & G. Petersen. 2004. Top Value Added Chemicals from Biomass Volume I — Results of Screening for Potential Candidates from Sugars and Synthesis Gas. ed. U. D. o. E. (DOE).

Wu, Z., Y. Huang, C. Zhang, D. Zhu, Z. Bian, M. Ding, L. Gao & Z. Yang (2010) A Simple and Efficient Way to Synthesize Optically Active Polyamides by Solution Polycondensation of Di-O-Methyl-L-Tartaryl Chloride with Diamines. *Journal of Applied Polymer Science,* 117**,** 3558-3567.

Yokoe, M., K. Aoi & M. Okada (2005) Biodegradable polymers based on renewable resources. IX. Synthesis and degradation behavior of polycarbonates based on 1,4 : 3,6-dianhydrohexitols and tartaric acid derivatives with pendant functional groups. *Journal of Polymer Science Part a-Polymer Chemistry,* 43**,** 3909-3919.

Zamora, F., K. Hakkou, A. Alla, M. Rivas, A. Martinez de Ilarduya, S. Munoz-Guerra & J. A. Galbis (2009) Butylene Copolyesters Based on Aldaric and Terephthalic Acids. Synthesis and Characterization. *Journal of Polymer Science Part a-Polymer Chemistry,* 47**,** 1168-1177.

Synthesis of D-glucaric acid acetate

2.1. Introduction

D-Glucaric acid (GA) is an aldaric acid based on an acyclic sugar main-chain, and it is a potential monomer for synthesis of polyesters and polyamides because of the carboxyl groups at two ends. To synthesize higher molecular weight polymer, it is better to prevent the formation of lactones. All the hydroxyl groups should be protected before polymerization. In some cases of aldaric acids, the acetyl groups were used to protect hydroxyl groups before polymerization, such as galactaric acid (Bachmann and Thiem 1992) and tartaric acid (Alla et al. 2005). Because acetyl group can be easily removed, acetyl group is considered as a potential protection group for D-glucaric acid.

GA-based polymers were difficult to synthesize efficiently because of easy lactones formation in equilibrium (Horton and Walaszek 1982, Brown et al. 2007), preventing efficient monomer or polymer synthesis; galactaric and mannaric acids do not easily form lactones, probably because of their stereochemical structures. In practice, GA is converted to the acyclic potassium salt by neutralization. However, protection of the hydroxyl groups of GA by acetyl groups is difficult because GA or the GA potassium salt is only soluble in water, and this prevents general reactions, which mainly proceed in organic solvents. In addition, GA derivatives are expected to be soluble in both water and organic solvents, because of their carboxyl groups, so it can be difficult to purify GA derivatives by extraction with other reagents. For these reasons, there have, as far as we know, been no reports of the direct syntheses of GA derivatives with complete acyclic structures from GA, and their polymers.

Because GA is chiral molecular, it is difficult to determine the chemical structure of GAA through NMR measurement. However, there are some research literatures about NMR analysis of chemical structure of GA (Styron et al. 2002, Denton et al. 2011, Enomoto-Rogers et al. 2016, Brown et al. 2007), which would help us analysis the chemical structure of GAA by NMR measurement.

In this chapter, we report the synthesis and characterization of D-glucaric acid acetate (GAA) with a complete acyclic structure and will use it as a class of monomer for polymerization.

2.2. Experimental Section

2.2.1. Materials

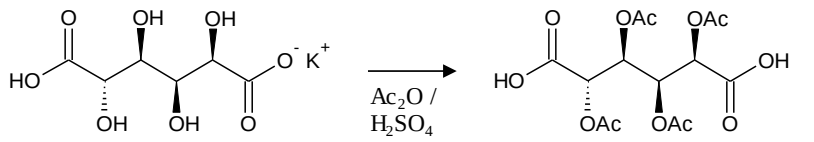
D-Glucaric acid monopotassium salt (GAK) was provided by the Ensuiko Sugar Refining Co., Ltd. (Yokohama, Japan). All other reagents were obtained commercially and used without further purification.

2.2.2. Instruments

^{1}H and ^{13}C NMR spectroscopies, double quantum filtered correlation spectroscopy (DQF-COSY), and heteronuclear single quantum coherence (HSQC) and heteronuclear multiple bond correlation (HMBC) spectroscopies were performed using a Varian INOVA500 (500 MHz) instrument at 25 °C, with chloroform-*d* as the solvent. The chemical shifts (δ) and coupling constants (J) were reported in parts per million (ppm) and hertz (Hz), respectively.

2.2.3. Synthesis of GAA

As shown in Scheme 2-1, the typical procedure for synthesis is as fellow. GAK (10 g) was dispersed in acetic anhydride (10 mL) at room temperature, and then concentrated sulfuric acid (50 mL) was added at 60 °C. The solution, which turned clear in a few minutes, was stirred for 3 h. The mixture was extracted with chloroform/acetone (7:3, v/v) and water. The organic phase was dried with Na_2SO_4, and concentrated to dryness to give GAA as a colorless solid (3.0 g, 30% yield). ^{1}H NMR ($CDCl_3$): δ = 2.07 (s, 3H, CH_3CO at C4), 2.08 (s, 3H, CH_3CO at C3), 2.15 (s, 3H, CH_3CO at C5), 2.19 (s, 3H, CH_3CO at C2), 5.22 (d, 1H, $J_{4,5}$ = 4.65, C5-H), 5.37 (d, 1H, $J_{2,3}$ = 3.90, C2-H), 5.60 (dd, 1H, $J_{4,5}$ = 4.65, $J_{4,3}$ = 6.22, C4-H), 5.81 (dd, 1H, $J_{3,2}$ = 3.90, $J_{3,4}$ = 6.22, C3-H), 6.9 (broad s, C1OOH and C6OOH). ^{13}C NMR ($CDCl_3$): δ = 20.31 (CH_3CO at C2), 20.36 (CH_3CO at C5), 20.42 (CH_3CO at C3), 20.46 (CH_3CO at C4), 69.20 (C3), 69.66 (C5), 69.81 (C4), 70.15 (C2), 169.73 (CH_3CO at C5), 170.07 (CH_3CO at C3), 170.14 (CH_3CO at C4), 170.19 (C6), 170.21 (C1), 170.47 (CH_3CO at C2).



D-Glucaric acid monopotassium (GAK)

D-Glucaric acid acetate (GAA)
Ac = Acetyl group (-$COCH_3$)

Scheme 2-1. Acetylation of D-glucaric acid.

2.3. Results and Discussion

2.3.1. Synthesis of GAA

GA and its monopotassium salt are soluble in water, but insoluble in organic solvents such as alcohols, dimethyl sulfoxide (DMSO), and *N*,*N*-dimethylformamide (DMF). GAA was synthesized from GAK using acetic anhydride as acetylating agent and concentrated sulfuric acid as catalyst, and GA easily dissolves in this mixed system.

GAA extraction was more complex than extraction of common compounds that can be easily extracted and separated using an organic solvent from organic / water systems. GAA is soluble in both aqueous and organic media and GAA potassium and sodium salts are soluble in water. We therefore tried to extract GAA into organic media from an organic solvent / water system. The solution was not neutralized with an alkali such as sodium hydrogen carbonate, to prevent salt formation and dissolution of GAA salts in aqueous media. When ethyl acetate was used as the organic medium, transesterification with ethyl acetate occurred under acidic conditions, and the carboxyl groups of GAA were esterified by the ethyl groups of ethyl acetate. When chloroform and diethyl ether, which are aprotic organic solvents with low polarities, were used as extraction media, no GAA was extracted and the yield was zero. This is because GAA has high polarity and is more soluble in acetic anhydride / sulfuric acid systems than in chloroform or diethyl ether. Organic media with higher polarities, obtained by mixing chloroform with a higher-polarity solvent, were therefore investigated to extract GAA more effectively. After several experiments, the highest GAA extraction was achieved using a chloroform / acetone (7:3, v/v) mixed solution; this mixture had the best polarity balance. When the proportion of acetone was higher, the organic and aqueous media formed an inseparable emulsion, and GAA could not be extracted. The obtained GAA was soluble in both water and organic solvents such as alcohols, chloroform, and DMSO. The acetyl groups were not hydrolyzed in chloroform. The obtained GAA exhibited high water absorbability, and should preserved in dry environment.

2.3.2. NMR analysis of GAA

2.3.2.1. 1D-NMR analysis of GAA

The ^{1}H and ^{13}C NMR spectra of GAA in chloroform are shown in Figure 2-1. The peak patterns and chemical shifts in the NMR spectra of GAA in deuterium oxide were the same as those in the spectra in chloroform, indicating that the GAA molecules were dispersed in

solution and there were no intermolecular interactions or interactions between GAA and solvent molecules.

In ^{1}H NMR spectra, the four peaks from acetyl groups can be found at about 2.1 ppm, and the four peaks from glucaric acid can be found at 5.2 - 5.9 ppm in ^{1}H-NMR spectra. The integrated areas ratio of them is 3 : 1. That means the four hydroxyl groups were fully protected by acetyl groups.

In ^{13}C NMR spectra, the four peaks from acetyl groups and four peaks from glucaric acid are found at 20.4 - 20.8 ppm and 69.2 - 70.6 ppm, separately. The six peaks at 170.0 - 171.0 ppm belongs to the four aldehyde groups of acetyl groups and two carboxyl groups of glucaric acid. There are no peaks from lactones can be found in ^{1}H, ^{13}C NMR spectra. That means the protection of four hydroxyl groups by acetyl groups were carried out successfully without producing lactones.

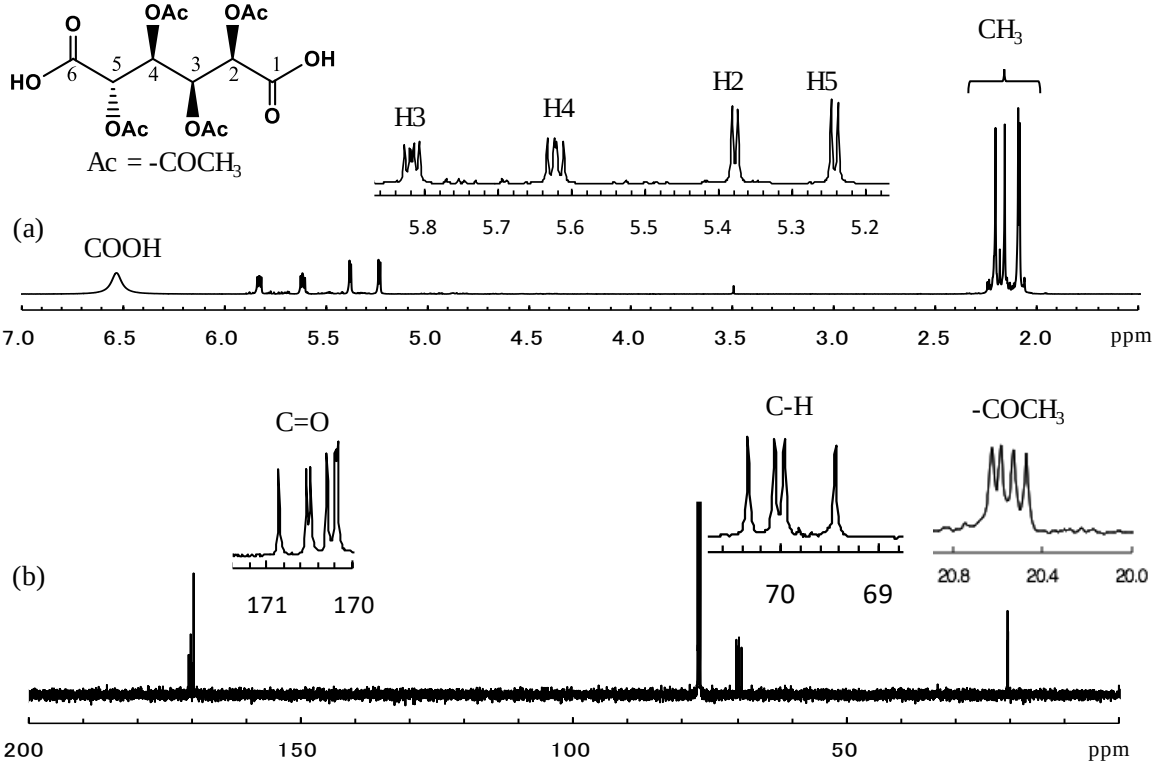


Figure 2-1. (a) ^{1}H, (b) ^{13}C NMR spectra of GAA.

2.3.2.2. 2D-NMR analysis of GAA

The assignments of the chemical shifts and coupling constants (*J*) of the four methine (CH) protons are listed in Table 2-1. The set of two doublets, which can be assigned to H2 or H5, appeared at higher field than the set of two double doublets, which can be assigned to H3 or H4; this is the opposite order from that for GA. Previous NMR studies of GA (Denton et al. 2011, Enomoto-Rogers et al. 2016) showed H doublets at lower field (5.37 ppm) with a smaller coupling constant, assigned to H2. All the proton, methyl, and carbonyl carbon peaks of the four acetyl groups were assigned based on the HSQC and HMBC spectra shown in Figure 2-2a and b, respectively.

GA tends to form a lactone in solution, and has two reactive groups, namely hydroxyl and carbonyl groups; therefore, it is difficult to use it as a monomer in various polymerizations. In this study, we successfully substituted only the hydroxyl groups of GA and obtained pure acyclic GAA, which is a promising monomer for novel bio-based polymers.

Table 2-1. ^{1}H and ^{13}C Chemical Shifts of GAA.

		Chemical shift (d)					
		C1	C2	C3	C4	C5	C6
^{1}H	C<u>*H*</u>		5.37 d $^{3}J_{H2H3}$ 3.90	5.81 dd $^{3}J_{H3H4}$ 6.22	5.60 dd $^{3}J_{H4H5}$ 4.65	5.22 d	
	C<u>*H*</u>$_3$CO		2.19	2.08	2.07	2.15	
	COO<u>*H*</u>	6.52					6.52
^{13}C	<u>*C*</u> H	170.21	70.15	69.20	69.81	69.66	170.19
	<u>*C*</u> H$_3$CO	-	20.31	20.42	20.46	20.36	-
	CH$_3$<u>*C*</u> O	-	170.47	170.07	170.14	169.73	-

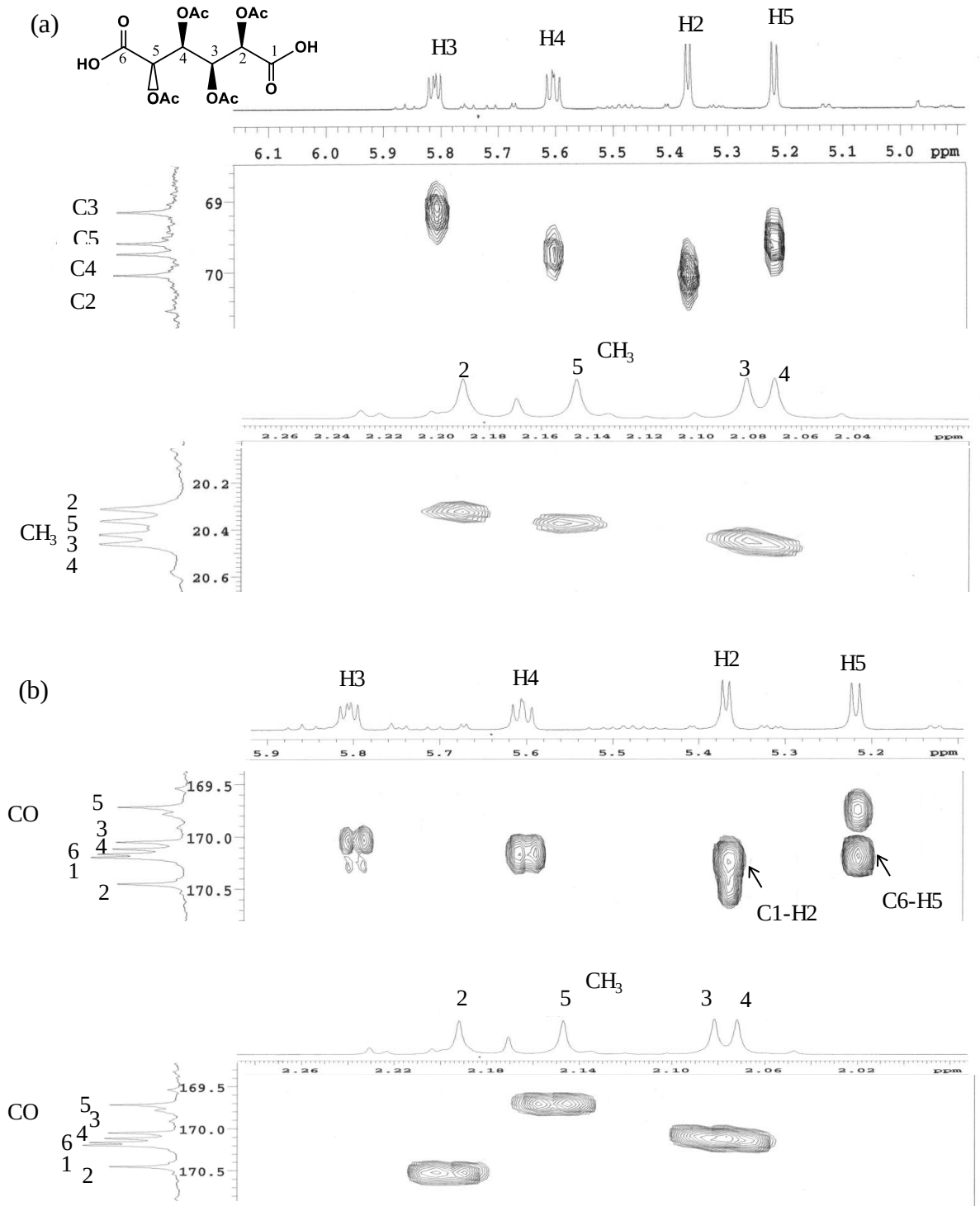


Figure 2-2. (a) HSQC and (b) HMBC NMR spectra of GAA.

2.3.2. Thermal stability of GAA

TGA curve of GAA is showed in Figure 2-3. 10% and 50% (wt) decomposition temperatures were $T_{d10\%}$ = 187.5 °C, $T_{d50\%}$ = 195.5 °C, respectively. When heated to about 150 °C, GAA started to decompose quickly. It is difficult to use GAA in bulk polymerization.

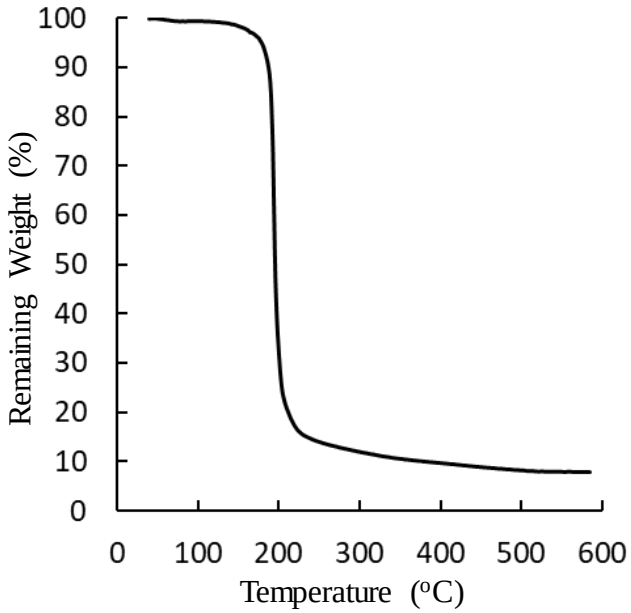


Figure 2-3. TGA thermogram of GAA

2.4. Conclusions

GAA with an acyclic structure, was synthesized successfully from GA using acetic anhydride and sulfuric acid. The chemical structure of GAA was analyzed by one-dimensional and two-dimensional NMR techniques that confirmed the fully acetylation of hydroxyl groups. The thermal stability of GAA was low.

References

Alla, A., J. Oxelbark, A. Rodriguez-Galan & S. Munoz-Guerra (2005) Acylated and hydroxylated polyamides derived from L-tartaric acid. *Polymer,* 46**,** 2854-2861.

Bachmann, F. & J. Thiem (1992) SYNTHESIS OF HYDROPHILIC CARBOHYDRATE-DERIVED POLYAMIDES. *Journal of Polymer Science Part a-Polymer Chemistry,* 30**,** 2059-2062.

Brown, J. M., M. Manley-Harris, R. J. Field & D. E. Kiely (2007) An NMR study of the equilibration of D-glucaric acid with lactone forms in aqueous acid solutions. *Journal of Carbohydrate Chemistry,* 26**,** 455-467.

Denton, T. T., K. I. Hardcastle, M. K. Dowd & D. E. Kiely (2011) Characterization of D-glucaric acid using NMR, X-ray crystal structure, and MM3 molecular modeling analyses. *Carbohydrate Research,* 346**,** 2551-2557.

Enomoto-Rogers, Y., H. Masaki, T. Ito, K. Furihata & T. Iwata (2016) Conformation analysis of D-glucaric acid in deuterium oxide by NMR based on its J(HH) and J(CH) coupling constants. *Magnetic Resonance in Chemistry,* 54**,** 561-567.

Horton, D. & Z. Walaszek (1982) CONFORMATIONS OF THE D-GLUCAROLACTONES AND D-GLUCARIC ACID IN SOLUTION. *Carbohydrate Research,* 105**,** 95-109.

Styron, S. D., A. D. French, J. D. Friedrich, C. H. Lake & D. E. Kiely (2002) 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). *Journal of Carbohydrate Chemistry,* 21**,** 27-51.

Chapter 3

Synthesis of aliphatic polyesters and aliphatic polyamides from D-glucaric acid

3.1. Introduction

In terms of polymer science, aldaric acids such as GA that have two carboxyl groups, one at either end, have significant potential as building blocks for the construction of polymers, including polyesters and polyamides. Carbohydrate-based nylon-type polyamides are considered as potential novel bio-based materials and received great attention recently owing to their biocompatibility, good thermal and mechanical properties (Galbis et al. 2016, Orgueira et al. 2001). Hashimoto et al. (Hashimoto, Okada and Honjou 1990, Hashimoto et al. 1993, Hashimoto, Wibullcksanakul and Okada 1995) and Kiely et al. (Kiely, Chen and Lin 1994, Chen and Kiely 1996, Kiely, Chen and Lin 2000) reported the synthesis of nylon-type polyamide from unprotect GA. They prepared dilactone or monolactones from GA, then used them as monomer to synthesize polyamides with diamines via ring-opening polymerization. The molecular weights of these GA-based polyamides are not high enough to use as a material. Furthermore, the self-organization behavior of these GA-based polyamides in strong polar organic solvent has been found (Rosu et al. 2015). In addition, GA derivatives are expected to be soluble in both water and organic solvents, because of their carboxyl groups, and it can be difficult to purify GA derivatives by extraction with other reagents. For these reasons, there have, as far as we know, been no reports of the direct syntheses of GA derivatives with complete acyclic structures from GA, and their polymers.

In chapter 2, we successfully synthesized acyclic D-glucaric acid acetate whose four hydroxyl groups were all protected to prevent undesired side reactions and to allow polymerization with counter monomers through carboxyl groups. Other acetyl groups protected aldaric acid-based monomers and their polymers via various synthetic routes, e.g., galactaric acid acetate and its polyamides (Mansour et al. 1990) and acetyl tartaric acid and its polyamides (Alla et al. 2005). Various polymers were obtained by polycondensations of these acetyl group protected aldaric-based monomers with aliphatic or aromatic diols and diamines using various methods, including solution, interfacial, and bulk polymerization. The obtained polymers generally do not have high weight-average molecular weights (M_w), and their use as plastic materials has not been well investigated.

In this chapter, we synthesized polyesters and polyamides from GAA and aliphatic diols or diamines, then analyzed their properties.

3.2. Experimental Section

3.2.1. Materials

GAA was synthesized as shown in Chapter 2. All other reagents were obtained commercially and used without further purification.

3.2.2. Instruments

3.2.2.1. NMR spectroscopy

^{1}H-NMR spectroscopies were performed using a Varian INOVA500 (500 MHz) instrument at 25 °C, with chloroform-*d* as the solvent. The chemical shifts (δ) and coupling constants (J) were reported in parts per million (ppm) and hertz (Hz), respectively.

3.2.2.2. Gel permeation chromatography (GPC)

The number-average molecular weights (M_ns), M_ws, and polydispersity indexes (M_w/M_n) of the GA-based polyesters and polyamides were estimated using GPC (SCL-10A, RID-10A, SIL-10Ai, CTO-10AC, and LC-10Ai, Shimadzu) in 20 mM LiCl/DMAc at 40 °C. The samples (5 mg mL^{-1}) were filtered using a poly(tetrafluoroethylene) syringe filter (Millex-LH 0.20 μm). A Shodex column (TSKgel α-M) was used. The flow rate was 0.6 mL min^{-1} for polyamides obtained by interfacial polymerization and 0.3 mL min^{-1} for polyesters and polyamides obtained by solution polymerization. A calibration curve was constructed using poly(ethylene oxide) (Sigma-Aldrich).

3.2.2.3. Thermogravimetric analysis (TGA)

TGA was performed in a nitrogen atmosphere using a STA6000 instrument (PerkinElmer). Thermograms were acquired at 40–600 °C at a heating rate of 10 °C min^{-1}.

3.2.2.4. Differential scanning calorimetry (DSC)

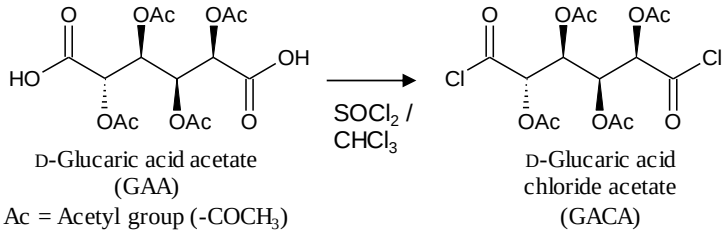
DSC was performed (DSC8500; PerkinElmer) in a nitrogen atmosphere. The samples (2 mg) were heated from 30 to 200 °C (first heating scan) at a heating rate of 10 °C min^{-1} and then immediately quenched to 0 °C. Second heating scans were performed from 0 to 200 °C at a heating rate of 10 °C min^{-1}.

3.2.2.5. Polarized optical microscopy (POM)

Samples were pressed between two glass plates and heated from 40 to 200 °C at a heating rate of 10 °C min^{-1}. The samples were observed using a Nikon E600 POL polarizing microscope equipped with a hot stage. Images were captured every 6 s.

3.2.3. Synthesis of D-glucaric acid chloride acetate (GACA)

As shown in Scheme 3-1, the typical procedure for syntheis is as fellow. GAA (1.0g, 2.6mmol) was dissolved in chloroform (5.0 mL). Then thionyl chloride (1.2mL, 16.5mmol) was added at room temperature. The reaction mixture was heated to 50 °C, and stirred for 3h. After concentrated by evaporator, the obtained GACA was used for polymerization without further purification.



D-Glucaric acid acetate (GAA)
Ac = Acetyl group (-$COCH_3$)

D-Glucaric acid chloride acetate (GACA)

Scheme 3-1. Acyl chlorination of GAA.

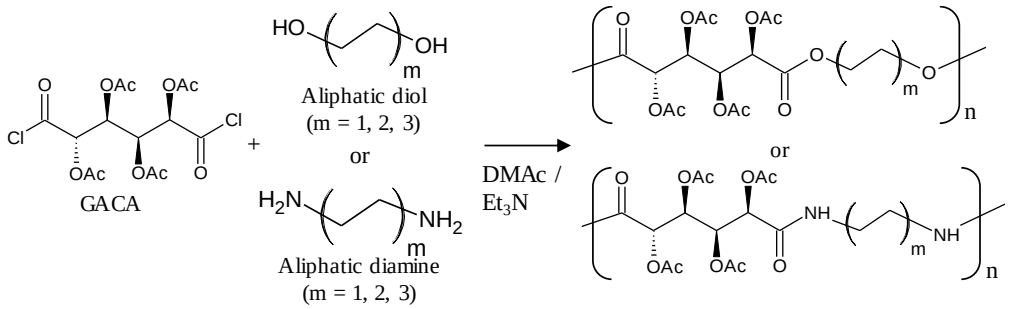
3.2.4. Synthesis of GAA-based polyesters in solution

As shown in Scheme 3-2, the typical procedure for polymerization of GACA with ethanediol (EO; *m* = 2) was as follows. GACA (ca. 1.0 g, 2.6 mmol) in dimethylacetamide (DMAc; 5.0 mL) was added dropwise to a solution of EO (147 µL, 2.6 mmol) and triethylamine (TEA; 734 µL, 2.6 mmol) in DMAc (5.0 mL). The reaction mixture was stirred overnight. The solution was concentrated, and the crude polyester was obtained. Other two kinds of polyesters were synthesized using 1,4-butanediol (BO, *m* = 4; 234 µL, 2.6 mmol) and 1,6-hexanediol (HO, *m* = 6; 312 mg, 2.6 mmol).

3.2.5. Synthesis of GAA-based polyamides in solution

As shown in Scheme 3-2, the typical procedure for polymerization of GACA with ethylenediamine (EA, *m* = 2) was as follows. GACA (ca. 1.0 g, 2.6 mmol) in DMAc (5.0 mL) was added dropwise to a solution of EA (176.4 µL, 2.6 mmol) and TEA (734 µL, 5.3 mmol) in DMAc (5.0 mL). The reaction mixture was stirred overnight. The solvent was evaporated

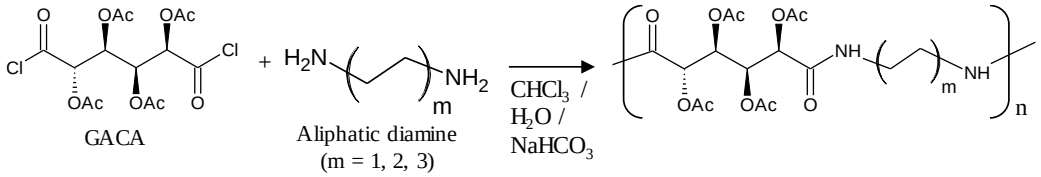
and freeze-drying, and the crude polyamide was obtained. Other two kinds of polyamides were synthesized using 1,4-butanediamine (BA; *m* = 4; 265 µL, 2.6 mmol) and 1,6-hexanediamine (HA; *m* = 6; 365 µL, 2.6 mmol). The molecular weights of the obtained polyamides were determined by gel-permeation chromatography (GPC) without purification.



Scheme 3-2. Solution polymerization of GACA and diamines or diols.

3.2.6. Synthesis of GAA-based polyamides by interfacial polymerization

As shown in Scheme 3-3, the typical procedure for polymerization of GACA with EA was as follows. EA (200 µL, 3.0 mmol) and sodium hydrogen carbonate (0.6 g) in water (10 mL) were added dropwise to a solution of GACA (ca. 1.0 g, 2.6 mmol) in chloroform (10 mL), over the surface of the chloroform solution. The two-phase solution was loaded into a flask. The crude polyamide was obtained from the reaction mixture by solvent evaporation using a rotary evaporator and then freeze-drying. The polymerization product (ca. 600 mg) was purified by dialysis against water using a cellulose dialysis membrane (molecular-weight cutoff = 1000), and a polyamide consisting of GAA and EA (4.1 mg, quantitative) was obtained. Other two kinds of polyamides were synthesized using BA (300 µL, 3.0 mmol) and HA (400 µl, 3.0 mmol); the yields of the pure polyamides were 1.7 mg (quantitative) and 4.2 mg (quantitative), respectively.



Scheme 3-3. Interfacial polymerization of GACA and diamines.

3.3. Results and Discussion

3.3.1. Solution polymerization of GAA-based polyesters

We first examined the solution polymerization of GAA with alkanediols. GAA was converted to glucaric acid chloride acetate (GACA) and then polymerized with diols in DMAc using TEA, as shown in Scheme 3-2. However, no solid polymeric products were obtained. The reaction products were amphiphilic and soluble in both water and organic solvents, including DMAc, DMF, and DMSO. No solid products were obtained by precipitation and purification. All the reaction products were collected by solvent evaporation and submitted to GPC analyses as mixtures with TEA. The GPC elution curves and molecular-weight distributions of the obtained compounds are shown in Figure 3-1a and b. The molecular weights of the obtained polymers are listed in Table 3-1. The polyesters of GAA and diols had M_ws ranged from 400 to 700, these values indicate that polymerization was incomplete.

3.3.2. The molecular weights of GAA-based polyamides

The solution polymerizations of GACA and diamines were examined as described in Scheme 3-2. The polymerization products obtained from GACA and alkyl diamines were amphiphilic. It was difficult to purify the polymers by precipitation. All the polymerization products, which contained TEA, were characterized using GPC. The GPC elution curves in Figure 3-1c show that the polymerization products gave a single peak, and no peaks from monomers were observed; this indicates complete polymerization of GAA. The molecular-weight distributions are shown in Figure 3-1d; the M_ws of polyamides consisting of GAA and EA, BA, and HA, were 7.0×10^3, 8.0×10^3, and 5.9×10^3, respectively, indicating successful polymerization of GAA.

The interfacial polymerization of GACA with alkyl diamines to give polyamides as described in Scheme 3-3 was also investigated. However, on addition of a diamine in sodium hydrogen carbonate aqueous solution to the surface of a chloroform solution of GACA a small amount of solid product appeared at the interface, and the product was too soft and emulsion-like for collection using tweezers in the same way as in polymerization of nylon-6,6. When we touched the interface with tweezers, the organic layer became turbid and no solid product was obtained. The two-phase solution was loaded into a flask, and the reaction mixture was collected by solvent evaporation using a rotary evaporator and subsequent freeze-drying. The main polymerization reaction may have occurred during rotation as a result of evaporation. It

was difficult to purify the polymers by precipitation because the products were soluble in both water and organic solvents.

The collected product mixtures, consisting of polymers, monomers, and bases, were submitted to GPC analyses. Figure 3-1e shows that the GPC elution curves contained two peaks. The first peak appeared at an earlier elution time and was assigned to the polyamide, and the second peak was assigned to monomers, i.e., GAA and diamines. The molecular-weight distributions are shown in Figure 3-1f. The M_ws of the polyamides consisting of GAA and EA, BA, HA were 20.8×10^3, 19.6×10^3 and 14.5×10^3, respectively. The molecular weights of the polyamides obtained by interfacial polymerization were significantly higher than those of the polyamides obtained by solution polymerization, although the monomer conversion rates were obviously higher for solution polymerization. In the case of interfacial polymerization, concentration of organic phase containing GACA was kept high during polymerization because the solvent was continuously evaporated throughout the reaction. It might be allowed efficient reaction between the terminal amino groups of polyamides and GACA and resulted in the elongation of the polymers. This shows that the reactivity of the GAA synthesized in this study is higher than that of GA with free hydroxyl groups, and acetylation of the GA hydroxyl groups promotes polymerization.

Table 3-1. Characterization of GAA-based polyesters and polyamides

Polymers	Comonomer (m)		Solvent	Catalyst	M_w ($\times 10^{-3}$)	M_n ($\times 10^{-3}$)	M_w/M_n	T_m (^oC)
Polyester	EO	2	DMAc	TEA	0.7	0.3	2.0	-
	BO	4	DMAc	TEA	0.4	0.1	2.9	-
	HO	6	DMAc	TEA	0.7	0.3	2.8	-
Polyamide	EA	2	DMAc	TEA	7.0	3.6	1.9	-
	BA	4	DMAc	TEA	8.0	3.9	2.0	-
	HA	6	DMAc	TEA	5.9	1.3	4.5	-
Polyamide	EA	2	$H_2O/CHCl_3$	$NaHCO_3$	20.8	8.8	2.4	119.5
	BA	4	$H_2O/CHCl_3$	$NaHCO_3$	19.6	6.9	2.8	139.4
	HA	6	$H_2O/CHCl_3$	$NaHCO_3$	14.5	6.8	2.1	141.7

GAA = 1.0g, [GAA]/ [comonomer] = 1:1

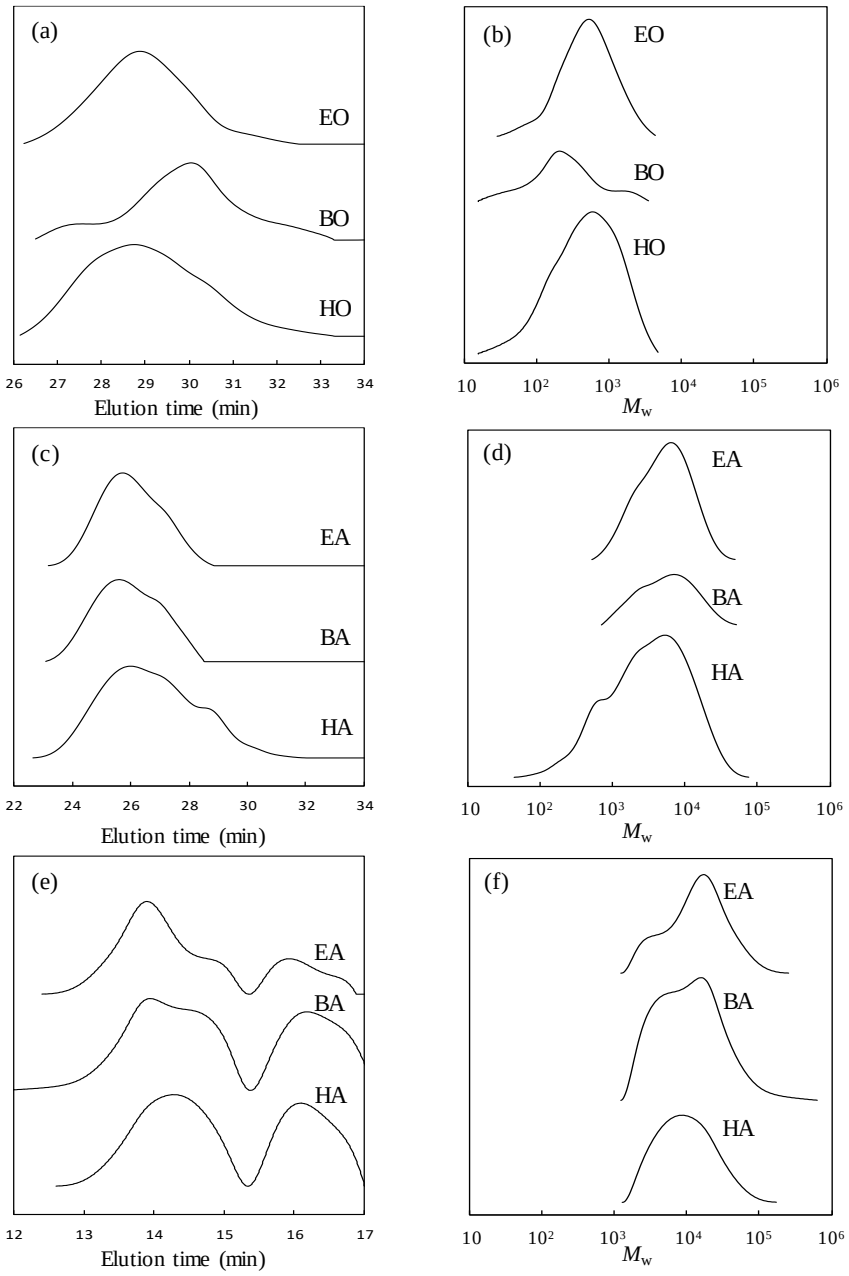


Figure 3-1. GPC elution curves and molecular weight distributions of (a) and (b) polyesters consisting of GAA and EO, BO, and HO, and polyamides consisting of GAA and EA, BA, and HA obtained by (c) and (d) solution polymerization, and (e) and (f) interfacial polymerization.

3.3.3. Chemical structures of GAA-based polyamides synthesized by interfacial polymerization

We tried to obtain NMR spectra of all the obtained polyesters and polyamides without purification to determine their molecular structures. However, the NMR spectra were complex because the peaks of remaining monomers, large amounts of TEA, and polymers overlapped and no clear peaks that could be assigned to pure polymer chains were observed.

We tried to purify the polyamides obtained by interfacial polymerization by dialysis against water using a dialysis membrane with a molecular-weight cutoff of 1000, which was the lowest value for our obtained products. The yields of the obtained polyamides were a few milligrams, indicating that most of the polymers went through the membrane. Improved purification methods need to be developed to increase the yields.

The ^{1}H NMR spectra of the polyamides consisting of GAA and EA, BA, and HA are shown in Figure 3-2. The broad peaks assigned to the methine protons of GAA are observed at 5–6 ppm; the broadening of this peak indicates successful polymerization of GA. The four broad peaks at 2 ppm are assigned to the methyl protons of acetyl groups, indicating that the acetyl groups were retained as hydroxyl-protecting groups during polymerization. The peak at 3.2 ppm is assigned to methylene protons adjacent to an amide group, indicating that an amide bond formed and polymerization proceeded. Other methylene protons were also observed, at 1.5 ppm for BA, 1.2 and 1.5 ppm for HA.

The molecular structures of glucaric and mannaric acids are symmetric, but GA has an asymmetric structure. We previously reported that the conformation of GA in solution is bent rather than fully extended, because of its asymmetric structure at C5. We suggest that this bent and asymmetric conformation could affect the molecular structure and that the properties of the obtained polyamides would be affected by the direction of the GAA monomer unit, namely head-to-tail or tail-to-head, in the polymer chain, similar to tacticity in polypropylene. Styron et al. examined the conformation of GA using computer modeling and also suggested that the asymmetric structure of GA would affect the structures and properties of GA-based polymers (Styron et al. 2002). In this study, the direction of the GAA monomer could not be determined using NMR spectroscopy. However, control of the tacticity of GAA-based polymers will be important for strict control of their properties, e.g., thermal and mechanical properties and crystallinity.

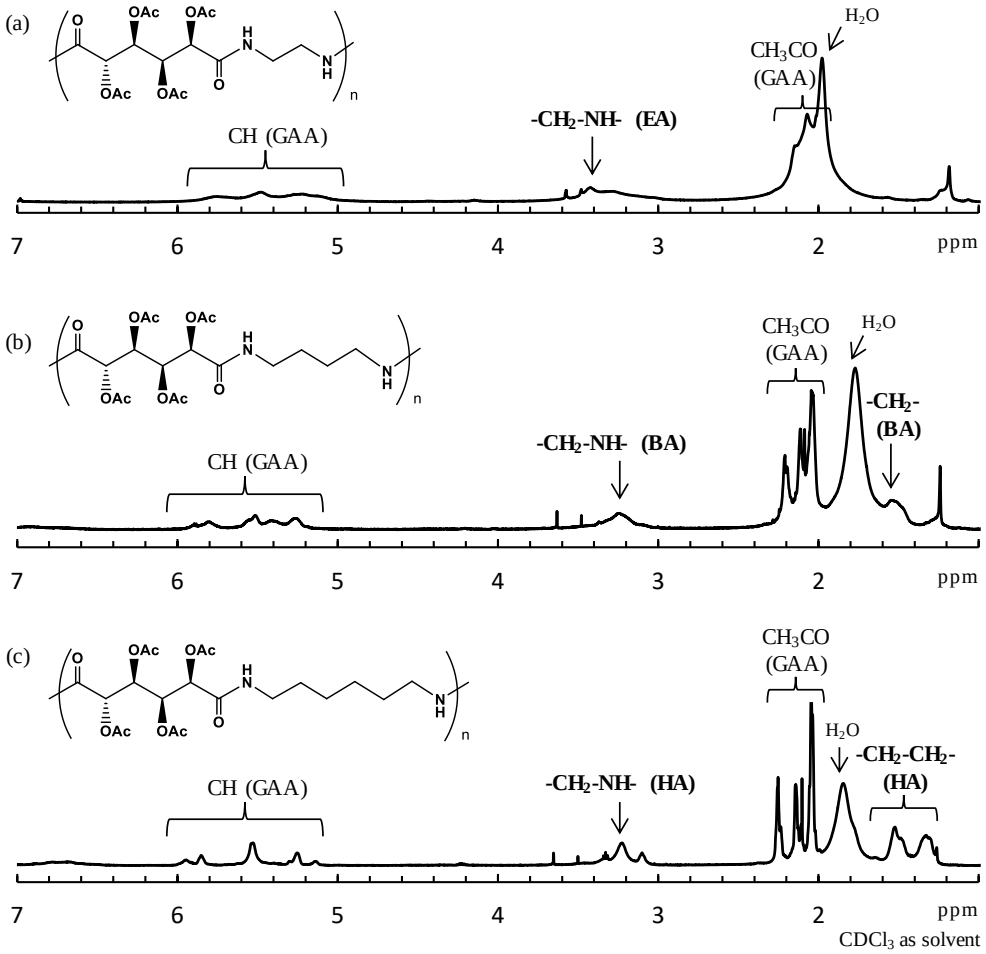


Figure 3-2. ^{1}H NMR spectra of the polyamide consisting of GAA and (a) EA, (b) BA, and (c) HA.

3.3.4. Thermal properties of GAA-based polyamides synthesized by interfacial polymerization

The thermal behaviors of the GAA-based polyamides were investigated using TGA and DSC. The samples were mixtures of the polyamides and GAA monomers because purification. was difficult. The TGA thermograms in Figure 3-3 show that the first weight losses of polyamides occurred at 150–200 °C; these are attributed to degradation of GAA and diamine monomers. The residues, amounting to about 40% of the total weights, were attributed to sodium chloride, which was formed during polymerization. We expected second weight losses at ca. 250 °C from degradation of the obtained polyamides.

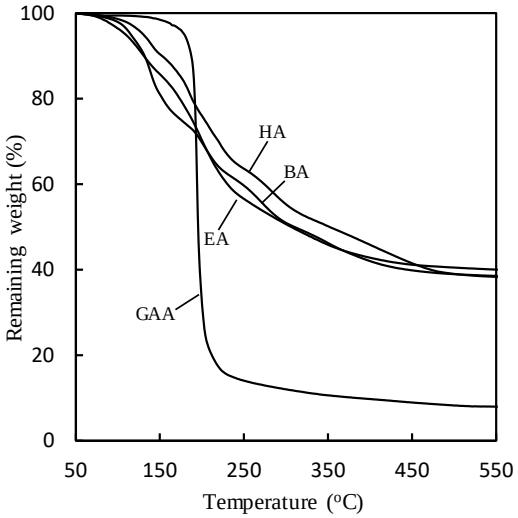


Figure 3-3. TGA thermograms of GAA and polyamides consisting of GAA and EA, BA, and HA obtained by interfacial polymerization.

Figure 3-4 shows the DSC curves of the GAA-based polyamides during the first heating scan. Endothermic peaks were observed for the polyamides with EA, BA, and HA at 119.5, 139.4, and 141.7 °C, respectively. The melting points (T_ms) of the GAA and HA monomers were observed at 50 and 44 °C, respectively. EA and BA could not be subjected to DSC because they were liquid at room temperature. These endothermic peaks were therefore attributed to the T_ms of the GAA-based polyamides, indicating that they were crystalline polymers. The TGA results show that degradation of these monomers occurred below 140 °C, supporting the conclusion that the endothermic peaks in the DSC curves at ca. 140 °C arose from polyamide melting rather than monomer degradation.

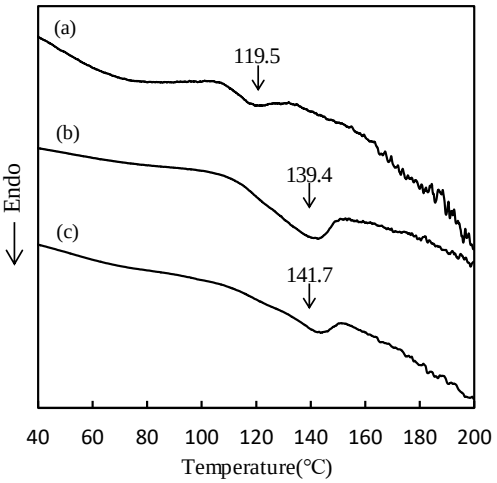


Figure 3-4. DSC thermograms of the polyamides consisting of GAA and (a) EA, (b) BA, and (c) HA, obtained by interfacial polymerization.

The POM observations shown in Figure 3-5 also inferred that the polyamides melted and turned clear at these T_ms and that the obtained GAA-based polyamides were thermoplastic polymers.

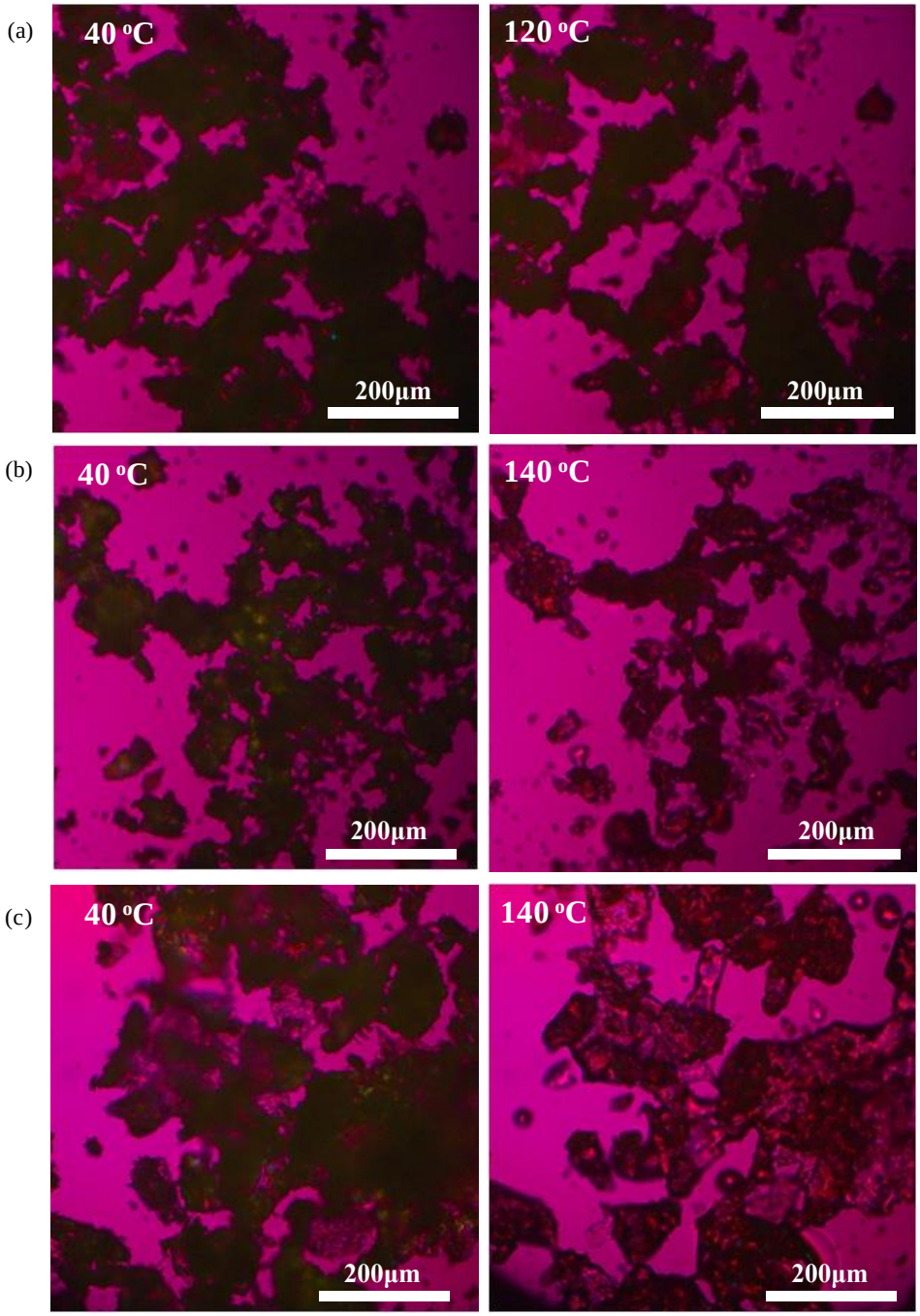


Figure 3-5. POM images of the polyamides consisting of GAA and (a) EA, (b) BA, and (c) HA obtained by interfacial polymerization.

Glass-transition temperature peaks were not observed for the polyamides, probably because they overlapped with the melting peak of the GAA monomer. The T_ms of the polyamides increased from 119.5 to 139.4 to 141.7 °C with increasing alkyl carbon number of the diamine monomer. This is contrary to the general tendency for T_m to decrease with increasing alkyl carbon number because of improved molecular motion. We suggest that this opposite trend is the result of steric hindrance by the acetyl groups in the GAA unit in the formation of amide hydrogen bonds, resulting in an increase in T_m. We suspect that more hydrogen bonds were formed between molecules when the amide bonds were sufficiently separated along the main chain by long diamine alkyl chains to allow amide bond formation.

3.4. Conclusions

Polymerization of GAA was performed with aliphatic diols (EO, BO, and HO) and diamines (EA, BA, and HA) via solution or interfacial polymerization. The GAA-based polyesters and polyamides dissolve in water, alcohol, and other common organic solvents. The M_ws of the polymers obtained via solution polymerization was less than 8 000. The M_ws of the polyamides obtained by interfacial polymerization were $14.5 \times 10^3 – 20.8 \times 10^3$. DSC and POM showed that the GAA-based polyamides were thermoplastic with T_ms at ca. 120–140 °C, indicating that these polyamides were crystalline. The T_m increased with increasing diamine alkyl carbon number, probably because of steric hindrance by acetyl groups in amide bond formation. It is important to improve the purification methods, yields, and molecular weights of GAA-based polymers for future applications of GA.

References

Alla, A., J. Oxelbark, A. Rodriguez-Galan & S. Munoz-Guerra (2005) Acylated and hydroxylated polyamides derived from L-tartaric acid. *Polymer,* 46**,** 2854-2861.

Chen, L. & D. E. Kiely (1996) Synthesis of stereoregular head,tail hydroxylated nylons derived from D-glucose. *Journal of Organic Chemistry,* 61**,** 5847-5851.

Galbis, J. A., M. D. Garcia-Martin, M. V. de Paz & E. Galbis (2016) Synthetic Polymers from Sugar-Based Monomers. *Chemical Reviews,* 116**,** 1600-1636.

Hashimoto, K., M. Okada & N. Honjou (1990) RING-OPENING POLYADDITION OF D-GLUCARO-1,4-6,3-DILACTONE WITH PARA-XYLYLENEDIAMINE. *Makromolekulare Chemie-Rapid Communications,* 11**,** 393-396.

Hashimoto, K., S. Wibullcksanakul & M. Okada (1995) MACROMOLECULAR-SYNTHESIS FROM SACCHARIC LACTONES - POLYADDITION OF D-GLUCARO-1,4/6,3-DILACTONES AND D-MANNARO-1,4/6,3-DILACTONES WITH DIISOCYANATES AND HYDROLYZABILITY OF THE RESULTING POLYURETHANES HAVING DILACTONE RINGS IN THE MAIN CHAINS. *Journal of Polymer Science Part a-Polymer Chemistry,* 33**,** 1495-1503.

Hashimoto, K., S. Wibullucksanakul, M. Matsuura & M. Okada (1993) MACROMOLECULAR-SYNTHESIS FROM SACCHARIC LACTONES - RING-OPENING POLYADDITION OF D-GLUCARO-1,4/6,3-DILACTONES AND D-MANNARO-1,4/6,3-DILACTONES WITH ALKYLENEDIAMINES. *Journal of Polymer Science Part a-Polymer Chemistry,* 31**,** 3141-3149.

Kiely, D. E., L. Chen & T. H. Lin (1994) HYDROXYLATED NYLONS BASED ON UNPROTECTED ESTERIFIED D-GLUCARIC ACID BY SIMPLE CONDENSATION-REACTIONS. *Journal of the American Chemical Society,* 116**,** 571-578.

--- (2000) Synthetic polyhydroxypolyamides from galactaric, xylaric, D-glucaric, and D-mannaric acids and alkylenediamine monomers - Some comparisons. *Journal of Polymer Science Part a-Polymer Chemistry,* 38**,** 594-603.

Mansour, E., S. H. Kandil, H. Hassan & M. A. E. Shaban (1990) SYNTHESIS OF CARBOHYDRATE-CONTAINING POLYAMIDES AND STUDY OF THEIR PROPERTIES. *European Polymer Journal,* 26**,** 267-276.

Orgueira, H. A., R. Erra-Balsells, H. Nonami & O. Varela (2001) Synthesis of chiral polyhydroxy polyamides having chains of defined regio and stereoregularity. *Macromolecules,* 34**,** 687-695.

Rosu, C., P. S. Russo, W. H. Daly, R. Cueto, J. A. Pople, R. A. Laine & Negulescu, II (2015) Sugar-Based Polyamides: Self-Organization in Strong Polar Organic Solvents. *Biomacromolecules,* 16**,** 3062-3072.

Chapter 4

Synthesis of aromatic polyamides from D-glucaric acid

This chapter is scheduled to be published in the form of a scientific journal within 5 years.

本章の内容は、学術雑誌論文として出版する計画があるため公表できない。５年以内に出版予定。

Chapter 5

Synthesis of three-component copolymers from D-glucaric acid

This chapter is scheduled to be published in the form of a scientific journal within 5 years.

本章の内容は、学術雑誌論文として出版する計画があるため公表できない。５年以内に出版予定。

Chapter 6

General conclusions

In chapter 2, GAA with an acyclic structure was synthesized successfully from GA using acetic anhydride and sulfuric acid to prevent the formation of lactones during polymerization. The chemical structure of GAA was confirmed by one-dimension (1D) and two-dimension (2D) NMR techniques. The ^{1}H and ^{13}C NMR peaks for GAA were assigned based on COSY, HSQC, and HMBC.

In chapter 3, GAA was converted to GACA for further application as a monomer. Polymerization of GAA was performed with aliphatic diols (EO, BO, and HO) and diamines (EA, BA, and HA) via solution or interfacial polymerization. The GAA-based polyesters and polyamides were dissolved in water, alcohol, and other common organic solvents. The weight-average molecular weights of the polyesters were 400 - 700; those of the polyamides obtained by solution and interfacial polymerizations were $5.9 \times 10^3 – 8.0 \times 10^3$ and $14.5 \times 10^3 – 20.8 \times 10^3$, respectively. The polyamides synthesized via interfacial polymerization are potential polymer materials because of their high molecular weight. DSC showed that the polyamides were thermoplastic and melted at ca. 140 °C that confirmed by POM, indicating crystallinity. The melting points increased with increasing number of diamine alkyl carbons, which probably because of steric hindrance by acetyl groups in amide bond formation. However, these aliphatic polyamides were soluble in water and common organic solvent, which make it very difficult to purify them.

The above results show that it is important to improve the purification methods, yields, and molecular weights of GAA-based polymers for future applications. However, these GAA-based polymers are expected to have a potential to be used as novel bio-based polymer materials.

LIST OF PUBLICATIONS

1. Yuxin Wu, Yukiko Enomoto-Rogers, Hisaharu Masaki and Tadahisa Iwata, Synthesis of crystalline and amphiphilic polymers from D-glucaric acid, *ACS Sustainable Chemistry & Engineering*, 4(7), 3812-3819 (2016)

2. Yuxin Wu, Yukiko Enomoto, Hisaharu Masaki and Tadahisa Iwata, Synthesis of polyamides from sugar derived D-glucaric acid and aromatic diamines, *Polymer International* (Submitted)

ACKNOWLEDGEMENTS

Firstly, I would like to express my sincere gratitude to my advisor Prof. Tadahisa Iwata for the continuous support of my Ph.D. study and related research, for his patience, motivation, and immense knowledge. His guidance helped me in all the time of research and writing of this thesis. I could not have imagined having a better advisor and mentor for my Ph.D. study.

My sincere thanks also goes to A/Prof. Yukiko Enomoto, who gave me advice and encouragement about synthesis planning, how to use the equipment and how to write a scientific paper.

I would also like to thank the rest of my thesis committee: Prof. Akio Takemura, A/Prof. Tomoya Yokoyama, and Prof. Hideki Abe (RIKEN), for their insightful comments and encouragement, but also for the hard question which incented me to widen my research from various perspectives.

I would like to express my sincere gratitude to Ensuiko Sugar Refining Co., Ltd. (Yokohama, Japan) and Dr. Hisaharu Masaki who kindly provided the raw material D-glucaric acid and had the opportunity to start this research.

I would like to thank Japan Society of Promotion of Science (JSPS) DC2 program (17J04203) for the support of my life and research.

I would also like to express my sincere gratitude to A/Prof. Satoshi Kimura and A/Prof. Daisuke Ishii (Tokyo University of Agriculture), Taizo Kabe who gave me adequate advice through seminars and research reports and taught me how to use experimental instruments.

I thanks my labmates, Zhigang Ling, Takehiro Dannjo, Wenjia Zhai, Tatsuya Goto, Chih-Ying Chien, Sakarin Puanglek, Hakyong Lee, Hongyi Gan and other master and undergraduate students, for the support in my research life.

Last but not the least, a special thanks to my family, for supporting me spiritually throughout writing this thesis and my life in general.

March 2018