Carbohydrate-based Building Blocks and Step-growth Polymers
synthesis, characterization and structure-properties relations

PROEFSCHRIFT

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Carbohydrate-based Building Blocks and Step-growth Polymers
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Abbreviation and symbols

1,4-BDO 1,4-butanediol
1,6-HDO 1,6-hexanediol
13C NMR carbon-13 Nuclear Magnetic Resonance spectroscopy
1D NMR 1-Dimensional Nuclear Magnetic Resonance spectroscopy
2D-COSY NMR 2-Dimensional Correlation Nuclear Magnetic Resonance spectroscopy
1H NMR hydrogen-1 Nuclear Magnetic Resonance spectroscopy
AA adipic acid
ATR-FTIR Attenuated Total Reflection Fourier-Transform InfraRed
BHT butylated hydroxytoluene
BH3-THF borane-tetrahydrofuran complex
BrA brassylic acid
BTf bismuth(III) triflate
CDCl3 deuterated chloroform
CHCl3 chloroform
(CH3)3COK potassium tert-butoxide
CH3CO2K potassium acetate
trans-CHDA trans-cyclohexanedicarboxylic acid
VT-CP/MAS Variable-temperature (VT) 13C{1H} cross-polarization/magic-angle spinning
CuCN copper cyanide
daII diaminoisoidide ((3S,6S)-hexahydrofuro[3,2-b]furan-3,6-diamine)
DAH isohexides (1,4,3,6-dianhydrohexitols)
DBTO dibutyltin(IV)oxide
DBU 1,8-diazabicyclo[5.4.0]undec-7-ene
DFT density functional theory
DMA dimethyl adipate
DMF dimethylformamide
DMSO dimethyl sulfoxide
DMSO-d6 deuterated dimethyl sulfoxide
DMT dimethyl terephthalate
DSC Differential Scanning Calorimetry
EG ethylene glycol
EA ethyl acetate
EtOH ethanol
FDA furan-2,5-dicarboxylic acid
Galx dimethyl 2,3,4,5-di-O-methylene galactarate
GLC gas-liquid chromatography
ΔH enthalpy of transition
HCl hydrogen chloride
HFIP  1,1,3,3,3-hexafluoro-2-propanol
II  isoidide (1,4:3,6-D-dianhydro-L-iditol)
IIDTF  isoidide bistri fluoride
(\((3S,6S)\)-hexahydrofuro[3,2-b]furan-3,6-diyiulfosulfonate)
IIDCA  isoidide 2,5-dicarboxylic acid (\((3S,6S)\)-hexahydrofuro[3,2-b]furan-3,6-dicarboxylic acid)
IIDMA  isoidide 2,5-dimethylamine
(\((3S,6S)\)-hexahydrofuro[3,2-b]furan-3,6-diyi dimethanamine)
IIDMC  isoidide-2,5-dimethylcarboxylate
IIDML  isoidide-2,5-dimethanol (\((3S,6S)\)-hexahydrofuro[3,2-b]furan-3,6-diyi dimethanol)
IIDN  isoidide-2,5-dinitrile (\((3S,6S)\)-hexahydrofuro[3,2-b]furan-3,6-dicarbonitrile)
IM  isomannide (1,4:3,6-dianhydro-D-glucitol)
IMDN  isomannide-2,5-dinitrile
IPA  isophthalic acid
IS  isosorbide-2,5-dihydroxyacetone
ISBTf  isorebitride bistri fluoride
(ISR,6S)-hexahydrofuro[3,2-b]furan-3,6-bis(trifluoromethanesulfonate)
ISDN  isorebitride-2,5-dinitrile (\((3R,6S)\)-hexahydrofuro[3,2-b]furan-3,6-dicarbonitrile)
KCN  potassium cyanide
KOH  potassium hydroxide
LiAlH4  lithium aluminium hydride
MALDI-Tof-MS  Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass
MgSO4  magnesium sulfate
MeOH  methanol
\(\text{Mn}\)  number-average molecular weight (g/mol)
\(\text{Mw}\)  weight-average molecular weight (g/mol)
MW  molecular weight
NaCN  sodium cyanide
\(\Phi\)  Cremer-Pople ring puckering phase angle
PBT  poly(butylene terephthalate)
PCT  poly(1,4-cyclohexylylmethylene terephthalate)
PDI  polydispersity index
PE-nAds  poly(alkylene adipates)
PE-nIIDCs  poly(alkylene isoidide dicarboxylates)
PETF  poly(ethylene furan-2,5-dicarboxylate)
PET  Poly(ethylene terephthalate)
\(pK_b\)  base dissociation constant
Q  Cremer-Pople ring puckering amplitude
SA  sebacic acid
SEC  size exclusion chromatography
SSPC  solid-state post-condensation
\(t\)  time [s]
T  temperature [°C]
\(T_{5\%}\)  temperature of 5% mass loss [°C]
\(T_{\text{max}}\)  temperature of maximal rate of decomposition [°C]
TA  terephthalic acid
TBAC  tetrabutylammonium cyanide
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>TBD</td>
<td>1,5,7-triazabicyclo[4.4.0]dec-5-ene</td>
</tr>
<tr>
<td>TBT</td>
<td>titanium(IV) butoxide</td>
</tr>
<tr>
<td>Te</td>
<td>crystallization temperature [°C]</td>
</tr>
<tr>
<td>Tcc</td>
<td>cold crystallization temperature [°C]</td>
</tr>
<tr>
<td>TEMP</td>
<td>((2,2,6,6-tetramethylpiperidin-1-yl)oxy)</td>
</tr>
<tr>
<td>Tf2O</td>
<td>trifluorosulfonic anhydride</td>
</tr>
<tr>
<td>Tg</td>
<td>glass transition temperature [°C]</td>
</tr>
<tr>
<td>TIP</td>
<td>titanium(IV) isopropoxide</td>
</tr>
<tr>
<td>TGA</td>
<td>thermogravimetric analysis</td>
</tr>
<tr>
<td>THF</td>
<td>tetrahydrofuran</td>
</tr>
<tr>
<td>Tm</td>
<td>melting temperature [°C]</td>
</tr>
<tr>
<td>TMAB</td>
<td>N-acetyl-N,N,N-trimethylammonium bromide</td>
</tr>
<tr>
<td>WAXS</td>
<td>wide-angle X-ray scattering</td>
</tr>
</tbody>
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Summary

Driven by the concern about the future petro-chemical feedstock availability, as well as the need for a green and sustainable society, renewable and bio-based materials have become the natural candidates for alternatives to petro-chemicals. As the most abundant biomass feedstock, carbohydrates are attracting significant attention from both academia and industry for the production of chemicals, fuels and energy. However, one major drawback of directly using carbohydrates in industrial processes is their limited thermal stability caused by the existence of multiple functional groups, for instance hydroxyl groups. Consequently, simplified or bi-functional carbohydrate-derived building blocks are often more attractive than the virgin carbohydrates for polymer chemists. In this thesis, we aim to 1) develop a new family of difunctional bio-based building blocks, and 2) utilize these new building blocks as AA monomers to synthesize step-growth polymers, such as polyesters and polyamides. Ideally, the new polymers are expected to be semicrystalline, preferably having high melting ($T_m$) and high glass transition temperatures ($T_g$), and can be used as the potential fully or partially bio-based engineering plastics.

Isohexides (1,4,3,6-dianhydrohexitols), a group of secondary, rigid diols, as well as their derivatives are interesting carbohydrate-derived building blocks for various types of step-growth polymers, such as polyesters, polyamides and polycarbonates. Due to the intrinsic rigidity of the structures, isohexides are capable of increasing the glass transition temperatures when incorporated into polymers. However, the relatively poor reactivity of the secondary hydroxyl groups of isohexides has been recognized as a main drawback, which often results in low molecular weight or discolored polymers. In order to overcome these problems, as well as utilizing the rigidity of the isohexide skeleton, a new family of 1-carbon extended isohexide-derivatives were designed and synthesized by transforming the less reactive secondary hydroxyl functionalities into more reactive ones. Based on a key dinitrile intermediate, viz. isoididedinitrile (IIDN), the novel isohexide-derived building blocks were obtained. They are: isoidide-2,5-dicarboxylic acid (IIDCA) and its dimethyl ester (IIDMC), isoidide-2,5-dimethanol (IIDML) and isoidide-2,5-dimethyleneamine (IIDMA). After optimization of the respective synthetic routes, these building blocks were obtained at sufficient scales (5–20 g/batch) and high purities (>99.5%) to be suitable for polymerizations.

Three series of polyesters based on the novel 1-carbon extended isohexides were synthesized. The first series of polyesters is based on isoidide dicarboxylic acid (IIDCA) and linear alkylene diols. Unexpectedly, they have rather low $T_m$ (60–100 °C) values whereas the recorded low $T_g$ values (~30–18 °C) were approximately expected. The second series of polyesters is fully based on renewable, isohexide-derived monomers. The combination of
both isohexide-based AA/BB monomers gave significantly higher \( T_g \) values (45–85 °C) than the partially linear aliphatic polyesters of the first series. Importantly, this part of the project revealed the promising characteristics (reactivity, rigidity and thermal stability) of isoidide-2,5-dimethanol (IIDML) for potential applications in performance polymers with high \( T_g \) and \( T_m \). Therefore, the third series of polyesters was entirely focused on IIDML-based semi-aromatic systems. The \( T_g \) and \( T_m \) values of these polyesters were found to exceed even those of the conventional PET and PBT polyesters, confirming our expectation that IIDML is a promising rigid cyclic diol for engineering plastic applications.

Two series of semicrystalline (co)polyamides were synthesized from the new isoidide 2,5-dimethyleneamine (IIDMA) or from a mixture of IIDMA and 1,6-hexamethylene diamine with the biobased dicarboxylic acids sebacic acid or brassylic acid. A combination of melt polymerization of nylon salts with solid-state polycondensation (SSPC) processes afforded the desired copolyamides with maximum number average molecular weight \( (M_n) \) of 49,000 g/mol. Analysis by temperature dependent solid state NMR and FT-IR spectroscopies revealed that the new diamine IIDMA exist in both the crystalline and amorphous phases of the copolyamides. Given the sufficiently high \( T_m \) values (~200 °C) of the copolyamides containing less than 50% of IIDMA, these bio-based semicrystalline copolyamides can be useful for engineering plastic applications.

By comparing the thermal properties of the polymers based on the new isohexide-based building blocks, i.e. IIDCA, IIDML and IIDMA, with relevant reference polymers, systematic structure-thermal properties studies of each series of polymers were conducted. This work objectively evaluated the relative rigidities, reactivities and thermal stabilities of these new building blocks with respect to those of the parent isohexides, as well as with respect to their linear, cyclic aliphatic and aromatic analogues. Both the experimental (i.e., single crystal X-ray diffraction) and computational-aided methods (i.e., Density Functional Theory (DFT)) were employed to elucidate the structural characteristics of the isohexide-based building blocks, as well as to understand the specific thermal properties of the polymers based thereon.

Additional efforts were invested to expand the dinitrile platform to the other stereo-isomers. The isomeric isohexide dinitriles were synthesized by base-induced epimerization. The strong non-nucleophilic organic base 1,8-diazabiclycloundec-7-ene (DBU) was found to be a suitable catalyst for such type of isomerization. A kinetic study on the epimerization of three dinitrile isomers revealed an equilibrium between the three possible isomers in THF. Single crystal X-ray diffraction studies demonstrated several structural characters of these molecules regarding their symmetry and linearity. Density Functional Theory (DFT) calculations further supported the base-induced epimerization mechanism.
This work concerns a pioneering study of deoxy-1-carbon-extended isohexide-based building blocks. All the monomers and polymers synthesized, characterized and evaluated in this thesis are entirely new. Suitable synthetic laboratory-scale protocols were developed for all the monomers and polymers. The reported study of the structure-thermal properties relations, as well as the crystal structure elucidation by single crystal X-ray diffraction and DFT, are also of high importance concerning the field of isohexide-based polymers and will certainly prove to be very useful for drawing conclusions on the industrial feasibility of such bio-based materials.
Samenvatting

Vanwege de onzekerheid over de toekomstige beschikbaarheid van petrochemische grondstoffen en het verlangen naar een groene en duurzame samenleving zijn hernieuwbare en biogebaarde producten vanzelfsprekende alternatieven. De meest voorkomende biomassa-grondstof, koolhydraten, krijgt veel aandacht van zowel de academische als de industriële wereld voor de productie van chemicaliën, brandstoffen en energie. Echter, de gelimiteerde thermische stabiliteit, door bijvoorbeeld meerdere hydroxylgroepen, is een groot nadeel voor het direct gebruikmaken van koolhydraten in industriële processen. Zodoende zijn vereenvoudigde of bifunctionele uit koolhydraten opgebouwde bouwstenen vaak aantrekkelijker voor polymeerchemici dan niet-gemodificeerde koolhydraten. Het uitgangspunt van dit proefschrift is 1) het ontwikkelen van een nieuwe serie bifunctionele biogebaarde bouwstenen en 2) deze nieuwe bouwstenen te gebruiken als AA monomeren om stapgroeipolymeren zoals polyesters en polyamides te synthetiseren. Indien deze nieuwe polymeren semikrystallijn zijn, en bij voorkeur een hoge smelt- ($T_m$) en glasovergangstemperatuur ($T_g$) hebben, zouden deze van toepassing kunnen zijn in volledig of deels biogebaarde hoogwaardige kunststoffen.

Isohexides (1,4,3,6-dianhydrohexitolen), een groep starre secundaire diolen, zijn, evenals hun derivaten, interessante uit koolhydraten ontwikkelde bouwstenen voor een verscheidenheid aan stapgroeipolymeren zoals polyesters, polyamides en polycarbonaten. Dankzij de starheid van de cyclische structuur is het mogelijk met isohexides de glasovergangstemperatuur te verhogen wanneer deze in polymeren worden ingebouwd. De relatief lage reactiviteit van de secundaire hydroxyl-groepen van isohexides is welbekend als het voornaamste nadeel en resulteert vaak in laag molecuulair gewicht of verkleurde polymeren. Om deze gevolgen te voorkomen, maar tegelijkertijd de starheid van het isohexide skelet te behouden is een nieuwe serie van koolstofverlengde isohexide derivaten ontworpen en gesynthetiseerd door de hydroxyl-groepen te modificeren naar functionele groepen met een hogere reactiviteit. Uitgaande van de belangrijke dinitril tussenvorm, namelijk isoididedinitril (IIDN)), werden deze nieuwe isohexide-derivaten verkregen. Deze zijn: isoidide-2,5-dicarbonzuur (IIDCA) en het dimethylester (IIDMC), isoidide-2,5-dimethanol (IIDML) en isoidide-2,5-dimethyleenamine (IIDMA). Na optimalisatie van de benodigde syntheses werden de monomeren in voldoende hoeveelheid (5-20 g opbrengst in de laatste synthese stap) en hoge zuiverheid (>99.5%) geschikt bevonden voor polymerisaties.

Drie polyester series uitgaande van de nieuwe koolstofverlengde isohexides werden gesynthetiseerd. De eerste serie is gebaseerd op isoidide dicarbonzuur (IIDCA) en lineaire alkaandiole. Deze polyesters hadden onverwacht lage $T_m$ (60–100 °C) waarden terwijl de
lage $T_g$ waarden (~30–18 °C) wel in de verwachting lagen. De tweede serie zijn polyesters volledig gebaseerd op hernieuwbare, isohexide derivaten. De combinatie van op isohexide gebaseerde AA/BB monomeren gaf aanzienlijk hogere $T_g$ waarden (45–85 °C) dan de deels lineair alifatische polyesters uit de eerste series. Dit deel van het project bracht de veelbelovende eigenschappen (reactiviteit, starheid en thermische stabilititeit) van isoidide-2,5-dimethanol (IIDML) naar voren voor mogelijke toepassing in polymeren met hoge $T_g$ en $T_m$. Daarom is een derde serie polyesters gesynthetiseerd, volledig gecentreerd rond IIDML-gebaseerde semi-aromatische systemen. De $T_g$ en $T_m$ waarden van deze polyesters overtroffen zelfs de veelgebruikte PET en PBT polyesters wat onze verwachtingen, dat IIDML een veelbelovend star en cyclisch diol is voor hoogwaardige kunststoffen, bevestigde.

Twee series semikristallijne (co)-polyamides werden gesynthetiseerd uit het nieuwe isoidide 2,5-dimethyleneamine (IIDMA) of uit mengsel van IIDMA en 1,6-hexamethyleen diamine met de biogebaseerde dicarbonzuren sebacinezuur of brassylzuur. Een combinatie van de smeltpolymerisatie van nylon zouten met vaste fase polycondensatie (solid-state polycondensation, SSPC) resulteerde in de gewenste copolyamides met een maximum getalgemiddelde molecuulmassa ($M_w$) van 49,000 g/mol. Analyse door temperatuur afhankelijke vaste fase NMR en FT-IR spectroscopie wees uit dat dit nieuwe diamine IIDMA voorkomt in zowel de kristallijne als de amorfe fase van de copolyamides. Vanwege de voldoende hoge $T_m$ waarden (~200 °C) van de copolyamides die minder dan 50% IIDMA bevatten zouden deze biogebaseerde, semikristallijne copolyamides kunnen voldoen als hoogwaardige kunststoffen.

Door het vergelijken van de thermische eigenschappen van polymeren gebaseerd op de nieuwe uit isohexide opgebouwde bouwstenen, namelijk IIDCA, IIDML en IIDMA, met relevante vergelijkbare polymeren werd een systematische structuur-thermische eigenschappen studie uitgevoerd. Hierin werden de relatieve starheid, reactiviteit en thermische stabilititeit van deze nieuwe bouwstenen vergeleken met de oorspronkelijke isohexides evenals hun lineaire, cyclo-alifatische en aromatische analoque verbindingen. Zowel experimentele (dwz. single crystal X-ray diffraction) en computationele methodes (dwz. Density Functional Theory (DFT)) werden ingezet om de structureigenschappen van de isohexide-gebaseerde bouwstenen en tevens de specifieke thermische eigenschappen van de daaruit ontwikkelde polyamide nader toe te lichten.

Extra aandacht werd besteed aan het uitbreiden van het isohexide dinitril naar de andere stereo-isomeren. Deze isomeren werden gesynthetiseerd door base-gekatalyseerde epimerisatie. De sterke niet-nucleofiele organische base 1,8-diazabicycloundec-7-ene (DBU) werd geschikt bevonden als katalysator voor dit type isomerisatie. Een kinetische studie wees uit dat de epimerisatie van drie mogelijke dinitril isomeren een evenwicht vertoonde in THF. Single crystal X-ray diffraction demonstreerde verscheidene structurele
karakteristieken van deze moleculen wat betreft hun symmetrie en lineariteit. Density Functional Theory (DFT) berekeningen ondersteunde het base-gekatalyseerde epimerisatiemechanisme.

Dit proefschrift bevat origineel onderzoek naar deoxy-1-koolstof verlengde isohexide-gebaseerde bouwstenen. Alle monomeren en polymeren die zijn gesynthetiseerd, gekarakteriseerd en geëvalueerd in dit proefschrift zijn volledig nieuw. Toepasbare werkwijzen zijn ontwikkeld voor synthese op laboratoriumschaal voor alle monomeren en polymeren. Het onderzoek naar de relaties tussen structuur en thermische eigenschappen en kristalstructuur door middel van single crystal X-ray diffraction en DFT zijn van belang voor het terrein van isohexide-gebaseerde polymeren en zal zeer waarschijnlijk bijdragen aan het trekken van conclusies over de industriële haalbaarheid van deze biogebaseerde producten.
Introduction

1.1 Renewable resources and biomass

For several thousands of years natural polymers have been indispensable for mankind to serve as food, to provide shelter and clothing and to serve as a source of energy. During the development of the human society, the use of natural polymers became more sophisticated, illustrated by the development of various technologies such as papermaking, textile manufacturing and wood processing. In the mid-nineteenth century the chemical modification of natural materials gave rise to the first commercial thermoplastic materials, like cellulose acetate and nitrate, and the first elastomer, i.e. vulcanized natural rubber. In the beginning of the twentieth century the development of various synthetic polymers (Bakelite, poly(vinylchloride), polystyrene, nylons, polyesters, etc.) brought the real breakthrough which significantly changed the life-style in modern society. Nowadays, these synthetic polymers are present in almost every aspect in our life and they are extensively used in the packaging industry, building and construction, thermal and electrical appliances, automotive industry, coating applications, as well as in demanding applications like military and aerospace.

A fundamental fact one should realize is that all developments of the polymer industry cannot be continued and not even be maintained without the abundant availability of raw materials, which are typically fossil resource based. For several decades, human beings have taken it for granted that fossil feed stocks are inexhaustible resources. In recent years, public awareness has been awoken by sharp increases in crude oil prices, concerns on fossil feedstock shortages as well as a deteriorating status of environmental conditions and climate change. In 1992, more than 180 governments agreed on a sustainable development in the 21st century during the United Nations Conferences on Environment and Development (UNCED), held in Rio de Janeiro. The “Rio declaration” claims “Human beings are at the center of concerns for sustainable development. They are entitled to a healthy and productive life in harmony with nature”.1 Over the last 20 years, various renewable
Chapter 1

resources have been evaluated as feedstock for the green and sustainable production of chemicals, fuels and energy. It is estimated that in 2050, use of renewable feed stocks will exceed those of the conventional fossil feed stock like e.g. coal, natural gas and oil, and become the major raw material resource for chemical industry (Figure 1-1).2

![Figure 1-1](image)

**Figure 1-1.** Raw materials used by the chemical industry in historical perspective. (a) Renewable feed stocks; (b) Coal; (c) Natural gas, oil.2

Concerning the production of chemicals, biomass is regarded as an essential renewable resource comprising a broad array of low and high molecular weight products, such as sugars, hydroxy and amino acids, lipids, and biopolymers such as cellulose, hemicellulose, chitin, starch, lignin and proteins.2 By far the most important and abundant class of biomass in terms of volume are carbohydrates, which comprise cellulose, semicellulose, starch and sucrose, and represent approximately 75% of the annual renewable biomass production (Figure 1-2).2,3 Only a minor fraction (ca. 4%) of this amount is used by man, the rest decays and recycles along natural pathways.2 Despite its ready availability, native carbohydrates are usually unsuitable for direct use in industrial processes for producing polymeric materials. The main reason is their limited thermal stability caused by the presence of a variety of reactive functional groups. Consequently, defunctionalization to obtain bifunctional carbohydrate-derived monomers is a practical strategy,4,5 yielding building blocks such as succinic acid6, furan-2,5-dicarboxylic acid (2,5-FDA or FDCA),7,9 and 1,4:3,6-dianhydrohexitols (isohexides) (Figure 1-3).10,11
Introduction

Figure 1-2. Distribution of types of natural products in biomass.²,³

<table>
<thead>
<tr>
<th>Natural Product</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lignin</td>
<td>20%</td>
</tr>
<tr>
<td>Fats, proteins, terpenoids, alkaloids, nucleic acids</td>
<td>20%</td>
</tr>
<tr>
<td>Semicellulose</td>
<td>25%</td>
</tr>
<tr>
<td>Cellulose</td>
<td>40%</td>
</tr>
<tr>
<td>Starch, sucrose</td>
<td>10%</td>
</tr>
<tr>
<td>Lignin</td>
<td>20%</td>
</tr>
<tr>
<td>Semicellulose</td>
<td>25%</td>
</tr>
<tr>
<td>Cellulose</td>
<td>40%</td>
</tr>
<tr>
<td>Starch, sucrose</td>
<td>10%</td>
</tr>
</tbody>
</table>

Succinic acid

Furan-2,5-dicarboxylic acid (2,5-FDCA)

1,4:3,6-dianhydrohexitols (isohexides)

Figure 1-3. Molecular structures of some representative bio-based difunctional building blocks.

Succinic acid is a useful component for producing commercially important polymers, such as polyamides and polyesters.¹²,¹³ FDCA has been extensively promoted as an important bio-based building block because of its claimed potential of substituting terephthalic acid (TA) in the production of thermoplastics.⁷–⁹ During the past years, the research activity concerning a family of sugar-derived bicyclic diols, namely the 1,4:3,6-dianhydrohexitols (isohexides, Figure 1-3), is continuously increasing. These molecules possess several unique features, as they are non-toxic, aliphatic, chiral, rigid and hydrophilic. Therefore, they attract significant attention in academia and industry. Although, to the best of our knowledge, no isohexide-based polymer has been commercialized thus far, the wide scope of research activities concerning these building blocks are indicative of their promising industrial potential. Isohexide-based chemistry is the main research topic of this thesis.
1.2 1,4;3,6-dianhydrohexitols (isohexides)

1.2.1 Structural characteristics of isohexides

Isohexides are a group of highly interesting bio-based compounds, which are found in three major isomeric forms, namely isosorbide (1,4;3,6-dianhydro-D-glucitol), isoidide (1,4;3,6-dianhydro-L-iditol) and isomannide (1,4;3,6-dianhydro-D-mannitol) (Figure 1-4). The central skeleton of the isohexides consists of two cis-fused tetrahydrofuran rings (2,6-dioxabicyclo[3,3,0]octane). The functional groups, viz. two secondary hydroxyl groups, are attached to carbons 2 and 5, respectively. The two tetrahydrofuran rings are not entirely planar but form a V-shape opening with dihedral angles of approximately 120°. The configurations of the three isohexide isomers are distinguished by the orientations of the hydroxyl groups, which are both endo for isomannide and both exo for isoidide, and 2-exo and 5-endo for isosorbide. These differences significantly influence their physical and chemical properties, including melting temperatures, reactivity and thermal stability.

Figure 1-4. Three isomeric 1,4;3,6-dianhydrohexitols (isohexides).
1.2.2 Preparation of isohexides

The preparation of isohexides comprises a limited number of (bio)organic transformations: sugar/polysaccharides such as sucrose, starch or cellulose are first depolymerized into monosaccharides (D-fructose, D-glucose) under acidic or enzymatic conditions and then hydrogenated into hexitols (D-glucitol, D-mannitol). Further dehydration of these sugar alcohols ultimately yields the three isohexide isomers (Scheme 1-1). Other hexitols, such as D-galactitol, D-gulitol, D-talitol and D-allitol can also serve as the precursors to produce isohexides.

![Scheme 1-1. Schematic synthetic pathway for the production of isohexides from biomass.](image)

Thus far, isosorbide is the only commercialized isohexide isomer produced at an industrial scale. As currently isosorbide is produced from food-grade precursors like starch or sucrose, extensive efforts have also been made to search for more sustainable biobased feedstocks, e.g. lignocellulosic biomass, which is abundantly available e.g. wood, straw,
agro-food residues.\textsuperscript{18-22} Isomannide is available from chemical suppliers, yet only in limited quantities compared to isosorbide.

The third isomer, isoidide, can be synthesized by hydrogenation of L-idose, followed by the acid-catalyzed cyclization of the resulting L-iditol.\textsuperscript{15,23,24} However, the lack of availability of L-idose from natural renewable resources severely limits this approach. Alternatively, as described by Thiem et al, isoidide can be synthesized from isosorbide in a 3-step fully stoichiometric route: protection of the \textit{exo}-hydroxyl by acetylation; transformation of the \textit{endo}-hydroxyl group into the \textit{exo}-benzoate ion via Mitsunobu inversion; and subsequent hydrolysis of both ester groups affording isoidide.\textsuperscript{25,26} More straightforward and atom-efficient methods have also been reported, for example the isomerization of isosorbide into a mixture of the three isomeric isohexides using a nickel catalyst under a hydrogen atmosphere.\textsuperscript{27} Highly pure L-iditol has been attempted by chromatographic fractionation from a mixture of L-iditol and L-sorbose as reported by Fuertes et al in 2006.\textsuperscript{28} Unfortunately, to date an efficient pathway is still lacking and isoidide remains a rare and expensive renewable compound.

1.2.3 Physical and chemical properties of isohexides

As shown in Figure 1-4, the \textit{endo}-hydroxyl groups form intramolecular hydrogen bonds with the oxygen atom in the opposite tetrahydrofuran ring, while the \textit{exo}-hydroxyl groups are not involved in such interactions. The two types of hydroxyl groups can e.g. be distinguished by Fourier transform infrared spectroscopy (FT-IR). According to the different absorption bands of O-H valence vibrations, the free \textit{exo} and the bonded \textit{endo} hydroxyl groups show absorptions at approximately 3625 cm\(^{-1}\) and 3540–3560 cm\(^{-1}\), respectively.

Depending on the specific reaction mechanism and conditions, the \textit{exo} and \textit{endo}-orientated hydroxyl groups (OH) exhibit different reactivities. Critical parameters are steric hindrance and/or intramolecular hydrogen bonding. The \textit{endo}-OH group appears to be more reactive than the \textit{exo}-orientated counterparts upon esterification with 4-toluenesulfonyl chloride\textsuperscript{29} or 4-(phenylazo)benzoyl chloride\textsuperscript{30} in pyridine. This was explained by an enhanced nucleophilicity of the \textit{endo}-OH being involved in the hydrogen bonding interactions.\textsuperscript{30,31} However, preferential cases have also been observed for \textit{exo}-OH e.g. the acetylation reaction of isosorbide, as summarized in a review article by Stoss and Hemmer.\textsuperscript{18} The \textit{exo}-orientated hydroxyl groups appear to be more reactive than the \textit{endo}-OH in the reaction of isosorbide with acetic anhydride in pyridine, while the \textit{endo}-acetylation product was found to be the major species when using pyridine hydrochloride. Therefore, when strong steric hindrance and/or a lack of activation of the \textit{endo}-OH are encountered, the reaction of the \textit{exo}-orientated hydroxyl groups will be predominating. Furthermore, in the
case of melt polymerization, the *exo*-OH is considerably more reactive than the *endo*-OH, as extensively demonstrated by many authors.\textsuperscript{32-34} This is assumed to be because that the less sterically-hindered is favorable for esterification and polymer chain growth.

The orientation of the hydroxyl groups also has a profound influence on the thermal stability of isohexides. The presence of *endo* hydroxyl groups has been observed to reduce the thermal and chemical stability of the bicyclic ring. Since *endo* hydroxyl groups are less reactive in e.g. (poly)esterification reactions due to steric hindrance, competitive reactions such as elimination of water or ring-opening cause the formation of unstable intermediates and a reduction of available end-groups. Therefore, isosorbide and isoidide are usually more thermally stable than isomannide during the melt polymerization.\textsuperscript{14} As isosorbide is known to be thermally stable up to 270 °C it can be used for polycondensation reactions in the melt.\textsuperscript{14}

### 1.2.4 The state of the art

#### 1.2.4.1 Brief history of isohexide chemistry

The earliest records of the research on “anhydrohexitols” dates back to the 1870’s to 1880’s when 1,4-anhydro-D-mannitol and 1,4:3,6-dianhydro-D-mannitol were studied by Bonchardaat\textsuperscript{35} and Fauconnier,\textsuperscript{36} respectively. However, general interest for this type of compounds remained low. In the 1940’s to 1950’s, isohexide chemistry entered a crucial stage. During this period, purification and structural characterization of the three isohexides were systematically conducted by different authors.\textsuperscript{15, 16, 37-39} Following a decrease in activities in the 1970’s to 1990’s the research interests for these compounds started to increase again.\textsuperscript{18} A range of derivatives were developed and the applications of isohexides were expanded to a rather wide scope, ranging from chemical and pharmaceutical intermediates to the food industry. An excellent review paper by Stoss and Hemmer from 1991 summarizes the major progress of the synthesis and applications of the parent isohexides and their derivatives during this period.\textsuperscript{18} Since the 1990s, along with the increased interest for sustainability and the exploration of biogenic chemicals, a sharp rise in the number of patent applications and publications concerning isohexide compounds can be seen. Several appealing features of isohexides, including their low toxicity, chirality and rigidity, have been recognized as attractive characteristics for an even wider scope of applications.
1.2.4.2 Major (industrial) applications of isohexides

Currently, of the three isomeric forms, isosorbide is attracting the majority of interest from both academia and industry, mainly due to its availability. The other two isomers, isomannide and isoidide, are basically limited to academic activities. In general, the applications of isohexides and their derivatives can be categorized into four groups:

1) Pharmaceutical applications. The pharmacodynamic properties of isosorbide make this molecule useful in pharmaceutical applications. Isosorbide was shown to have diuretic activity, being able to reduce the pressure of the intraocular and the cerebrospinal liquid, and as a consequence has been used to treat hydrocephalus and glaucoma.\(^{40}\) Isosorbide nitrate and dinitrate have been used as vasodilators since 1939 by lowering portal pressure and decreasing cardiac output.\(^{41}\) Moreover, the non-toxic isosorbide dimethyl ether has been propagated as a high boiling point (234°C) green solvent for the pharmaceutical industry exhibiting,\(^{11,42}\) Currently, commercial application of isosorbide is mainly limited to the above mentioned examples.

2) Fine chemical and fuel production. Some alkyl derivatives of isohexide are promising green solvents for cosmetic compositions and can be used as fuels, fuel additives and surfactants.\(^{11}\) Ditetrahydrofuran (2,6-dioxabicyclo[3,3,0]octane), a defunctionalized isohexide, has also been claimed to be a promising solvent by Wiggins\(^ {43}\) and Cope et al.\(^ {44}\) The production of isohexide-based surfactants is achieved by mono-substitution of its hydroxyl groups by alkyl chains, which creates a significant difference in the polarity of the remaining hydroxyl groups and the long, highly non-polar alkylester tails. Moreover, isosorbide diesters have shown excellent plasticizing effects.\(^ {45-47}\) “POLYSORB ID37” is a (pre-)commercial product developed by the French company Roquette Frères.\(^ {48}\)

3) Organic synthesis and catalysis. The chirality of isohexides and their derivatives has been utilized in synthesizing a variety of sophisticated molecules, such as chiral ionic liquids,\(^{49-51}\) phase-transfer catalysts,\(^ {52}\) and ligands for asymmetric catalysis (amino alcohols, amines, mono- and diphosphines, diphosphites, bis-diaminophosphites, etc.).\(^ {53-62}\)

4) Polymers. Di-functional isohexides and their derivatives are ideal AA/AB building blocks for the synthesis of step-growth polymers. A wide range of isohexide-based homo and copolymers have been reported. The rigidity and \(T_g\)-enhancing ability of isohexides, combined with low toxicity and chirality are important properties for a variety of applications, ranging from performance polymers to optical materials and biodegradable/biocompatible materials.\(^ {10,11,63}\)
1.3 Isohexide-based monomers and polymers

1.3.1 Key features of isohexides for polymer synthesis

One of the most explored fields concerning the application of isohexides are polymeric materials, mostly referring to step-growth polymers. A first review paper was published by Braun and Bergman in 1992,\textsuperscript{64} in which the early developments of isohexide-based polyesters, polycarbonates and polyurethanes were discussed. Later on, Kricheldorf presented another progress report\textsuperscript{63}, mainly focusing on isohexide-derived polyesters with special optical and liquid crystalline properties. Recently, an excellent review paper was published by Fenouillot et al.\textsuperscript{10}, which not only covers the most important and latest results on this subject, but also the commercial applicability as well as the industrial potential of isohexide-derived monomers. The scope of isohexide-based polymers has been remarkably broadened and encompasses even more classes than those already mentioned, such as polyamides, poly(ester amides), poly(ester imide)s and polyethers. It will be obvious that for some of these classes isohexide-derivatives are required. The potential industrial applications of these polymers include performance polymers (packaging and engineering plastics), liquid crystalline materials, powder coatings, plasticizers and biomedical materials. Additional information regarding this topic can be obtained from other review papers, in which the progress of the isohexide-based monomers and polymers are interpreted from different perspectives.\textsuperscript{11,65}

Given the broad interest in isohexides for polymer chemistry, it is important to realize the key features of isohexides. These are briefly summarized below:

1) The parent isohexides originate from biomass. Therefore, their derivatives are in principle biogenic. Incorporation of these building blocks into polymers will yield a novel generation of polymeric materials, partially or fully based on renewable feed stocks, which is desirable with regard to sustainability.

2) Low toxicity. As mentioned in §1.2.4.2, isosorbide and isosorbide nitrate and dinitrate have been used as drugs since long time ago.\textsuperscript{40,41} Isosorbide dimethyl ether is a promising green solvent for the pharmaceutical industry.\textsuperscript{11,42} Some of the isohexide-based polymers, such as polyesters and poly(ester amide)s, have been proven to be sensitive to hydrolysis or enzymatic degradation, and thus may be (bio)degradable. When come into post-use or consumer phase, after degrading of these polymers, the released building blocks do not have adverse ecological effects. This feature has been utilized to produce biodegradable materials, drug delivery formulations or other general biomedical materials.\textsuperscript{10,11}
3) Isohexides and their derivatives are chiral molecules. Several types of isohexide-based polymers, including poly(ester amide)s, poly(ester imide)s and polycarbonates, show interesting properties as liquid-crystalline polymers.

4) Isohexides are rigid molecules. This is probably the most relevant feature of isohexides for polymer applications. The introduction of the highly rigid isohexides into the main chain of polymer molecules has been found to significantly increase the glass transition temperatures ($T_g$) of the corresponding materials. For instance, by increasing the isosorbide content incorporated in poly(ethylene terephthalate) (PET), the $T_g$ value of the copolyester can be enhanced from 80 °C to 200 °C (Figure 1-5). Such an effect can broaden the application window of these polymers, which has been successfully shown for e.g. PET,66-69 PBT,70,71 as well as for succinic acid-based powder coatings.32,34,72-74

![Figure 1-5. Comonomer effect of isosorbide, 1,4-cyclohexanedicarboxylic acid (IPA) on the glass transition temperature ($T_g$) of poly(ethylene terephthalate) (PET).48](image)

**1.3.2 Major drawbacks of isohexides**

Despite the promising and unique properties of isohexides, it is important to address a few drawbacks limiting their industrial application. The first is the sometimes encountered insufficient purity of isosorbide which frequently results in polymers with discoloration and low molecular weights. Isohexide isomers, incompletely dehydrated products (sorbitan), degradation products and residues from chemical transformations are the main sources of these impurities.10 In this regard, better purification methods or improved synthetic procedures are required. The second drawback is the relatively low reactivity of the secondary hydroxyl groups of the parent isohexides in comparison with primary diols such as ethylene glycol or 1,4-butanediol. This is considered to be the most critical issue impeding
the industrial production of isohexide-based polymers. There is ample evidence and experience that it is difficult to obtain high-molecular-weight polymers or polymers with a high percentage incorporation of isohexides via melt polymerization. High polymerization temperatures or prolonged reaction times have adverse effects on molecular weights and color formation, caused by chain scission and/or thermal degradation.\(^{34,69,74}\) Moreover, some types of polymers like e.g. polyamides and polyurethanes can only be produced from the standard isohexides (or their derivatives) with great difficulty. Therefore, either milder or improved polymerization procedures or more reactive isohexide derivatives need to be developed.

In order to avoid thermal degradation, solid-state post-condensation (SSPC) is a useful method to enhance the molecular weight of the semicrystalline prepolymermrs, as extensively shown in the industrial production of PET and nylon.\(^ {75}\) However, the assymmetric structure of isosorbide often results in amorphous polymers, the molecular weights of which are therefore impossible to be enhanced by SSPC. In addition, the high tendency of water absorption can be another drawback of the isohexide-based polyesters, which is mainly caused by the rather hydrophilic \textit{cis}-fused tetrahydrofuran skeleton. This often lowers the \(T_g\) and/or reduces the dimensional stability of the polymers in humid environment, and therefore has adverse influence on their thermal and/or mechanical properties. Nevertheless, such feature of the isohexide-based polymers, on the other hands, can be advantageous to provide good water dispersion performance and thus be used in e.g. waterborne coating applications.

**1.3.3 Strategies to overcome the drawbacks of isohexides**

For reducing the side reactions that occur during the polymerization procedures, a few aspects can be considered. To minimize the thermo-oxidation of isohexides, the reaction systems can be carefully deoxygenated by alternating operations of vacuuming and inert gas purging, or by adding additives such as antioxidants (phenolic or phosphorous compounds) or color-correcting agents (e.g. cadmium oxide).\(^ {76,77}\) Furthermore, it is also very important to develop more efficient catalyst systems. An antimony-based bimetallic catalytic system was found to be able to increase the isosorbide percentage in PEIT (poly(ethylene-co-isosorbide terephthalate)) by approximately 10\%, yet at the expense of severe discolouration.\(^ {78}\) Thus far, it remains challenging to find the most effective catalysts for the polymerization of isohexides.
Apart from adapting the synthetic methodology, it can be more effective to overcome the intrinsic reactivity drawback of the parent isohexide by developing more reactive derivatives. The key concept is preserving the central bicyclic skeleton for the desired rigidity, while modifying the secondary hydroxyl groups into primary ones or into other reactive functional groups, either on one side or on both sides of the molecule. This could be realized by chain extension on the oxygen atoms or by substitution of the mentioned oxygen atoms with other functional groups (-NH₂ and -NCO) (Scheme 1-2). Theoretically, any functional group that reacts with a secondary hydroxyl group from any type of compound should be able to yield new building blocks through chain extension on the hydroxyl groups. Therefore, this protocol is by far the most frequently explored method and a number of isohexide-derivatives have been developed. However, one should be aware that the Tₘ-enhancing effect of the isohexide skeleton in the polymers can be compromised by the more flexible extended chain parts, such as flexible alkylene oxide extensions. In contrast, the second strategy, explained below, is expected to be capable of preserving the overall rigidity of the polymer chains to a large extent (Scheme 1-2). This strategy advocates the direct replacement of the secondary hydroxyl groups by more reactive functional groups. In other words, the functional groups are attached directly or closely to the central bicyclic skeleton without introducing additional flexible moieties. Since this strategy usually requires several stoichiometric steps, the number of available examples is much smaller than that of the derivatives obtained through chain extension on the oxygen atom. Thus far, the derived functional groups are: halogen (X), azide (N₃), amine (NH₂), isocyanate (NCO) and thioisocyanate (NCS). Given the beneficial structural rigidity and improved reactivity of the new derivatives, we believe this method has a great potential of generating new isohexide-based monomers, capable of realizing breakthroughs.
1.3.4 Key monomers and polymers derived from isohexides

In this work, we aim to develop new rigid isohexide derivatives for step-growth polymerization. Therefore, those molecules obtained through direct replacement of the functional groups directly linked to the rings of the parent isohexides (Scheme 1-2) are of interest. The number of such monomers is fairly small. The most extensively explored species are the isohexides with mono- or di- amino groups or isocyanate groups, which can be used as AA or AB monomers to synthesize step-growth polymers. The molecular structures, IUPAC names and the references describing the synthetic protocols of these monomers are listed in Table 1-1.

The mono- or di-deoxyamino-isohexides are useful building blocks for synthesizing polyamides or poly(ester amide)s, as well as precursors of isocyanato-isohexides for polyurethane and polyurea synthesis. Among all the possible AA or AB monomers with the amine groups directly attached to the isohexide skeleton, diaminoisoidide (DAII) is the most explored species (Table 1-1). To the best of our knowledge, seven synthetic routes have been reported to convert the original secondary hydroxyl groups to amine groups, as exemplified for DAII (see Appendix A, Scheme A-1). The first five routes all involve the nucleophilic substitution of the activated isohexides (bismesylates or bistosylates) by nitrogen-containing nucleophiles (like e.g. azide, phthalimide, ammonia and benzyl amine). Some of these routes suffer from severe drawbacks restricting even laboratory-scale production, such as high risk of explosion (route 1)\(^{90}\) and low overall isolated yield of DAII (< 12%, route 2; 34%, route 3\(^{90,92}\) ). Recently, by optimizing reaction conditions (solvent, reactant ratio, reaction temperature, reaction time) of route 3, Van Es and co-workers managed to raise the overall isolated yield of IIDA to 47% (route 4, Scheme A-1)\(^{90}\). Although stoichiometric steps are involved, this reaction is advantageous for being safe, readily reproducible and being capable of affording the resin grade IIDA at a relatively satisfactory lab-scale (>50 g/batch). In the meantime, Thiyagarajan and Van Es et al. developed a more sustainable route by hydrogenating the corresponding bisbenzylamine intermediates to IIDA or to the isomeric diaminoisosorbose (ISDA) in the presence of Pearlman’s catalyst, Pd(OH)\(_2\)/C (route 5). The products can be obtained in good overall isolated yields of >80% and with high purities (>99.5%)\(^{89}\). Similar strategies have also been described in other literature\(^{93-95}\). The direct amination of hydroxyl groups by treating isomannide with ammonia, as described in route 6, is theoretically an ideal protocol from a green-chemistry point of view\(^{96}\). However, it is speculated that it remains difficult to stereo-specifically obtain the desired product both with satisfactory quantity and purity in this way. Another route innovatively involves biological catalysts in both reaction steps, \textit{viz.} first in the transformation from isomannide into isohexide-diketone and then for the conversion into dideoxy-diamino isohexides by enzymatic transamidation\(^{97}\).
Table 1-1. AA or AB type isohexide-based monomers obtained through replacement of functional groups directly connected to the isohexide skeleton.

<table>
<thead>
<tr>
<th>structure</th>
<th>IUPAC name (abbreviation)</th>
<th>type</th>
<th>references</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Structure" /></td>
<td>(3S,6S)-hexahydrofuro[3,2-b]furan-3,6-diamine (diaminoisoidide, DAII)</td>
<td>AA</td>
<td>23, 89, 90, 93, 97–101</td>
</tr>
<tr>
<td><img src="image2" alt="Structure" /></td>
<td>(3R,6R)-hexahydrofuro[3,2-b]furan-3,6-diamine (diaminoisomannide, DAIM)</td>
<td>AA</td>
<td>97–100</td>
</tr>
<tr>
<td><img src="image3" alt="Structure" /></td>
<td>(3R,6S)-hexahydrofuro[3,2-b]furan-3,6-diamine (diaminoisosorbide, DAIS)</td>
<td>AA</td>
<td>23, 97–100</td>
</tr>
<tr>
<td><img src="image4" alt="Structure" /></td>
<td>(3R,6R)-6-aminohexahydrofuro[3,2-b]furan-3-ol</td>
<td>AB</td>
<td>55, 94, 95, 98, 102–105</td>
</tr>
<tr>
<td><img src="image5" alt="Structure" /></td>
<td>(3R,6R)-6-aminohexahydrofuro[3,2-b]furan-3-ol</td>
<td>AB</td>
<td>98, 102–104, 106, 107</td>
</tr>
<tr>
<td><img src="image6" alt="Structure" /></td>
<td>(3S,6R)-6-aminohexahydrofuro[3,2-b]furan-3-ol</td>
<td>AB</td>
<td>98, 100, 102, 104</td>
</tr>
<tr>
<td><img src="image7" alt="Structure" /></td>
<td>(3S,6S)-6-aminohexahydrofuro[3,2-b]furan-3-ol</td>
<td>AB</td>
<td>90, 98, 100, 102–104</td>
</tr>
<tr>
<td><img src="image8" alt="Structure" /></td>
<td>(3S,6S)-3,6-diisocyanatohexahydrofuro [3,2-b]furan</td>
<td>AA</td>
<td>83, 86–88, 109</td>
</tr>
<tr>
<td><img src="image9" alt="Structure" /></td>
<td>(3R,6S)-3,6-diisocyanatohexahydrofuro [3,2-b]furan</td>
<td>AA</td>
<td>83</td>
</tr>
<tr>
<td><img src="image10" alt="Structure" /></td>
<td>(3R,6R)-3,6-diisocyanatohexahydrofuro [3,2-b]furan</td>
<td>AA</td>
<td>83</td>
</tr>
</tbody>
</table>
The mono- or di-deoxy isocyanato isohexides are promising AB or AA monomers for polyurethane and polyurea preparation (Series II and III, Table 1-1). The number of such monomers is fairly small. The most extensively explored species are the isohexides with mono- or di- amino groups or isocyanate groups, which can be used as AA or AB monomers to synthesize step-growth polymers. The molecular structures, IUPAC names and the references describing the synthetic protocols of these monomers are listed in Table 1-1. According to the literature, thus far, the isocyanate group (N=C=O) was uniformly obtained by phosgenation starting from either isohexide free diamine or from the diamine.HCl salt (for the synthetic route, see Appendix A, scheme A-2 and A-3). As described in the first papers published by Bachmann and co-workers, the highly toxic phosphene gas (dispersed in toluene) was used as a phosgenation reagent, which should be cautiously handled. The reported isolated yields of the isocyanato products were as high as >90%. However, reproduction of the same reactions by Thiyagarajan and Van Es et al. was not successful. They experienced very poor solubility of the HCl salt of diaminoisoidide (IIDA) in toluene, which resulted in poor isolated yileds (~10%). Later on, Thiyagarajan and Van Es et al. adapted the synthetic route by using the less toxic diphosgene/triphosgene as well as the more polar ethyl acetate as the phosgenation reagent and the solvent, respectively (Scheme A-3). The obtained highest overall isolated yield was about 47%. In addition, another interesting monomer, namely 2,5-deoxy-dithioisocyanato isodide, is shown in Table 1-1 as well. This compound was also prepared by Bachmann et al. From an objective point of view, both routes suffer from the troublesome practical handling of the highly toxic phosgenation reagents and the poor isolated yields. Investigation into the potential applications of isocyanato-isohexides remains limited.

In addition to these rather toxic isocyanate routes, recently Thiyagarajan and Van Es et al. probed the non-isocyanate route via the Boc- (tert-butyl) or CBC- (carprolactam) protected intermediates (Scheme A-4, Appendix A). Although being not successful thus far, these attempts are of significant importance from an ecological point of view.
1.4 Aim and scope of this study

Due to the relatively low reactivity of the parent isohexides, despite a diversity of available isohexide-based building blocks, the synthesis of polymers containing high percentages of isohexides, as well as the investigation of their full thermo-mechanical potentials have been restricted so far. This work was motivated by the ambition of probing a breakthrough approach within the area of isohexide chemistry and carbohydrate chemistry. The research project focusing on this topic, sponsored by the Dutch Polymer Institute (DPI), is entitled “GREENER”, which stands for “Green Rigid building blocks for Engineering plastics with ENhanced pERformance”. In other words, we aimed to develop a new family of rigid bio-based building blocks (mainly referring to isohexides), as well as new step-growth polymers with high glass transition \( T_g \) and melting \( T_m \) temperatures suitable for a variety of applications, preferably in the performance polymer area. The ideal outcome was to develop fully or partially bio-based engineering plastics with thermal and mechanical properties competing or even exceeding those of the conventional petro-based materials, e.g. poly(ethylene terephthalate) (PET) and poly(butylene terephthalate) (PBT).

From the monomer perspective, the main goal was to develop a new family of isohexide-based building blocks with a variety of versatile functional groups. They should serve as the monomers or the precursors of other potential monomers meeting the requirement of synthesizing a wide scope of step-growth polymers, such as polyesters, polyamides, poly(ester amide)s, polycarbonates, etc. In order to improve the reactivity while preserving the structural rigidity, the synthetic strategy for obtaining these building blocks was focused on the direct replacement of the hydroxyl functionalities of the parent isohexides, as described in § 1.3.3. This constitutes the pioneering study of these compounds. Given the different physical and chemical properties of the isohexide compounds, the required synthetic and purification protocols were significantly different from the conventional aliphatic/aromatic counterparts. In order to be used as monomers for step-growth polymer synthesis, the new compounds were obtained in high purity (>99.0%) to allow for the generation of high molecular weight polymers. Moreover, for feasible polymer synthesis, the synthetic procedure was readily reproducible and afforded sufficient amounts of the desired monomers in a relatively short time. Therefore, the synthetic route to these targeted monomers was fully or as much as possible optimized to approach satisfactory isolated yields for each building block. The syntheses and structural characterizations of the novel monomers, as well as the supply of certain quantities of the monomers for polymerization experiments were accomplished as the initial tasks of this work.

The second goal was to develop series of novel homo- or copolymers, which are either partially or fully bio-based, from the newly-developed isohexide-based building blocks. Given the versatile character of the newly designed isohexide-based monomers, a wide
Introduction

range of polymers, such as polyesters, polyamides, poly(ester amide)s, polycarbonates and polyurethanes, could be the potential targets. Considering the numerous possible co-monomer species, a completely new array of carbohydrate-based step-growth polymers is expected to arise. The research activities of this part of the project encompassed:

1) Synthesis of fully or partially bio-based step-growth polymers.

2) Structural characterization of the synthesized polymers and investigation of their thermal/mechanical properties.

3) Structure-(thermal) properties relations study of the synthesized polymers. Define the relative characters (reactivity, rigidity, molecular conformation, etc.) of the novel isohexide-based monomers developed in this work with respect to the parent isohexides, as well as their petrochemical based linear/cyclic aliphatic or aromatic counterparts.

The work presented in this thesis is the result of a research collaboration between Food & Biobased Research in Wageningen (FBR, part of the Wageningen University and Research Centre, WUR) and the Laboratory of Polymer Chemistry (SPC) of the Technical University of Eindhoven (TU/e).

1.5 Outline of the thesis

The research project of which the results are summarized in this thesis encompasses a broad array of disciplines, ranging from synthesis and purification of monomers and step-growth polymers to the optimization of the several synthetic routes, as well as to employing different analytical and characterization techniques. The thesis consists of eight chapters, describing the development of novel isohexide-based building blocks and the polymers based thereon.

Chapter 2 focuses on the innovative design of the novel isohexide-based building blocks. The key concept is to achieve a 1-carbon-deoxy extension of the original hydroxyl groups, as shown in Scheme 1-2. A versatile exo-exo configured dinitrile intermediate was obtained in a stereo-specific manner, which further yielded a family of exo-exo di-functional isohexide-derivatives, including isoidide dicarboxylic acid (IIDCA, -COOH) and its dimethyl ester (IIDMC, -COOCH₃), isoidide-2,5-dimethanol (IIDML, -CH₂OH) and isoidide-2,5-dimethylenamine (IIDMA, -CH₂NH₂).

In Chapter 3 the possibility of synthesizing the isomeric dinitrile intermediates with exo-endo and endo-endo configurations is described.

Chapter 4 describes the synthesis of a series of aliphatic polyesters by combining isoidide dicarboxylic acid (IIDCA) and its dimethyl ester (IIDMC) with linear α,ω-alkylene diols. A detailed structure-thermal properties relations study demonstrates the relative rigidity of IIDCA/IIDMC with respect to the relevant linear counterpart monomers.
Chapter 1

In Chapter 5, the focus is on a series of fully renewable polyesters solely based on the isohexide-derived monomers, including isoidide dicarboxylic acid (IIDCA) and different isohexide-based diols (isosorbide, isomannide, isoidide and isoidide 2,5-dimethanol). A structure-thermal properties relations study, even following a broader approach as compared to the polyesters reported in Chapter 4, reveals the relative rigidity of the involved new isohexide-based building blocks, IIDCA/IIDMC and IIDML, with respect to the parent isohexides and other relevant counterparts.

Motivated by the promising findings regarding the new diol, isoidide 2,5-dimethanol (IIDML) from Chapter 5, in Chapter 6, we explored the potential of IIDML as a rigid diol to synthesize high $T_g$ and high $T_m$ polyesters with applicability as engineering plastics. IIDML was polymerized with conventional aromatic dicarboxylic acids, as well as the biobased FDCA. Thermal properties analysis confirmed the high rigidity of IIDML.

In Chapter 7, the synthesis of two series of (co)polyamides is described. One series is based on isoidide-2,5-dimethyleneamine (IIDMA), 1,6-hexamethylenediamine and sebacic acid, while the other series is based on IIDMA, 1,6-hexamethylenediamine and brassylc acid. (Co)polyamides with different monomer compositions were obtained for each series of polymers. By using different characterization and testing techniques, detailed crystal structural properties as well as the related thermal properties are discussed.

The final section of this thesis, Chapter 8, will present an epilogue to highlight the key results and conclusions obtained from the work presented in Chapters 2 to 8. The contribution of the work described in this thesis to isohexide chemistry in general as well as to the field of step-growth polymers in particular will be evaluated from a scientific and fundamental research point of view. Moreover, in the final “technology assessment” section, the potential industrial applications of the monomers and polymers disclosed in this thesis will be outlined, along with some additional suggestions and expectations regarding the future development of this area.

For more information regarding some necessary analytical results of different chapters one can refer to the enclosed “Appendices A-F”.

REFERENCES

Introduction

Chapter 1

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2

Novel isohexide derivatives: chiral building blocks from renewable resources

Abstract

With the aim to increase reactivity while at the same time retain rigidity, in this chapter, we describe the synthesis of a new family of C2/C5 one-carbon extended isohexides derivatives in a stereo-controlled manner. The optimized cyanation step was optimized affording the key intermediate isoidide dinitrile (IIDN) with high purity and good isolated yield (80%). All the new building blocks, namely, isoidide dicarboxylic acid (IIDCA) and its dimethyl ester (IIDMC), isoidide 2,5-dimethanol (IIDML) and isoidide 2,5-dimethyleneamine (IIDMA) were obtained with resin grade purities, which are sufficient for polymerizations. Single crystal X-ray diffraction and DFT study on IIDCA revealed several unique structural properties. These chiral and rigid bio-based building blocks can have a wide scope of applications in pharmaceutical, cholesteric liquid crystals and as building blocks for high performance polymers.

2.1 Introduction

The combination of rapidly depleting fossil resources and growing concerns about green-house gas emissions and global warming have stimulated extensive research on the use of biomass for energy, fuels and chemicals.\textsuperscript{1,6} Although bio-based chemicals have the potential to reduce the amount of fossil feedstock consumed in the chemical industry today, the most abundant type of bio-based feedstock, i.e. carbohydrates, is often unsuitable for current high temperature industrial chemical processes. Compared to hydrophobic aliphatic or aromatic feedstocks with a low degree of functionalisation, carbohydrates such as polysaccharides are complex, over-functionalized hydrophilic materials. One approach to overcome these drawbacks is to reduce the number of functional groups resulting in more stable, industrially applicable bifunctional bio-based building blocks\textsuperscript{1,7} such as furan-2,5-dicarboxylic acid,\textsuperscript{8} levulinic acid,\textsuperscript{9,12} and isohexide.\textsuperscript{13-15}

In chapter 1, we have indicated that, due to their chirality and intrinsic rigidity, isohexides have been the subject of intensive research in various fields of applications, ranging from catalysis\textsuperscript{16-20} to pharmaceuticals,\textsuperscript{21,22} liquid crystalline materials\textsuperscript{14} and polymers.\textsuperscript{13,14} In the latter case, it was shown that incorporation of these rigid diols into e.g. polyesters increases the glass transition temperature ($T_g$), allowing for new high temperature applications of such polymers. Various authors have demonstrated these effects for polyethylene terephthalate (PET),\textsuperscript{23-26} while we have shown comparable effects in polybutylene terephthalate (PBT)\textsuperscript{27} as well as in succinic acid-based powder coatings.\textsuperscript{28,29}

Despite the apparent benefits of incorporating isohexides into polymers such as polyesters, one major drawback remains. The limited reactivity of the sterically hindered secondary hydroxyl groups impedes the formation of high molecular weight (MW) polymers under common melt polycondensation conditions. Since isohexides reduce the crystallinity in polyesters, amorphous polymers are obtained which require high MWs in order to achieve the desired mechanical properties. Increasing the reaction temperatures or reaction times in order to increase the MWs often has detrimental effects (discoloration, chain scission) due to the limited thermal stability of the isohexides at high temperatures (>250 °C).\textsuperscript{23,24,29,30}

In order for isohexides to be successfully applied in commercial polymers, either new, milder polymerization procedures or more reactive isohexide derivatives need to be developed. To avoid losing rigidity and hence the $T_g$ of the polymers,\textsuperscript{31-33} following the second strategy (§ 1.3.3) as has been demonstrated by several authors,\textsuperscript{34-37} we decided to explore the potential of a 1-carbon extension of the bicyclic isohexide skeleton by direct substitution of the hydroxyl functionalities (Scheme 2-1). In this way it is expected that rigidity will be retained, while the reactivity of the functional groups is significantly increased. Here we report the first successful 1-carbon extension of an isohexide skeleton on
both C2 and C5, which gives way to a completely new family of bio-based chiral building blocks.\textsuperscript{38}

\begin{center}
\includegraphics[width=0.5\textwidth]{Scheme.png}
\end{center}

**Scheme 2-1.** Retro synthetic strategy towards new isohexide-based building blocks: FG (Functional group): -NH\textsubscript{2}, -NCO, -COOH, -COOMe, -CH\textsubscript{2}OH, -CH\textsubscript{2}NH\textsubscript{2}, etc.; LG (Leaving group): -OT\textsubscript{f}, -OMs, -OT\textsubscript{i}, -X.

### 2.2 Experimental Section

#### Materials and general methods

Isomannide (I, Sigma-Aldrich), trifluoromethanesulfonic anhydride (≥99\%, Aldrich), Dichloromethane (Merck, p.a.), pyridine (Merck, p.a.), hydrochloric acid (reagent grade, 37\%, Sigma-Aldrich), tetrahydrofuran (anhydrous, ≥99.9\%, Sigma-Aldrich), potassium cyanide (extra pure, Merck), 18-crown-6 (≥99\%, Fluka), chloroform (Merck, p.a.), methanol (Merck, p.a.), lithium aluminum hydride (LiAlH\textsubscript{4}, reagent grade, Aldrich), borane-tetrahydrofuran complex (BH\textsubscript{3}-THF) in THF solution (1.0 M, Sigma-Aldrich), hydrochloride in diethyl ether solution (2.0 M, Sigma-aldrich), chloroform-d (99.8 atom \% Aldrich), D\textsubscript{2}O (≥99.8\%, Merck), methanol-d\textsubscript{4} (99.8 atom \% D, contains 0.05\% (v/v) TMS, Aldrich), activated carbon (Norit, CN1), magnesium sulfate (Acros Organics, 99\% extra pure, dried, contains 3 to 4 moles of water), Celite\textsuperscript{®} 545 coarse (Fluka). Amberlyst\textsuperscript{®} A26 (Aldrich) hydroxide form (Strongly basic, macroreticular resin with quaternary ammonium functionality from Rohm&Haas Co); prior to use, the resin was washed with demineralised water by sonication in an ultrasonic bath at RT for 10 min. The water layer was subsequently removed by decantation. This procedure was repeated 5 times, until the water layer remained colourless. All the chemicals were used as received, unless denoted otherwise. Melting point was measured on a Thermal Fisher Scientific IA 9000 Series digital melting point apparatus. NMR spectra were recorded on a Bruker Avance III spectrometer operating at 400.17 MHz (1H) and 100.62 MHz (13C) at room temperature. Gas chromatography was performed on an Interscience Focus GC equipped with an AS 3000 series auto sampler. Fourier transform infrared (FT-IR) spectra were obtained on a Varian Scinitar 1000 FT-IR spectrometer equipped with a Pike MIRacle ATR Diamond/ZnSe single reflection plate and a DTGS-detector. The measurement resolution was set at 4 cm\textsuperscript{-1}, and the spectra were collected in the range 4000-650 cm\textsuperscript{-1} with 32 co-added scans. High resolution mass spectra were recorded on a Bruker microOTOF-Q instrument in positive ion mode (capillary potential of 4500 V).

#### Synthesis and analytical data of the synthesized compounds

\((3R,6R)-\text{hexahydrofuro}[3,2-b]furan-3,6-diyl bis(trifluoromethanesulfonate}) (2): A 500 mL 3-necked round-bottom flask, equipped with a mechanical stirrer and a dropping funnel, was charged with 1 (36.5 g,
0.25 mol), pyridine (49 mL) and dichloromethane (150 mL). The colorless solution was cooled down to −10 °C. Next, trifluoromethanesulfonic anhydride (0.6 mol, 100 mL) was added drop wise over 1 h. After stirring at room temperature for an additional 3 h, the reaction mixture was poured onto ice-water (0.5 L) and stirred. The organic layer was separated, and the water layer was extracted with chloroform (3 x 150 mL). The combined organic layers were subsequently washed with aqueous HCl (1.0 M, 3 x 150 mL), water (2 x 150 mL), dried over MgSO4, and decolorized with activated carbon. After filtration over a glass filter containing Celite, the resulting clear solution was evaporated under reduced pressure using a rotary evaporator. Finally, pure product 2 was obtained by recrystallisation from ethanol as colorless needles. Yield: 95 g, 93% (purity: 100%, GLC); mp: 62–63 °C; 1H NMR (CDCl3), δ = 5.22 (dd, 2H), 4.77 (m, 2H), 4.15 ppm (m, 4H); 13C NMR (CDCl3), δ = 118.48 (q, J13C = 319 Hz), 83.43, 80.32, 70.86 ppm; FT-IR: 2943, 2901, 1415, 1248, 1197, 987 cm−1; HR-MS (Q-TOF): m/z [M+Na]+, calcd for C10H14O6: 432.9457, found: 432.9463.

(3S,6S)-hexahydrofuro[3,2-b]furan-3,6-dicarboxylic acid (5): A 100 mL one-necked round-bottom flask, equipped with a magnetic stirrer and a reflux condenser, was charged with diester 4 (2.3 g, 1.0 mmol) and aqueous HCl solution (1.0 M, 30 mL). The reaction mixture was stirred under reflux for 24 h and then cooled down to room temperature. After removal of the solvent under reduced pressure using a rotary evaporator, the crude diacid was subsequently recrystallised from diethyl ether affording the pure 5 as a white solid. The single crystal was obtained from diethyl ether/petroleum ether mixture by slow evaporation. Yield: 1.70 g, 84% (purity: 99.0%, 1H NMR); mp: 121–123 °C. 1H NMR (D2O): δ =
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4.98 (s, 2H), 4.12 (bm, 4H), 3.25 ppm(bs, 2H); 13C NMR (CDCl3): δ = 177.73, 83.30, 72.25, 53.86 ppm; FT-IR: 1692 cm⁻¹ (C=O); HR-MS (Q-Tof): m/z [M+Na]⁺, calcd for CsHsO6: 225.0370, found: 225.0368.

((3S,6S)-hexahydrofuro[3,2-b]furan-3,6-diyl)dimethanol (6): Dry THF (10 mL) and LiAlH₄ (0.22 g, 6 mmol) were charged to a 100 mL three-necked round-bottom flask equipped with a magnetic stirrer, pressure equalizing dropping funnel, and a reflux condenser. To this grey slurry a solution of 4 (0.345 g, 1.5 mmol) in dry THF (10 mL) was added at 0 °C under a nitrogen atmosphere. When addition was complete, the reaction was stirred at room temperature for 1 h and then refluxed for 4 h. Next, the reaction mixture was cooled to 0 °C, and carefully quenched with aqueous sodium hydroxide (10%, 0.3 mL), water (0.85 mL), and aqueous sodium hydroxide (10%, 0.2 mL). After stirring for 20 min., the mixture was diluted with ethyl acetate (EA, 30 mL), filtered through Celite (EA wash), and concentrated under reduced pressure to give 0.275 g oil-like crude product. The pure diester was obtained as a colorless oil by flash chromatography (methanol: dichloromethane, 1:10). Yield: 0.15 g, 58% (purity 99.0%, 1H NMR); 13C NMR (CDCl3): δ = 4.47 (s, 2H), 3.99 (m, 2H), 3.68 (m, 2H), 3.60 (d, 4H), 2.80 (bs, 1H, OH), 2.45 ppm (m, 2H); 13C NMR (CDCl3): δ = 85.48, 69.96, 62.16, 49.19 ppm; FT-IR: 3358 (O-H), 2947, 2874, 1032 cm⁻¹; HR-MS (Q-Tof): m/z [M+Na]⁺, calcd for CsHsO6: 197.0784, found: 197.0778.

((3S,6S)-hexahydrofuro[3,2-b]furan-3,6-diyl)dimethanamide hydrochloride salt (7): A 250 mL three-necked round-bottom flask, equipped with a magnetic stirrer, pressure equalizing dropping funnel, and a reflux condenser, was charged with BH₃·THF complex in THF solution (1.0 M, 50 mL). Next, a solution of 3 (0.6 g, 4.88 mmol) in THF (20 mL) was added drop wise at room temperature under a nitrogen flow in 20 min. After addition was complete, the reaction was refluxed for another 16 h. Next, methanol (30 mL) was added carefully to quench the reaction, during which hydrogen gas was released vigorously. When no more gas evolved, hydrogenchloride in diethyl ether solution (2.0 M, 30 mL) was added drop wise and a white precipitate formed immediately. The suspension was then filtered over a glass filter (G-3), and the collected gum-like solid was dried in an oven (70 °C, 1 atm.) for 1h, to give the crude diamine HCl salt as white hard powdered solid. Finally, the pure white diamine HCl salt (6e) was obtained after repeating washing with ethanol (3 x 20 mL) and drying under vacuum (35 °C, <1 mbar). Yield: 1.19 g, 66%; 1H NMR (D2O): δ = 4.45 (s, 2H), 4.01 (m, 2H), 3.67 (m, 2H), 3.54 (d, 4H), 2.42 ppm (m, 2H); 13C NMR (D2O): δ = 85.24, 69.79, 61.70, 49.38 ppm; FT-IR: 3364, 2917, 2883, 2851, 1601, 1213, 1060 cm⁻¹; HR-MS (Q-Tof): m/z [M-2(HCl)+H]⁺, calcd for CsHsN2O4Cl: 173.1285, found: 173.1282.

((3S,6S)-hexahydrofuro[3,2-b]furan-3,6-diyl)dimethanamine (8): Diamine HCl salt (7) (0.19 g, 0.78 mmol) was dissolved in demineralised water (20 mL) giving a colorless solution. To this solution was added freshly washed Amberlyst A 26-OH (0.75 g, 3.2 mmol). The resulting suspension was sonicated in an ultrasonic bath for 1 h at 30 °C. After the reaction was complete, the suspension was filtered over a glass filter (G-3) containing Celite, and the IEX-resin was washed thoroughly with water (3 x 15 mL) and methanol (3 x 15 mL). The combined clear colourless solutions were evaporated to dryness using a rotary film evaporator to afford the pure diamine (8) as a white solid. Yield: 0.1 g, 74.6% (purity: 99.0%, 1H NMR); 1H NMR (CD3OD): δ = 4.37 (s, 2H), 3.97 (m, 2H), 3.60 (m, 2H), 2.74 (m, 4H), 2.32 ppm (m, 2H); 13C NMR (CD3OD): δ=87.28, 71.51, 49.94, 42.63 ppm; FT-IR: 3342, 3275, 3174, 2938, 2878, 1605, 1093 cm⁻¹; HR-MS (Q-Tof): m/z [M+H]⁺, calcd for CsHsN2O6: 173.1285, found: 173.1281.
2.3 Results and Discussion

2.3.1 Synthesis

In order to assess the viability and flexibility of this approach, we decided to devise a strategy based on nucleophilic substitution of activated hydroxyl groups by cyanide, yielding a versatile dinitrile which can function as a new platform chemical (Scheme 2-2). Since Sn2 reactions on isohexide endo-hydroxyl groups are strongly favoured over exo-substitution for steric reasons,39,40 we decided to use isomannide as starting material.

Contrary to expectations neither the bistosylate nor the bismesylate of isomannide showed any reactivity towards cyanation. Despite trying a broad range of reaction conditions (KCN/NaCN/CuCN in DMSO, DMF, CH3CN, THF, CHCl3/H2O, CH3CN/H2O, with or without phase transfer catalysts 18-crown-6, TMAB (N-acetyl-N,N,N,N-trimethylammonium bromide) or TBAC (tetrabutylammonium cyanide)), the bistosylate turned out to be remarkably persistent. Only the highly activated bistriflate,41 obtained by reacting isomannide (I) with trifluorosulfonic anhydride (Tf2O) and pyridine in dichloromethane, gave the desired dinitrile (3, Scheme 2-2). The absolute stereochemistry of the product (exo-exo conformation) was confirmed by 1-D and 2-D 1H-NMR, 13C-NMR, as well as single crystal X-ray diffraction (Figure 2-1).

Scheme 2-2. Synthesis of isohexide-based momomers: a. Tf2O, pyridine, CH2Cl2, −10–0 °C, 2 h, 95%; b. KCN, 18-crown-6, dry THF, 0 °C, 3 h, 80%; c. MeOH/ HCl (c) (1:1, v/v), reflux, 3.5 h, 73%; d. 1N HCl aq., reflux, 16 h, 80%; e. LiAlH4, dry THF, −10–0 °C, 1 h, then reflux 4 h, 58%; f. BH3·THF complex in THF (1.0 M), reflux 14 h, then HCl in diethyl ether solution (2.0 M), 66%; g. Amberlyst-26 (-OH), sonication, 30 °C, 1 h, 75%.
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Figure 2-1. Molecular structure of 3 in the crystal. Displacement ellipsoids are drawn at the 50% probability level.

Table 2-1. Cyanation conditions for conversion of 2 into 3.

<table>
<thead>
<tr>
<th>No.</th>
<th>Ratio&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Temperature(°C)</th>
<th>Time (h)</th>
<th>3&lt;sup&gt;c&lt;/sup&gt; (%)</th>
<th>Yield&lt;sup&gt;d&lt;/sup&gt; (%)</th>
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<td>1</td>
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<td>RT</td>
<td>21</td>
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<tr>
<td>2</td>
<td>1: 6: 0.5</td>
<td>RT</td>
<td>24</td>
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<td>24</td>
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<td>8</td>
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<td>−10–0</td>
<td>3</td>
<td>95</td>
<td>80</td>
</tr>
</tbody>
</table>

<sup>a</sup>All the reactions were performed in THF. <sup>b</sup>Molar ratio of bistriflate (2):KCN:18-crown-6. <sup>c</sup>Data based on the percentage of 3 derived from <sup>1</sup>H NMR and GLC analysis of the crude product. <sup>d</sup>Yield of the isolated, analytically pure (>99.9%, <sup>1</sup>H NMR and GLC) dinitrile. <sup>e</sup>Reactions conducted on small scale (3 mmol of bistriflate) without further isolation.

Since dinitrile (3) is the key intermediate in our strategy we explored several ways to optimize the isolated yield. To this end, reaction parameters such as temperature, time and reactant ratios were varied. A synoptic overview of reaction conditions is given in Table 2-1. By starting from a preformed 1:1 complex of KCN and 18-crown-6 the required reaction time is reduced to 3 h. This combination of low temperature and highly active reactants ensures a very high degree of selectivity towards the desired dinitrile (95% selectivity in the crude product according to GLC analysis). The product obtained after column chromatography (petroleum ether: ethyl acetate, 2:1) has a purity of >99.9% according to GLC analysis.

With the new high purity dinitrile (3) in hand subsequent transformations of the nitrile group were investigated. Our first focus was on the hydrolysis of the dinitrile to the
corresponding diacid (5). This new conformationally rigid symmetrical diacid is a novel potential bio-based alternative to terephthalic acid (TA) for a wide range of potential applications.

Various aqueous nitrile hydrolysis procedures (both acidic and basic) gave unsatisfactory results, since none of the wide range of conditions that were investigated gave full conversion of the nitrile groups. Due to the high polarity of mono nitrile-mono acid and diacid, effective separation of the desired 5 from the crude reaction mixture turned out to be very difficult. In order to circumvent these problems it was decided to take a different approach and attempt a direct methanolysis of 3 to yield the dimethyl ester (4). Various reaction conditions were effective (see Table A-1, Appendix A), but the highest selectivity for the diester (at full conversion of the starting material) was obtained by refluxing 3 in a 1:1 mixture of HCl (c) and MeOH.\textsuperscript{43,44} Monitoring the reaction in time by GLC revealed that 2-3 h at reflux is sufficient to achieve \textgreater 95\% conversion to the diester. At this point partial hydrolysis of the diester to monoacid and diacid is still negligible, which allows for a simple and effective purification by flash column chromatography (petroleum ether: ethyl acetate, 5:1). In this way high purity (\textgreater 99.5\%) diester was obtained as a colorless liquid in 73\% isolated yield.

Next, diacid (5) was conveniently obtained by hydrolysis of high purity diester (4) in 1N HCl. The resulting colorless oil was recrystallized from hexane/diethyl ether, affording the diacid (5) as a white solid in high isolated yield (84\%) and high purity (99.0\%).

Also starting from diester (4), the third building block, the corresponding diol (6), was prepared by conventional reduction with lithium aluminium hydride (LiAlH\textsubscript{4}) in anhydrous THF at reflux. The pure diol was obtained as a colorless oil by flash column chromatography (dichloromethane: methanol, 10:1).

The final building block, diamine (8), was obtained by reduction of dinitrile (3) with borane-tetrahydrofuran complex (BH\textsubscript{3}-THF) (1.0 M) in THF solution. After work-up, first the white diamine-HCl salt (7) was obtained, which was transformed into the free diamine by treatment with Amberlyst-26 (-OH) basic ion exchange resin. Diamine (8) was thus obtained as a white solid in 99.0\% purity and 50\% isolated yield.

2.3.2 Crystal structure

Given the unique characteristics of diacid 5 (rigid, chiral, and aliphatic), it is important to elucidate its molecular structure on a more detailed level. Single-crystal X-ray analysis of 5 resulted in a number of remarkable observations, which are supported by high level DFT\textsuperscript{45} calculations. The first distinctive feature of 5 is the V-shape of the two cis-fused furan rings. Single-crystal X-ray diffraction showed two independent conformers, 5a and 5b, in the
crystal matrix, which differ mainly in the conformation of one five-membered ring (Figure 2-2). The dihedral angle between the two rings cannot be given precisely, because they are not planar and hence cannot be defined by a plane unique for each of them (Figure 2-3). It may be described in terms of various planes through sets of four or of three atoms, or in terms of various torsion angles. In Table 2-2 two relevant torsion angles are compared. The molecular structure of 5a is in good agreement with the previously described wide-open (120°) skeleton of isosorbide.\textsuperscript{13,15,46} However, one of the five-membered rings of molecule 5b has a different geometry (C12 is pointing outwards), which results in significant differences between the two torsion angles (Table 2-2). From the crystal packing it appears that hydrogen bonding between the carboxylic acid groups is responsible for the differences in the geometries of the five-membered rings (see Appendix B, Figure B-1). DFT results confirm that the conformers 5a and 5b differ only 1.7 kcal/mol in the gas phase. (A third conformer 5c with a similar energy as 5b was calculated but not detected with X-ray diffraction; 5c has C12 and C62 both pointing outwards; see Appendix B, Table B-2). These results suggest that the isohexide skeleton is much more flexible than previously assumed.

![Figure 2-2. Quaternion fit\textsuperscript{47} of the two independent conformers of 5, showing their different conformations.](image)

<table>
<thead>
<tr>
<th>Torsion angle</th>
<th>5a</th>
<th>5b</th>
</tr>
</thead>
<tbody>
<tr>
<td>C51-C41-C31-C21</td>
<td>-121.31(11)</td>
<td>-130.53(12)</td>
</tr>
<tr>
<td>O21-C31-C41-O11</td>
<td>117.35(12)</td>
<td>102.98(13)</td>
</tr>
</tbody>
</table>
Since the number of known biogenic rigid difunctional building blocks is fairly small, it is of interest to compare the structural properties of diacid 5 with those of three relevant known rigid diacids. TA is the obvious petrochemical based benchmark, since it is a rigid, aromatic bulk-chemical. trans-Cyclohexane dicarboxylic acid (CHDA) makes an interesting comparison, since like in the case of 5, it is chiral and aliphatic, yet displays cyclohexane-related ring flexibility. Furan-2,5-dicarboxylic acid (2,5-FDA) was chosen as the third reference, since it is increasingly promoted as bio-based alternative to terephthalic acid (TA), being both rigid and aromatic, albeit not a linear diacid. In Table 2-3, experimental (single-crystal X-ray diffraction) and computational (DFT) results for all four diacids are compared.

Generically, all four diacids can be regarded as conformationally-restricted analogues of adipic acid. Thus, for the convenience of comparison, carbons between two carboxylic groups of the four molecules are re-labelled as C2-C5 (Figure 2-4) and comparisons are restricted to the distances and angles related to these atoms.
As shown in Table 2-3, the gas phase DFT data are generally in good agreement with the X-ray diffraction results. The distance D between C1 and C6 is highly comparable for 5 and both TA and CHDA. The angle α, here defined as the C1-C2-C5/C6-C5-C2 angle, is a measure for the (non) linearity of the carboxylic acid groups. In the highly symmetrical TA this angle is obviously close to 180°, whereas both CHDA and 2,5-FDA are considerably less linear. This can result in significant differences with regard to e.g. crystallization behaviour and properties of polymers based on these building blocks. In this respect 5 shows an even larger degree of non-linearity. A further distinct feature of 5 is expressed by the angle β, here defined as the C1-C2-C5-C6 dihedral angle, which clearly shows that in 5a and 5c the C1-C2 and C5-C6 bonds are not in the same plane. The differences observed here for 5a–5c again point to a high degree of flexibility of the five-membered rings. The angle γ, here defined as the (projected) angle between the C1-C2 and the C5-C6 bonds, serves as another indicator for the linearity of the molecules. Whereas TA and trans-CHDA are fully linear, 2,5-FDA is obviously not. Since in the case of 5a–c the C1-C2 and C5-C6 bonds are not in the same plane, only projected angles can be given with values ranging from 77 to 118°. This suggests that the carboxylic acid groups in 5 are situated more or less perpendicular to each other.

Thus, the data from Table 2-3 show that whereas diacid 5 is similar to the other diacids in some respects overall it has rather unique characteristics, which will result in new interesting properties of the polymer materials based on this type of building block.

### 2.4 Conclusion

In conclusion, we report the first stereo-controlled synthesis of a new family of C2/C5 carbon extended isohexides. These bio-based chiral rigid building blocks can have a wide scope of applications, ranging from pharmaceuticals and cholesteric liquid crystals to building blocks for performance polymers. Detailed structural analysis of isoidide dicarboxylic acid (5) underlines its unique properties. Applications in the fields of polymer chemistry and catalysis are currently under investigation. The aim of this work is to show the wide range of promising possibilities of a renewable platform for biobased difunctional chemicals derived from the new stereo-specific dinitrile. A logical follow up on this work will be e.g. replacing the currently petro-based organic solvents by green solvents as well as the development of more sustainable, catalytic routes towards C2/C5 carbon extended isohexides. We will address these issues in our future work.
Table 2-3. Structural data of rigid diacids.

<table>
<thead>
<tr>
<th>Name</th>
<th>Symmetry</th>
<th>D (Å)</th>
<th>α (°)</th>
<th>β (°)</th>
<th>γ (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X-ray</td>
<td>DFT</td>
<td>X-ray</td>
<td>DFT</td>
<td>X-ray</td>
</tr>
<tr>
<td>5a</td>
<td>C₁</td>
<td>C₂</td>
<td>5.715(2)</td>
<td>5.92</td>
<td>145.79(10)/127.20(9)</td>
</tr>
<tr>
<td>5b</td>
<td>C₁</td>
<td>C₁</td>
<td>5.715(2)</td>
<td>5.92</td>
<td>145.79(10)/127.20(9)</td>
</tr>
<tr>
<td>5c</td>
<td>–</td>
<td>C₂</td>
<td>–</td>
<td>6.13</td>
<td>–</td>
</tr>
<tr>
<td>TA⁸⁸</td>
<td>C₁</td>
<td>C₂₈</td>
<td>5.731</td>
<td>5.77</td>
<td>179.2</td>
</tr>
<tr>
<td>trans-CHDA (eq-eq)⁹⁶</td>
<td>C₁</td>
<td>C₁</td>
<td>5.808</td>
<td>5.84</td>
<td>153.3</td>
</tr>
<tr>
<td>2,5-FDA⁹⁰</td>
<td>C₅</td>
<td>C₅₀</td>
<td>4.830</td>
<td>4.88</td>
<td>154.7</td>
</tr>
</tbody>
</table>

*Interatomic distance between C1-C6 (carboxylic acid groups). °C1-C2-C5/C6-C5-C2 angle. †C1-C2-C5-C6 dihedral angle. ‡Actual or projected angle between the C1-C2 bond and the C5-C6 bond.
REFERENCES

42. CCDC 792545 (compound 3) and 796497 (compound 5) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via [www.ccdc.cam.ac.uk/data_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif).
3

Isohexide dinitriles: a versatile family of renewable platform chemicals

Abstract

Novel 2/5 1-carbon extended isohexide dinitriles are now synthetically accessible by a convenient, selective base-catalyzed epimerization procedure. Kinetic experiments using the strong organic base 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) show that all three possible isohexide isomers are in a dynamic equilibrium. An epimerization mechanism is proposed based on DFT calculations. Structural identification of all three possible isomers is based on NMR analysis as well as single crystal X-ray crystallography. DFT calculations confirmed that the observed crystal structures are indeed the lowest energy conformers of these isohexide derivatives.
3.1 Introduction

The transformation of readily available, yet structurally-complex biomass into simple and high added-value molecules is currently one of the central topics for both academia and industry. Isohexides (1,4;3,6-dianhydrohexitols) are a family of rigid bicyclic diols, which can be derived from cellulose or starch. Three different isomeric isohexides are known, namely isomannide (IM, 1,4;3,6-dianhydro-D-glucitol), isosorbide (IS, 1,4;3,6-dianhydro-D-mannitol) and isoidide (II, 1,4;3,6-D-dianhydro-L-iditol). These biobased molecules are highly interesting owing to several key features: all three isomers are non-toxic, chiral, aliphatic, bifunctional and rigid.\(^{1,2,4}\)

In recent years, the continuously increasing number of papers and patents dealing with isohexide chemistry is indicative of the broad scope of (potential) applications for these molecules.\(^{1-4}\) Besides the direct use of the parent isohexides, a number of derivatives have also been synthesized for various purposes. This is accomplished by modification of the hydroxyl groups at the 2- and 5-position of the bicyclic ring. One approach is the chain extension on the oxygen atoms of the original hydroxyl groups. For instance, reacting isosorbide with ethylene carbonate in the presence of potassium carbonate yields a 2,5-bis(2-hydroxyethyl)isosorbide.\(^{5}\) Alternatively, the direct replacement of the original hydroxyl groups by new functional groups (\(-\text{NH}_2, -\text{NCO}, -\text{COOH}, \text{CH}_2\text{OH}, -\text{CH}_2\text{NH}_2\)) has also been reported.\(^{6-17}\) Hence, the application window of the parent isohexides can be significantly broadened.\(^{1,4}\) Current applications include the use of isosorbide dinitrate as a vasodilator for treating cardiac or vascular diseases.\(^{18-20}\) Furthermore, isosorbide alkyl derivatives have been propagated as green solvents for pharmaceutical or cosmetic compositions,\(^{4,21}\) while isosorbide diesters are excellent plasticisers for PVC.\(^{22-24}\) In the field of synthetic organic chemistry, the chirality of isohexides and derivatives has been exploited in the synthesis of a variety of sophisticated molecules, such as chiral ionic liquids,\(^{25-27}\) phase-transfer catalysts,\(^{28}\) and ligands for asymmetric catalysis (amino alcohols, amines, mono- and diphosphines, diphosphites, bis-diaminophosphites, \textit{etc.}).\(^{29-38}\) Difunctional isohexide derivatives are also interesting building blocks for various step-growth polymers with potential applications ranging from performance polymers to biodegradable/biocompatible materials and optical materials.\(^{1,3,4}\)

As we are interested in developing value-added biobased materials, we have been involved in the development of novel synthetic routes for isohexide-based building blocks,\(^{6,7}\) as well as new polymers based on these monomers.\(^{39-47}\)

In Chapter 2, we reported the synthesis of a new family of 2,5-deoxy 1-carbon-extended isohexides(Scheme 3-1). The aim is to overcome some of the drawbacks associated with the use of the parent isohexides in the synthesis of step-growth polymers, such as low reactivity and moderate thermal stability.\(^{41}\)
Thus far, our synthetic approach (Scheme 3-1) is based on the stereo-specific conversion, i.e. conversion of the endo-endo configured isomannide bistriflate (IMBTf) to the exo-exo configured isoidide dinitrile (IIDN) via Walden inversion in the presence of a cyanide anion. IIDN then serves as a key intermediate for the subsequent transformations into a family of bi-functional building blocks, including isoidide 2,5-dicarboxylic acid (IIDCA), isoidide 2,5-dimethylester (IIDMC), isoidide 2,5-dimethanol (IIDML) and isoidide 2,5-dimethylene amine (IIDMA). We have successfully shown that IIDCA and IIDMC, as well as IIDML are rigid AA type monomers from which novel polyesters have been obtained, as described in Chapters 3 to 5. Furthermore, these new molecules can have various additional applications, including catalysis, pharmaceuticals and liquid crystalline materials.

Unfortunately, the current synthetic strategy only gives access to the isohexide derivatives with the exo-exo configuration. Derivatives with the exo-endo or endo-endo configuration cannot be synthesized via the same protocol, since Walden inversion of an exo-triflate group is sterically unfavorable. As the orientation of the substituents at the 2 and 5 position in isohexides can have a dramatic influence on physical and chemical properties, investigation of the effects of the substituent orientation in the new 1-carbon extended isohexides is important in order to unlock their full potential. Hence, an alternative synthetic route towards the exo-endo and endo-endo isomers is highly desired.

In this chapter, we describe the synthesis of isosorbide dinitrile (ISDN) and isomannide dinitrile (IMDN) by a convenient base-catalyzed epimerization protocol, starting from isoidide dinitrile (IIDN). A reaction mechanism for the epimerization reaction is proposed based on experimental data and density functional theory (DFT) calculations. The molecular structures of three dinitrile isomers were analyzed by 1D and 2D NMR spectroscopy, single crystal X-ray diffraction and DFT calculations.
3.2 Experimental section

Materials and general methods

Isohexide dinitrile ((3S,6S)-hexahydrofuro[3,2-b]furan-3,6-dicarbonitrile) was synthesized according to the procedure described in Chapter 2.18 Tetrahydrofuran (anhydrous, ≥99.9%, Sigma-Aldrich), potassium cyanide (extra pure, Merck), 18-crown-6 (≥99%, Fluka), chloroform (Merck, p.a.), methanol (Merck, p.a.), magnesium sulfate (Airos Organics, 99% extra pure, dried, contains 3 to 4 moles of water), Celite® 545 coarse (Fluka), potassium hydroxide (p.a. Sigma-Aldrich), potassium tert-butoxide (reagent grade, Sigma-Aldrich), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, puriss, ≥99.0% (GC), Fluka). NMR spectra were recorded on a Bruker Avance III spectrometer operating at 400.17 MHz (1H) and 100.62 MHz (13C) at room temperature. Gas chromatography was performed on an Interscience Focus GC equipped with an AS 3000 series auto sampler. Fourier transform infrared (FT-IR) spectra were obtained on a Varian Scimitar 1000 FT-IR spectrometer equipped with a Pike MIRacle ATR Diamond/ZnSe single reflection plate and a DTGS-detector. The measurement resolution was set at 4 cm\(^{-1}\), and the spectra were collected in the range 4000-650 cm\(^{-1}\) with 32 co-added scans. High resolution mass spectra were recorded on a Bruker microTOF-Q instrument in positive ion mode (capillary potential of 4500 V).

\[
(3S,6S)-\text{hexahydrofuro}[3,2-b]furan-3,6-\text{dicarbonitrile} \; (\text{IIDN}):^1\text{H NMR (CDCl}_3\text{)}: \delta = 5.02 \; (s, 2H), 4.14 \; (s, 4H), 3.19 \; ppm \; (m, 2H); ^13\text{C NMR (CDCl}_3\text{)}: 117.22, 86.20, 70.34, 36.70 \; ppm; \text{FT-IR:} \; 2492, 2901, 2248 \; (C=N), 1487 \; cm\(^{-1}\); \text{HR-MS (Q-Tof):} \; m/z \; [M+Na]^+\text{, calcd for } \text{C}_9\text{H}_9\text{N}_2\text{O}_2\text{: } 187.0478, \text{found: } 187.0474.
\]

\[
(3R,6S)-\text{hexahydrofuro}[3,2-b]furan-3,6-\text{dicarbonitrile} \; (\text{ISDN}): ^1\text{H NMR (CDCl}_3\text{)}: \delta = 4.96 \; (m, 1H), 4.91 \; (m, 1H), 4.26 \; (m, 2H), 3.98 \; (m, 1H), 3.24 \; (m, 2H); ^13\text{C NMR (CDCl}_3\text{)}: 117.40, 115.10, 86.77, 82.32, 70.91, 69.65, 37.08, 35.75 \; ppm; \text{FT-IR:} \; 3006, 2954, 2885, 2245 \; (C=N), 1468 \; cm\(^{-1}\); \text{HR-MS (Q-Tof):} \; m/z \; [M+Na]^+\text{, calcd for } \text{C}_9\text{H}_9\text{N}_2\text{O}_2\text{: } 187.0478, \text{found: } 187.0475.
\]

\[
(3R,6R)-\text{hexahydrofuro}[3,2-b]furan-3,6-\text{dicarbonitrile} \; (\text{IMDN}): ^1\text{H NMR (CDCl}_3\text{)}: \delta = 4.85 \; (d, 2H), 4.26 \; (t, 2H), 4.08 \; (t, 2H), 3.31 \; (m, 2H); ^13\text{C NMR (CDCl}_3\text{)}: 115.23, 82.81, 70.47, 36.18; \text{FT-IR:} \; 2991, 2939, 2895, 2249 \; (C=N), 1486 \; cm\(^{-1}\); \text{HR-MS (Q-Tof):} \; m/z \; [M+Na]^+\text{, calcd for } \text{C}_9\text{H}_9\text{N}_2\text{O}_2\text{: } 187.0478, \text{found: } 187.0473.
\]

Epimerization procedure

Isohexide dinitrile (250 mg, 1.52 mmol), a base and anhydrous THF (25 mL) were charged into a two-necked round-bottom flask. An additional portion of 18-crown-6 (0.2 equiv. with respect to isoheide dinitrile) is needed in the case of a potassium base. After initiation of the reaction, a GLC sample was taken at a certain time interval to follow the epimerization conversion. To prepare the GLC samples, 1 mL of the reaction mixture was taken from the flask. After partitioning in a mixture of an aqueous HCl solution (1.0 mL, 1.5 N) and 2 mL of chloroform (2.0 mL), the water layer was removed with a Pasteur pipette. The remaining organic layer was dried over MgSO\(_4\) and filtered. The filtrate was injected into the GC-FID.

X-ray crystal structure determinations

Reflections were measured on a Bruker Kappa ApexII diffractometer with sealed tube and Triumph monochromator (\(\lambda = 0.71073 \; \text{Å}\) at a temperature of 150(2) K. Intensity data were integrated
Isohexide dinitriles: a versatile family of renewable platform chemicals

with the SAINT software. Absorption correction and scaling was performed based on multiple measured reflections with SADABS. The structures were solved by Direct Methods using the programs SHELXS-97. Least-squares refinement was performed with SHELXL-97 against F2 of all reflections. Non-hydrogen atoms were refined freely with anisotropic displacement parameters. Hydrogen atoms were located in difference Fourier maps and refined with a riding model. Geometry calculations and checking for full symmetry were performed with the PLATON program.

CCDC 890377 (IMDN) and 890378 (ISDN) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

**IMDN:** C8H8N2O2, Fw = 164.16, colorless plate, 0.64 x 0.46 x 0.08 mm3, monoclinic, P21 (no. 4), a = 5.6599(3), b = 9.1663(5), c = 7.8939(5) Å, β = 106.0095(16)°, V = 393.65(4) Å3, Z = 2, Ds = 1.385 g/cm3, μ = 0.10 mm-1. 7873 Reflections were measured up to a resolution of (sin θ/λ)max = 0.65 Å-1. Friedel pairs were merged. 956 Reflections were unique (Rint = 0.018), of which 936 were observed [I>2σ(I)]. The absolute structure was assigned according to the synthesis. 109 Parameters were refined with one restraint. R1/wR2 [I > 2σ(I)]: 0.0304 / 0.0803. R1/wR2 [all refl.]: 0.0309 / 0.0809. S = 1.055. Residual electron density between -0.16 and 0.29 e/Å3.

**ISDN:** C8H8N2O2, Fw = 164.16, colorless block, 0.70 x 0.48 x 0.44 mm3, orthorhombic, P2221 (no. 19), a = 6.7519(4), b = 8.3266(5), c = 13.4595(8) Å, V = 756.70(8) Å3, Z = 4, Ds = 1.441 g/cm3, μ = 0.11 mm-1. 17965 Reflections were measured up to a resolution of (sin θ/λ)max = 0.65 Å-1. Friedel pairs were merged. 1024 Reflections were unique (Rint = 0.019), of which 1010 were observed [I>2σ(I)]. The absolute structure was confirmed by a Hooft analysis prior to the merging of Friedel pairs. 109 Parameters were refined with no restraints. R1/wR2 [I > 2σ(I)]: 0.0263 / 0.0711. R1/wR2 [all refl.]: 0.0265 / 0.0714. S = 1.095. Residual electron density between -0.13 and 0.26 e/Å3.

### 3.3 Results and discussion

#### 3.3.1 Synthesis of isohexide isomers

As described in Chapter 2, isoidide dinitrile (IIDN) can be efficiently synthesized from isomannide bistri fluoride via a Sn2 substitution by cyanide anions, affording IIDN in approximately 80% isolated yield after column chromatography. When the same cyanation conditions (isohexide bistri fluoride / KCN/ 18-crown-6/ tetrahydrofuran (THF), -10–0 °C) were applied to either isosorbide bistri fluoride (ISBTf) or isoidide bistri fluoride (IIBTf), severe degradation of the starting material was observed and no significant amounts of the desired product could be isolated (Scheme 3-2). Sn2 substitution of exo-leaving groups in isohexides has been known to be unfavorable due to steric hindrance. As schematically shown in Scheme 2, E2 elimination under basic conditions can give unstable vinyl ethers, while α-deprotonation can give ring-opened side products.

During the synthesis of IIDN, we observed an interesting phenomenon: small amounts of the dinitrile epimers ISDN and IMDN were observed occasionally, depending on reaction time and temperature, as well as on the excess of KCN/18-crown-6 used. Regarding the
mechanism of such an epimerization side reaction, the possibility of free radical-induced epimerization was first excluded. This was supported by the results of the cyanation reactions conducted in THF solution in the presence of radical scavengers, e.g. TEMPO ((2,2,6,6-tetramethylpiperidin-1-yl)oxyl) and BHT (butylated hydroxytoluene). Both conditions showed the formation of isomers. Given that potassium cyanide is a relatively strong base (pKb in water = 2.9) and the basicity in THF will even increase in the presence of a phase-transfer catalyst, for instance, crown ether, we speculated that base-induced epimerization was the most likely mechanism. According to literature, catalytic epimerization of readily available isohexide derivatives has been an attractive strategy to obtain the synthetically less accessible isomers. In the 1960’s, Wright et al. reported a catalytic epimerization protocol to obtain isoidide and isomannide from isosorbide by using a nickel catalyst under a hydrogen atmosphere. Based on our previous results, starting from isomannide, IIDN can be readily obtained in rather good yield (80%) in two steps and in high purity (>99.9%). Therefore, we decided to explore the viability of a base-catalyzed epimerization reaction of IIDN in order to obtain ISDN and IMDN.

In order to investigate the viability of the epimerization reaction as a synthetic procedure, IIDN was exposed to a series of inorganic bases with different basicities in THF at room temperature (Scheme 3-3). Addition of 18-crown-6 was applied in order to increase the solubility of the potassium salts. The reaction conditions and the corresponding
compositions of three isohexide isomers are shown in Table 3-1. Relatively strong bases like potassium tert-butoxide ($pK_b = -3$), potassium hydroxide ($pK_b = 0.5$) and potassium cyanide ($pK_b = 0.5$) gave swift epimerization (entry 1 to 3). At the same time, significant degradation was observed as indicated by severe discoloration of the reaction mixtures. Nevertheless, epimerization equilibria appeared to be reached in about 0.5 h in both cases. The approximate molar product ratios are IIDN : ISDN : IIDN = 4 : 5 : 1 as obtained by GLC analysis. In contrast, the weak base potassium acetate ($pK_b = 9.24$) showed low epimerization activity (entry 4); only 13% of ISDN and almost no IMDN was observed after 24 h. However, no discoloration occurred over this extended time-span, indicating that these mild conditions are highly selective. Although the combination of potassium salts with 18-crown-6 can effectively induce epimerization, the results were unsatisfactory with regard to either selectivity or reactivity. Moreover, rather tedious isolation/purification procedures were required due to the complicated composition of the crude products. We therefore explored the potential of using a fully soluble, strong and non-nucleophilic organic base, which does not require the presence of 18-crown-6. Initial experiments with DBU (1,8-diazabicyclo[5.4.0]undec-7-ene, $pK_b = 2.0$) showed that DBU is capable of effectively inducing epimerization, affording a similar equilibrium molar ratio of IIDN : ISDN : IIDN = 4 : 5 : 1 after 26 h (entry 5). Moreover, the DBU-induced epimerization reaction also showed good selectivity towards the epimers, given the absence of the aforementioned discoloration in the case of the strong potassium bases.

The pure dinitrile isomers were separated by column chromatography (ethyl acetate/petroleum ether mixture, V/V, 1:8) of the crude reaction mixtures obtained with DBU. All three isomers were thus obtained in good purity ($>99.0\%$), while the combined total isolated yield exceeded 90% ($\geq 5.0$ g scale), confirming that this procedure is highly selective towards the targeted product. The molecular structures of the three isomers were fully characterized by NMR, FT-IR, GC-MS and high resolution MS.

**Scheme 3-3.** Base-induced epimerization reactions of IIDN in THF solutions.
Table 3-1. Epimerization results using various bases in THF solutions.

<table>
<thead>
<tr>
<th>entry</th>
<th>base</th>
<th>( pK_\text{b} )</th>
<th>t (h)</th>
<th>color</th>
<th>IIDN</th>
<th>ISDN</th>
<th>IMDN</th>
<th>product composition (%)^\text{c}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(CH$_3$)$_2$CO$_2$K</td>
<td>3.0\text{a}</td>
<td>0.5</td>
<td>brownish</td>
<td>38.7</td>
<td>51.6</td>
<td>9.7</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>KOH</td>
<td>0.5\text{a}</td>
<td>0.5</td>
<td>brownish</td>
<td>39.1</td>
<td>48.0</td>
<td>12.9</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>KCN</td>
<td>2.9\text{a}</td>
<td>0.5</td>
<td>brownish</td>
<td>45.2</td>
<td>44.3</td>
<td>10.5</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>CH$_3$CO$_2$K</td>
<td>9.24\text{a}</td>
<td>24</td>
<td>colorless</td>
<td>86.6</td>
<td>13.4</td>
<td>trace</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>DBU\text{d}</td>
<td>2.0</td>
<td>26</td>
<td>colorless</td>
<td>39.6</td>
<td>50.1</td>
<td>10.3</td>
<td></td>
</tr>
</tbody>
</table>

^aAll reaction performed at room temperature. The reactant molar ratio is: IIDN: 18-crown-6: base = 1: 0.1: 0.2. \(^b pK_b\) values in H$_2$O. \(^c Data derived from the GLC analysis of the ethyl acetate layer after partition in ethyl acetate/water biphasic of the sample directly taken from the reaction mixture. \(^dNo 18$-crown-6$ was used. Reaction was performed at 50 °C with 0.5 equiv. of DBU.

NMR spectroscopy is a powerful technique for characterizing the molecular structures of isoxides, since the different isomers give very distinct spectra. The $^1$H and $^{13}$C spectra of the three isoxide dinitrile isomers are presented in Figure 3-1. The stereo-configurations of the three isomers can be distinguished by several typical features. The bridge protons H3/4 appear as a singlet at around 5.0 ppm for the exo-exo configured IIDN. This is mainly due to symmetry and an dihedral angle of approximately 90° and thereby a negligible vicinal coupling constant between the adjacent protons H2 and H3, as well as between the protons H4 and H5, respectively.\text{61} For the endo-end configuration IMDN, the signals of the bridge protons H3/4 are apparently shifted upfield. Due to magnetic inequivalence, they display a more complicated multiplicity at around 4.85 ppm.\text{61} In the case of ISDN, due to structural asymmetry, different coupling constants exist between the bridge protons H3/4 with the neighboring protons H2/5, respectively. Now, the bridge protons H3/4 appear as a quasi-doublet (H3) and a triplet (H4) at 4.96 and 4.91 ppm, respectively.\text{61} Furthermore, the (a)symmetry of the three isomers is also reflected in their respective $^{13}$C NMR spectra. For the asymmetrical ISDN eight signals are found instead of only four signals for the symmetrical IIDN and IMDN.\text{61} In addition, the nitrile groups exhibit a very distinctive signal at approximately 115 ppm. Overall, both the $^1$H and $^{13}$C NMR spectra of the asymmetrical exo-end configuration ISDN appear as an average of the spectra of the symmetrical isomers. 2D COSY NMR spectra of the three isomers confirm the assignments based on the 1D spectra (see Appendix C, Figure C-1).
Figure 3-1. $^1H$ NMR (a) and $^{13}C$ NMR (b) spectra of isohexide dinitriles recorded in CDCl$_3$ at room temperature.
3.3.2. Epimerization kinetics and study of the mechanism

In order to improve the efficacy of the epimerization reaction as a synthetic tool, as well as to elucidate the epimerization mechanism, a kinetic study was performed. Epimerization reactions were carried out on all three purified isohexide dinitriles in THF solution at 50 °C in the presence of DBU. Samples were taken at specific time intervals and the ratio of isomers was analyzed by gas chromatography (GC-FID). To avoid the \textit{in-situ} thermal-induced epimerization during the GC analysis, special care was taken to remove DBU from the samples prior to GC analysis by ethyl acetate/water extraction, followed by a rapid filtration on silica gel. Figure 3-2 shows the curves of the fraction of three dinitrile isomers versus reaction time obtained for the epimerization reactions. When starting from IIDN (Figure 3-2a), a dynamic equilibrium is reached in approximately 26 h. The final isomer molar ratio is IIDN:ISDN:IMDN = 35:50:15. The formation of ISDN is rapid within the first 10 h, while the amount of IMDN is almost negligible. When starting from pure ISDN, equilibrium is reached in 20 h, eventually giving a same product ratio (Figure 3-2b). In the case of IMDN, it is clear that the epimerization rates are significantly higher than those of the previous two cases, as indicated by the higher slopes of the kinetic curves, especially during the initial 5–7 h (Figure 3-2c). Again, the same final equilibrium molar ratio is obtained. Overall, it is clear that the ISDN concentration reaches a steady state of around 50% within 25 h, while IIDN and IMDN become stable in 48 h with final concentrations of approximately 35% and 15%, respectively. The trends in Figure 3-2 conclusively show that a dynamic epimerization equilibrium exists for all three isomers under the investigated basic conditions. The apparent preference for the \textit{exo-endo} ISDN is different from the data reported by Wright \textit{et al.} These authors reported a molar ratio of isoidide : isosorbide : isomannide = 60 : 30 : 10 for the catalytic epimerization of isohexides by means of dehydrogenation-rehydrogenation.\textsuperscript{59} The isomer ratio was observed to be independent of the configuration of the starting material as well.

In order to understand this difference in selectivity, we performed density functional theory (DFT) calculations on the three isohexide isomers in the forms of molecules and anions in both the gas phase and in THF. Since strong electron withdrawing groups like nitriles increase the acidity of \( \alpha \)-protons, we assume that the base abstracts a proton at C2 or C5 generating a carbanion (Scheme 3-3). Previous work by Paolucci \textit{et al.} has shown that an unstabilized negative charge at C2/C5 results in ring-opening of the isohexide skeleton, forming a reactive 2,5-dihydrofuran species. This reaction has been shown to proceed at temperatures as low as \(-78 \, ^\circ\text{C}\).\textsuperscript{30} Given that the DBU-catalyzed epimerization at 50 °C, as described in the kinetics study, did not cause any ring-opening side-reaction, charge stabilization by the nitrile group appears to be very efficient.
Figure 3-2. Epimerization kinetics curves of the molar percentage (%) of isomers versus reaction time (h): (a) epimerization of IIDN; (b) epimerization of ISDN; (c) epimerization of IMDN. A typical epimerization experiment is performed in the presence of isohexide dinitriles (1.0 mmol), DBU (0.5 mmol) and THF (25 mL) at 50 °C under a nitrogen atmosphere. Samples for GLC analysis were taken at intervals over a period of 48 h.
Scheme 3-3. Deprotonation-reprotonation epimerization pathway of isohexide dinitriles through stabilization of the carbanion by the nitrile group.

All DFT calculations were performed using the Amsterdam Density Functional (ADF) program supported by density functional theory at BP86/TZ2P for geometry optimization and energies.\textsuperscript{62,63} Solvation in tetrahydrofuran (THF) was simulated using the conductor-like screening model (COSMO).\textsuperscript{64-68} All stationary points were verified to be minima through vibrational analysis.

The relative energies between the molecules and anions are given in Table 3-2. The two cis-fused tetrahydrofuran rings of the three isohexide dinitriles have the possibility to pucker on C1 and C6. This can result in different conformations (up-up, up-down, down-up and down-down). The computations show that in the gas phase, the exo-exo IIDN is the most stable form, whereas in THF the energy difference among the three conformers is negligible. For the corresponding anions, the same trend is encountered. As indicated by the energy values in Table 3-1, the up-down conformations of IIDN and ISDN, as well as the up-up conformation of ISDN appear to be the most stable configurations by showing the lowest energy (Figure 3-3). Notably, they are the same types of conformations as found in the crystal structures. (Figure 3-4 in the later section).
Table 3.2 Relative energies (in kcal/mol) and dihedral angles of three isohexide isomers in the forms of molecules and anions in both gas phase and THF solution.\textsuperscript{c}

<table>
<thead>
<tr>
<th>species</th>
<th>C1/C6 \textsuperscript{b}</th>
<th>gas phase</th>
<th>THF</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>molecule</td>
<td>anion</td>
<td>dihedral angle\textsuperscript{c}</td>
</tr>
<tr>
<td>IIDN</td>
<td>D/U</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>U/U</td>
<td>0.7</td>
<td>1.2</td>
</tr>
<tr>
<td></td>
<td>D/D</td>
<td>0.4</td>
<td>0.0</td>
</tr>
<tr>
<td>ISDN</td>
<td>U/U</td>
<td>1.2</td>
<td>1.2</td>
</tr>
<tr>
<td></td>
<td>D/U</td>
<td>0.5</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>U/D</td>
<td>1.4</td>
<td>1.2</td>
</tr>
<tr>
<td></td>
<td>D/D</td>
<td>3.0</td>
<td>0.0</td>
</tr>
<tr>
<td>IMDN</td>
<td>U/U</td>
<td>1.8</td>
<td>1.2</td>
</tr>
<tr>
<td></td>
<td>D/U</td>
<td>2.5</td>
<td>1.2</td>
</tr>
<tr>
<td></td>
<td>D/D</td>
<td>1.8</td>
<td>4.3</td>
</tr>
<tr>
<td>CH\textsubscript{3}</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

\textsuperscript{c}Computed at the BP86/TZ2P level of theory using COSMO to estimate the solvent effects by THF. The data in bold belong to the configurations same as those found in single crystal X-ray diffraction study (Figure 3-4).\textsuperscript{b}Conformers with different puckering directions of C1 and C6. U: up; D: down. \textsuperscript{c}Dihedral angle between the plains defined by C1C2C3 and C4C2C3, see Figure C-1, Appendix C.

Under basic conditions, deprotonation of the sp\textsuperscript{3} hybridized 2/5 carbon atoms of isohexide dinitrile is expected to initially give a sp\textsuperscript{3} hybridized α-nitrile carbanion with a tetrahedral conformation (Scheme 3-3). In order for epimerization to occur, conformational inversion of this carbanion is required to enable reprotonation from the opposite side. The dihedral angle formed by the planes C1C2C3 and C4C2C3 (see Figure C-2, Appendix C) serves as a measure for the degree of pyramidalization of the carbanion. According to the DFT calculations, the (mono) isohexide dinitrile carbanions have almost planar configurations in the gas phase with dihedral angles of nearly 180°, and slightly pyramidal configurations in THF solution with dihedral angles in the range of 150–160° (Table 3-2). In contrast, the corresponding dihedral angle of the fully pyramidal methylide anion is 110° (Table 3-2). At the same time, the distances between the carbanion and its neighboring carbon atoms of the sp\textsuperscript{2} hybridized carbanion, \textit{viz.} the bond lengths of C1-C2 and C2-C3, were also observed to be shortened by up to 0.08 Å (Figure 3-3). In THF, the calculated barrier for sp\textsuperscript{3}-sp\textsuperscript{2} rehybridization is only 0.4 kcal/mol, and therefore virtually negligible. Thus, rehybridization of the tetrahedral carbanion to a planar sp\textsuperscript{2} hybrid is believed to be a feasible course.
Figure 3-3. Bond lengths (in Å) for IIDN, ISDN and IMDN and anions thereof. Computations conducted at the BP86/TZ2P level of theory using COSMO to estimate the solvent effects by THF (top and side view are presented) and the increase in atomic Voronoi Deformation Density (VDD) Charges (only charge increments larger than 0.04 electrons are shown).
From previous work, it is known that substituents at the carbanion, particularly nitrile groups stabilize a planar structure.\textsuperscript{70, 71} In our case, the stabilization is accomplished by donation of charge from the isohexide dinitrile carbanion into the $\pi^*$ orbitals of the neighboring cyano-group. During this course, a dynamic equilibrium is formed between the original nitrile group and imine anion (Scheme 3-3). Therefore C-N bond is shortened by 0.03 Å (Figure 3-3). The planar sp\textsuperscript{2} hybridized carbanion makes it possible for the H\textsuperscript{+} to attack from both sides giving as a result a mixture of these three structures. In the case of catalytic epimerization of isosorbide under hydrogen pressure using a dehydrogenation-hydrogenation catalyst, Wright et al.\textsuperscript{59} also postulated a sp\textsuperscript{2}-hybridized intermediate (ketone). These authors observed a preference for \textit{exo}-substitution (75\%) which resulted in an overall preference for the isoidide isomer (57\%). In the case of the isohexide dinitriles the observed product ratio amounts to a 60\% preference for \textit{exo}-substitution and hence a preference for ISDN (50\%). Given the large differences in reaction temperature between Wright’s and our reaction (220–240 °C versus 50 °C respectively), care should be taken in comparing the epimeric molar ratio values. Moreover, as shown in Figure 3-3, carbanion formation under basic conditions additionally causes elongation of C–O (ether) bonds, in particular the C3–O2 bond, by up to 0.09Å, which is thought to be caused by the lone pair charge donation from C2 or C5 into the neighboring $\sigma^*$ orbital of the ether bonds (see increase of atomic charges shown in Figure 1). Without the presence of electron-stabilizing groups on C2 or C5, like e.g. a nitrile, such an elongation of the C-O bond can result in a ring opening side reaction, as reported by Paolucci et al.\textsuperscript{30}

\textbf{3.3.3 X-ray crystal structures}

The orientation of the functional groups in isohexides has a profound influence on both physical and chemical properties such as reactivity and thermal stability.\textsuperscript{1,4,16} When used as building blocks for synthesizing step-growth polymers, factors like rigidity, symmetry and linearity can have dramatic effects on molecular weight build-up, thermal properties, degree of crystallization and crystallization rates of the polymers. We have recently reported a number of studies which focused not only on the structural characterization of the building blocks, but also the structure-property relations in the ensuing polymers. Studies on novel isohexide-based polyamides and polyesters showed that, whereas isohexides in general have a profound effect on e.g. the glass transition temperature and crystallinity, the orientation and type of substituents at the 2/5 positions can have a dramatic influence on various properties.\textsuperscript{16,39-41}

Previously, by a single crystal X-ray diffraction study and DFT calculations, we have shown that isoidide-2,5-dicarboxylic acid (IIDCA, Scheme 3-1) can adopt different
conformations due to puckering of the five-membered rings.\textsuperscript{16} Significant differences were observed for a few structural parameters, such as the planarity of the rings, symmetry and linearity of the molecules among different conformers. DFT results showed that the free energy of these conformers only differ by approximately 1 kcal/mol. The existence of three types of conformers suggests a higher than expected flexibility of the bicyclic skeleton. In order to expand our understanding of the structural properties of isohexide derivatives, we conducted an in-depth analysis of the three dinitrile isomers by X-ray crystal structure determinations and DFT calculation.

Single crystals of all three dinitriles were obtained by crystallization of high purity isomers from ethyl acetate/n-hexane, and subsequently analyzed by single crystal X-ray diffraction techniques (Figure 3-4). Analysis of the crystal structures shows that the tetrahydrofuran rings of each isomer are non-planar due to ring puckering on C1 and C6 (Figure 3-4): C1 is puckered upward in all three isomers, while C6 points downward in IIDN and ISDN and upward in IMDN (Table 3-3). The corresponding Cremer-Pople puckering parameters (Q, $\Phi$)\textsuperscript{72} based on X-ray crystal structures quantitatively describe the degree of puckering of each ring, which can be found in Table 3-3. However, it should be noted that, the description on puckering up/down directions is only meaningful when the rings are in an envelope conformation. In ISDN, ring b has a twist conformation, thus an up/down comparison is impossible. In IMDN, both rings are in envelope conformation, but the pivot atoms (C2, C5) are different from IIDN (C1, C6). A simple up/down does not reflect this situation.

Analysis of the torsion angles defined by O1-C4-C3-C2 and O2-C3-C4-C5, shows that going from IIDN (0°, or virtually co-planar), via ISDN (5-9°) to IMDN (25°), the 5-membered rings become severely twisted. Since the two cis-fused tetrahydrofuran rings are not planar, the dihedral angles between them, \textit{viz}. the V-shape opening angles, cannot be given precisely. It may be described in terms of various planes through sets of three or four atoms, or in terms of various torsion angles. According to the dihedral angle formed by the two least-square planes defined by O1-C4-C3-C2 and O2-C3-C4-C5, respectively, the V-shape angles of the three isomers are in good agreement with the previously described 120° opening of the isohexide skeleton.\textsuperscript{1,3,4} Nevertheless, a significant difference of 50° between the two torsion angles, i.e. O1-C4-C3-O2 and C2-C3-C4-C5 was observed for the highly deformed IMDN (Table 3-3). It is widely accepted that the bicyclic isohexide skeleton is a rigid moiety.\textsuperscript{1,3,4} However, based on the above observations, it is clear that this skeleton can deform to a large extent. A similar phenomenon has been observed in the case of isoidide dicarboxylic acid (IIDCA).\textsuperscript{16}

The degree of linearity and symmetry of the molecules is governed by the orientation of the nitrile groups. Interestingly, in all three isomers the nitrile groups adopt an equatorial
conformation (Figure 3-4). The distances between the two nitrile groups (defined as D, Table 3-3) are rather comparable (~5.8 Å) for all three isomers. Therefore, the relative positions of C2 and C5 are not much affected by the different degrees of deformation of the bicyclic skeletons. The angle α, here defined as the C8-C5-C2/C7-C2-C5 angle, is a measure for the (non)linearity of the nitrile groups. Since in none of the three isomers an α angle of 180° is encountered, all three dinitriles are non-linear. A further distinct feature is expressed by the angle β, here defined as the C8-C5-C2-C7 torsion angle. In the case of IIDN, both nitrile groups are virtually located in the same plane by showing a torsion angle of almost 0°, while the angle gradually increases when going to ISDN (25°), and finally IMDN (62°). These observations on β angles suggest that the two nitrile groups are virtually located in a same plane for IIDN and are gradually separated to the two almost perpendicular planes for IMDN. The last parameter describing the relative positions of the two nitrile groups is defined as γ, which represents the projected angles between the two nitrile groups of the three isomers. Owing to a more “stretched” exo-exo structure, IIDN displays an apparently higher γ angle than the other two isomers.

According to these X-ray diffraction data, the three dinitriles apparently display varying degrees of deformation and are all lacking symmetry. For all the three isomers, the energy barriers for 5-membered ring conformational changes, as indicated by the energy values of different conformers for each isomer, differ by less than 2 kcal/mol in THF and by less than 3 kcal/mol in the gas phase (Table 3-2). This is supported by the fact that the configurations of IIDN and IMDN, determined by solution NMR spectroscopy at room temperature, are fully symmetrical, suggesting an overall stereo-chemistry effect of all the coexisting conformers.

Based on the above comprehensive structural comparisons, it is obvious that the deformations and differences in all the investigated structural parameters point to deviations from symmetry of the molecules as well as the flexibility of the bicyclic ring structure. The apparent dynamic equilibrium between the isohexide ring conformers at room temperature shows that isohexides are more flexible than previously thought of, given the significant changes in the angles between the substituents for the various ring conformations.
Figure 3-5. Displacement ellipsoids of three isohexide dinitrile isomers in the crystal (50% probability level).
Table 3-3. Structural characteristics and values of structural parameters of isohexide dinitrile isomers derived from single crystal X-ray structure determinations and DFT calculations.\(^a\)

<table>
<thead>
<tr>
<th>parameters</th>
<th>IIDN(^b)</th>
<th>ISDN</th>
<th>IMDN</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1/C6 PD(^a)</td>
<td>U/D</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>2-CN/5-CN</td>
<td>eq./eq.</td>
<td>eq./eq.</td>
<td>eq./eq.</td>
</tr>
<tr>
<td>Q(_a)(Å)</td>
<td>0.3944(13)</td>
<td>0.4039(13)</td>
<td>0.3596(17)</td>
</tr>
<tr>
<td>(\Phi_a)(°)</td>
<td>217.31(19)</td>
<td>224.75(19)</td>
<td>256.6(3)</td>
</tr>
<tr>
<td>(Q_b)(Å)</td>
<td>0.3659(12)</td>
<td>0.3940(13)</td>
<td>0.3558(17)</td>
</tr>
<tr>
<td>(\Phi_b)(°)</td>
<td>30.0(2)</td>
<td>24.36(19)</td>
<td>259.3(3)</td>
</tr>
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<td>(Tors_a)1-C4-C3-C2(°)</td>
<td>0.09(12)</td>
<td>–5.32(12)</td>
<td>–23.86(15)</td>
</tr>
<tr>
<td>(Tors_a)2-C3-C4-C3(°)</td>
<td>–4.99(11)</td>
<td>–9.36(12)</td>
<td>–24.87(14)</td>
</tr>
<tr>
<td>(A)(°)</td>
<td>62.83(8)</td>
<td>61.81(8)</td>
<td>63.86(11)</td>
</tr>
<tr>
<td>(Tors_a)1-C4-C3-C2(°)</td>
<td>–119.40(9)</td>
<td>–125.08(10)</td>
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</tr>
<tr>
<td>(Tors_a)1-C3-C4-C3(°)</td>
<td>114.49(10)</td>
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<tr>
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<td>5.8869(19)</td>
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<td>–154.99(18)</td>
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<tr>
<td>(\gamma)(°)</td>
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<td>30.45</td>
<td>47.99</td>
</tr>
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</table>

\(^a\)Abbreviations: PD: puckering direction; U: up; D: down; Q: Cremer-Pople ring puckering amplitude of a/b rings; \(\Phi\): Cremer-Pople ring puckering phase angle of a/b rings. \(Tors\): torsion angle; \(^b\)Dihedral angle between the two least-square planes defined by O1-C4-C3-C2 and O2-C3-C4-C5; \(^c\)The distance between two nitrile groups, defined by the interatomic distance of C7-C8; \(^d\)C8-C5-C2/C7-C2-C5 angle; \(^e\)Improper torsion angle C8-C5-C2-C7; \(^f\)Actual or projected angle between the C8-C5 bond and the C2-C7 bond.

3.4 Conclusions

In conclusion, a group of sugar-derived bicyclic dinitriles, \textit{viz.} isomeric isohexide dinitriles, were successfully synthesized by a convenient base-catalyzed epimerization procedure. Although various bases are effective, the strong organic base DBU was found to be the most suitable one, combining high selectivity with high reactivity. This procedure allows for a significant expansion of available 1-carbon extended isohexide derivatives, some of which have already shown highly interesting effects in step-growth polymers. A detailed structural analysis of all three possible isomers by single crystal X-ray diffraction and DFT calculations shows that several structural parameters, such as dihedral and torsion
angles, can vary over a wide range. The main learning from this chapter is that the bicyclic isohexide skeleton is significantly more flexible than anticipated based on existing literature.

REFERENCES

Chapter 3


Semicrystalline polyesters based on isoidide dicarboxylic acid (IIDCA)

Abstract

Isohexides, like e.g. isosorbide, are well-known carbohydrate-based rigid diols which are capable of dramatically increasing the glass transition temperature of polyesters. However, their relatively low reactivity has thus far hampered large scale industrial applications in the polymer field. Recently, with the aim to increase reactivity while at the same time retain rigidity, we have developed a new isoidide dicarboxylic acid (IIDCA) by transforming the secondary hydroxyls into carboxylate functionalities. Here we report the first polymers based on IIDCA and linear α,ω-diols. The novel polyesters were obtained via melt polymerization and exhibited weight average molecular weights in the range of 13,000–34,000 g/mol and polydispersities close to 2.0. NMR analyses showed that the exo-exo configuration of the isoidide dicarboxylate units was preserved during synthesis. Both differential scanning calorimetry and wide-angle X-ray diffraction analyses showed that the IIDCA polyesters are semi-crystalline materials. A systematic study on structure-thermal properties relations among relevant series of polyesters, such as isomeric polymers based on isoidide, revealed several interesting differences in melting and glass transition temperatures, which are thought to be related to variations in chain packing and free volume.

4.1 Introduction

In chapter 2, we described the synthesis of a new 1-carbon extended isohexide derivative, namely isoidide dicarboxylic acid (IIDCA, Figure 4-1).\(^2\) It was anticipated that substitution of the secondary hydroxyl groups by a carbon functionality directly attached to the bicyclic ring would result in a higher reactivity with retention of rigidity. Since polyesters are some of the most widely used polymers, our first focus was to investigate the effect of IIDCA incorporation into a series of linear aliphatic polyesters. The synthesis, structural characterization and thermal properties of the first polyesters based on IIDCA and linear \(\alpha,\omega\)-diols HO-(CH\(_2\))\(_n\)-OH (PE-\(n\)IIDCs, \(n = 2, 4, 6, 8, 10, 12\)) is described here. Some of the aliphatic diols are bio-based or can potentially be derived from biomass, such as ethylene glycol,\(^3,4\) 1,4-butanediol\(^4,6\) or 1,10-decanediol, a potential derivative of the castor-oil-derived sebacic acid.\(^7\) Thus, the polyesters based on these diols and IIDCA are fully bio-based. Furthermore, in order to investigate the effect of IIDCA incorporation on the polyester properties, as well as to verify the aforementioned hypothesis concerning the reactivity and rigidity, the structure-thermal properties relations were studied by comparing the thermal properties of a range of relevant polyesters.

![Figure 4-1. Structure of isoidide dicarboxylic acid (IIDCA) prepared from isomannide.](image)

4.2 Experimental section

Materials and general methods

Isomannide (95%), pyridine (Merck, p.a.), hydrochloric acid (reagent grade, 37%), tetrahydrofuran (anhydrous, \(\geq 99.9\%\)), 18-crown-6 (\(\geq 99\%\)), ethylene glycol (anhydrous, 99.8%), 1,4-butanediol (\(\geq 99\%\)), 1,6-hexanediol (99%), 1,8-octanediol (98%), 1,10-decanediol (98%), 1,12-dodecanediol (99%), titanium(IV) isopropoxide (97%), dibutyltin(IV) oxide (DBTO, 98%), 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD, 98%), chloroform-D (99.8 atom % D), trifluoroacetic acid (99%) were purchased from Sigma-Aldrich. 1,1,1,3,3,3-Hexafluoro-2-propanol (HFIP), methanol and chloroform and dichloromethane were purchased from Biosolve. Potassium cyanide (extra pure) and
trifluoromethanesulfonic anhydride (≥99%) were purchased from Merck. All chemicals were used as received, unless noted otherwise.

Characterization

Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Avance III spectrometer operating at 400.17 MHz (1H) and 100.62 MHz (13C) at room temperature. 2D NMR spectra were recorded on a Varian Unity 500 plus spectrometer at room temperature. Chemical shifts were referenced to residual signals of CDCl3. Correlation spectra (COSY) were acquired using standard programs provided by a Varian spectrometer library with the following parameters: spectral width SW1 = SW2 = 6075.3 Hz, acquisition time 0.221 s, relaxation delay 1.4 s, and number of scans 8 x 300 increments. Fourier transform infrared (FT-IR) spectra were obtained on a Varian Scimitar 1000 FT-IR spectrometer equipped with a Pike MIRacle ATR Diamond/ZnSe single reflection plate and a DTGS-detector. The measurement resolution was set at 4 cm−1 and the spectra were collected in the range 4000–650 cm−1 with 32 co-added scans. Size exclusion chromatography (SEC) in hexafluoropropylpentane (HFIP) was performed on a system equipped with a Waters 1515 Isocratic HPLC pump, a Waters 2414 refractive index detector (35 °C), a Waters 2707 auto sampler, and a PSS PFG guard column followed by 2 PFG-linear-XL (7 μm, 8 x 300 mm) columns in series at 40 °C. HFIP with potassium trifluoroacetate (3 g/L) was used as eluent at a flow rate of 0.8 mL/min. The molecular weights were calculated against polymethyl methacrylate standards (Polymer Laboratories, Mn = 580 Da up to Mn = 7.1 x 10⁶ Da).

The thermal stability of the polymers was determined by thermogravimetric analysis (TGA) with a TGA Q500 apparatus from TA Instruments. The samples were heated from 30 °C to 600 °C at a heating rate of 10 °C /min under a nitrogen flow of 60 mL/min. Glass transition temperatures and melting temperatures were measured by differential scanning calorimetry (DSC) using a DSC Q100 from TA Instruments. The measurements were carried out at a heating and cooling rate of 10 °C /min from −60 °C to 150 °C. Data acquisition was carried out using Pyris 7 software.

MALDI-Tof-MS spectra were recorded on a Voyager DE-STR from Applied Biosystems. Calibrations were carried out with poly(ethylene oxide) standards for the lower mass range and polystyrene standards for the higher mass range. The mass accuracy was better than 0.2 Dalton. The mass resolution was approximately m/z 12,000. DCTB (trans-2-[3-(4-tert-butylphenyl)-2-methyl-2-propenylidene]malononitrile) was used as matrix. Potassium trifluoroacetate (5 mg/mL) and the polyester sample (1 mg/mL) in HFIP were premixed in a ratio of 5:1:5. The mixture was subsequently hand-spotted on the target and left to dry. Spectra were recorded in reflector mode at positive polarity.

Analysis of the crystalline structure of the materials was performed using wide-angle X-ray scattering measurements by means of computer controlled goniometer coupled to a sealed-tube source of CuKα radiation (Philips), operating at 50 kV and 30 mA. The CuKα line was filtered using electronic filtering and the usual thin Ni filter. The data were collected at room temperature. The 1D profiles were subsequently background-corrected and normalized.

Monomer synthesis

(3S,6S)-hexahydrofuro[3,2-b]furan-3,6-dicarboxylic acid (IIDCA) and its dimethyl ester (3S,6S)-dimethyl hexahydrofuro[3,2-b]furan-3,6-dicarboxylate (IIDMC) were synthesized and purified according to the reported procedure.¹² The purity and stereo chemistry of the monomers were confirmed by GC, GC-MS, 1H NMR, 13C NMR and FT-IR.
Polymerization

Poly(alkylene isoididedicarboxylates) (PE-nIIDCs) were synthesized from IIDCA or IIDMC in combination with linear \( \alpha,\omega \)-diols HO-(CH\(_2\))\(_n\)-OH \((n = 2, 4, 6, 8, 10, 12)\). The model polymerization based on IIDCA or IIDMC and 1,4-butanediol was first investigated, and the synthesis follows procedure A (see below). The pristine DBTO (1.0 mol %, with respect to IIDCA/IIDMC), bismuth(III) triflate (1.0 mol %) and TBD (5 mol %) or 0.1 mL titanium(IV) isopropoxide in toluene solution (0.1 mmol/mL) were used as the catalysts. The syntheses of entire series of PE-nIIDCs follow the same procedure A using IIDMC as monomer and DBTO as catalyst. For comparison, poly(alkylene adipate)s (PE-nAd)s were synthesized as well from dimethyl adipate with the corresponding linear aliphatic \( \alpha,\omega \)-diols according to the reported procedure. The syntheses are summarized as procedure B.

Procedure A. IIDCA (0.202 g, 1.0 mmol) or IIDMC (0.230 g, 1.0 mmol) and \( \alpha,\omega \)-diol (2.0 mmol) were charged into a 10 mL round bottom flask located inside a Kugelrohr oven. The apparatus was flushed with nitrogen several times at room temperature to remove oxygen. Then the Kugelrohr oven was internally heated to 130 °C and maintained at this temperature for 5–10 min until the reactants turned into a clear melt. Next, catalyst was added into the flask. The pre-polymerization was carried out at 130 °C under a continuous flow of nitrogen for 3 h for the polymerizations based on IIDCA, 5–18 h for the polymerizations based on IIDMC. Subsequently, the polymerization temperatures were adjusted to the desired range of 130 to 200 °C as shown in the Table 1. At the same time vacuum (0.01–0.05 mbar) was applied step-wise to the reaction system to remove the excess diol and condensates. After 3 h, the resulting polymer melt was cooled down and dissolved in chloroform and precipitated into methanol, filtered and dried in vacuo at 30 °C for 24 h.

Procedure B. A 1.0–1.2/1 molar ratio mixture of the corresponding diol to dimethyl adipate and titanium(IV) butoxide (TBT) catalyst (0.5 mol % with respect to dimethyl adipate) were charged into a 100 mL three-necked round-bottom flask equipped with a mechanical stirrer, a nitrogen inlet and a vacuum distillation outlet. The apparatus was flushed with nitrogen several times at room temperature to remove oxygen. Transesterifications were carried out under a low nitrogen flow for 5 h at 180 °C, followed by the polycondenations for 3 h at 200 °C under reduced pressure (0.01–0.05 mbar). The resulting polymers were dissolved in chloroform and precipitated into methanol, filtered and dried in vacuo at 30 °C for 24 h.

**PE-2IIDC.** \(^1\)H NMR (CDCl\(_3\), \( \delta \), ppm): 170.99 (C=O), 85.80, 69.91, 62.56, 51.41. \(^1\)C NMR (CDCl\(_3\), \( \delta \), ppm): 4.91 (s, 2H), 4.35 (m, 4H), 4.10 (m, 2H), 4.02 (m, 2H), 3.15 (m, 2H). FT-IR, \( \nu \) (cm\(^{-1}\)): 3448, 2956, 2877, 1723 (C=O), 1476, 1447, 1381, 1315, 1171, 1061, 1027, 911, 800, 761.

**PE-4IIDC.** \(^1\)H NMR (CDCl\(_3\), \( \delta \), ppm): 171.19 (C=O), 85.89, 69.99, 64.53, 51.55, 25.12. \(^1\)C NMR (CDCl\(_3\), \( \delta \), ppm): 4.91 (s, 2H), 4.15 (m, 4H), 4.10 (m, 2H), 4.02 (m, 2H), 3.12 (m, 2H), 1.73 (m, 4H). FT-IR, \( \nu \) (cm\(^{-1}\)): 2958, 2883, 1721 (C=O), 1472, 1451, 1359, 1296, 1257, 1176, 1067, 962, 931, 814, 682.

**PE-6IIDC.** \(^1\)H NMR (CDCl\(_3\), \( \delta \), ppm): 171.32 (C=O), 85.84, 69.97, 65.16, 51.54, 28.30, 25.58. \(^1\)H NMR [(CDCl\(_3\), \( \delta \), ppm): 4.92 (s, 2H), 4.12 (m, 6H), 4.02 (m, 2H), 3.12 (m, 2H), 1.66 (m, 4H), 1.38 (m, 4H). FT-IR, \( \nu \) (cm\(^{-1}\)): 3540, 2933, 2867, 1721 (C=O), 1472, 1350, 1299, 1192, 1071, 1013, 938, 819, 765.

**PE-8IIDC.** \(^1\)H NMR (CDCl\(_3\), \( \delta \), ppm): 171.31 (C=O), 85.91, 69.96, 65.24, 51.63, 29.15, 28.44, 25.70. \(^1\)H NMR (CDCl\(_3\), \( \delta \), ppm): 4.91 (s, 2H), 4.12 (m, 6H), 4.03 (m, 2H), 3.12 (m, 2H), 1.64 (m, 4H), 1.32 (m, 8H). FT-IR, \( \nu \) (cm\(^{-1}\)): 3442, 2928, 2853, 1724 (C=O), 1472, 1300, 1074, 1022, 937, 818, 766, 725.

**PE-10IIDC.** \(^1\)C NMR (CDCl\(_3\), \( \delta \), ppm): 171.31 (C=O), 85.92, 69.97, 65.25, 51.65, 29.34, 29.12, 28.48, 25.78. \(^1\)H NMR (CDCl\(_3\), \( \delta \), ppm): 4.92 (s, 2H), 4.09 (m, 6H), 4.02 (m, 2H), 3.12 (m, 2H), 1.65 (m, 4H), 1.28 (m, 12H). FT-IR, \( \nu \) (cm\(^{-1}\)): 2924, 2853, 1724 (C=O), 1471, 1359, 1292, 1183, 1075, 1015, 968, 905, 723, 688.

**PE-12IIDC.** \(^1\)C NMR (CDCl\(_3\), \( \delta \), ppm): 171.31 (C=O), 85.92, 69.98, 65.28, 51.65, 29.48, 29.43, 29.17, 28.49, 25.79. \(^1\)H NMR (CDCl\(_3\), \( \delta \), ppm): 4.92 (s, 2H), 4.11 (m, 6H), 4.03 (m, 2H), 3.12 (m, 2H), 1.63 (m, 4H), 1.27 (m, 16H). FT-IR, \( \nu \) (cm\(^{-1}\)): 2919, 2851, 1726 (C=O), 1466, 1351, 1297, 1195, 1075, 1031, 969, 818, 766, 722.
**Semicrystalline polyesters based on isoidide dicarboxylic acid (IIDCA)**

*PE-4Ad.* $^{13}$C NMR (CDCl$_3$, δ, ppm): 173.36 (C=O), 63.73, 33.75, 25.22, 24.28. $^1$H NMR (CDCl$_3$, δ, ppm): 4.10 (t, 4H), 2.33 (t, 4H), 1.69 (m, 8H).

*PE-6Ad.* $^{13}$C NMR (CDCl$_3$, δ, ppm): 173.35 (C=O), 64.26, 33.88, 28.50, 25.57, 24.39. $^1$H NMR (CDCl$_3$, δ, ppm): 4.06 (t, 4H), 2.32 (t, 4H), 1.64 (m, 8H). 1.38 (m, 4H).

*PE-8Ad.* $^{13}$C NMR (CDCl$_3$, δ, ppm): 173.37 (C=O), 64.42, 33.91, 29.09, 28.58, 25.81, 24.41. $^1$H NMR (CDCl$_3$, δ, ppm): 4.06 (t, 4H), 2.32 (t, 4H), 1.67 (m, 8H). 1.32 (m, 8H).

*PE-10Ad.* $^{13}$C NMR (CDCl$_3$, δ, ppm): 173.36 (C=O), 64.46, 33.91, 29.39, 29.17, 28.60, 25.86, 24.39. $^1$H NMR (CDCl$_3$, δ, ppm): 4.06 (t, 4H), 2.32 (t, 4H), 1.63 (m, 8H). 1.29 (m, 12H).

*PE-12Ad.* $^{13}$C NMR (CDCl$_3$, δ, ppm): 173.37(C=O), 64.44, 33.87, 29.46, 29.43, 29.17, 28.56, 25.54, 24.37. $^1$H NMR (CDCl$_3$, δ, ppm): 4.05 (t, 4H), 2.31 (t, 4H), 1.61 (m, 8H). 1.27 (m, 16H).

### 4.3 Results and discussion

#### 4.3.1 Synthesis and molecular Characterization of the polyesters

By reacting isoidide dicarboxylic acid (IIDCA) or its dimethyl ester (IIDMC) with linear $\alpha,\omega$-diols HO-(CH$_2$)$_n$-OH ($n = 2, 4, 6, 8, 10, 12$), a series of aliphatic polyesters (PE-nIIDCs, Scheme 4-1) was obtained by melt polymerization.

![Scheme 4-1. Polymerization of IIDCA/IIDMC and $\alpha,\omega$-diols yielding aliphatic polyesters.](image)

In order to find the optimal reaction conditions for the new diacid, the reaction of IIDCA/IIDMC with 1,4-butanediol was conducted on 1.0 mmol scale to vary conditions like temperature, reaction time and catalyst. A conventional 2-stage melt polymerization was performed using titanium(IV) isopropoxide as the catalyst: pre-polymerization at 130 °C under nitrogen, followed by further polymerization at elevated temperature ranging from 130–200 °C (see Table 4-1) under reduced pressure (0.01–0.05 mbar). The results are listed in Table 1. When IIDCA is used as a monomer, the reaction temperature has a significant effect on the PDI. Apparently, at temperatures exceeding 130 °C side-reactions occurred, eventually leading to severe gel formation at temperatures above 170 °C (entry 3 and 4, Table 4-1). Whereas thus far we have been unsuccessful in elucidating the cross-linking
mechanism, it is reasonable to assume that acid catalyzed ring opening of the cyclic ethers is involved, as described by other authors.\textsuperscript{18,10} Hence, the best results (entry 1 and 5) were obtained at 130 °C for both the diacid (IIDCA) and the dimethylene (IIDMC) with $M_n$ values around 10,000 g/mol and PDI values close to 2.0. These results already show that despite the rather low polymerization temperature and short reaction times, it is possible to obtain virtually colorless polymers with sufficient molecular weights, showing the increased reactivity of IIDCA compared to the parent isohexides.

**Table 4-1.** Effect of the polymerization conditions on molecular weight distribution of polyesters based on IIDCA and 1,4-butandiol.\textsuperscript{a}

<table>
<thead>
<tr>
<th>entry</th>
<th>monomer</th>
<th>catalyst</th>
<th>T (°C)</th>
<th>$M_n$ (g/mol)</th>
<th>$M_w$ (g/mol)</th>
<th>PDI</th>
<th>Yield\textsuperscript{d} (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>IIDCA</td>
<td>TIP</td>
<td>130</td>
<td>10,300</td>
<td>24,300</td>
<td>2.3</td>
<td>57</td>
</tr>
<tr>
<td>2</td>
<td>IIDCA</td>
<td>TIP</td>
<td>150</td>
<td>17,300</td>
<td>72,400</td>
<td>4.2</td>
<td>51</td>
</tr>
<tr>
<td>3</td>
<td>IIDCA</td>
<td>TIP</td>
<td>170</td>
<td>8,400</td>
<td>31,200</td>
<td>3.7\textsuperscript{b}</td>
<td>41</td>
</tr>
<tr>
<td>4</td>
<td>IIDCA</td>
<td>TIP</td>
<td>190–200</td>
<td>gelation\textsuperscript{c}</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>IIDMC</td>
<td>TIP</td>
<td>130</td>
<td>10,900</td>
<td>24,400</td>
<td>2.2</td>
<td>36</td>
</tr>
<tr>
<td>6</td>
<td>IIDMC</td>
<td>TBD</td>
<td>120</td>
<td>oligomer, $M_n &lt; 1000$ g/mol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>IIDCA</td>
<td>BTf</td>
<td>130</td>
<td>10,900</td>
<td>39,600</td>
<td>3.6</td>
<td>80</td>
</tr>
<tr>
<td>8</td>
<td>IIDMC</td>
<td>DBTO</td>
<td>130</td>
<td>8,700</td>
<td>17,100</td>
<td>1.9</td>
<td>82</td>
</tr>
<tr>
<td>9</td>
<td>IIDMC</td>
<td>DBTO</td>
<td>150</td>
<td>14,100</td>
<td>34,100</td>
<td>2.4</td>
<td>95</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Polymerization conditions: (1) Prepolymerization at 130 °C for 3 h under N\textsubscript{2}; then polymerization at 130–200 °C for 3 h at 0.01–0.05 mbar; (2) TIP = titanium(IV) isopropoxide; TBD = 1,5,7-triazabicyclo[4.4.0]dec-5-ene; BTf = bismuth(III) triflate; DBTO = dibutyltin(IV) oxide. Molar ratio of the reactants and catalyst: IIDCA: 1,4-BDO: TIP = 1: 2: 0.01. \textsuperscript{b}Sample partially soluble in HFIP, PDI value derived from the HFIP-SEC results of the soluble part of the sample. \textsuperscript{c}Sample insoluble in HFIP. \textsuperscript{d}Isolated yields after precipitation from methanol.

In order to investigate the effect of the catalyst on both molecular weight build-up and polydispersity, besides the titanium(IV) catalyst, dibutyltin oxide (DBTO), bismuth(III) triflate and the guanidine base 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) were used (Table 4-1).\textsuperscript{11-13} Whereas the bismuth(III) triflate and TBD catalysts gave unsatisfactory results, DBTO in combination with the dimethylene IIDMC afforded polyesters in high isolated yields with sufficiently high molecular weights and acceptable PDI values.

Based on these results a series of novel aliphatic polyesters was synthesized from IIDMC and linear $\alpha,\omega$-diols HO-(CH$_2$)$_n$-OH ($n = 2, 4, 6, 8, 10, 12$), using DBTO as catalyst at 150 °C for 3 h. In view of the same number of carbon atoms (four) between the two carboxylates, IIDCA can be regarded as a conformationally restricted counterpart of adipic acid. A series of analogous poly(alkylene adipate)s was synthesized as well for comparison according to the known procedure.\textsuperscript{8,9} The polymerization results are presented in Table 4-2.
In general, the IIDCA polyesters were obtained in good to excellent yields with $M_n$ values around 10,000 g/mol and satisfactory PDI values. Poly(ethylene isoididedicarboxylate) (PE-2IIDC) was obtained with a lower $M_n$ value of approximately 6,000 g/mol, which is probably due to the imbalance of stoichiometry caused by the fast distillation of volatile ethylene glycol using the Kugelrohr oven. When comparing polyesters based on the parent isohexides, activated dicarboxylic acids, such as diacid chlorides, are typically needed to obtain sufficiently high molecular weight. Here, we show that IIDCA yields high molecular weight polyesters as such, indicating a higher combined reactivity of this novel and renewable dicarboxylic acid with primary diols, compared to the combination of the secondary isohexide diols with conventional aliphatic dicarboxylic acids. When compared to the series of corresponding adipates it is clear that the molecular weights obtained for the latter are about twice as high as those of the IIDCA polyesters. This is mainly due to the fact that the polymerization temperature of the polyadipates (200 °C) is considerably higher than that of the corresponding isodidide dicarboxylates (150 °C).

Table 4-2. Molecular weights, polydispersities and isolated yields of the polyesters prepared from IIDMC or dimethyladipate and linear $\alpha,\omega$-diols at 150 °C

<table>
<thead>
<tr>
<th>polyester</th>
<th>PE-$n$IIDCs</th>
<th></th>
<th></th>
<th>PE-$n$Ads</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>PE-2IIDC</td>
<td>6,100</td>
<td>13,100</td>
<td>2.1</td>
<td>81</td>
<td>PE-2Ad</td>
<td>19,600</td>
<td>39,000</td>
</tr>
<tr>
<td>PE-4IIDC</td>
<td>14,100</td>
<td>34,100</td>
<td>2.4</td>
<td>95</td>
<td>PE-4Ad</td>
<td>27,100</td>
<td>48,400</td>
</tr>
<tr>
<td>PE-6IIDC</td>
<td>10,200</td>
<td>22,800</td>
<td>2.2</td>
<td>97</td>
<td>PE-6Ad</td>
<td>24,300</td>
<td>47,800</td>
</tr>
<tr>
<td>PE-8IIDC</td>
<td>10,000</td>
<td>17,100</td>
<td>1.7</td>
<td>73</td>
<td>PE-8Ad</td>
<td>10,400</td>
<td>19,000</td>
</tr>
<tr>
<td>PE-10IIDC</td>
<td>11,800</td>
<td>24,600</td>
<td>2.1</td>
<td>85</td>
<td>PE-10Ad</td>
<td>21,600</td>
<td>48,700</td>
</tr>
<tr>
<td>PE-12IIDC</td>
<td>8,800</td>
<td>18,000</td>
<td>2.0</td>
<td>97</td>
<td>PE-12Ad</td>
<td>19,100</td>
<td>40,500</td>
</tr>
</tbody>
</table>

*a* Syntheses of PE-$n$IIDCs and PE-$n$Ads follow procedure A in the experimental section. $M_n$: number-average molecular weight, $M_w$: weight-average molecular weight, PDI: polydispersity index. *b* Isolated yield after precipitation from methanol.
The chemical structure of the new polyesters was analyzed by 1D and 2D nuclear magnetic resonance (NMR) spectroscopy. As an example, the 2D $^1$H COSY and $^{13}$C NMR spectra of PE-4IIDC are presented in Figure 4-2. All proton and carbon signals from the repeating unit of the polymer are found at the expected chemical shift values with matching multiplicities. The stereochemistry of PE-4IIDC can be clearly illustrated by the resonances of the isohexide unit: there is no $^1$H-$^1$H dihedral coupling between the bridge protons 3/4 with the neighboring protons 2/5 based on the 2D-COSY NMR spectrum, thus the bridge protons 3/4 appear as a singlet at 4.8–4.9 ppm in the $^1$H NMR spectrum. This indicates that the adjacent protons 2/5 have no dihedral coupling with the bridge protons 3/4 and adopt an endo-orientation. Logically, the 2- and 5- carboxylate groups should be in an exo orientation.2,19,20 This feature was found to be typical for the entire series of IIDCA polyesters, confirming that the stereochemistry of the isohexides moieties was retained under the applied polymerization conditions. Furthermore, the number of $^{13}$C signals (Figure 4-2b) reveals a symmetrical structure of the repeating unit of PE-4IIDC. This proves that there is at least no formation of exo-endo type of epimerization products under the polymerization conditions.
Semicrystalline polyesters based on isoidide dicarboxylic acid (IIDCA)

Figure 4-3. Section of the MALDI-ToF MS spectrum of poly(hexamethylene isoididedicarboxylate) (PE-6IIDC) synthesized at 150 °C, signals cationized with K⁺: (A) linear chains with one methyl ester and one hydroxyl end-group; (B) linear chains with two hydroxyl end-groups; (C) linear chains with two methyl ester end-groups; (D) cyclics.

Furthermore, the synthesized polyesters were studied by MALDI-ToF-MS spectroscopy. The entire series of polyesters showed similar MALDI-ToF-MS patterns, which may differ in the abundance of product species. A representative mass spectrum of poly(hexamethylene isoididedicarboxylate) (PE-6IIDC) is shown Figure 4-3, together with the structures of four possible chemical compositions. For the observed four sets of MS signals, the mass intervals are all equal to 284 Da, which exactly matches the molar mass of the repeating unit of PE-6IIDC. It was found that products A and B are the most abundant ones for most of the
polyesters, although this conclusion should be drawn with care since MALDI-ToF-MS is not a quantitative analysis technique. Despite the fact that diols were used in excess for all polymerizations, the obtained polyesters were not fully OH end-capped. This may be due to the faster distillation of volatile diols by the rotating Kugelrohr oven set-up than by the conventional vertical mechanical stirrer set-up. The existence of species C (Figure 4-3) was observed to be much less abundant for the polyesters containing diols with longer alkylene chains than for the polyesters based on the shorter ones. This is mainly due to lower volatility of long chain diols. The intensities of the peaks attributed to the cyclic products D are rather low for all polyesters, usually below 10%. Furthermore, no signals corresponding to branched or ring-opening related side products were observed in the MALDI-ToF-MS spectra for none of the polyesters, indicating that the polymerization conditions are sufficiently mild to leave the monomers intact.

All new polymers were additionally analyzed by FT-IR spectroscopy (Figure 4-4). All functional groups showed the expected vibration signals and the entire series of polyesters give similar FT-IR absorption patterns. The formation of ester bonds was confirmed by the characteristic C=O stretching band at ~1720 cm⁻¹.

![Figure 4-4. FT-IR spectra of PE-nIIDCs recorded at room temperature. The spectra show frequency ranges of 650–3300 cm⁻¹.](image)

**4.3.2 Thermal properties of polyesters**

The thermal stability of the new polyesters was determined by thermogravimetric analysis (TGA). TGA curves of PE-nIIDCs and PE-nAds, measured from 30 °C to 600 °C under nitrogen atmosphere, are shown in Figure 4-5. The temperatures at 5% weight loss and the maximal decomposition rates of the polyester are shown in Table 4-3. The IIDCA polyesters
are thermally stable up to 280–300 °C. Two narrow degradation steps were observed for all of them with maximal decomposition rates at approx. 320 °C and 390 °C respectively (see the TGA curves of the derivatives of remaining weight versus temperature in Appendix D, Figure D-1). About 30–40% and 40–50% of the initial weights were lost during each step, and 10–20% of the initial weights were left at 600 °C. The adipate reference polymers display slightly different degradation behavior with a narrow onset degradation temperature window from 250 to 300 °C, except for poly(butylene adipate), which showed a higher onset temperature at approximately 330 °C. Only one major decomposition step was observed for all polyadipates. The maximal decomposition rates of the polyadipates appeared at about 350 °C with no appreciable residues above 420 °C. It is known that the thermal stability of polymers is related to the molecular weights, the higher molecular weight polymer usually being more stable. Given that the molecular weights of IIDCA polyesters are on average half of those of the polyadipates, in view of the onset decomposition temperatures, it is concluded that the thermal stability of the new polyesters is quite similar to that of the polyadipates.

Next, the thermal transitions of the new polyesters were studied by differential scanning calorimetry (DSC). The first and second heating curves of the IIDCA polyesters, measured from −50–150 °C, are shown in Figure 4-6, while the thermal data are summarized in Table 4-3.

Linear polyadipates are highly crystalline polymers as evidenced by sharp and intense melting and crystallization peaks. The observed melting temperatures of the PE-ηAds are in the range of 64–80 °C with enthalpy values greater than 80 J/g, while the crystallization
temperatures fall into the range of 35–63 °C with enthalpy values greater than 50 J/g. Both parameters steadily increase with the number of methylene units in the diol segment. With regard to the IIDCA polyesters, as is apparent from the first heating DSC curves (Figure 4-6a), all the precipitated IIDCA polyesters are semi-crystalline, as evidenced by the melting exotherms. However, the recorded melting enthalpies are considerably lower than those of the corresponding polyadipates, suggesting lower degrees of crystallinity. Whereas the polyester from ethylene glycol and IIDCA (PE-2IIDC) has a melting point of 125 °C, increasing the diol chain length results in a rapid decrease of the $T_m$ to 50–70 °C. In addition, the IIDCA polyesters display bi\tri-modal melting peaks which is indicative of imperfect polymer crystals or coexistence of different crystal forms.

![DSC curves of IIDCA polyesters](image)

**Figure 4-6.** DSC curves of IIDCA polyesters measured between −50 °C to 150 °C at 10 °C/min heating and cooling rate: (a) first heating curves; (b) second heating curves.
Table 4-3. Thermal properties of IIDCA and adipic acid polyesters measured by TGA and DSC.\textsuperscript{a}

<table>
<thead>
<tr>
<th>polyester</th>
<th>TGA</th>
<th>DSC</th>
<th></th>
<th>TGA</th>
<th>DSC</th>
<th></th>
<th>TGA</th>
<th>DSC</th>
<th></th>
<th>TGA</th>
<th>DSC</th>
<th></th>
<th>TGA</th>
<th>DSC</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$T_{5%}$ (°C)</td>
<td>$T_{\text{max}}$ (°C)</td>
<td>$T_g$ (°C)</td>
<td>$T_m$ (°C)</td>
<td>$\Delta H_m$ (J/g)</td>
<td>$T_c$ (°C)</td>
<td>$\Delta H_c$ (J/g)</td>
<td>$T_g$ (°C)</td>
<td>$T_m$ (°C)</td>
<td>$\Delta H_m$ (J/g)</td>
<td>$T_c$ (°C)</td>
<td>$\Delta H_c$ (J/g)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PE-2IIDC</td>
<td>279</td>
<td>315/384</td>
<td>–</td>
<td>125</td>
<td>33.6</td>
<td>–</td>
<td>–</td>
<td>18</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PE-4IIDC</td>
<td>303</td>
<td>320/392</td>
<td>0</td>
<td>47/62\textsuperscript{b}</td>
<td>32.4</td>
<td>–</td>
<td>–</td>
<td>0</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PE-6IIDC</td>
<td>297</td>
<td>317/397</td>
<td>–20</td>
<td>54</td>
<td>39.6</td>
<td>–</td>
<td>–</td>
<td>–20</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PE-8IIDC</td>
<td>287</td>
<td>325/395</td>
<td>–27</td>
<td>43/51/55\textsuperscript{b}</td>
<td>46.4</td>
<td>–</td>
<td>–</td>
<td>–30</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PE-10IIDC</td>
<td>286</td>
<td>319/404</td>
<td>–33</td>
<td>43/54\textsuperscript{b}</td>
<td>38.8</td>
<td>–</td>
<td>–</td>
<td>–33</td>
<td>20</td>
<td>26.2</td>
<td>48</td>
<td>26.6</td>
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<td></td>
<td></td>
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<tr>
<td>PE-12IIDC</td>
<td>285</td>
<td>324/402</td>
<td>–29</td>
<td>57/64</td>
<td>56.2</td>
<td>26/32</td>
<td>37.0</td>
<td>–30</td>
<td>39</td>
<td>9.7</td>
<td>64</td>
<td>32.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PE-2Ad</td>
<td>317</td>
<td>384</td>
<td>–43</td>
<td>49</td>
<td>56</td>
<td>7</td>
<td>33.4</td>
<td>–44</td>
<td>4</td>
<td>15.1</td>
<td>49</td>
<td>51.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PE-4Ad</td>
<td>330</td>
<td>401</td>
<td>–63\textsuperscript{b,21}</td>
<td>64</td>
<td>86.7</td>
<td>35</td>
<td>51.6</td>
<td>–61\textsuperscript{b,21}</td>
<td>–</td>
<td>53/57</td>
<td>55.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PE-6Ad</td>
<td>291</td>
<td>345</td>
<td>–73\textsuperscript{22}</td>
<td>60</td>
<td>106.0</td>
<td>43</td>
<td>80.1</td>
<td>–73\textsuperscript{22}</td>
<td>–</td>
<td>–</td>
<td>60</td>
<td>77.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PE-8Ad</td>
<td>251</td>
<td>353</td>
<td>n.d.</td>
<td>67</td>
<td>137.0</td>
<td>52</td>
<td>107.3</td>
<td>n.d.</td>
<td>–</td>
<td>–</td>
<td>52</td>
<td>103.9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PE-10Ad</td>
<td>286</td>
<td>368</td>
<td>n.d.</td>
<td>76</td>
<td>112.9</td>
<td>58</td>
<td>107.9</td>
<td>n.d.</td>
<td>–</td>
<td>–</td>
<td>75</td>
<td>111.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PE-12Ad</td>
<td>294</td>
<td>348</td>
<td>n.d.</td>
<td>80</td>
<td>148.8</td>
<td>63</td>
<td>99.0</td>
<td>n.d.</td>
<td>–</td>
<td>–</td>
<td>76</td>
<td>114.8</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\textsuperscript{a}$T_{5\%}$ = temperature of 5% mass loss, $T_{\text{max}}$ = temperature of maximal rate of decomposition, $T_g$ = glass transition temperature, $T_m$ = melting temperature, $T_c$ = crystallization temperature, $T_{cc}$ = cold crystallization temperature upon heating, $\Delta H$ = enthalpy of transition. \textsuperscript{b} Multiple melting temperatures.
Chapter 4

As seen from Table 4-3, the clear absence of crystallization and melting peaks in the 10 °C/min DSC cooling and second heating runs indicates that the IIDCA polyesters do not (readily) crystallize from the melt,\textsuperscript{10,27} except for PE-12IIDC which crystallized around 30 °C with moderate crystallization enthalpy (Δ\textit{H} = 37 J/g). Furthermore, PE-10IIDC and PE-12IIDC show cold crystallization behavior in the second DSC heating runs, which is attributed to the known crystallization behavior of long chain aliphatic diols and diacids.\textsuperscript{23,28} In the following section, we will present an in-depth discussion of the relations between chemical structures and thermal transitions.

4.3.3 Wide-angle X-ray diffraction

DSC has shown that all IIDCA-based polyesters are semi-crystalline materials. The X-ray diffraction analysis corroborated the DSC results since, as shown in Figure 4-7, the diffraction patterns recorded for all the synthesized polyesters are indicative of semi-crystalline characteristics by showing sharp reflection peaks at different diffraction angles.

As seen from the overlay of diffractograms in Figure 4-7, it seems that the number of methylene units in the alkylene chain determines how the polymer chain packs. When the number of methylene unit increases from \( n = 2 \) to 6, the diffraction patterns of these three polyesters undergo substantial changes, which is evidenced by the changing in the location of diffraction peaks in terms of the values of 2theta angles, as well as the different intensities. Thus, their crystallographic forms are expected to be rather different. Further increase of \( n = 6 \) to 12 does not lead to remarkable change in diffraction patterns. However, additional signals were observed in the range of 2theta angles of 3–10°, which are absent in the diffractograms of the polyesters with shorter alkylene chains (\( n = 2 \) and 4). Moreover, these signals shift towards lower values of 2theta angle with increasing chain length, indicating an increase of the interplane distance.

Based on the X-ray diffraction patterns, the above mentioned interplane distances for PE-6IIDC to PE-12IIDC are: 1.479 nm (\( n = 6 \)), 1.667 nm (\( n = 8 \)), 1.841 nm (\( n = 10 \)) and 2.055 nm (\( n = 12 \)). Furthermore, theoretical calculations were performed to determine the length of the basic units of the synthesized polyesters. Geometry optimization were carried out at the PM6\textsuperscript{29} semi-empirical level of theory using the Gaussian09 package program.\textsuperscript{30} The obtained lengths of different basic units are: 0.894 nm (\( n = 2 \)), 1.213 nm (\( n = 4 \)), 1.458 nm (\( n = 6 \)), 1.705 nm (\( n = 8 \)), 1.954 nm (\( n = 10 \)) and 2.204 nm (\( n = 12 \)). Thus, the theoretical simulation results are reliable for further assignment of the diffraction signals. For the polyesters containing six and more methylene groups, the signals appearing in the range of 3–10° of 2theta angle are indexed to the 001 plane. In contrast, for polyesters contain two or four methylene units, the
lack of signals within the same range of 2theta angles is the evidence of lacking proper regularity along the chain. Further research will be focused on the full elucidation of the crystallographic structures of these IIDCA-based polyesters.

Figure 4-7. X-ray powder diffraction profiles of IIDCA-based polyesters.

4.3.4 Structure-thermal properties relations

Since that IIDCA is a new AA type monomer for polycondensates, we want to evaluate the effect of IIDCA incorporation on the polyester properties by comparison with series of relevant, aliphatic polyesters (having the same number of carbon atoms between the ester linkages), thereby obtaining the underlying structure-thermal properties relations. As mentioned earlier, IIDCA can be regarded as a conformationally-restricted and renewable counterpart of adipic acid. Therefore, comparison with a series of (substituted) polyadipates will give insight into the effects of the extended bicyclic structure. Apart from the unsubstituted polyadipates, polyesters based on the sugar-derived dimethyl 2,3:4,5-di-O-methylene galactarate (Galx) make an interesting comparison (Figure 4-8). In Galx, the number of carbon atoms between its two carbonyls is four, as is the case in adipic acid. However, Galx contains two five-membered acetal rings, which make it a conformationally-restricted dicarboxylic acid. Lavilla et al. have recently described a systematic study of the synthesis and the properties of polyesters derived from Galx and α,ω-diols (PE-nGalx). Although in IIDCA free rotation is only possible around the C2-COOH
and the C5-COOH bonds, in the case of Galx additional rotation around the C3-C4 bond is possible, making this monomer in theory more flexible.

We intended to preserve the rigidity induced by the bicyclic ring structure as much as possible. It is hence also of interest to compare the thermal properties of the IIDCA polyesters with those of isoidide- based linear aliphatic polyesters (PE-mII, Figure 4-8). Given the fact that the main difference between these two sets of polyesters is that the ester linkage is reversed, they can be regarded as isomeric analogues. Okada et al.\textsuperscript{15} reported a series of polyesters composed of isohexides and linear \( \alpha,\omega \)-dicarboxylic acids for biodegradability studies, while Noordover et al.\textsuperscript{10,19,32} described the synthesis and properties of isohexides- and succinic acid- based polyesters for powder coating applications.

![Figure 4-8. Structures of the compared polyester series: \( n (= 2, 4, 6, 8, 10, 12) \) refers to the number of methylene units of \( \alpha,\omega \)-diols; \( m (= 2, 4, 8) \) refers to the number of methylene units of \( \alpha,\omega \)-dicarboxylic acids.](image)

Based on our own results as well as literature data,\textsuperscript{8,10,15,21,22,33} the \( T_m \) and \( T_g \) values of these polyesters versus the number of methylene units are plotted in Figure 4-9. For reference, these thermal transition values together with the exact corresponding molecular weights data are provided in Table 4-4. The polygalactarates (PE-\( n \)Galx) were prepared by Lavilla et al.\textsuperscript{8} from Galx and \( \alpha,\omega \)-diols through melt polymerization. The \( M_n \) values of these polyesters are in the range of 16,000–18,000 g/mol. Poly(isoidide succinate) (PE-2II) was synthesized by Noordover et al.\textsuperscript{10} from succinic acid and isoidide with \( M_n \) value around 3,100 g/mol. This relatively low molecular weight polyester prepared by melt
polymerization was claimed to be suitable for powder coating applications. Poly(isoidide adipate) (PE-4II) and poly(isoidide sebacate) (PE-8II) were prepared by Okada et al.\textsuperscript{15} via interfacial polymerization using isoidide and the activated dicarboxylic chloride. The obtained $M_n$ values are around 30,000 g/mol. It is known that the value of $T_g$ is influenced by the polymer chain length. At higher molar masses the glass temperature is essentially constant when measured by any given method, but decreases as the molar mass of the sample is lowered.\textsuperscript{34} Here, given that most of the polyesters in comparison have molecular weights greater than 10,000 g/mol, we assume that the influence of the molar mass on $T_g$ values is rather small. Although the differences between synthetic protocols and molecular weights for these polymers preclude a quantitative comparison, the data presented in Figure 4-9 clearly show a (qualitative) trend.

Figure 4-9a shows that for the polyadipates and polygalactarates $T_m$ steadily increases with increasing chain length of the aliphatic diols, while the differences between the two types of polyesters become smaller. This trend is in agreement with the empirical observation that the thermal properties of polyesters approach those of polyethylene with increasing number of the methylene units incorporated into the polyester main chain.\textsuperscript{35} In contrast, the $T_m$ values of the isoidide-based polyesters are significantly higher (>70 °C) than those of the polyadipates and polygalactarates. One may argue that for this series of polyesters, the $M_n$ values are generally higher than other series. However, this is certainly not the case for the PE-$m$IIIs with $m = 2$. This polyester has a $M_n$ value of only about 3,000 g/mol, but exhibits the highest $T_m$ among all polyesters discussed in this study. In this case, increasing the chain length of the dicarboxylic acids still leads to an almost linear decrease in $T_m$, which may eventually converge to the values of the other polyesters. Obviously, the structural change overrules the molecular weight influence on $T_g$. When examining the melting temperatures of the IIDCA polyesters, we surprisingly found that, with the exception of PE-2IIDC, PE-nIIDCs have lower melting temperatures than all the reference polymers, even including the polyadipates. The possible cause of this phenomenon is discussed below. In general, the melting temperatures of PE-nIIDCs showed a continuous decrease with increasing alkylene chain length of the linear diol units, while PE-12IIDC starts to show a slight increase of the melting temperature. This is thought to be caused by the similar “polyethylene effect” as other reference polyesters.
Figure 4-9. Melting temperatures (a) and glass transition temperatures (b) of the polyester series versus the number of the methylene units: \( n \) for IIDCA, adipic acid or Glax polyesters; \( m \) for isoidide polyesters. Data derived from our own and literature results.8,10,15,21,22,33 N.B. for clarity reasons, trend lines are drawn to guide the eye only.

Table 4-4. Molecular weights and thermal transition data of PE-\( n \)Glax and PE-mIIDCs.

<table>
<thead>
<tr>
<th>( n ) or ( m )</th>
<th>PE-( n )Glax( ^8 )</th>
<th>PE-mIIDCs( ^{10,15} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( n ) or ( m )</td>
<td>( T_g ) (°C)</td>
<td>( T_m ) (°C)</td>
</tr>
<tr>
<td>2</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>4</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>6</td>
<td>6</td>
<td>71</td>
</tr>
<tr>
<td>8</td>
<td>–8</td>
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</tr>
<tr>
<td>10</td>
<td>–13</td>
<td>78</td>
</tr>
<tr>
<td>12</td>
<td>–17</td>
<td>83</td>
</tr>
</tbody>
</table>

\(^{n} n \) refers to the number of the methylene units in the linear aliphatic diols incorporated into the IIDCA, adipic acid or Glax polyesters; \( m \) refers to the number of the methylene units in the linear dicarboxylic acid incorporated into the isoidide polyesters.

With regard to estimating the intrinsic rigidity of IIDCA, the data of the glass transition temperatures for the four series of polyesters are presented in Figure 4-9b. Although the molecular weights of IIDCA polyesters are only about half of those of the unsubstituted polyadipates, the former still show \( T_g \) values approx. 50–70 °C higher than the latter8,9 confirming our hypothesis that IIDCA is capable of inducing rigidity in the polymer chain. When compared to the isoidide polyesters, it is clear that the IIDCA-based polyesters display about 20-50 °C lower \( T_g \) values. If one is not convinced by the fact that the high molecular weight polyesters PE-4II and PE-8II exhibit \( T_g \) values about 45 °C and 30 °C higher than PE-4IIDC and PE-8IIDC respectively, this is illustrated most clearly by comparison of PE-2IIDC (ethylene glycol + IIDCA) with PE-2IIIs (succinic acid + isoidide). Despite the lower \( M_n \) value of the latter, a dramatic decrease in \( T_g \) of 45 °C was observed.
Thus, it is concluded that, although the same number of methylene units is present in the respective polymer backbones, the combination of IIDCA with linear aliphatic diols results in more flexible polymer chains than the ‘reversed’ isomeric polyesters based on II and linear aliphatic diacids. Most surprising however is the observed difference in \( T_s \) between IIDCA polyesters and the polygalactarates. Contrary to expectations the IIDCA polyesters have \( T_s \) values approx. 15–20 °C lower than the polygalactarates, despite the potentially higher degree of rotational freedom of the latter around the C3–C4 bond. To elucidate this apparent discrepancy, density functional theory (DFT) calculations were performed on the diethyl esters of IIDCA and GalX, respectively.\(^{36}\) The computations show that the energy barrier for a 360° rotation around the ester bond of the IIDCA-based diester is 2.7 kcal/mol, whereas the energy barrier for rotation around the ester bond of the GalX-based diester is 4.2 kcal/mol (see Appendix D, Figure D-1, Table D-2). Furthermore, the rotation of the IIDCA-based diester yields essentially a single-well potential, whereas the energy barrier for rotation around the ester bond of the GalX-based diester corresponds to a double-well potential. This may indicate that GalX provides more rigidity to the polyester chain than IIDCA, leading to the observed higher \( T_s \) values. It is not clear yet if the higher molecular weights of the polygalactarates are also partly responsible for the observed differences, however, as mentioned earlier, we expect that the influence of molecular weights on \( T_s \) should be rather small.

Overall we can conclude that incorporation of IIDCA in linear aliphatic polyesters does increase the \( T_s \), however less pronounced than anticipated. These unexpected results can be attributed to several factors. Our previous conformational studies of IIDCA based on both single crystal X-ray diffraction as well as DFT calculations have shown that the V-shaped bicyclic isohexide skeleton of IIDCA is more flexible than previously assumed.\(^2\) Puckering of the 5-membered rings is a low activation energy transition (approx. 1.7 kcal) giving rise to different conformers, which could contribute to increased flexibility. A similar phenomenon can be found in the structures of other isohexide derivatives: the extensive conformational analysis of diaminoisoidide by DFT revealed a number of stable conformers with favorable energy profiles, which can be explained by the inherent flexibility of the isohexide units as well.\(^37\) The structural flexibility of the polymer main chain is regarded to be the main factor determining the glass transition temperature. Although we are currently not able to evaluate the structural flexibility variations of different isohexide derivatives, for example isoidide and IIDCA, the existence of different conformers at least suggests that the rigidity of the isohexide skeleton can be influenced by the specific substituents or functionalities.

Furthermore, due to ring puckering the angle between both carboxylate groups in IIDCA can differ between 85° and 118°, resulting in kinked polymer chains. This could result
in a considerable amount of free volume which prevents close packing of polymer chains, and hence results in an increase of entropy and decrease of \( T_m \). In GalX rotation around the C3–C4 bond may allow the change of the polymer chains towards a favorable orientation for a closer crystal packing, which is not permitted by the bicyclic skeleton in the case of IIDCA. We believe this could be the reason explaining why PE-nIIDCs are in general not able to crystallize from the melt, as found by the DSC analysis. Since \( T_m \) is a first-order thermodynamic transition, whereas \( T_g \) is not, there is no simple relation between them. According to the empirical correlation that \( T_g \) is about 0.5–0.8 times \( T_m \) in Kelvin,\(^{34}\) the dramatic decrease in the melting temperatures is assumed to (partially) explain the decrease of the glass transition temperatures.

### 4.4 Conclusions

For the first time, polymers based on the novel bio-based isoidide dicarboxylic acid (IIDCA) and \( \alpha,\omega \)-diols have been successfully synthesized via melt polymerization. A series of polyesters with weight average molecular weights in the range of 13,000–34,000 g/mol and PDI values close to 2.0 was obtained under rather mild polymerization conditions, indicating a higher reactivity of IIDCA compared to the parent isohexides. The exo-exo configuration of the isohexide skeleton was preserved after melt polymerization as indicated by NMR analyses. Both differential scanning calorimetry and wide-angle X-ray diffraction analyses showed that the IIDCA polyesters are semi-crystalline materials. Comparison with a corresponding series of polyadiplates shows that IIDCA increases the glass transition temperatures by approx. 50–70 °C compared to adipic acid, confirming our hypothesis that the 1-carbon extended isohexides combines increased reactivity with retention of rigidity. Comparison with the parent isohexides (i.e. isoidide) also shows that IIDCA is less effective than isoidide in inducing rigidity in the polymer chain. Although in the literature it is widely accepted that isohexide-based building blocks are rigid molecules, we have found that specific structural modification of the parent isohexide molecules can result in significant differences in the effects these building blocks have on the rigidity of polymers. In addition, we found that, although dimethyl 2,3:4,5-di-O-methylene galactarate (GalX) monomer may seem more flexible than IIDCA, the former structure is more effective in increasing the polyester \( T_g \) and \( T_m \). Preliminary DFT simulations confirm the higher rigidity of the GalX compared to IIDCA. In this paper, by combining synthesis, structural characterizations, and thermal analysis, we have shown that the new isohexide derivative isoidide dicarboxylic acid (IIDCA) is a highly interesting bio-based building block for polycondensates. We are currently expanding our structure-property relation studies to other isohexide derivatives, and will address this in our future work.
REFERENCES

Chapter 4


Abstract

In this chapter, we present a novel series of bio-based polyesters solely based on renewable isohexide-derived building blocks, synthesized via melt polymerization. Isoidide dicarboxylic acid (IIDCA) was polymerized with cyclic renewable diols such as isosorbide (IS), isomannide (IM), isoidide (II) and the novel 2,5-methylene-extended isoidide dimethanol (IIDML). Both IIDCA and IIDML were developed to increase the reactivity of the isohexide building block, while retaining rigidity and hence the beneficial effects on Tg. Compared to the parent isohexides, IIDML showed a markedly higher reactivity, resulting in three to four times higher weight average molecular weight (Mw) values of the synthesized polyesters. The molecular structure of the novel polyesters was analyzed by ¹H, ¹³C and 2D-COSY NMR techniques, confirming that the stereo-configurations of the isohexide moieties were preserved under the applied polymerization conditions. The II/IS-based polyesters have high Tg values noted of 70 °C and 85 °C, respectively, while the IIDML-based polyester has a lower Tg of approximately 45 °C, yet with an higher degree of crystallinity than the parent isohexide-based polyesters. A systematic study on structure-thermal properties relations comparing these novel polyesters with e.g. aliphatic polyesters reveals that, when incorporated into polyesters, both IIDCA and IIDML are able to increase the Tg by approximately 70 °C, which is comparable to the parent isohexides. Given the enhanced reactivity, high thermal stability and the retained ability to increase the Tg, IIDML is a promising renewable building block for performance polymers.
5.1 Introduction

In chapter 4, we reported a series of linear polyesters based on isoidide dicarboxylic acid (IIDCA) and α,ω-diols, which display melting and glass transition temperatures in the range of 50–120 °C and −35–20 °C, respectively.\textsuperscript{1} By comparison with a range of analogous polyadipates, it was concluded that incorporation of IIDCA into the backbone of linear polyesters increases the glass transition temperature by 50–70 °C. Nevertheless, the melting and glass transition temperatures of these polyesters are apparently insufficient for engineering plastic applications. In this chapter, in order to obtain polyesters with improved thermal properties, instead of using flexible linear diols, IIDCA was melt polymerized with a range of rigid isohexide-derived diols, viz. isosorbide, isomannide, isoidide and the new one-carbon extended diol IIDML (Scheme 5-1). The synthetic route of IIDCA and IIDML is schematically presented in Scheme 5-2. Although quite some information has been reported concerning the incorporation of isohexides or their derivatives into various aliphatic or semi-aromatic (co-)polymers,\textsuperscript{2,4} homo- or co-polymers fully based on AB or AA type isohexides or their derivatives are rather rare. More concretely, the main chains of these polymers basically only comprise the isohexide bicyclic skeleton and functional linkages, such as ester groups. The reported examples are: 1) poly(isohexide carbonate)s prepared by phosgenation or reacting isosorbide with its bischloroformate derivative;\textsuperscript{5,9} 2) the polyurethanes prepared from the AB-monomer 2-deoxy-isocyanato-isoidide or from the isohexide bischloroformates and and diaminoisohexide;\textsuperscript{10,12} 3) polyureas prepared from isohexide diisocyanates and diamines.\textsuperscript{11} These polymers were shown to have interesting optical properties and/or to be biodegradable. Importantly, the direct coupling of two isohexide moieties results in high glass transition temperatures. For instance, poly(isosorbide carbonate) has a \( T_g \) value within the range of 150–170 °C, depending the specific molecular weight of the polymer.\textsuperscript{6,8} Such a high glass transition temperature of this aliphatic polycarbonate can even compete with that of the commercially available bisphenol-A polycarbonate.

In this chapter, we report the synthesis, characterization, and thermal properties of a series of novel polyesters, prepared by the direct coupling of isohexide-based diols and dicarboxylic acids. Since our main interest lies in the development of effective bio-based rigid building blocks for performance polymers, it is crucial to have insight into the effects that isohexide derivatives have on polymer properties. Therefore, to elucidate the effects the various building blocks have on e.g. glass transition temperature and crystallinity, we have conducted a systematic structure-thermal properties relations study on a range of relevant polyesters.
5.2 Experimental section

Materials:

Isosorbide (98.5%, gifts from Roquette Frères) and isomannide (95%, Sigma-Aldrich) were purified by recrystallization from ethanol with the final purities >99.5%. Isoidide (99.8%) is also a gift from Roquette Frères. (3S,6S)-Dimethyl hexahydrofuro[3,2-b]furan-3,6-dicarboxylate (IIDMC) and ((3S,6S)-hexahydrofuro[3,2-b]furan-3,6-diyl)dimethanol (IIDML) were synthesized according to the reported procedure. Dimethyl adipate (DMA, 99%), dibutylltin(IV)oxide (98%), chloroform-D (99.8 atom %
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D) were purchased from Sigma-Aldrich. 1,1,1,3,3,3-Hexafluoro-2-propanol (HFIP), methanol and chloroform were purchased from Biosolve.

Characterization:

Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Avance III spectrometer operating at 400.17 MHz (1H) and 100.62 MHz (13C) at room temperature. 2D NMR spectra were recorded on a Varian Unity 500 plus spectrometer at room temperature. Chemical shifts were referenced to residual signals of CDCl3. Correlation spectra (COSY) were acquired using standard programs provided by a Varian spectrometer library with the following parameters: spectral width SW1 = SW2 = 6075.3 Hz, acquisition time 0.221 s, relaxation delay 1.4 s, and number of scans 8 × 300 increments. Fourier transform infrared (FT-IR) spectra were obtained on a Varian Scimitar 1000 FT-IR spectrometer equipped with a Pike MIRacle ATR Diamond/ZnSe single reflection plate and a DTGS-detector. The measurement resolution was set at 4 cm⁻¹, and the spectra were collected in the range 4000–650 cm⁻¹ with 32 co-added scans. Size exclusion chromatography (SEC) in hexafluoroisopropanol (HFIP) was performed on a system equipped with a Waters 1515 Isocratic HPLC pump, a Waters 2414 refractive index detector (35 °C), a Waters 2707 auto sampler, and a PSS PFG guard column followed by 2 PFG-linear-XL (7 μm, 8 × 300 mm) columns in series at 40 °C. HFIP with potassium trifluoroacetate (3 g/L) was used as eluent at a flow rate of 0.8 mL/min. The molecular weights were calculated against poly(methyl methacrylate) standards (Polymer Laboratories, Mn = 580 Da up to Mw = 7.1 × 106 Da).

The thermal stability of the polymers was determined by thermogravimetric analysis (TGA) with a TGA Q500 apparatus from TA Instruments. The samples were heated from 30 to 600 °C at a heating rate of 10 °C/min under a nitrogen flow of 60 mL/min. Glass transition temperatures (Tg) and melting temperatures (Tm) were measured by differential scanning calorimetry (DSC) using a DSC Q100 from TA Instruments. The measurements were carried out at a heating and cooling rate of 10 °C/min from −60 °C to 150 °C. Data acquisition was carried out using Pyris 7 software.

MALDI-ToF-MS spectra were recorded on a Voyager DE-STR from Applied Biosystems. Calibrations were carried out with poly(ethylene oxide) standards for the lower mass range and polystyrene standards for the higher mass range. The mass accuracy was better than 0.2 Dalton, the mass resolution was approximately m/z 12,000. DCTB (trans-2-[3-(4-tert-butylphenyl)-2-methyl-2-propenylidene]malononitrile) was used as matrix. Potassium trifluoroacetate (5 mg/mL) and the polyester sample (1 mg/mL) in HFIP were premixed in a ratio of 5:1:5. The mixture was subsequently hand-spotted on the target and left to dry. Spectra were recorded in reflector mode at positive polarity.

Analysis of the crystalline structure of the materials was performed using wide-angle X-ray scattering measurements by means of a computer-controlled goniometer coupled to a sealed-tube source of CuKα radiation (Philips), operating at 50 kV and 30 mA. The CuKα line was filtered using electronic filtering and the usual thin Ni filter. The data were collected at room temperature. The 1D profiles were subsequently background-corrected and normalized. The degree of crystallinity was calculated on the basis of the diffractograms. Reflection signal deconvolution between the crystalline phase and the overlapped amorphous halo was performed using WAXSFit software designed by M. Rabiej of the University of Bielsko-Biała. The software allows to approximate the shape of the peaks with a linear combination of Gauss and Lorentz, or Gauss and Cauchy functions and adjusts their settings and magnitudes to the experimental curve with a “genetic” minimizing algorithm. Such calculated surfaces of peaks, corresponding to given crystallographic planes and amorphous halo allowed to determine the degree of crystallinity of the sample.
Monomer synthesis:

(3S,6S)-dimethyl hexahydrofurfo[3,2-b]furan-3,6-dicarboxylate (isoidide dimethylcarboxylate, IIDMC) and ((3S,6S)-hexahydrofurfo[3,2-b]furan-3,6-diyldimethanol (IIDML) were synthesized and purified according to the reported procedure.13,14 The purity and stereo-chemistry of the monomers were confirmed by GC, GC-MS, FT-IR, 1H, 13C and 2D-COSY NMR.

Melt Polymerization:

Procedure A: This example is representative for all conducted polymerizations listed in Table 5-1 except PIII-2. IIDMC (0.230 g, 1.0 mmol) and isosorbide (0.365 g, 2.5 mmol) were charged into a 10 mL round bottom flask located inside a Kugelrohr oven. The apparatus was flushed with nitrogen several times at room temperature to remove oxygen. Then the Kugelrohr oven was internally heated to 130 °C at a rotating speed of 20 rpm for the whole procedure. The polymerization was maintained at this temperature for 5–10 min until the reactants turned into a clear, homogenous mixture. Next, 0.01 mmol dibutyltin oxide (DBTO) was added into the flask. The pre-polymerization was carried out at 130 °C under a continuous flow of nitrogen for 5 h. Subsequently, the reaction temperature was increased to 150 °C and vacuum (0.01–0.05 mbar) was applied step-wise and maintained for 3 h. The resulting polymer melt was cooled down, dissolved in chloroform and precipitated into methanol, filtered and dried in vacuo. The polyester synthesized from isomannide (PIIml) was obtained directly from the melt without further purification.

Procedure B: described for poly(isoidide isodidedicarboxylate) (PIII-2, Table 5-1). IIDMC (0.690 g, 3.0 mmol) and isoidide (1.010 g, 7.5 mmol) were charged into a 50 mL 3-neck round bottom flask equipped with mechanical stirrer, vigreux column and a Dean-Stark type condenser. The apparatus was flushed with nitrogen several times at room temperature to remove oxygen. Then the reaction mixture was heated to 130 °C and maintained at this temperature for 5–10 min until the reactants turned into a clear melt. Next, 0.01 mmol DBTO was added into the flask. The pre-polymerization was carried out at 130 °C under a continuous flow of nitrogen for 5 h. Subsequently, the reaction temperature was increased to 150 °C and vacuum (0.01–0.05 mbar) was applied step-wise and maintained for 3 h. The resulting product was cooled down, dissolved in chloroform and precipitated into methanol, filtered and dried in vacuo.

Poly(isosorbide isodidedicarboxylate) (PIISI): 1H NMR (CDCl3, δ, ppm): 5.21 (m, 2H; CH-1S), 4.91 (m, 2H; exo-CH, IS), 4.97 (m, 2H; endo-CH, IS), 3.90–4.11 (m, 8H; CH2), 3.16 (m, 2H; CH). 13C NMR (CDCl3, δ, ppm): 170.53, 170.48, 170.24, 170.18 (C=O), 85.84 (CH), 85.77 (CH), 80.57 (CH), 78.39 (CH), 74.42 (CH), 72.92 (CH2), 72.19 (CH2), 70.59 (CH2), 69.89 (CH2), 51.28 (CH2), 51.22 (CH2); FT-IR (cm⁻¹): 3463, 2925, 2877, 1730 (C=O), 1465, 1364, 1299, 1257, 1172, 1068, 1025, 912, 770. Isolated yield: 39%.

Poly(isomannide isodidedicarboxylate) (PIIml): 1H NMR (CDCl3, δ, ppm): 5.17 (m, 2H; CH-IM), 4.94 (s, 2H; CH), 4.00–4.20 (m, 6H; CH2), 3.81 (m, 2H; CH2), 3.22 (m, 2H); FT-IR (cm⁻¹): 2953, 2879, 1730 (C=O), 1470, 1361, 1300, 1251, 1172, 1037, 1031, 919, 779. Isolated yield: 30%.

Poly(isoidide isodidedicarboxylate) (PIII): 1H NMR (CDCl3, δ, ppm): 5.24 (d, J = 3.0 Hz, 2H; CH), 4.91 (s, 2H; CH), 4.64 (s, 2H; CH2), 4.02 (m, 4H; CH2), 3.96 (m, 4H; CH2), 3.89 (m, 2H; CH2), 3.14 (m, 2H); 13C NMR (CDCl3, δ, ppm): 170.22 (C=O), 85.73 (CH), 85.27 (CH), 78.21 (CH), 72.44 (CH2), 69.95 (CH2), 51.43(CH); FT-IR (cm⁻¹): 2953, 2879, 1730 (C=O), 1470, 1361, 1300, 1251, 1172, 1037, 1031, 919, 779. Isolated yield: 65%.

Poly(isoididedimethylene isodidedicarboxylate) (PIIEI): 1H NMR (CDCl3, δ, ppm): 4.91 (s, 2H; CH), 4.42 (s, 2H; CH), 3.97–4.48 (m, 10H; CH2), 3.63 (m, 2H; CH2), 3.31 (m, 2H; CH2), 2.59 (m, 2H; CH); 13C NMR (CDCl3, δ, ppm): 171.06 (C=O), 85.81 (CH), 85.23 (CH), 69.94 (CH2), 69.72 (CH2), 63.99 (CH2).
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51.45 (CH), 46.04 (CH); FT-IR (cm⁻¹): 3458, 2949, 2877, 1730 (C=O), 1470 (CH₃), 1360, 1294, 1177, 1072, 1012, 968, 907, 809. Isolated yield: 87%.

Poly(isooxalidedimethylene adipate) (Plm): ¹H NMR (CDCl₃, δ, ppm): 4.41 (s, 2H; CH), 3.97–4.09 (m, 6H; CH and CH₂), 3.63 (m, 2H; CH₂), 2.26 (m, 2H; CH₃), 2.35 (m, 4H; CH₂), 1.63 (m, 4H; CH₂); ¹³C NMR (CDCl₃, δ, ppm: FT-IR (cm⁻¹): 173.00 (C=O), 85.22 (CH), 69.84 (CH₂), 63.21 (CH₂), 46.19 (CH), 33.67 (CH₃), 24.23 (CH₂); FT-IR (cm⁻¹): 3446, 2946, 2875, 1727(C=O), 1465, 1373, 1260, 1167, 1048, 965, 734. Isolated yield: 83%.

5.3 Results and discussion

5.3.1 Synthesis and molecular characterization of the polyesters

The fully isohexide-based polyesters were synthesized in the melt by reacting isoidide dimethylcarboxylate (IIDMC) with the corresponding isohehexide-based diols, including isosorbide (IS), isoidide (II), isomannide (IM) and isoidide dimethanol (IIDML). The polymerizations were performed according to the previously reported procedure. Excess diol (1.5 equivalent with respect to IIDMC) was used to compensate for evaporation. The molecular weights, polydispersities and isolated yields of the synthesized polyesters are presented in Table 5-1.

Table 5-1. Molecular weights, polydispersities and isolated yields of the polyesters based on IIDMC and isohexide-diols

<table>
<thead>
<tr>
<th>entry</th>
<th>diester</th>
<th>diol</th>
<th>M_n (g/mol)</th>
<th>M_w (g/mol)</th>
<th>PDI</th>
<th>yield (%)</th>
<th>end-groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>PlsI</td>
<td>IIDMC</td>
<td>IS</td>
<td>2,600</td>
<td>3,300</td>
<td>1.4</td>
<td>39</td>
<td>A, B, C</td>
</tr>
<tr>
<td>PlmI</td>
<td>IIDMC</td>
<td>IM</td>
<td>1,200</td>
<td>1,700</td>
<td>1.4</td>
<td>30*</td>
<td>B, A</td>
</tr>
<tr>
<td>PlII-1</td>
<td>IIDMC</td>
<td>II</td>
<td>2,500</td>
<td>3,600</td>
<td>1.4</td>
<td>65</td>
<td>B, A, C</td>
</tr>
<tr>
<td>PlII-2</td>
<td>IIDMC</td>
<td>II</td>
<td>2,500</td>
<td>3,600</td>
<td>1.4</td>
<td>77</td>
<td>C, A</td>
</tr>
<tr>
<td>PII</td>
<td>IIDMC</td>
<td>IIDML</td>
<td>5,400</td>
<td>10,400</td>
<td>2.0</td>
<td>87</td>
<td>A, B, C, D</td>
</tr>
<tr>
<td>PleA</td>
<td>dimethyl adipate</td>
<td>IIDML</td>
<td>12,100</td>
<td>26,500</td>
<td>2.1</td>
<td>83</td>
<td>C, D</td>
</tr>
</tbody>
</table>

*Mo: number-average molecular weight, M_w: weight-average molecular weight, PDI: polydispersity index. Molecular weights obtained from HFIP-SEC. All polymerizations follow Procedure A described in the Experimental Section unless noted otherwise. Polymerization following Procedure B. Polymerization conditions: 1) Prepolymerization at 150–170 °C for 5 h under N₂; then polymerization at 180–200 °C for 3 h at 0.01 mbar. Isolated yield after precipitation from methanol. Polymer directly obtained from the melt without further purification. As identified from the MALDI-ToF-MS spectra, codes refer to the structures depicted in Figure 5-2. Bold codes refer to the species with the highest intensity for each product present in the spectra.

It has been frequently reported that the secondary hydroxyl groups of the parent isohehexides are relatively unreactive, which often leads to unsatisfactory molecular weights.
and/or severely discolored polymers. Depending on the polymerization conditions, the exo- and endo-hydroxyl groups display different reactivities: in esterification reactions the endo-hydroxyl group is usually less reactive under melt polymerization conditions, which is thought to be due to steric hindrance and/or the intramolecular hydrogen bonding formed between the endo-hydroxyl proton and the oxygen atom in the neighboring ring. Moreover, the stereochemistry of 2- and 5-substituents also influences the relative thermal stability of the isohexide bicyclic skeletons: the exo-substituenced isohexides are usually more thermally stable. Thus, both the reactivity and the thermal stability of the three isomers are basically in the order of isomannide < isosorbide < isoidide. Our observations during the synthesis of the fully isohexide-based polyesters are in agreement with these findings. Poly(isomannide isoididecarboxylate) (PIml) was obtained as a brownish polymer with a rather low number-average molecular weight (Mn) value of 1,200 g/mol, which underlines the poor thermal stability (color) and low reactivity (low Mn) of the endo-hydroxyl groups. Isosorbide and isoidide were more reactive, yielding polyesters with Mn values of 2,500 g/mol (PIsI and PIiI, Table 5-1). PIiI was prepared via two slightly different procedures by using a Kugelrohr oven or a mechanical stirrer for mixing, respectively. The two polyesters PIiI-1 and PIiI-2 have comparable Mn values, but differ in the predominating species based on the end-group analysis by MALDI-ToF-MS spectroscopy, which will be discussed in a later section. The higher degree of discoloration of poly(isosorbide isodidicarboxylate) (PIsI) points to the lower reactivity and thermal stability of the endo-hydroxyl group. The isolated yields are in the order of isoidide > isosorbide > isomannide, while the PDI values of 1.4 indicate incomplete conversion of the functional groups.

The polymerization of IIDCA with IIDML was performed under similar conditions, yielding a colorless polymer. The purified polyester was isolated in 87% yield, with the Mn value of 5,400 g/mol and the polydispersity of 2.0 (PIel). This confirms that the one-carbon extension strategy is effective to increase the reactivity (degree of conversion of functional groups and higher molecular weight, higher isolated yield and equilibrium PDI of the obtained polyesters) as well as the thermal stability (colorless product).

In our previous study we have shown that IIDCA/IIDMC will give branched or cross-linked products if the polymerization temperature exceeds 170 °C. Thus, melt polymerization was performed within a relatively low temperature range of 150–160 °C to avoid or to limit side-reactions. In this study, we used comparable polymerization conditions to prepare all IIDMC-based polyesters. According to the literature, melt polymerization of the parent isohexides can be conducted at temperatures as high as 200 °C. In order to investigate the thermal stability of IIDML at higher polymerization temperatures, it was reacted with dimethyl adipate (DMA) at 200 °C, yielding the novel
polyadipate PleA. This polyester was obtained with considerably higher $M_n$ value (12,100 g/mol) than PleI. Given the fact that high molecular weight isohexide-based polyesters have almost exclusively been prepared from diacid chlorides by interfacial or solution polymerizations, the results for PleI and PleA prove that IIDML is significantly more reactive than the parent isohexides under melt polymerization conditions. Furthermore, no epimerization (based on NMR analysis, see further), branching or cross-linking (based on HFIP-SEC and MALDI-ToF-MS analysis) was observed for PleA, confirming that IIDML is thermally stable up to at least 200 °C. Moreover, PleA was obtained as a colorless product indicating that the thermal stability of IIDML is higher than that of the parent isohexides.

The molecular structure of the novel polyesters was analyzed by $^1$H NMR, $^{13}$C NMR and 2D COSY spectroscopy. Representative NMR spectra of PII and Ple are shown in Figure 5-1. In general, all proton and carbon signals from the repeating units of the polymers can be found at the expected chemical shift values with matching multiplicities. The low intensity signals indicated by dots in the $^{13}$C NMR spectrum of PII are assigned as the resonances coming from the IIDMC and II end-groups.

With regard to the stereochemistry, the \textit{exo-exo} configurations of the isohexide units existing in PII and Ple can be elucidated by examining the $^1$H and $^{13}$C resonances. In the \textit{exo-exo} type of isohexides, the bridge protons at C3 and C4 have no dihedral coupling with the protons at C2 or C5 if these are in the \textit{endo}-conformation (and hence the substituents are \textit{exo}-orientated).\textsuperscript{13,18,30} For symmetrical isohexides, like isoidide, IIDML or IIDCA, C3 and C4 are identical, resulting in a singlet for the bridge protons in the $^1$H-NMR spectrum. In the case of the PII (Figure 5-1a), the bridge protons c/d and j/i thus appear as two singlets at 4.9 and 4.6 ppm, respectively. The NMR analysis of the IIDML-based polyester PleA gave similar results. Thus our comprehensive NMR analysis has shown that the original stereochemistry of the monomers was preserved during the polymerization.

In the case of PII, the asymmetry of isosorbide results in more complex NMR spectra. Apart from the increased complexity already observed in the monomer, the occurrence of stereo-irregularity in the polyester (\textit{i.e. exo-exo, exo-endo, and endo-endo} triads) results in a significant overlap of signals (see Supporting Information). For PII, since the $M_n$ is rather low (1,200 g/mol, Table 5-1), it is expected that, on average, trimeric species were formed. The NMR analysis of PleA is more straightforward due to the symmetry of the monomers. The \textit{exo-exo} configuration of the isohexide unit again follows from $^1$H-NMR, comparable to PII and Ple. In addition, no side-products were observed, confirming the satisfactory thermal stability of IIDML at 200 °C. More information about the NMR spectra can be found in Appendix E.
Fully isohexide-based polyesters: synthesis, characterization and structure-properties relations

![Chemical structures](image)

**Figure 5-1.** 2D COSY and $^{13}$C NMR spectra of polyesters based on isoidide (PiiI, a and b) and IIDML (Piel, c and d) recorded in CDCl$_3$, respectively. The (*) symbols indicate the position of end-group signals.

![FT-IR spectra](image)

**Figure 5-2.** FT-IR spectra of the fully isohexide-based polyesters recorded at room temperature. The spectra show frequency ranges of 650–3300 cm$^{-1}$. 89
The fully isohexide-based polyesters were further characterized by infrared spectroscopy. The entire series of polyesters exhibit similar FT-IR absorption patterns: the formation of ester bonds was confirmed by the very characteristic C=O stretching signals which appeared at around 1720 cm\(^{-1}\). The FT-IR spectra of all the synthesized polyesters are presented in Figure 5-2.

All new polyesters were also studied by MALDI-ToF-MS spectroscopy. The representative mass spectra of two isoidide-based polyester samples PIiI-1 and PIiI-2 are shown in Figure 5-3, together with the structures of the four possible molecular polyester species. According to the respective MS spectra, the observed species are presented in Table 5-1. The species having the highest intensity is highlighted in bold. In view of the MALDI-Tof-MS spectra of PIiI-1 and PIiI-2, the mass intervals are all equal to 312 Da, which exactly matches the theoretical molar mass of the repeating unit of PIiI. However, the two polyesters are different in terms of the predominating end-group moieties. For PIiI-1, no cyclics (D, Figure 5-3a) were observed, while the other MS signals are assigned as three sets of polymer species terminated with different hydroxyl or methyl ester end-groups (A, B and C). In contrast, the OH-terminated polymer C appears to have the highest intensity for PIiI-2, accompanied by a low intensity of A without the presence of B or D. The major reason causing the different distributions of the end-groups is thought to be the use of different polymerization set-ups. As described in the Experimental Section, a Kugelrohr oven or mechanical stirrer was used to afford efficient mixing of the reactants during the polymerizations (Procedure A and B). Since most of the polymerizations in this study were performed at quite small scale (1 mmol of IIDMC), the Kugelrohr oven is a rather convenient set-up which achieves efficient mixing of the reactants by continuously forming thin films through rotation of the reactor. However, the increased surface area of the thin films also causes more evaporation of the volatile reactants. Although an excess of diol was used in both cases, it is obvious that a larger amount of diols evaporated during Procedure A compared to B. Based on the MALDI-ToF-MS results, the OH-terminated species C is the predominant species only for PIiI-2 but not for PIiI-1. Nevertheless, given that the molecular weights of PIiI-1 and PIiI-2 are rather similar, the polymerization efficiencies of two procedures are fairly comparable. For larger scale polymerizations or to obtain fully OH-terminated polymers, Procedure B using the mechanical stirrer set-up is preferred.
Figure 5-3. Section of the MALDI-ToF MS spectra of poly(isoidide isoididedicarboxylate) (Plil-1, a; Plil-2, b) synthesized at 150 °C, signals cationized with K⁺: (A) linear chains with one methyl ester and one hydroxyl end-group; (B) linear chains with two methyl ester end-groups; (C) linear chains with two hydroxyl end-groups; (D) cyclic structures.
5.3.2 Thermal properties of polyesters

Thermal properties of the synthesized polyesters were determined by thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC). Since the obtained brownish isomannide-based polyester PImI is basically a mixture of short oligomers, the thermal properties for this polymer will not be discussed in detail.

TGA analysis of the IIDCA-based polyesters shows that the thermal stability of these polyesters increases in the order isosorbide < isoidide < IIDML, in the temperature range 270–300 °C (Figure 5-4, Table 5-2). The values of 5% weight loss temperatures of PleI and PleA show that the IIDCA moieties are rather thermally stable when incorporated into the polymer chains and comparable to linear alkylenedicarboxylic acid-polyesters. The IIDCA-based polyesters (PIsI to PIeI) show two major decomposition steps at 300–350 °C and at 350–500 °C, respectively. Approximately 30 wt % and 50 wt % of the initial weight is lost during each step which leads to approximately 20 wt % residual weight at 600 °C. These degradation profiles are in agreement with our previous observation concerning polyesters based on IIDCA and linear aliphatic α,ω-diols. However, polyadipate PIeA shows one major decomposition step at the temperature range of 300 to 380 °C. During this step, almost 75 wt % of the initial mass of the polymer is lost, resulting in only 8 wt % residual weight at 600 °C. Linear poly(alkylene dicarboxylates) are known to decompose almost completely under the same TGA conditions. Hence, the residual weights observed for PIsI to PIeI are mainly the degradation products of the isohexide moieties. Similar thermal decomposition phenomena have been reported for other polymer systems containing cyclic ethers.

![TGA traces of polyesters recorded from 30–600 °C at 10 °C/min under N2 atmosphere.](image)

**Figure 5-4.** TGA traces of polyesters recorded from 30–600 °C at 10 °C/min under N2 atmosphere.
Figure 5-5. First heating (a) and second heating (b) DSC curves of fully isohexide-based polyesters. The experiments carried out from -50 °C to 180 °C at the heating rate of 10 °C/min.

The melting and crystallization temperatures, enthalpy of the transitions and glass transition temperatures were studied by differential scanning calorimetry (DSC, Figure 5-5 and Table 5-2). As observed from DSC analysis the polyesters with relatively high isosorbide contents are predominantly amorphous materials due to the asymmetry of isosorbide, which results in the formation of stereo-irregular polymers, unless in some cases when long alkylene unit exists in the polymer chain. In contrast, polyesters containing the symmetrical isomers, especially isoidide, are often semi-crystalline. DSC analysis shows that poly(isosorbide isoididedicarboxylate) (PIsI) has a weak and broad melting endotherm ranging from 125–168 °C in the first DSC heating run (Figure 5-5a). The melting enthalpy of approximately 5 J/g is rather low, and therefore the melting and crystallization of this polymer from melt was not observed in the second DSC heating run (Figure 5-5b). For poly(isoidide isoididedicarboxylate) (PIiI), a more pronounced but broad melting endotherm around 110–150 °C with higher melting enthalpy of 15 J/g was observed during the first heating run. Again, the melting transition was absent in the second DSC heating run, as was any (cold) crystallization behavior during the cooling and heating runs, which suggests either a low degree of crystallinity or a slow crystallization rate from the melt (Figure 5-5). These phenomena were further confirmed by the wide-angle X-ray diffraction (WAXD) analysis, as described in the next section. Although this polyester contains both exo-
exo oriented monomers, the combination still does not seem to be favorable for a regular crystal packing.

Compared with the isohexide-based polyesters, the IIDML-based polyester PIeI has a higher crystallinity. A fairly pronounced bimodal melting peak at 133/144 °C can be seen in the second heating run with a much higher melting enthalpy of approximately 30 J/g. Bimodal melting peaks are indicative of imperfect polymer crystals or of the coexistence of different crystal forms (Figure 5-5).\textsuperscript{31,34-38} (Cold) crystallization exotherms were observed at 91 °C and 87 °C during the first cooling and second heating runs respectively (for the DSC cooling curves, see Appendix E, Figure E-3). Thus, it can be concluded that the incorporation of IIDML into the backbone of the IIDCA-based polyesters leads to the polyesters revealing higher degrees of crystallinity in comparison with the polyesters based on the parent isohexides, including the exo-exo oriented isoidide. Furthermore, DSC analysis of the polyadipate PIeA shows sharp and intense melting and crystallization peaks, which resembles the typical thermal behavior of linear poly(alkylene adipates). Thus, both DSC thermograms of PIeI and PIeA show that incorporation of IIDML increases/improves the degrees of the crystallinity of the synthesized polyesters. This can be beneficial to provide satisfactory mechanical properties and to increase molecular weight by solid-state post condensation (SSPC) just below \( T_m \). More examples showing that the SSPC is an efficient method of raising the molecular weight of the IIDML-based polymers will be presented in Chapter 6.

As can be clearly seen from the second heating curves in Figure 5-5b, all polyesters showed pronounced glass transition behavior. The glass transition temperatures of PIIsI and PIiI were noted around 73 °C and 85 °C, respectively. Given the relatively low molecular weights of these polyesters (\( M_n \) values around 2,500 g/mol), one can expect that with an increased molecular weight of these materials their \( T_g \) values will increase as well. Thus, the \( T_g \) values obtained for these fully bio-based aliphatic polyesters are rather remarkable and are even comparable to those of high molecular weight semi-aromatic polyesters such as the well-known poly(ethylene terephthalate) (PET, \( T_g = 85 °C \)) or the bio-based, semi-aromatic poly(ethylene furan-2,5-dicarboxylate) (PEF, \( T_g = 80 °C \)) and significantly higher than the bio-based aliphatic poly(lactic acid) (PLA, \( T_g = 60-65 °C \)). Compared with PIIsI and PIiI, poly(isoididedimethylene isoididedicarboxylate) (PIeI) has a lower \( T_g \) of 48 °C due to the presence of two extra methylene units in the structure of IIDML unit. However, this value is still in the same range as for the high molecular weight semi-aromatic poly(butylene terephthalate) (PBT). Moreover, the \( T_g \) of the poly(isoididedimethylene adipate) (PIeA, \( T_g = -5 °C \)) is approximately 70 °C higher than that of the linear analogue poly(hexamethylene adipate),\textsuperscript{39} confirming that incorporation of IIDML has a dramatic effect on \( T_g \). A detailed structure-thermal properties relations study is discussed in a later section.
Table 5-2. Thermal properties of isohexide-based polyesters measured by TGA and DSC

<table>
<thead>
<tr>
<th>entry</th>
<th>TGA</th>
<th>DSC first heating</th>
<th>DSC cooling</th>
<th>DSC second heating</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T5% (°C)</td>
<td>Tg (°C)</td>
<td>Tm (°C)</td>
<td>ΔHm (J/g)</td>
</tr>
<tr>
<td>PlsI</td>
<td>274</td>
<td>75</td>
<td>125-168(^b)</td>
<td>4.3(^b)</td>
</tr>
<tr>
<td>PlmI</td>
<td>267</td>
<td>29</td>
<td>89</td>
<td>2.2</td>
</tr>
<tr>
<td>PII</td>
<td>286</td>
<td>-</td>
<td>109-143(^b)</td>
<td>15.4(^b)</td>
</tr>
<tr>
<td>PlIeI</td>
<td>298</td>
<td>-</td>
<td>118-150(^b)</td>
<td>45.5</td>
</tr>
<tr>
<td>PlmA</td>
<td>296</td>
<td>2.3</td>
<td>88</td>
<td>35.7</td>
</tr>
</tbody>
</table>

\(^a\)T5\% = temperature at 5% mass loss, \(T_{\text{max}}\) = temperature at maximal rate of decomposition, \(T_g\) = glass transition temperature, \(T_m\) = melting temperature, \(T_c\) = crystallization temperature, \(T_{cc}\) = cold crystallization temperature, \(\Delta H\) = enthalpy of transition. DSC data derived from the second heating and cooling runs.

\(^b\)Data derived from rather broad melting endotherms.
5.3.3. Wide-angle X-ray diffraction

![Figure 5-6. X-ray powder diffraction profiles of IIDCA-based polyesters (a) and the exemplary result of the peak deconvolution applied to the poly(isoididedimethylene adipate) (PleA).](image)

To support the DSC observations, a wide-angle X-ray diffraction (WAXD) study was conducted for all the synthesized polyesters. The diffraction profiles are presented in Figure 5-6a. The degrees of crystallinity were estimated according to the ratio between the surfaces of peaks, corresponding to crystalline and amorphous component. The exemplary result of the peak deconvolution applied to the poly(isoididedimethylene adipate) (PleA) is shown in Figure 5-6b. As can be seen from Figure 5-6a, the X-ray diffraction profiles are in line with the DSC results: since isosorbide possesses an asymmetric endo-exo configuration, Plsl is a completely amorphous polyester giving a rather broad diffraction signal. All other
Fully isohexide-based polyesters: synthesis, characterization and structure-properties relations

polyesters are semi-crystalline materials showing some sharp reflections on top of an amorphous halo at 2theta angles ranging from 10–25 ° due to the incorporation of symmetric isohexide monomers (isoidide, isomannide and IIDML). The estimated degrees of crystallinity of PII and PlmI are 32% and 31%, respectively. Such degrees of crystallinity seem insufficient to enable a proper and fast crystallization of the polymer chains from the melt, which further resulted in the absence of a crystallization exotherm and a melting endotherm during the cooling and second heating DSC runs, respectively. The IIDML-based polyesters, PleI and PleA, have substantially higher degrees of crystallinity of 42% and 51%, respectively. The strongly emphasized signals arising from the crystalline phase in connection with a relatively weak signal representative of the amorphous phase indicate the existence of ordered structures. This confirms the previous DSC observation that polymers based on IIDML have an improved ability to crystallize compared to polyesters based on the parent isohexides. Furthermore, PleA has a rather different diffraction pattern than PleI by showing additional signals located at 2theta angles of around 12°, 18° and 22°, which are indicative of the existence of crystalline alkylene chains.

5.3.4 Structure-thermal properties relations

Since our interest is focused on developing rigid bio-based building blocks for performance polymers, it is crucial to understand how the various isohexide derivatives influence polymer properties. By comparing the polymer properties of a range of polyesters containing various types of analogous building blocks one can study the structure-properties relations and, ideally, attribute specific effects to the respective monomers. Previously, by investigating a series of polyesters based on IIDCA and linear α,ω-diols, we reported that incorporation of isoidide dicarboxylic acid (IIDCA) increases the $T_g$ of the materials by 50–70 °C relative to adipic acid-based analogues. Here, by investigating a series of polyesters based on IIDCA and isohexides, the interaction of IIDCA with rigid co-monomers, as well as assess the rigidity of the new bismethylene extended diol IIDML was studied.

IIDCA can be regarded as a conformationally-restricted counterpart of adipic acid, with 4 carbon atoms separating the two carboxylic acid groups (Figure 5-7). Similarly, the parent isohexides and IIDML can be regarded as the comparing counterparts of a 1,4-butanediol and 1,6-hexanediol, respectively (Figure 5-7). Table 5-3 gives an overview of the $T_g$, $T_m$ and $M_n$ values of four series of relevant polyesters. The comparison of the data in Table 5-3 can be conducted either between polyadipates and IIDCA-based polyesters (series I v.s. series III; series II v.s. series IV) to show the $T_g$-increasing effect of IIDCA with respect to adipic acid
or between/within series I and II, or III and IV to show the $T_g$-increasing ability of IIDML with respect to the parent isohexides and their acyclic analogues. It should be noted that these thermal data are based on literature data.$^{16,31,39-41}$ Although the differences between synthetic protocols and molecular weights for these polymers preclude a quantitative comparison, a (qualitative) trend can be clearly observed by the data presented in Table 5-3.

![Figure 5-7. Structure correlations between isohexides monomers and their linear analogues.](image)

**Table 5-3. Molecular weights, melting and glass transition temperatures of four series of relevant polyesters.a**

<table>
<thead>
<tr>
<th>series</th>
<th>diol</th>
<th>$M_n$ (g/mol)</th>
<th>$T_m$ (°C)</th>
<th>$T_g$ (°C)</th>
<th>series</th>
<th>diol</th>
<th>$M_n$ (g/mol)</th>
<th>$T_m$ (°C)</th>
<th>$T_g$ (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>IS$^{11,b}$</td>
<td>26,000</td>
<td>21</td>
<td></td>
<td>IS (Plsl)</td>
<td>2,300</td>
<td>125-168</td>
<td>73</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IM$^{11,b}$</td>
<td>16,000</td>
<td>28</td>
<td></td>
<td>IM (Plml)</td>
<td>1,200</td>
<td>89</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td></td>
<td>II$^{11,b}$</td>
<td>34,000</td>
<td>164</td>
<td>46</td>
<td>II (PlII)</td>
<td>2,600</td>
<td>109-143</td>
<td>85</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>1,4-BDO$^{16,c}$</td>
<td>27,100</td>
<td>64</td>
<td>-63</td>
<td>1,4-BDO$^{16}$</td>
<td>14,100</td>
<td>62</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IIDML (PleA)</td>
<td>12,100</td>
<td>90</td>
<td>-6</td>
<td>IIDML (PleI)</td>
<td>5,400</td>
<td>140</td>
<td>48</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1,6-HDO$^{39,c}$</td>
<td>24,300</td>
<td>60</td>
<td>-73</td>
<td>1,6-HDO$^{39,c}$</td>
<td>10,200</td>
<td>54</td>
<td>-20</td>
<td></td>
</tr>
</tbody>
</table>

$a$1,4-BDO = 1,4-butanediol; 1,6-HDO = 1,6-hexanediol; $T_g$ = glass transition temperature; $T_m$ = melting temperature. $b$Polymers synthesized from adipoylchloride and isohexides at 160 °C by melt polymerization.$^{41}$ $c$Polymers synthesized from dimethyladipate and 1,4-BDO or 1,6-HDO by melt polymerization.

Comparison within series I shows the profound influence on the thermal properties of incorporating isohexides versus 1,4-BDO within the polyadipate series. The isohexide-based polyadipates (series I) containing endo-hydroxyl groups are amorphous, while the incorporation of isoidide instead ofisosorbide or isomannide into the backbone of the
aliphatic polyesters improves the ability of polymer to crystallize. Exchanging 1,4-BDO by isoidide results in an increase of $T_m$ of 100 °C, while the $T_g$ increases by a formidable 109 °C. Comparison of the polyadipates based on the conformational analogues isoidide and IIDML (series I and II) shows that the latter is less rigid than the former since the $T_m$ is decreased by 74 °C, while the $T_g$ is decreased by 52 °C, although such decrements might be overestimated given the relatively low molecular weight of the PleA compared to the polymers based on isoidide. This is understandable considering that the additional methylene units allow for more chain flexibility. However, IIDML is still fairly rigid compared to the linear analogue 1,6-HDO (series II), resulting in a considerable increase in $T_g$ of 67 °C for their polyadipates.

The effect of substituting adipic acid by IIDCA in the all-isohexide based polyesters becomes clear from comparing series I and III, with II and IV respectively. Based on the $T_g$ values of polyesters of sufficient molecular weights, it is clear that the incorporation of IIDCA increases $T_g$ by: 63 °C in the case of 1,4-BDO, 53 °C for 1.6-HDO and 54 °C for IIDML. So on average, IIDCA increases the $T_g$ by 50–60 °C compared to adipic acid, which is in line with our previous results. Comparison of IIDML and isoidide in the IIDCA-polyesters (series III and IV) shows a similar trend as in the case of the polyadipates (series I and II), as mentioned earlier: isoidide is more effective than IIDML in increasing the $T_g$ by 37 °C, even though IIDML yields higher molecular weight polyesters. Compared to 1,6-HDO, IIDML increases the $T_g$ of the polyester by 68 °C, which is similar to the polyadipates. Overall, it is clear that both IIDCA and IIDML have a profound influence on the $T_g$ values of the synthesized polyesters. The combination of isohexide based-diols with IIDCA results in a significant increase in $T_g$ of the materials. This is best illustrated by comparing the linear aliphatic polyadipates with the corresponding fully isohexide-based polyesters, viz. poly(butylene adipate) and poly(hexamethylene adipate) v.s. isoidide-IIDCA (PIil) and IIDML-IIDCA (PIel) polyesters, respectively. In the former case the total increase in $T_g$ is a staggering 148 °C, while in the latter case it is 121 °C.

5.4 Conclusions

In conclusion, we successfully synthesized a novel series of polyesters fully based on renewable isohexide building blocks by melt polymerization. The recently developed isoidide dicarboxylic acid (IIDCA) was polymerized with all three parent isohexides as well as with the new 2,5-bismethylene-extended isoidide dimethanol (IIDML). Additionally, a novel IIDML-based polyadipate was synthesized as a reference polymer. Based on the molecular weights, polydispersities, color formation and isolated yields, we can conclude
that IIDML is a more reactive and more thermally stable diol than the parent isohexides. Furthermore, the NMR analyses showed that the original stereo-configurations of the isohexide moieties incorporated into the polyesters were preserved under melt polymerization conditions. DSC measurements showed that the IIDCA-isohexide polyesters are predominantly high $T_g$ amorphous polymers, while the IIDML-based polyesters are semi-crystalline, which was further confirmed with the wide-angle X-ray diffraction study.

A systematic structure-thermal properties analysis showed that all isohexide derivatives are rigid molecules which are capable of increasing the glass transition temperature with respect to linear aliphatic polyesters in the order isoidide > IIDML > IIDCA.

Overall, we have shown that the one-carbon extension on the 2/5 carbons of the isohexides is very effective for improving both reactivity and thermal stability, while retaining sufficient rigidity to increase $T_g$ of aliphatic polyesters. Moreover, one-carbon-extension introduces adequate flexibility to allow for crystallization. Hence, we conclude that IIDML is a novel, highly interesting rigid bio-based diol. We are currently further exploring the full potential of this new building block.

REFERENCES

Abstract

In this chapter, we describe a series of semi-aromatic polyesters based on isoidide-2,5-dimethanol (IIDML) and various aromatic dicarboxylic acids, viz. terephthalic acid, isophthalic acid and furan-2,5-dicarboxylic acid. These novel polyesters were obtained via melt polymerization, optionally followed by solid-state post-condensation (SSPC). The resulting polyesters have number average molecular weights ($M_n$) ranging from 7,700–30,000 g/mol and minor discoloration. The molecular structure of the polyesters was analyzed by $^1$H and $^{13}$C NMR spectroscopy, which confirms that the stereo-configuration of the isohexide moieties was preserved under the applied polymerization conditions. These semi-aromatic polyesters are thermally stable up to 380 °C, which is comparable to those of commercial products like poly(ethylene terephthalate) (PET) or poly(butylene terephthalate) (PBT). Poly(isoidide 2,5-dimethylene terephthalate) (PIeT) and poly(isoidide 2,5-dimethylene furan-2,5-dicarboxylate) (PIeF) are semi-crystalline materials with high glass transition (105 °C and 94 °C, respectively) and melting temperatures (290 °C and 250 °C, respectively). These values exceed those of PET or PBT, and are comparable to those of poly(1,4-cyclohexylmethylene terephthalate) (PCT). The amorphous poly(isoidide 2,5-dimethylene isophthalate) (PIeIP) exhibits a $T_g$ of 88 °C, which is about 22 °C higher than that of poly(ethylene isophthalate) (PEI). Given the enhanced reactivity, excellent thermal stability and the ability to dramatically increase $T_g$ and $T_m$, IIDML is a promising renewable building block for application in (partially) bio-based performance polymers.
6.1 Introduction

Semi-aromatic (or aliphatic-aromatic) polyesters are an essential class of polymers displaying a number of useful properties, such as high heat distortion temperatures, good mechanical properties, good chemical resistance and electrical insulation properties.\(^1\) Commercially important examples of this family are poly(ethylene terephthalate) (PET) and poly(butylene terephthalate) (PBT). These polyesters have been extensively used as engineering plastics for various industrial applications, including bottle containers, packaging materials, textile and industrial fibers and components for electronic and automotive applications. To widen the application window, the properties of these polyesters can be improved or adjusted through modification of their chemical or physical structures, e.g. by copolymerization, by blending with other polymers, or by using additives. For instance, incorporation of the rigid 1,4-cyclohexylene ring into PET enhances the glass transition temperature and thus the thermal and mechanical properties at enhanced temperatures of the resulting copolyester.\(^1,3\) Isophthalic acid (IPA) is also frequently used as a co-monomer to fine-tune certain properties of PET, such as melting temperature and degree of crystallinity.\(^1,3\)

With regard to the development of more sustainable semi-aromatic polymers, bio-based building blocks can be used to replace the petrochemical-based monomers to obtain comparable polymer properties. Alternatively, they can be introduced into existing petrochemical-based polyesters to improve or modify their properties. One example of the first approach is the carbohydrate-derived furan-2,5-dicarboxylic acid (FDCA). Poly(ethylene furan-2,5-dicarboxylate) (PEF) displays a \(T_g\) of 85 °C, comparable to that of poly(ethylene terephthalate) (PET) and a \(T_m\) of 223 °C, comparable to that of poly(butylene terephthalate) (PBT).\(^4,5\) Thus, FDCA is being advocated as a promising renewable alternative in polyesters for the petrochemical-based terephthalic acid (TA). With regard to the second approach, an essential group of renewable building blocks are the isohexides (1,4:3,6-dianhydrohexitols, DAH). Isohexides are a group of rigid secondary diols based on C6-sugar alcohols, which are found in three major isomeric forms, namely isosorbide (1,4:3,6-dianhydroisorbitol), isoidide (1,4:3,6-dianhydrodithiol) and isomannide (1,4:3,6-dianhydromannitol). Starting from starch or cellulose via several steps of (bio-)organic transformations, they can ultimately be derived from D-sorbitol, D-mannitol and L-iditol, respectively.\(^6-9\) In recent years, isohexides, especially the commercially available isosorbide, and their derivatives have found numerous uses in polycondensates, such as polyesters, polyamides, polycarbonates and polyurethanes.\(^10\) The potential industrial applications of these polymers encompass liquid crystalline materials, powder coatings, plasticizers, etc.\(^10-13\) Isohexides have shown great potential in enhancing the \(T_g\) of step-growth polymers, as exemplified in the case of commercial semi-aromatic polyesters such as PET,\(^14-17\) and
polybutylene terephthalate (PBT).\textsuperscript{18} Another important development regarding semi-aromatic polyesters are those polyesters based entirely on rigid bio-based dicarboxylic acids and diols. Some of these display even higher $T_m$ and $T_g$ values than the conventional polyesters, e.g. PET or PBT. In the 1990s, Storbeck \textit{et al.} reported a series of fully bio-based polyesters based on isohexides and 2,5-FDCA synthesized by solution polymerization, with $T_g$ values of such polyesters in the range of 191–196 °C.\textsuperscript{19} Later on, Okada \textit{et al.} reported another series of fully bio-based polyesters based on isohexides and difuranic diesters, i.e. bis(5-(methoxycarbonyl)-2-furyl) methane and 1,1-bis(5-(methoxycarbonyl)-2-furyl)ethane, with $T_g$ values of approximately 100–112 °C.\textsuperscript{20} Compared to PET or PBT, the combination of two rigid biobased AA/BB monomers affords even higher rigidities and thus higher $T_g$ values.

Restricted by the relatively low reactivity of the secondary hydroxyl groups of the parent isohexides, it is difficult to obtain isohexide-based polyesters with high molecular weights and low discoloration via an industrially-relevant preparative method like melt polymerization.\textsuperscript{15,16,21,22} In order to overcome these drawbacks we have developed a family of new isohexide-based building blocks which combine rigidity and improved reactivity, as described in Chapter 2. This family includes the novel diol isoidide-2,5-dimethanol (IIDML). The synthesis of the first IIDML-based (aliphatic) polyesters is presented in Chapter 5. In comparison with the parent isohexides, IIDML has shown an improved reactivity by yielding polyesters with considerably higher molecular weights. Furthermore, IIDML was shown to be rigid, resulting in increased $T_g$ values by 50–70 °C when compared to the flexible linear analogue 1,6-hexanediol. It was also noticed that, owing to the presence of two additional methylene units at C2 and C5, IIDML improves the crystallization behavior of the polymers compared to the parent isohexides.

\begin{equation}
\text{MeOOC-} \text{Ar-COOMe} + \xrightarrow{\text{melt polymerization}} \text{Prepolymer} \xrightarrow{\text{SSPC}} \text{SSPC}
\end{equation}

\textbf{Scheme 6-1.} Synthesis of semi-aromatic polyesters based on IIDML and aromatic dimethylesters via melt polymerization and solid-state post-condensation (SSPC).

As a continuing study of using IIDML for step-growth polymer synthesis, but also with the aim of investigating its potential for engineering plastic applications, in this chapter we
report the synthesis and characterization of a series of semi-aromatic polyesters based on IIDML and three commercially relevant aromatic dicarboxylic acid monomers, viz. the petrochemical based terephthalic acid (TA) and isophthalic acid (IPA), as well as the bio-based furan-2,5-dicarboxylic acid (2,5-FDCA) (Scheme 6-1). A detailed study concerning the structural-thermal property relations will give insights into the rigidity and Tₐr-enhancing ability of IIDML in such semi-aromatic systems.

6.2 Experimental section

Materials

((35,65S)-Hexahydrofuro[3,2-b]furan-3,6-diyl)dimethanol (IIDML) was synthesized according to the reported procedure described in Chapter 2 with purity >99.5% (GLC). 2,5-Furandicarboxylic acid (FDCA) was kindly supplied by Avantium. Hydrochloric acid (HCl, 37 wt %), anhydrous magnesium sulphate (MgSO₄), a methanolic solution of potassium hydroxide (KOH, 0.5 N), dimethyl terephthalate (DMT, ≥99%), dimethyl isophthalate (99%), titanium(IV) isopropoxide (97%), dibutyltin(IV) oxide (98%) and chloroform-D (99.8 atom % D) were purchased from Sigma-Aldrich. Trifluoroacetic acid-d₄ (99.5 atom % D) was purchased from Cambridge Isotope Laboratories, Inc. 1,1,1,3,3,3-Hexafluoro-2-propanol (HFIP) methanol and chloroform were purchased from Biosolve. All purchased chemicals and solvents were used as received, unless otherwise stated.

Characterization

Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Avance III spectrometer operating at 400.17 MHz (¹H) and 100.62 MHz (¹³C) at room temperature. Fourier transform infrared (FT-IR) spectra were recorded with a Varian Scimitar 1000 FT-IR spectrometer equipped with a Pike Miraclipse ATR Diamond/ZnSe single reflection plate and a DTGS-detector. The measurement resolution was set at 4 cm⁻¹, and the spectra were collected in the range 4000–650 cm⁻¹ with 32 co-added scans. Size exclusion chromatography (SEC) in hexafluorosipropanol (HFIP) was performed at 40 °C on a system equipped with a Waters 1515 Isocratic HPLC pump, a Waters 2414 refractive index detector (35 °C), a Waters 2707 auto sampler and a PSS PFG guard column followed by 2 PFG-linear-XL (7 μm, 8 × 300 mm) columns in series. HFIP with potassium trifluoroacetate (3 g/L) was used as eluent at a flow rate of 0.8 mL/min. The molecular weights were calculated against polymethyl methacrylate standards (Polymer Laboratories, M_p = 580 Da up to M_p = 7.1 × 106 Da). The thermal stability of the polymers was determined by thermogravimetric analysis (TGA) with a TGA Q500 apparatus from TA Instruments. The samples were heated from 30 to 600 °C at a heating rate of 10°C /min under a nitrogen flow of 60 mL/min. Glass transition temperatures (T_g) and melting temperatures (T_m) were measured by differential scanning calorimetry (DSC) using a DSC Q100 from TA Instruments. The measurements were carried out at a heating and cooling rate of 10°C /min from −50 °C to 320 °C.

Analysis of the crystalline structure of the materials was performed using wide-angle X-ray scattering (WAXS) techniques by means of a computer-controlled goniometer coupled to a sealed-tube source of CuKα radiation (Philips), operating at 50 kV and 30 mA. The CuKα line was filtered using electronic filtering and the usual thin Ni filter. The data were collected at room temperature. The 1D profiles were subsequently background-corrected and normalized.

The degree of crystallinity was calculated on the basis of diffractograms. Since reflections from the crystalline phase and the amorphous halo frequently overlap each other, it was necessary to
Semi-aromatic polyesters from isoidide-2,5-dimethanol (IIDML)

separate them. Analysis of diffraction profiles of the examined samples and separation of peaks was performed using WAXSFit software designed by M. Rabiej of the University of Bielsko-Biała (AHT).\textsuperscript{25} The software allows to approximate the shape of the peaks with a linear combination of Gauss and Lorentz or Gauss and Cauchy functions and to adjust their settings and magnitudes to the experimental curve with a “genetic” minimizing algorithm. Such calculated surfaces of peaks, corresponding to given crystallographic planes, and of the amorphous halo allowed to determine the degree of crystallinity of the samples.

Monomer synthesis

\textit{Synthesis of (\textit{3S,6S})-hexahydrofuro[3,2-b]furan-3,6-diyl]dimethanol (IIDML):} IIDML was synthesized and purified according to the procedure described in Chapter 2\textsuperscript{23,24} The purities and stereo chemistry of the monomers were analyzed by GC, GC-MS, FT-IR, \textit{\textsuperscript{1}H}, \textit{\textsuperscript{13}C} and 2D-COSY NMR.

\textit{Synthesis of dimethyl-2,5-furandicarboxylate (DM-FDCA):} 2,5-Furandicarboxylic acid (10 g, 0.064 mol) was reacted with methanol (118.7 g, 3.4 mol) in the presence of hydrochloric acid (1 mL) as a catalyst. This reaction was allowed to continue for 18 h and subsequently the catalyst was deactivated by adding 30 mL of a 0.5 N methanolic KOH solution. The solvent was evaporated and the obtained white solid product was dissolved in CHCl\textsubscript{3}. The solution was filtered and washed with brine (1 x 200 mL) and demi-water (2 x 200 mL). Subsequently, this solution was dried over MgSO\textsubscript{4}. Then the solution was filtered and the solvent evaporated using a rotary evaporator. The obtained solids were recrystallized from CHCl\textsubscript{3} affording white crystals. Yield: 80%. Purity: > 99.5%. \textit{\textsuperscript{1}H} NMR (CDCl\textsubscript{3}, \textit{\delta}, ppm): 3.94 (s, 6H), 7.23 (d, 2H). \textit{\textsuperscript{13}C} NMR (CDCl\textsubscript{3}, \textit{\delta}, ppm): 52.36 (OCH\textsubscript{3}), 118.44 (furan ring C3 and C4), 146.67 (furan ring C2 and C5), 158.29 (C=O), FT-IR (cm\textsuperscript{-1}): 3118 (\textit{\textsuperscript{=CH}}); 2964 (C-H); 1719 (C=O); 1583, 1515 (C=C); 1264 (C-O); 987, 834, 765 (\textit{\textsuperscript{=CH}}).

Melt Polymerization

\textit{Procedure A:} This example is representative for poly(isoididedimethylene terephthalate) and poly(isoididedimethylene furan-2,5-dicarboxylate) (PleT and PleF-a, Table 6-1): IIDML (0.26 g, 1.5 mmol) and dimethyl 2,5-furandicarboxylate (0.18 g, 1.0 mmol) were charged into a 10 mL round bottom flask located inside a Kugelrohr oven. The apparatus was flushed with nitrogen several times at room temperature to remove oxygen, and then internally heated to 150 °C and rotated at a speed of 20 rpm. The reactants gradually turned into a clear homogeneous melt in about 5–10 min. Next, 0.01 mmol of dibutyltin(IV) oxide was added into the flask and the pre-polymerization was continued at a rotation speed of 20 rpm under N\textsubscript{2} atmosphere. The polymerization temperature was then increased from 150 °C to 180 °C step wise in 30 min. After about 1 h polymerization at 180 °C, the formed polyester started to crystallize into a white solid. After cooling down to room temperature, the resulting polymer was dissolved in TFA/CHCl\textsubscript{3} (V/V = 1:4) and precipitated into methanol giving a white suspension. The precipitate was collected by filtration and further dried \textit{in vacuo}. The product was ground to a powder and subsequently subjected to solid-state post-condensation between its T\textsubscript{g} and T\textsubscript{x} (see further) to further increase the molecular weight.

\textit{Procedure B:} The synthesis of PleF-b (Table 6-1): IIDML (0.26 g, 1.5 mmol) and dimethyl 2,5-furandicarboxylate (0.18 g, 1.0 mmol) were charged into a 10 mL round bottom flask located inside a Kugelrohr oven. The apparatus was flushed with nitrogen several times at room temperature to remove oxygen, and then heated to 150 °C and rotated at a speed of 20 rpm. The reactants gradually turned into a clear homogeneous melt in about 5–10 min. Next, 0.01 mmol of dibutyltin(IV) oxide was added into the flask and the pre-polymerization was continued at a rotation speed of 20 rpm under N\textsubscript{2} atmosphere. The polymerization temperature was increased step-wise from 150 °C to 180 °C in 30 min. After about 1 h polymerization at 180 °C, the formed polyester started to crystallize into a white solid. Then the polymerization temperature was raised to about 260 °C. The prepolymer gradually
melted and the reaction mixture was kept at this temperature for 2h at a rotating speed of 20 rpm. During the course of the reaction, discoloration of the reaction mixture into a brownish melt was observed. After cooling down to room temperature, the resulting polymer was dissolved in TFA/CHCl₃ (V/V = 1:4) and precipitated into methanol. The white precipitate was collected by filtration and further dried in vacuo.

Procedure C: The preparation of poly(isoididedimethylene isophthalate) (PIeIP, Table 6-1) follows a conventional two-stage melt polymerization: IDML (0.260 g, 1.5 mmol) and dimethyl isophthalate (0.194 g, 1.0 mmol) were charged into a 10 mL round bottom flask located inside a Kugelrohr oven. The apparatus was flushed with nitrogen several times at room temperature to remove oxygen. Then the Kugelrohr oven was internally heated to 140 °C at a rotating speed of 20 rpm. After 5–10 min, the reactants turned into a clear homogenous melt. Next, 0.01 mmol dibutyltin oxide (DBTO) was added into the flask. The pre-polymerization temperature was further increased to 180 °C and maintained at this temperature for 3 h. Subsequently, the reaction temperature was increased to 230 °C and vacuum (0.01–0.05 mbar) was applied step-wise and maintained for 3 h. The resulting polymer was cooled down, dissolved in chloroform and precipitated into methanol forming a white suspension. The product was collected by filtration and further dried in vacuo to afford PieIP as a white solid.

Solid-state Post-condensation (SSPC)

In order to increase the molecular weight of the melt-synthesized polyester prepolymers (PieT and PieF-a, Table 6-1), solid state post-condensation (SSPC) was applied. SSPC of the prepolymers was carried out between their $T_g$ and $T_m$ in a glass tube reactor (2.5 cm diameter) equipped with a sintered glass plate at the bottom on which the polyester powder was deposited. Below this glass plate the SSPC reactor was fitted with an inert gas inlet through which preheated N₂ gas was introduced. The SSPC reactor was immersed into a salt bath preheated to the desired temperature. The reactor was heated using a salt mixture of KNO₃ (53 wt %), NaNO₂ (40 wt %), NaNO₃ (7 wt %). SSPC was carried out in N₂ atmosphere at a gas flow rate of 2.5 L/min.

Table 6-1. Temperatures and reaction times of the prepolymerization and melt polymerization or solid-state post-condensation.

<table>
<thead>
<tr>
<th>symbol</th>
<th>prepolymerization</th>
<th>melt Polymerization</th>
<th>SSPC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T(°C) t(h)</td>
<td>T(°C) t(h)</td>
<td>T(°C) t(h)</td>
</tr>
<tr>
<td>PieT</td>
<td>180 1</td>
<td>220–240 3</td>
<td>240 4</td>
</tr>
<tr>
<td>PieIP</td>
<td>180 3</td>
<td>230–260 2</td>
<td>230 4</td>
</tr>
<tr>
<td>PieF-a</td>
<td>180 1</td>
<td>230–260 2</td>
<td>–   –</td>
</tr>
<tr>
<td>PieF-b</td>
<td>180 1</td>
<td>230–260 2</td>
<td>–   –</td>
</tr>
</tbody>
</table>

Poly(isoidide2,5-dimethylene terephthalate) (PieT), before SSPC: ¹H NMR (CDCl₃, δ, ppm): 8.10 (s, 4H), 4.92 (s, 2H), 4.86-4.84 (end-group), 4.45 (m, 4H), 4.42 (end-group), 4.31 (m, 2H), 4.26 (end-group) 4.04 (m, 2H), 3.96 (end-group). ¹³C NMR (CDCl₃, δ, ppm): 167.3, 133.2, 129.9, 85.5, 85.3, 85.1, 69.9, 69.6, 65.9, 64.3, 45.4, 45.1; FT-IR (cm⁻¹): 2943, 2877, 1711 (C=O), 1454, 1406, 1270, 1123, 1094, 1050, 1016, 975, 889, 727

Poly(isoidide 2,5-dimethylene isophthalate) (PieIP), after melt polymerization: ¹H NMR (CDCl₃, δ, ppm): 8.65 (s, 1H), 8.20 (d, 2H), 7.52 (t, 1H), 4.60 (s, 2H), 4.34 (m, 4H), 4.09 (m, 2H), 3.76 (m, 2H), 2.78 (m, 2H), ¹³C NMR (CDCl₃, δ, ppm): 165.3, 133.8, 130.2, 128.7, 85.3, 69.8, 64.1, 46.2.; FT-IR (cm⁻¹): 2950, 2878, 1720 (C=O), 1301, 1231, 1138, 1074, 1052, 971, 726

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Poly(isoididedimethylene furan-2,5-dicarboxylate) (PieF), after SPPC: $^1$H NMR (CDCl$_3$, δ, ppm): 4.91 (s, 2H), 4.35 (m, 4H), 4.10 (m, 2H), 4.02 (m, 2H), 3.15 (m, 2H). $^{13}$C NMR (CDCl$_3$, δ, ppm): 170.99 (C=O), 153.68, 149.98, 148.69, 147.62, 129.12, 127.42, 121.03, 114.21, 111.89, 105.79, 99.51, 98.67, 97.34, 76.62.

6.3 Results and discussion

6.3.1 Synthesis and molecular characterization

Due to the relatively low reactivity of the secondary hydroxyl groups of the parent isohexides, the reported high molecular weight isohexide-based semi-aromatic polyesters are almost exclusively prepared by reaction with dicarboxylic acid chlorides.$^{15-17,19}$ These methods are either too expensive or not suitable to be used in an industrial setting. Previously we have shown that the primary hydroxyl groups of IIDML are more reactive than the secondary ones of the parent isohexides, as described in Chapter 5. Here, we aim to synthesize the targeted semi-aromatic polyesters by means of industrially feasible methods, i.e. melt polymerization and solid-state post-condensation (SSPC).

Poly(isoidide-2,5-bismethylene terephthalate) (PieT) and poly(isoidide-2,5-bismethylene furan-2,5-dicarboxylate) (PieF) were synthesized by melt polymerization and followed by SPPC. During the synthesis, both polyesters start to crystallize rapidly from the melt after polymerization at 180 °C for about 1 h. The crystallized PieT and PieF prepolymer are white solids having relatively low molecular weights ($M_n = 2,300$ g/mol and 6,900 g/mol, respectively, Table 6-2) and rather high melting points (around 284 °C and 250 °C, respectively). Further increasing the polymerization temperature causes discoloration and thermal degradation of the two prepolymer. For PieF, although a higher molecular weight product ($M_n = 13,400$ g/mol, PieF-b, Table 6-2) can be obtained by continuing the melt polymerization at 260 °C, the thermal degradation was observed to be significant, as evidenced by the brownish color of the final product and a relatively high PDI value of 2.9. The prepolymer of PieT displays an even higher melting point of 280-290 °C. Continuing melt polymerization is detrimental to this low molecular weight prepolymer. Therefore, to obtain the desired PieT and PieF with low discoloration, high molecular weights and satisfactory PDI values, SPPC was applied to the prepolymer to further increase the molecular weight.$^{26}$ The SPPC of PieT was attempted at two temperatures: 200 °C and 240 °C. The plots of the number average molecular weight ($M_n$) and polydispersity index (PDI) values versus the reaction times are shown in Figure 6-1a. It can be clearly seen that the polymerization temperature plays a crucial role in increasing the molecular weight: 23 h SPPC of PieT at 200 °C resulted in a product with $M_n$ of 4,700 g/mol, which only doubled the
initial molecular weight \( (M_n = 2,300 \text{ g/mol}) \). When SSPC was performed at 240 °C, a comparable molecular weight \( (M_n = \approx 5,000 \text{ g/mol}) \) can be achieved in only 0.5 h. After 5 h at 240 °C, PlTeT was obtained as a white to slightly grayish material with \( M_n = 7,700 \text{ g/mol} \) based on the HFIP-SEC analysis. A sufficiently high SSPC temperature increases the mobility and the diffusion rate of the polymer chain.\(^{26} \) The reactive chain ends can more easily find and react with each other so as to enhance the molecular weight at a higher rate.\(^{26} \) The empirical rule concerning the suitable SSPC temperature is that it should be higher than the \( T_g \) but lower than the \( T_m \), and most preferably around 20–30 °C below the \( T_m \) of prepolymer.\(^{26} \) Given that the \( T_m \) of PlTeT is 290 °C, SSPC is expected to be most effective at 260–270 °C. However, high SSPC temperatures (>250 °C) or prolonged reaction times (>5 h) probably result in side-reactions resulting in the formation of insoluble cross-linked product in HFIP. Similar phenomena have been reported for the parent isohexides and their derivatives and other cyclic ether monomers.\(^{27-29} \) A possible cause for this is the ring-opening side reaction involving the ether linkages of these rings.

### Table 6-2. Molecular weights and polydispersities of the synthesized IIDML-based polyesters\(^a\)

<table>
<thead>
<tr>
<th>Symbol</th>
<th>before SSP</th>
<th>after SSP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( M_n ) (g/mol)</td>
<td>( M_w ) (g/mol)</td>
</tr>
<tr>
<td>PlTeT</td>
<td>2,300</td>
<td>3,900</td>
</tr>
<tr>
<td>PlIP</td>
<td>9,800</td>
<td>67,600</td>
</tr>
<tr>
<td>PlF-a</td>
<td>6,900</td>
<td>15,200</td>
</tr>
<tr>
<td>PlF-b</td>
<td>13,400</td>
<td>38,700</td>
</tr>
</tbody>
</table>

\(^a\)\( M_n \): number-average molecular weight, \( M_w \): weight-average molecular weight, PDI: polydispersity index. Molecular weights determined by HFIP-SEC against PMMA standards.
Semi-aromatic polyesters from isoidide-2,5-dimethanol (IIDML)

Figure 6-1. Plots of number average molecular weight ($M_n$) and polydispersity index (PDI) values versus solid-state post-condensation (SSPC) duration: (a) SSPC of PleT at 200 °C and 240 °C; (b) SSPC of PleF at 200 °C and 230 °C. N. B. for clarity reasons, trend lines are drawn to guide the eye only.

The melting point of the PleF prepolymer was determined to be around 250 °C. According to the aforementioned empirical rule, the optimal SSPC temperature is expected to be around 220–230 °C. It can be clearly seen from Figure 6-1b that the molecular weight increases rather rapidly at 230 °C: after only 0.5 h, the $M_n$ value of PleF had more than tripled (to 21,000 g/mol) with respect to the initial molecular weight; while after 4 h $M_n$ had increased to > 30,000 g/mol. When the SSPC reaction is performed at a lower temperature of 200 °C, more than 24 h is needed to achieve a comparable molecular weight. Moreover, the color formation is rather minor after SSPC, affording slightly grayish high molecular weight polyesters.
Since poly(isoidide 2,5-bismethylene isophthalate) (PIeIP) is an amorphous material, the molecular weight cannot be enhanced by means of SSPC. A conventional two-stage polycondensation procedure was applied: pre-polymerization at 180 °C under N₂ atmosphere, followed by polymerization at 230 °C under reduced pressure (0.01–0.05 mbar). After precipitation from methanol, PIeIP was obtained as a white material with $M_n = 9,800$ g/mol. A rather high PDI value of 6.9 was observed according HFIP-SEC analysis. Given the good solubility of PIeIP in HFIP, it is speculated that a small fraction of the formed polyester might form a branched product by ring opening. A similar phenomenon has been observed previously for the isoidide dicarboxylic acid (IIDCA)-based polyesters, as described in Chapter 4.29

The molecular structures of the new semi-aromatic polyesters were analyzed by nuclear magnetic resonance (NMR) spectroscopy. The bridge protons $a$ of the three polyesters appear as singlets located at 4.6–4.9 ppm (Figure 6-2a), which confirms the exo-exo configuration of the incorporated IIDML units. These characteristic signals have been discussed in detail for isoidide dicarboxylic acid (IIDCA)-based polyesters in Chapters 4 and 5. During melt polymerization, 0.5 molar equivalent excess of diol (with respect to the respective dimethyl esters) was used to compensate for the weight loss caused by evaporation. The presence of the IIDML end-groups are indicated as dots in the $^1$H and $^{13}$C NMR spectra shown in Figure 6-2b.
Figure 6-2. NMR spectra of the semi-aromatic polyesters recorded in TFA/CHCl₃ (V/V = 1:4) for PleT and PleF and in CDCl₃ for PleIP, 400M Hz: (a) ¹H NMR spectra of the semi-aromatic polyesters; (b) ¹³C NMR spectra of the semi-aromatic polyesters; (•) indicating the presence of IIDML-end groups.
The polyesters were further characterized by infrared spectroscopy. The FT-IR spectra are presented in Figure 6-3 and the absorptions of the major valence vibrations are collected in Table 6-3. The formation of ester bonds was confirmed by the very characteristic C=O stretching signals appearing at 1710–1720 cm\(^{-1}\) as well as by the multiple ester C–O–C stretching vibration absorptions in the region of 1200–1300 cm\(^{-1}\). The C–H asymmetric and symmetric stretching vibrations of the methylene groups in the bicyclic skeleton appear as two major bands at 2950 cm\(^{-1}\) and 2880 cm\(^{-1}\), respectively. The C-H stretching signals of the furan ring appear at 3154 cm\(^{-1}\) and 3118 cm\(^{-1}\), while the C=C absorptions of the furan or phenyl rings are located at around 1580–1600 cm\(^{-1}\).

![Figure 6-3. FT-IR spectra of semi-aromatic polyesters recorded at room temperature. The spectra show the frequency ranges of 650–3300 cm\(^{-1}\)](image)

Table 6-3. FT-IR absorptions of the synthesized polyesters recorded at room temperature.

<table>
<thead>
<tr>
<th>assignment</th>
<th>wave number (cm(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PleT</td>
</tr>
<tr>
<td>=C-H (Fu)</td>
<td>–</td>
</tr>
<tr>
<td>C-H (CH(_2))</td>
<td>2947, 2878</td>
</tr>
<tr>
<td>C=O (ester)</td>
<td>1710</td>
</tr>
<tr>
<td>C=C (Fu/Ph)</td>
<td>1581</td>
</tr>
<tr>
<td>C-O-C (ester)</td>
<td>1261</td>
</tr>
<tr>
<td>Disubstituted Fu/Ph</td>
<td>937, 825, 726</td>
</tr>
</tbody>
</table>
6.3.2 Thermal properties of the synthesized polyesters

The thermal stability of the synthesized semi-aromatic polyesters was investigated by thermogravimetric analysis (TGA) under N₂ atmosphere. The TGA traces of the IIDML-based polyesters are depicted in Figure 6-4. The collected thermal data are listed in Table 6-4. The thermal profiles of all the polyesters undergo a major degradation step with the maximum weight loss temperatures around 410–430 °C. The 5% weight loss temperatures were observed at approximately 380 °C for PleT, PleIP and for the high molecular weight PleF-a. The thermal stability of these new semi-aromatic polyesters are comparable to those of PEF (degradation temperature \( T_d = 389 \) °C), PET (\( T_d = 407 \) °C) and PBT (\( T_d =384 \) °C).³⁰ The relatively low molecular weight polyester PleF-b, prepared by the melt polymerization only, appeared to be less thermally stable than the high molecular weight PleF-a obtained after SSPC and exhibited a 30 °C lower temperature for a weight loss of 5%. Moreover, the residual weights at 600 °C of PleT and PleF-a are about 20–30% higher than those of the low molecular weight polyesters PleIP and PleF-b. Further investigation on the occurring degradation mechanisms can be helpful to explain the observed differences.

![Figure 6-4. TGA traces of polyesters recorded from 30–600 °C at 10 °C/min under N₂ atmosphere. The molecular weights of the TGA samples are in accordance with the results presented in Table 6-2. For the preparation methods it is referred to the Experimental section.](image)

The melting, crystallization and glass transition phenomena as well as the enthalpies of the transitions of the synthesized polyesters were analyzed by differential scanning calorimetry (DSC). The second heating and cooling curves are presented in Figure 6-5. The
thermal transition temperatures and the corresponding enthalpy values are listed in Table 6-4. Both P1eT and P1eF are semi-crystalline materials indicated by the pronounced melting endotherms and crystallization exotherms. P1eT has rather high melting and crystallization temperatures of 284 °C and 248 °C, respectively. The enthalpies for both transitions are higher than 50.0 J/g, suggesting a relatively high degree of crystallinity. For the polyfuranate P1eF the thermal properties were investigated for two samples with different molecular weights, \textit{viz.} P1eF-a and P1eF-b. Rather comparable \( T_m \) values were observed for both samples, which are in the range of 240–250 °C and which are about 20–30 °C lower than that of P1eT. The recorded melting enthalpies are influenced by the molecular weights of the specimens. The high molecular weight sample P1eF-a has a melting enthalpy of approx. 25.0 J/g, which is about half of that of the low molecular weight sample P1eF-b (49.2 J/g). Presumably, the high molecular weight polymers have higher melt viscosity because of their higher degrees of chain entanglements than the low molecular weight polymers, impeding the fast and efficient chain alignment and thereby resulting in lower degrees of crystallinity. Suitable nucleating additives and/or annealing treatments can be helpful to enhance the degree of crystallinity. This effect will be discussed in a later section concerning the WAXD study. Furthermore, the second melting enthalpies of both samples are rather comparable to their crystallization enthalpies, indicating that they are able to crystallize rather efficiently from the melt at a cooling rate of 10 °C/min. The molecular weight of P1eF also influences the crystallization temperatures \( T_c \): an approximately 10 °C lower \( T_c \) value was observed for the high molecular weight P1eF-a than for the low molecular weight P1eF-b. Thus far, IIDML is the first isohexide-based diol that can be incorporated for the full 100% into high molecular weight homo-polyesters via melt polymerization with retention of crystallization from the melt. Given the multiple benefits of these IIDML-based polyesters, including their high molecular weights, their low degrees of discoloration, their high thermal stability and their crystallizability from the melt, these polyesters are promising partially renewability materials to allow for industrial production.
Semi-aromatic polyesters from isoidide-2,5-dimethanol (IIDML)

Figure 6-5. Second heating (a) and second cooling (b) DSC curves of semi-aromatic polyesters recorded from −50–300 °C at heating and cooling rates of 10 °C/min.

The polyisophthalate PleIP appears to have a very poor crystallizability. The DSC measurement of PleIP was performed on the sample obtained after precipitation from chloroform solution into methanol. Although a weak melting endotherm with a fairly low melting enthalpy of 6.5 J/g can be observed during the first heating run, it is no longer present during the second heating run (Figure 6-5a). The wide-angle X-ray diffraction study on the polyesters studied in this work will provide further insights regarding the estimated degrees of crystallinity and will be discussed in a later section. A rather pronounced glass transition behavior can be observed for PleIP at around 88 °C, which is approximately 26 °C higher than the glass transition temperature of poly(ethylene isophthalate) \( T_g = 62 °C \).\(^{31} \) For
Chapter 6

the semi-crystalline PleF and PleT, the glass transitions are considerably less pronounced than in the case of PleIP when the same cooling rate of 10 °C/min is applied. The two polyfuranurate samples PleF-a and PleF-b, in spite of their different molecular weights, exhibit comparable glass transition temperatures of about 93 °C. The glass transition of PleT could only be observed after a very rapid DSC cooling scan with a cooling rate of 100 °C/min from the melt. This is probably due to the relatively low molecular weight as well as a corresponding high degree of crystallinity. The recorded $T_g$ value of PleT is 105 °C, which is 12 °C higher than that of PleF, and 25 °C or 60 °C higher than those of PET or PBT, respectively, while it is also about 25 °C higher than that of PEF.

To summarize, the IIDML-based semi-aromatic polyesters combine high thermal stability with high melting and glass transition temperatures, which can compete with or even exceed those of the commercially available analogues PET and PBT, and of PEF, which most probably will become industrially relevant as soon as furandicarboxylic acid is commercially available at kiloton scale. To obtain an overview of the rigidity of IIDML with respect to the parent isohexides and other linear (e.g. 1,6-hexanediol) and cyclic (e.g. 1,4-cyclohexanediol) diols, a detailed study concerning structure-property relations will be presented later.

The polysisophthalate PleIP appears to have a very poor crystallizability. The DSC measurement of PleIP was performed on the sample obtained after precipitation from chloroform solution into methanol. Although a weak melting endotherm with a fairly low melting enthalpy of 6.5 J/g can be observed during the first heating run, it is no longer present during the second heating run (Figure 6-5a). The wide-angle X-ray diffraction study on the polyesters studied in this work will provide further insights regarding the estimated degrees of crystallinity and will be discussed in a later section. A rather pronounced glass transition behavior can be observed for PleIP at around 88 °C, which is approximately 26 °C higher than the glass transition temperature of poly(ethylene isophthalate) ($T_g = 62$ °C). For the semi-crystalline PleF and PleT, the glass transitions are considerably less pronounced than in the case of PleIP when the same cooling rate of 10 °C/min is applied. The two polyfuranurate samples PleF-a and PleF-b, in spite of their different molecular weights, exhibit comparable glass transition temperatures of about 93 °C. The glass transition of PleT could only be observed after a very rapid DSC cooling scan with a cooling rate of 100 °C/min from the melt. This is probably due to the relatively low molecular weight as well as a corresponding high degree of crystallinity. The recorded $T_g$ value of PleT is 105 °C, which is 12 °C higher than that of PleF, and 25 °C or 60 °C higher than those of PET or PBT, respectively, while it is also about 25 °C higher than that of PEF.
Table 6-4. Thermal stabilities, glass transition, melting and crystallization temperatures, and enthalpies of the transitions determined by thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC).\textsuperscript{a}

<table>
<thead>
<tr>
<th>entry</th>
<th>TGA   </th>
<th>DSC</th>
<th>first heating</th>
<th>first cooling</th>
<th>second heating</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T5%  (°C)</td>
<td>T_max  (°C)</td>
<td>T_g (°C)</td>
<td>T_m (°C)</td>
<td>ΔH_m (J/g)</td>
</tr>
<tr>
<td>PIeT</td>
<td>385</td>
<td>417</td>
<td>–</td>
<td>268/277/296</td>
<td>–</td>
</tr>
<tr>
<td>PIeIP</td>
<td>386</td>
<td>429</td>
<td>90</td>
<td>158</td>
<td>6.5</td>
</tr>
<tr>
<td>PIeF-a\textsuperscript{b}</td>
<td>376</td>
<td>411</td>
<td>–</td>
<td>236/252</td>
<td>39.4</td>
</tr>
<tr>
<td>PIeF-b\textsuperscript{c}</td>
<td>347</td>
<td>398</td>
<td>96</td>
<td>248</td>
<td>49.6</td>
</tr>
</tbody>
</table>

\textsuperscript{a}T_{5\%} = temperature at 5\% weight loss, T_{\text{max}} = temperature at maximum rate of decomposition, T_g = glass transition temperature, T_m = melting temperature, T_c = crystallization temperature, ΔH = enthalpy of transition. DSC data derived from the second heating and cooling runs. \textsuperscript{b}DSC sample: PIeF-a: M_n = 30,300 g/mol, PDI = 2.0; \textsuperscript{c}DSC samples: PIeF-b: M_n = 13,400 g/mol, PDI = 2.2. \textsuperscript{d}T_g obtained by rapid quenching of the polymer melt at a cooling rate of 100 °C /min.
To summarize, the IIDML-based semi-aromatic polyesters combine high thermal stability with high melting and glass transition temperatures, which can compete with or even exceed those of the commercially available analogues PET and PBT, and of PEF, which most probably will become industrially relevant as soon as furandicarboxylic acid is commercially available at kiloton scale. To obtain an overview of the rigidity of IIDML with respect to the parent isohexides and other linear (e.g. 1,6-hexanediol) and cyclic (e.g. 1,4-cyclohexanediol) diols, a detailed study concerning structure-property relations will be presented later.

6.3.3 Wide angle X-Ray diffraction (WAXD) study

Wide-angle X-ray diffractograms of the synthesized semi-aromatic polyesters are represented in Figure 6-6. The degrees of crystallinity were estimated from the ratio of the surfaces of peaks corresponding to crystalline and amorphous domains, respectively. Due to the overlapping of diffraction signals, peak deconvolution is necessary to distinguish the separate signals arising from the crystalline and amorphous regions. The deconvolution results of the diffractogram of poly(isoidide-2,5-bismethylene terephthalate) (PliT) is representatively shown in Figure 6-7. As shown in Figure 6-6, PliT and Pief are semi-crystalline materials, as evidenced by the sharp diffraction signals. The estimated degrees of crystallinity of PliT and Pief are 66% and 42%, respectively. In contrast, the polyisophthalate PleIP is an amorphous material. According to the DSC analysis as mentioned earlier, a weak melting endotherm was present for PleIP during the first DSC heating run. However, the recorded first heating melting enthalpy is very low (6.5 J/g), indicating a low fraction of crystalline region in the analyzed sample, which was obtained after precipitation from solution. As discussed above this minor crystallinity is lost upon crystallization from the melt. One might argue that the diffractogram of PleIP shows a very small crystalline peak around $2\theta \approx 18^\circ$, just ‘escaping’ from the amorphous halo, but on the other hand one might conclude that these crystals may contain many defects making them “invisible” for the WAXD technique.
Semi-aromatic polyesters from isoidide-2,5-dimethanol (IIDML)

Figure 6-6. X-ray powder diffraction profiles of as synthesized IIDML-based polyesters.

Figure 6-7. Example of the peak separation by deconvolution, applied to poly(isoidide-2,5-bismethylene terephthalate) (PleT)

The degree of crystallinity of the obtained polyesters is also dependent on the synthetic method. The diffractograms of a few PleF samples are presented in Figure 6-8. These samples are different with respect to the synthetic method as well as the molecular weights. Since all the diffraction profiles are comparable, the crystal packing patterns of these samples are not substantially affected by the synthetic procedure nor by $M_n$. In other words, they have identical crystal unit cells. The two polyfurandicarboxylate samples obtained from melt polymerization, i.e. PleF-a prepolymer and PleF-b, have similar degrees of crystallinity
amounting to 16.0% and 19.9% respectively. SSPC apparently increases the degree of crystallinity significantly, since starting from the same prepolymer PleF-a \((M_n = 6,900 \text{ g/mol})\), SSPC at 200 °C for 23 h yields a polyester with a much enhanced degree of crystallinity of 33.8% \((M_n = 27,700 \text{ g/mol})\). Remarkably SSPC at 230°C for only 4 h results in a polyester with an even higher degree of crystallinity of 42.2% \((M_n = 30,300 \text{ g/mol})\). The observed difference in the degrees of crystallinity is mainly induced by the SSPC conditions, in particular the reaction temperature. As mentioned earlier in the synthesis section, sufficient high SSPC temperature increases the mobility of the polymer chains. Therefore, they have the opportunity to adjust their position for obtaining more ordered chain alignment patterns which, as a result, enhances the degree of crystallinity of the polymer sample.

![Figure 6-8. X-ray powder diffraction profiles of polyfurandicarboxylates synthesized by melt polymerization or SSPC, showing the different degrees of crystallinity.](image)

**6.3.4 Structure-thermal properties relations**

According to the DSC analysis, the synthesized IIDML-based semi-aromatic polyesters exhibit fairly high melting and glass transition temperatures. In order to become an overview of the rigidity and the \(T_g\)-enhancing ability of IIDML, a study on structure-thermal properties relations was conducted by comparing the thermal properties of these IIDML-based polyesters, *viz.* the melting and crystallization temperatures, with a series of other relevant polyesters. The molecular structures of the relevant diols for the structure-thermal properties study are shown in Figure 6-9.
Figure 6-9. Molecular structures of the relevant linear and cyclic diols for the structure-property relations study.

The $T_g$-increasing effect of IIDML, and hence its inherent rigidity, becomes clear by comparing the $T_g$ values of IIDML-based polyesters with a series of analogous polyesters. With six carbon atoms separating the two hydroxyl groups, 1,6-hexanediol (1,6-HDO) can be regarded as the flexible linear analogue of IIDML (Figure 6-9). Moreover, the corresponding semi-aromatic polyesters based on ethylene glycol and 1,4-butanediol (1,4-BDO) are also within the range of comparison. The thermal data of these polyesters are presented in Table 6-5 (series II to IV). In order to eliminate the effect of molecular weight on thermal properties, the thermal data listed in Table 6-5 are based on the respective high molecular weight (> 10,000 g/mol) polyesters reported in literature. Figure 6-10a shows the trend of the $T_g$ values of three types of polymers for each diol, viz. polyterephthalates, polyisophthalates and polyfuranoates. It is clear that the IIDML-based polyesters have considerably higher $T_g$ values than all the linear diol-based polyesters. When comparing with the polyterephthalates, the $T_g$ of PteT (105 °C) is about 100 °C, 60 °C and 35 °C higher than those of PHT, PBT and PET, respectively. Similar trends are observed for the corresponding polyisophthalates and polyfuranoates. Therefore, the $T_g$-enhancing ability of IIDML is considerably higher than that of the linear $\alpha,\omega$-diols, even higher than that of the shortest diol ethylene glycol, but this trend is as expected in view of the bicyclic structure of the IIDML. Due to the existence of two additional flexible methylene units at the 2- and 5-positions of the isoidide skeleton, the IIDML-based polyesters display about 90–100 °C lower glass transition temperatures than those of the parent isohexides-based semi-aromatic polyesters (Series V, Table 6-5). Thus, IIDML is significantly less rigid than the parent isohexides. A similar trend has been noticed in Chapter 5 in the case of the fully isohexide-based polyesters. However, when compared with another cyclic diol, viz. the petrochemical-based 1,4-cyclohexanedimethanol (CHDM), the $T_g$ of PteT is 15 °C higher than that of the corresponding poly(1,4-
cyclohexylenedimethylene terephthalate) (PCT), which has a \( T_g \) of 90 °C when containing 100% trans-isomer.\(^{13}\) Hence, we can conclude that IIDML has a higher structural rigidity than trans-CHDM.

Concerning the melting temperatures, the IIDML-based polyesters exhibit considerably higher \( T_m \) values than all the polyesters derived from the three linear diols (Figure 6-10b, Table 6-5). For instance, the \( T_m \) of PleT, PleIP and PleF are about 30 °C, 26 °C and 13 °C higher than those of PET, PEI and PEF, respectively. Compared to the parent isohexide-based polyesters, interestingly, the \( T_m \) of PleT (292 °C) is even about 30 °C higher than that of poly(isoidide terephthalate) (PIT, \( T_m = 261°C \)) as reported by Storbeck et al.\(^{17, 32}\) Such a high \( T_m \) value approaches that of PCT containing 100% trans-CHDM (\( T_m = 315 °C \)).\(^{1}\) Given the high \( T_g \) and \( T_m \) values of these semi-aromatic polyesters, it can be concluded that IIDML is a rigid molecule.

It should be noted that, as mentioned by Storbeck et al, the melting endotherm of poly(isoidide terephthalate) (PIT) was only present in the first DSC heating thermogram and is absent in the second DSC heating run.\(^{9, 29}\) This is thought to be related to the rather low degree of crystallinity or slow rate of crystallization of PIT from the melt. As described earlier, both PleT and PleF display rather pronounced melting and crystallization transitions. Thus, compared to isoidide, IIDML obviously improves the crystallization of the investigated semi-aromatic polyester systems. This is believed to be caused by the presence of the additional methylene units. Compared to the parent isohexides, more specifically isoidide, on the one hand the flexibility of the methylene units decreases the stiffness of the polymer chain, thereby lowering the \( T_g \), and on the other hand the flexible methylene units are expected to allow for necessary polymer chain adjustments in the viscous melt towards better crystal packing, which is beneficial for the formation of more perfect crystals, resulting in an increase of the \( T_m \). If the entropy (\( \Delta S_c \)) of the crystal is reduced, the respective entropy upon melting (\( \Delta H_m \)) increases, which further results in a lower \( \Delta H_m / \Delta S_m \), viz. \( T_m \). This is believed to be the reason why PleT displays a lower \( T_g \) but a higher \( T_m \) than PIT. The larger value of \( T_m - T_g \), the so-called ‘crystallization window’, of the IIDML-based polyesters with respect to II-based polyesters explains their better crystallizability from the melt.

Although it is widely accepted that isohexides and derivatives are rigid molecules, as described for the isoidide dicarboxylic acid (IIDCA)-based polyesters in chapters 3 and 4, their effects on polymer properties, i.e. \( T_g \), \( T_m \) and crystallinity, are highly dependent on the specific molecular structures. Modification of the functional groups can result in large differences in every aspect of the polymer properties.
Semi-aromatic polyesters from isoidide-2,5-dimethanol (IIDML)

Figure 6-10. Comparison of (a) glass transition temperatures ($T_g$) and (b) the melting ($T_m$) of the IIDML-based polyesters with relevant polyesters based on linear diols, including ethylene glycol, 1,4-BDO and 1,6-HDO. The plots are based on the data collected for series I-V, Table 6-5.

Table 6-5. Molecular weights, melting and glass transition temperatures of analogous polyesters.a

<table>
<thead>
<tr>
<th>series</th>
<th>polyester</th>
<th>diol</th>
<th>diacid</th>
<th>$M_n$ (g/mol)</th>
<th>$T_m$ (°C)</th>
<th>$T_g$ (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>PleT</td>
<td>IIDML</td>
<td>TA</td>
<td>7,700</td>
<td>292</td>
<td>105</td>
</tr>
<tr>
<td></td>
<td>PleIP</td>
<td>IIDML</td>
<td>ITA</td>
<td>9,800</td>
<td>158</td>
<td>88</td>
</tr>
<tr>
<td></td>
<td>PleF</td>
<td>IIDML</td>
<td>2,5-FDCA</td>
<td>30,300</td>
<td>248</td>
<td>93</td>
</tr>
<tr>
<td></td>
<td>PHT</td>
<td>1,6-HDO</td>
<td>TA</td>
<td>39,000</td>
<td>143</td>
<td>9</td>
</tr>
<tr>
<td>II</td>
<td>PHF</td>
<td>1,6-HDO</td>
<td>ITA</td>
<td>7,200</td>
<td>–</td>
<td>–6</td>
</tr>
<tr>
<td></td>
<td>PHF</td>
<td>1,6-HDO</td>
<td>2,5-FDCA</td>
<td>32,100</td>
<td>148</td>
<td>28</td>
</tr>
<tr>
<td>III</td>
<td>PBT</td>
<td>1,4-BDO</td>
<td>TA</td>
<td>–</td>
<td>225</td>
<td>35-48</td>
</tr>
<tr>
<td></td>
<td>PBI</td>
<td>1,4-BDO</td>
<td>ITA</td>
<td>13,000</td>
<td>156</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>PBF</td>
<td>1,4-BDO</td>
<td>2,5-FDCA</td>
<td>17,800</td>
<td>172</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>PET</td>
<td>1,2-EG</td>
<td>TA</td>
<td>–</td>
<td>250-260</td>
<td>70</td>
</tr>
<tr>
<td>IV</td>
<td>PEI</td>
<td>1,2-EG</td>
<td>ITA</td>
<td>38,700</td>
<td>132</td>
<td>62</td>
</tr>
<tr>
<td></td>
<td>PEF</td>
<td>1,2-EG</td>
<td>2,5-FDCA</td>
<td>22,400</td>
<td>215</td>
<td>80</td>
</tr>
<tr>
<td>V</td>
<td>PIT</td>
<td>isoidide</td>
<td>TA</td>
<td>14,500</td>
<td>261</td>
<td>209</td>
</tr>
<tr>
<td></td>
<td>PIF</td>
<td>isoidide</td>
<td>2,5-FDCA</td>
<td>21,500</td>
<td>–</td>
<td>196</td>
</tr>
</tbody>
</table>

a1,4-BDO = 1,4-butanediol; 1,6-HDO = 1,6-hexanediol; $T_g$ = glass transition temperature; $T_m$ = melting temperature. bPolyesters synthesized from adipoylchloride and isohexides at 160 °C by melt polymerization. cPolyesters synthesized from dimethyladipate and 1,4-BDO or 1,6-HDO by melt polymerization.

In view of the above, it can be concluded that IIDML is a rigid bio-based monomer capable of increasing both the glass transition and melting temperatures of polyesters. For
the investigated semi-aromatic systems, the $T_g$-increasing ability of IIDML is lower than those of the parent isohexides, but higher than that of the most rigid linear aliphatic diol, ethylene glycol, and close to that of trans-CHDM. Given the high $T_g$ and $T_m$ values, these IIDML-based semi-aromatic polyesters may find applications as engineering plastics. The monomer IIDML can also be used as a renewable (co)monomer for modifying or improving the properties of existing polyesters, such as $T_w$, $T_m$ as well as the degree of the crystallinity.

6.4 Conclusions

In this Chapter, we have described the synthesis and characterization of a series of novel semi-aromatic polyesters based on the new rigid bio-based primary diol isoididedimethanol (IIDML). Polyesters of IIDML with terephthalic acid, isophthalic acid and furan-2,5-dicarboxylic acid, were obtained via melt polymerization and subsequent solid-state polycondensation (SSPC). IIDML showed an excellent thermal stability and a dramatically improved reactivity compared to the parent isohexides. The desired polyesters were obtained with very low discoloration and high molecular weights. In particular, the molecular weight of poly(isoidide-2,5-dimethylene furan-2,5-dicarboxylate) (PIeF) exceeds 30,000 g/mol after a relatively short SSPC reaction time. TGA analysis revealed that the IIDML-based semi-aromatic polyesters have similar thermal stabilities as the known poly(ethylene terephthalate) (PET) and poly(butylene terephthalate) (PBT) as well as poly(ethylene furan-2,5-dicarboxylate) (PEF). DSC and WAXD analyses showed that both the poly(isoididedimethylene terephthalate) (PIeT) and PIeF are semi-crystalline materials with high melting and glass transition temperatures, which exceed those of PET, PBT and PEF, and compete with that of poly(1,4-cyclohexylmethylene terephthalate) (PCT). The amorphous poly(isoididedimethylene isophthalate) (PIeIP) also displays considerably higher $T_g$ and $T_m$ values than analogous polyesters based on linear or cyclic diols. As evidenced by the structure-thermal properties study, IIDML is a promising bio-based rigid diol monomer possessing remarkable $T_g$ and $T_m$-enhancing abilities. Thus far, IIDML is the first isohexide-based diol that can be incorporated for the full 100% into polyesters via melt polymerization. Given the multiple benefits of these IIDML-based polyesters, including high molecular weights, low degrees of discoloration, high thermal stability, superior $T_g$ and $T_m$ values compared to PET and PBT, as well as good crystallizability from the melt, these polyesters are promising candidates for industrial production of new semi- or fully-biobased engineering plastics, as soon as IIDML is synthesized on kiloton scale.
REFERENCES

Investigation of polyamides based on isoidide-2,5-dimethyleneamine

Abstract

Novel, semicrystalline polyamides and copolyamides were synthesized from a new carbohydrate-based diamine, namely isoidide-2,5-dimethyleneamine (IIDMA). In combination with 1,6-hexamethylene diamine (1,6-HDA) as well as the bio-based sebacic acid (SA) or brassyllic acid (BrA). The desired copolyamides were obtained via melt polymerization of the nylon salts followed by solid-state polycondensation (SSPC) process. Depending on the chemical compositions, the number average molecular weights ($M_n$) of the polyamides were in the range of 4,000–49,000 g/mol. With increasing IIDMA content in the synthesized copolyamides, their corresponding glass transition temperatures ($T_g$) increase from 50 °C to approximately 60–67 °C, while the melting temperatures ($T_m$) decrease from 220 °C to 160 °C. The chemical structures of the polyamides were analyzed by NMR and FT-IR spectroscopy. Both differential scanning calorimetry (DSC) and wide angle X-ray diffraction (WAXD) analyses revealed the semicrystalline character of these novel (co-)polyamides. Variable-temperature (VT) $^{13}$C{'H} cross-polarization/magic-angle spinning (CP/MAS) NMR and FT-IR techniques were employed to study the crystal structures as well as the distribution of the IIDMA moieties over the crystalline and amorphous phases of the copolyamides. The performed ab initio calculations reveal that the stability of the IIDMA moieties is due to a pronounced “boat” conformation of the bicyclic rings. The incorporation of methylene segments in between the isohexide group and the amide groups enables the hydrogen bonds formation and organization of the polymer chain fragments. Given the sufficiently high $T_m$ values (~200 °C) of the copolyamides containing less than 50% of IIDMA, these bio-based semicrystalline copolyamides can be useful for engineering plastic applications.

The work described in this chapter was carried out in collaboration with Dr. Lidia Jasinska-Walc.
Chapter 7

7.1 Introduction

The various commercially available polyamides (PAs) belong to one of the most important classes of semicrystalline polymers owing to their good thermal and mechanical properties. Concerning the versatile applications of PAs, often in demanding conditions, some naturally-occurring polyamides formed from amino acids, e.g. wool or silk, can be used for textile production. Recently, PAs such as PA 6.6, PA 6 and PA 6.10 have gradually substituted wool and silk and have been applied in a wide range of applications. Nowadays, owing to their excellent physicochemical and mechanical properties, PAs form one of the most important groups of step-growth polymers, and are extensively used in industry for injection molding, extrusion and film or fiber applications. Nevertheless, a fundamental fact one should realize is that all developments in the polyamide industry cannot be continued and not even be maintained without the abundant availability of raw materials, which are typically fossil resource based.

With the growing concern of the fossil feedstock shortage and the relating environmental issues of fossil feedstock consumption, biomass is regarded as a promising resource for producing sustainable chemicals, fuels and energy. Among numerous existing biomass monomers, the carbohydrate-derived 1,4:3,6-dianhydrohexitols (isohexides) are highly interesting building blocks for step-growth polymerization. These isohexides are a group of rigid secondary diols derived from C6-sugars, which are found in three major isomeric forms, namely isosorbide (1,4:3,6-dianhydro-D-glucitol, IS, with 2-endo, 5-exo oriented hydroxyl groups), isomannide (1,4:3,6-dianhydro-D-mannitol, IM, with 2-endo, 5-endo oriented hydroxyl groups) and isoide (1,4:3,6-dianhydro-L-iditol, II, with 2-exo, 5-exo oriented hydroxyl groups). These molecules can be obtained from starch or cellulose via a few (bio)organic transformations and therefore are considered as biogenic. In recent years, extensive interests raised from both academia and industry focusing on the utilization of isohexides for various types of step-growth polymers, such as polyesters, polyamides, polycarbonates and polyurethanes. One of the most appealing features of the isohexides is their intrinsic rigidity originating from the bicyclic rings, which can significantly enhance the glass transition temperature \( T_g \) and thereby broaden the application window of polymers. Such effects have been demonstrated by several authors for the isohexide-modified poly(ethylene terephthalate) (PET)\(^8\text{-}^{11} \), poly(butylene terephthalate) (PBT)\(^12 \) as well for succinic-acid based powder coatings.\(^13\text{-}^{16} \) The potential industrial applications of the isohexide-based polymers encompass packaging, (powder) coating resins, performance polymers as well as optical or bio-medical materials.\(^13\text{-}^{17}\text{-}^{21} \)

Despite these promising and unique properties of isohexides, the relatively poor reactivity of their secondary hydroxyl groups at the 2- and 5- positions has been recognized as a major drawback, which often results in low molecular weights (MW) and severely
colored polymers. Moreover, as bifunctional alcohols, the parent isohexide apparently is limited to be directly used as monomer for the synthesis of certain types of step-growth polymers like e.g. PAs. Hence, a number of isohexide-derivatives have been reported for better reactivity and/or diverse functionalities.

In order to synthesize PAs, the parent isohexide has been transformed into a few aminoderivatives through chain extension on the oxygen atom of the 2/5-hydroxyl groups (-OH) by e.g. propylamine (-(CH2)3NH3), phenylamine (PhNH2) or benzylamine (PhCH2NH2), or through the direct replacement of the 2/5-hydroxyl groups by amine (-NH2) groups. Since the functional groups are directly attached to the bicyclic skeleton of isohexide, the latter strategy has been proven to be able to retain the structural rigidity to a large extent. Following such a strategy, thus far three isomeric isohexide-based diamines have been generated, namely diamino-isosorbide (DAIS), diamino-isomannide (DAIM) and diamino-isoidide (DAII). Thiem et al. reported the first PAs derived from these isohexide-based diamines in combination with several aromatic or aliphatic diacyl chlorides via interfacial polymerization. These PAs show high degrees of polymerization and $T_\text{m}$ values in the range of 50–70 °C, which are significantly higher than those of commercially available PA 6 or PA-66. Recently, our studies on isohexide-derived PAs presented the comprehensive analyses concerning the preparation of series of fully bio-based copolyamides (co-PAs) by incorporating DAII or DAIS into PA 4.10 or PA 4.13. The synthetic protocol, starting with the preparation of the corresponding ‘nylon salts’, combines a conventional melt-polymerization with a solid-state post-polycondensation (SSPC), affording the desired co-PAs with number-average molecular weights ($M_n$) above 20,000 g/mol. In comparison to PA 4.10 or PA 4.13, these isohexide-derived co-PAs exhibit lower degrees of hydrogen bond density and thus have lower melting points.

We are interested in developing versatile isohexide-based building blocks as well as in their applications in step-growth polymerization. In Chapter 2, with the aim to develop novel isohexide derivatives with improved reactivity and preserved rigidity, we reported a new family of isohexide-based bifunctional monomers. The original hydroxyl groups were replaced by several 1-carbon extended functionalities including carboxylates (-COOH, -COOCH3), methylenehydroxyl (-CH2OH) and methyleneamine (-CH2NH2). Subsequently, several partially or fully bio-based polysters from these building blocks, including isoidide dicarboxylic acid (IIDCA) and isoidide dimethanol (IIDML), were synthesized. The sufficiently high molecular weights ($M_n = 10,000–30,000$ g/mol) as well as the appropriate thermal properties of the resulting polysters revealed their improved reactivity and largely-preserved structural rigidity of the novel monomers.

In this chapter, we present a series of (co)polyamides based on a novel one-carbon extended isohexide diamine, namely isoidide-2,5-dimethylene amine (IIDMA), which can be
Chapter 7

synthesized from isomannide via a dinitrile intermediate (IIDN) (Scheme 7-1).\textsuperscript{31} Compared to the known secondary isohexide-based diamines, like diaminoisoidide (DAII) or diaminoisosorbide (DAIS), IIDMA is a primary diamine and therefore is expected to exhibit higher reactivity. In this work, the synthesis, chemical structure characterization, thermal properties and crystal structure analysis of the PAs based on IIDMA, 1,6-hexamethylene diamine (1,6-HDA) and the bio-based dicarboxylic acids, including sebacic acid (SA) and brassylic acid (BrA), will be described. The molecular structure of the synthesized PAs was characterized by nuclear magnetic resonance (NMR) spectroscopy. In addition, FT-IR spectroscopy, wide angle X-ray scattering (WAXD) and solid-state NMR spectroscopy were employed to elucidate the hydrogen bonding nature and chain packing capabilities as well as the distribution of IIDMA over the crystalline and amorphous phases of the PAs.

Scheme 7-1. Chemical structure of isoidide dimethylene amine (IIDMA) prepared from isomannide via the dinitrile intermediate.

7.2 Experimental section

Materials

((3S,6S)-hexahydrofuro[3,2-b]furan-3,6-diyl)dimethanamine (IIDMA) was prepared according to the method described in Chapter 2.\textsuperscript{31} Isomannide (Sigma-Aldrich), trifluoromethanesulfonic anhydride (>99%, Aldrich), dichloromethane (Merck, p.a.), pyridine (Merck, p.a.), tetrahydrofuran (anhydrous, ≥99.9%, Sigma-Aldrich), potassium cyanide (extra pure, Merck), 18-crown-6 (>99%, Fluka), chloroform (Merck, p.a.), borane-tetrahydrofuran complex (BH\textsubscript{3}-THF) in THF solution (1.0 M, Sigma-Aldrich), hydrochloride in diethyl ether solution (2.0 M, Sigma-Aldrich), 1,6-hexamethylene diamine (98%, Sigma-Aldrich), sebacic acid (99%, Sigma-Aldrich), brassylic acid (1,11-undecanedicarboxylic acid, Sigma-Aldrich, 94%, purified by recrystallization from toluene), chloroform-d (99.8 atom % D), trifluoroacetic acid-d (99.5 atom % D, Sigma-Aldrich), D\textsubscript{2}O (>99.8%, Merck), methanol-d\textsubscript{4} (99.8 atom % D, contains 0.05 % (v/v) TMS, Aldrich), 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP, Biosolve), activated carbon (Norit, CN1), magnesium sulfate (Acros Organics, 99% extra pure, dried, contains 3 to 4 moles of water), Celite® 545 coarse (Fluka). Amberlyst\textsuperscript{®} A26 (Aldrich) hydroxide form (strongly basic, macroreticular resin with quaternary ammonium functionality from Rohm&Haas Co; prior to use, the resin was washed with demineralized water by sonication in an ultrasonic bath at RT for 10 min. The water layer was subsequently removed by decantation. This procedure was repeated 5 times, until the water layer remained colorless).
Characterization

$^1$H NMR and $^{13}$C NMR spectra were recorded at room temperature using a Varian Mercury Vx spectrometer operating at frequencies of 400 MHz and 100.62 MHz for $^1$H and $^{13}$C, respectively. For $^1$H NMR experiments, the spectral width was 6402.0 Hz, acquisition time 1.998 s and the number of recorded scans equal to 64. $^{13}$C NMR spectra were recorded with a spectral width of 24154.6 Hz, an acquisition time of 1.300 s, and 256 scans.

Size exclusion chromatography (SEC) in hexafluoroisopropanol (HFIP) was performed on a system equipped with a Waters 1515 Isocratic HPLC pump, a Waters 2414 refractive index detector (35 °C), a Waters 2707 auto sampler, and a PSS PFG guard column followed by 2 PFG-linear-XL (7 μm, 8×300 mm) columns in series at 40 °C. HFIP with potassium trifluoroacetate (3 g/L) was used as eluent at a flow rate of 0.8 mL/min. The molecular weights were calculated against poly(methyl methacrylate) standards (Polymer Laboratories, $M_p = 580$ Da up to $M_p = 7.1 \times 106$ Da).

The thermal stability of the polymers was determined by thermogravimetric analysis (TGA) with a TGA Q500 apparatus from TA Instruments. The samples were heated from 30 to 600 °C at a heating rate of 10 °C/min under a nitrogen flow of 60 mL/min.

Glass transition temperatures ($T_g$) and melting temperatures ($T_m$) were measured by differential scanning calorimetry (DSC) using a DSC Q100 from TA Instruments. The measurements were carried out at a heating and cooling rate of 10 °C/min from −60 °C to 180–250 °C. The transitions were deduced from the second heating and cooling curves.

Variable-temperature (VT) $^{13}$C/$^1$H cross-polarization/magic-angle spinning (CP/MAS) NMR experiments were carried out on a Bruker ASX-500 spectrometer employing a double-resonance probe for rotors with 4.0 mm outside diameter. These experiments utilized 10.0 kHz MAS and a 4 μs π/2 pulse for $^1$H. All VT $^{13}$C/$^1$H CP/MAS NMR spectra were recorded using a CP contact time of 3.0 ms and TPPM decoupling during acquisition. The temperature was controlled using a Bruker temperature control unit in the range from 30 °C to 180 °C. The VT $^{13}$C/$^1$H CP/MAS NMR spectra were recorded under isothermal conditions at intervals of 10 °C. A heating rate of 2 °C/min was employed between temperatures. Reported temperatures are corrected for friction- induced heating due to spinning using $^{207}$Pb MAS NMR of Pb(NO$_3$)$_2$ as a NMR thermometer. The 2D $^1$H/$^1$H Double-Quantum Single-Quantum (DQ-SQ) correlation and $^{13}$C/$^1$H Frequency-Switched Lee-Goldburg HETero-nuclear CORrelation (FSLG-HETCOR) experiments were recorded on a Bruker AVANCE-III 850 spectrometer using a double-resonance probe for rotors with 2.5 mm outside diameter. These experiments employed spinning frequencies of 29762 Hz and 15000 Hz, respectively. DQ excitation was performed using the BaBa sequence and the FSLG-HETCOR experiment used a CP time of 2.0 ms. Chemical shifts for $^1$H and $^{13}$C MAS NMR are reported relative to TMS using solid adamantane as an external reference. CP conditions were optimized using L-alanine. All samples were annealed just below their melting temperature for 5 min under a flow of nitrogen gas before NMR analysis to remove precipitation-induced structural conformations.

Geometry optimization and $^{13}$C NMR chemical shift calculations were performed within the Gaussian03 program package. The geometries of the conformations obtained by merging results from a set of 1D potential energy surface (1D-PES) scanning procedure via B97-D/6-311G** were further optimized at the same level. The most abundant conformer with respect to energy has been proceeded for further NMR chemical shifts calculations at the B97-D/6-311G** level of theory. Further details about information on the 1D-PES procedure, comparison of B97-D and MP2 results, and the NMR chemical shift calculations are given in Appendix F.

Fourier transform infrared spectra (FT-IR) were obtained using a Varian 610-IR spectrometer equipped with a FT-IR microscope. The spectra were recorded in a transmission mode with a resolution of 2 cm$^{-1}$. PA films obtained from 1,1,1,3,3,3-hexafluoroisopropanol were analyzed on a zinc selenium disk and heated from 30 °C to the temperatures slightly above the melting points of the polyamides. For this purpose a Linkam TMS94 hotstage and controller were used. The samples were cooled in 10 °C steps and reheated with the same heating steps. The spectra from the second heating
run were collected. Varian Resolution Pro software version 4.0.5.009 was used for the analysis of the spectra.

Analysis of the crystalline structure of the materials was performed using wide-angle X-ray scattering measurements by means of a computer-controlled goniometer coupled to a sealed-tube source of CuK\(\alpha\) radiation (Philips), operating at 50 kV and 30 mA. The CuK\(\alpha\) line was filtered using electronic filtering and the usual thin Ni filter. The data were collected at room temperature. The 1D profiles were subsequently background-corrected and normalized. Since reflections from the different crystallographic phases frequently overlap each other, it was necessary to separate them by deconvolution. Analysis of diffraction profiles of the examined samples and peak deconvolution were performed using WAXSFit software designed by M. Rabiej at the University of Bielsko-Biała (AHT). The software allows to approximate the shape of the peaks with a linear combination of Gauss and Lorentz or Gauss and Cauchy functions and adjusts their settings and magnitudes to the experimental curve with a “genetic” minimizing algorithm.

Isoidide-2,5-dimethylamine (IIDMA)-Sebacic Acid Salt: To a solution of sebacic acid (1.2 g, 0.006 mol) in ethanol (10 mL) at 50 °C, a solution of IIDMA (1.0 g, 0.006 mol) in an ethanol/water mixture (3 mL, 2:1, v/v) was added dropwise. During the addition, a precipitate was formed. The mixture was stirred at 80 °C for 1 h and then at 50 °C for 1 h. The crude product was filtered and recrystallized from an ethanol/water mixture (10:1, v/v) to afford the salt as white crystals. Yield: 1.9 g, 85%. \(1^H\) NMR (D$_2$O, ppm): \(\delta = 4.62\) (s, 2H), 4.10 (m, 2H), 3.75 (m, 2H), 3.10 (m, 4H), 2.60 (m, 2H), 2.17 (t, 4H), 1.55 (m, 4H), 1.30 (m, 8H).

1,6-Hexamethylene diamine-Sebacic Acid Salt: To a solution of sebacic acid (4.6 g, 0.04 mol) in ethanol (200 mL) at 50 °C a solution of 1,6-hexamethylene diamine (8.1 g, 0.04 mol) in ethanol (10 mL) was added dropwise. During the addition, a precipitate was formed. The mixture was stirred at 80 °C for 1 h and then at 50 °C for 1 h. The crude product was filtered and recrystallized from ethanol/water mixture (10:1, v/v) to afford the salt as white crystals. Yield: 11.8 g, 93%. \(1^H\) NMR (D$_2$O, ppm): \(\delta = 2.85\) (s, 4H), 2.02 (m, 4H), 1.54 (m, 4H), 1.40 (m, 4H), 1.28 (m, 4H), 1.15 (m, 8H).

Isoidide-2,5-dimethylamine (IIDMA)-Brassylic Acid Salt: To a solution of brassylic acid (1.5 g, 0.006 mol) in ethanol (20 mL) at 50 °C, a solution of IIDMA (1.0 g, 0.006 mol) in an ethanol/water mixture (3 mL, 2:1, v/v) was added dropwise. During the addition, a precipitate was formed. The mixture was stirred at 80 °C for 1 h and then at 50 °C for 1 h. The crude product was filtered and recrystallized from ethanol/water mixture (10:1, v/v) to afford the salt as white crystals. Yield: 2.0 g, 81%. \(1^H\) NMR (D$_2$O, ppm): \(\delta = 4.47\) (s, 2H), 3.96 (m, 2H), 3.59 (m, 2H), 2.93 (m, 4H), 2.46 (m, 2H), 2.03 (t, 4H), 1.40 (m, 4H), 1.13 (m, 16H).

1,6-Hexamethylene diamine-Brassylic Acid Salt: To a solution of brassylic acid (1.5 g, 0.006 mol) in ethanol (20 mL) at 50 °C, a solution of 1,6-hexamethylene diamine (0.69 g, 0.006 mol) in ethanol (3 mL) was added dropwise. During the addition, a precipitate was formed. The mixture was stirred at 80 °C for 1 h and then at 50 °C for 1 h. The crude product was filtered and recrystallized from ethanol/water mixture (10:1, v/v) to afford the salt as white crystals. Yield: 2.1 g, 96%. \(1^H\) NMR (D$_2$O, ppm): \(\delta = 2.84\) (t, 4H), 2.01 (t, 4H), 1.53 (m, 4H), 1.39 (m, 4H), 1.27 (m, 4H), 1.13 (m, 16H).

Synthesis of the Polyamides: A three-necked round-bottom flask equipped with an overhead mechanical stirrer, a Dean-Stark type condenser and vigereux column was charged with 1,6-hexamethylene diamine-sebacic acid salt (0.5 g), isoidide-2,5-dimethylamine-sebacic acid salt (0.5 g), 1,6-hexamethylene diamine (0.05 g, 0.43 mmol), isoidide-2,5-dimethylamine (0.05 g, 0.29 mmol) and Irganox 1330 (0.01 g) and the mixture was stirred at 170–175 °C for 30 min under argon atmosphere. Then the temperature was raised to 190 °C and the polycondensation process was continued for 2 h. After cooling down to room temperature, the synthesized prepolymer was isolated from the flask and
ground into powder, washed with demineralized water at 80 °C, filtered and dried under reduced pressure at 80 °C. The resulting product was subsequently submitted to solid-state polymerization carried out about 20–30 °C below the melting point of the prepolymer for 5 h under Ar atmosphere. Analogous conditions of the polymerization process were applied for all the investigated polyamides.

7.3 Results and discussion

7.3.1 Synthesis and molecular characterization of the IIDMA-derived (co)polyamides.

Two series of novel (co)polyamides were synthesized from isoidide-2,5-dimethyleneamine (IIDMA), 1,6-hexamethylyene diamine (1,6-DAH), in combination with either sebacic acid (SA) or brassylic acid (BrA). The synthetic protocol comprises a solvent-free melt polycondensation process starting from the corresponding nylon salts, followed by an optional solid-state postcondensation (SSPC), as described previously for the diaminoisoidide (DAII) or diaminoisosorbide (DAIS)-derived PAs.\textsuperscript{17,18} When the IIDMA content was below 75 mol%, the two series of PA prepolymerm were obtained with \( M_n \) values ranging from 6,700–21,500 g/mol, which were further enhanced to 12,400–49,000 g/mol by SSPC (Table 7-1, entry 2, 3, 4, 7, 8). The SSPC temperatures were approximately 20–30 °C lower than the corresponding melting points of the prepolymer.\textsuperscript{40} According to the previous studies, series of melt polymerizations of SA, 1,4-butanediame and the secondary isohehexide-based diamines, viz. diaminoisoidide (DAII, \textit{exo-exo} oriented diamine) or diaminoisosorbide (DAIS, \textit{exo-end} oriented diamine)\textsuperscript{17-19} gave the corresponding polyamide prepolymerm with \( M_n \) values in the ranges of 2,500-6,500 g/mol and 5,600-8,100 g/mol, respectively. Given the significantly higher molecular weights of IIDMA-based polyamide prepolymerm, we expect a considerably higher reactivity of the primary amine groups of IIDMA than the secondary amine groups of DAII and DAIS. However, such conclusion should be drawn with care since different reactivities of the used diamines, i.e., 1,4-diaminobutane and 1,6-hexamethylenediame, may exist under the applied melt polymerization conditions (although we believe that this is not likely). As also presented for DAII- and DAIS-based polyamides,\textsuperscript{17,18} interfacial polymerization of the diamines and sebacoyl chloride afforded lower molecular weight materials. Therefore, regardless of diamine configuration, the procedure consisting of melt polymerization in combination with SSPC can be considered as a suitable route towards the family of isoidide-derived products. However, as presented in Table 7-1, the attempt to enhance the molecular weight of the polymer derived from IIDMA and sebacic acid (PA 5) was unsuccessful. Due to the relatively low melting temperature of this product (157.7 °C), SSPC process carried out at
around 140 °C was ineffective. Despite the limited thermal stability of the sugar-derived monomers for high temperature polymerization processes, the applied short melt polymerization in combination with SSPC allowed the successful preparation of the PAs with minor degrees of discoloration and high molecular weights.\textsuperscript{17-19} When comparing the weighted-in and the incorporated molar ratio of the diamines, a slight preferential incorporation of 1,6-HDA residues over IIDMA was observed. The reasons can be a lower reactivity of IIDMA, most probably due to the proximity of the ring structure and/or a lower thermal stability of IIDMA than 1,6-DAH. Nevertheless, as shown in Table 7-1, the applied two-step polymerization conditions lead to the successful preparation of the desired products with close to expected chemical compositions.

![1H NMR spectrum of the polyamide synthesized from SA and IIDMA (PA5) and the chemical structure of the repeating unit of the homo- and copolyamides. Proton and carbon labels shown in the scheme were used for the analysis of the liquid-state and solid-state NMR spectra. The symbol (•) indicates the resonances cause by the IIDMA end-groups.](image)

Figure 7-1. \textsuperscript{1}H NMR spectrum of the polyamide synthesized from SA and IIDMA (PA5) and the chemical structure of the repeating unit of the homo- and copolyamides. Proton and carbon labels shown in the scheme were used for the analysis of the liquid-state and solid-state NMR spectra. The symbol (•) indicates the resonances cause by the IIDMA end-groups.

The molecular structure of the synthesized IIDMA-based polyamides was analyzed by \textsuperscript{1}H and 2D \textsuperscript{1}H-\textsuperscript{1}H COSY nuclear magnetic resonance (NMR) spectroscopy. As exemplified by the \textsuperscript{1}H NMR spectrum of the polyamide based on IIDMA and SA (PA5) in Figure 7-1, all proton signals from the repeating unit of the polymer are found at the expected chemical shift values with matching multiplicities. The stereochemistry of the IIDMA moieties in PA5
can be clearly identified by the resonances of the isohexide unit: based on the 2D $^1$H-$^1$H COSY NMR spectrum (see Appendix F, Figure F-1), there is no $^1$H-$^1$H dihedral coupling between the $\beta_{\text{IIDMA}}$ bridge protons with the neighboring $\alpha_{\text{IIDMA}}$ protons. Thus, the bridge $\beta_{\text{IIDMA}}$ protons appear as a singlet at 4.25 ppm in the $^1$H NMR spectrum (Figure F-1). Therefore, the adjacent $\alpha_{\text{IIDMA}}$ protons have no dihedral coupling with the $\beta_{\text{IIDMA}}$ bridge protons and adopt an endo-orientation. Logically, the methyleneamine groups should be in an exo orientation. This feature has been frequently illustrated in other isohexide-based polymers.$^{9,15,17,18,21}$ Given the fact that the molecular weight of PA5 is in a low range ($M_n = 3,900$ g/mol), the low intensity signals as indicated by dots are assumed to come from the IIDMA end-groups. Overall, we conclude that the stereo-configuration of IIDMA moieties were preserved during the applied polymerization conditions.

**Table 7-1.** Chemical compositions, molecular weights and polydispersity indices of the homo- and copolyamides synthesized from isoidide-2,5-dimethyleneamine (IIDMA), 1,6-hexamethylenediamine (1,6-DAH), sebacic acid (SA) and brassicic acid (BrA).

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<th>Symbol</th>
<th>Feed molar ratio (IIDMA/1,6-DAH)$^a$</th>
<th>Built-in molar ratio (IIDMA/1,6-DAH)$^b$</th>
<th>Prepolymer $\alpha_{\text{IIDMA}}$ (g/mol)$^c$</th>
<th>PDI$^c$</th>
<th>After SSP $\alpha_{\text{IIDMA}}$ (g/mol)$^c$</th>
<th>PDI$^c$</th>
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<td>–</td>
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<td>2.1</td>
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<td>68/32</td>
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<td>1.2</td>
<td>–</td>
<td>–</td>
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<tr>
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<td>0/100</td>
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<td>17,400</td>
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<td>1.7</td>
<td>13,900</td>
<td>2.3</td>
</tr>
</tbody>
</table>

$^a$Ratio determined by weighed-in monomers; $^b$Ratio determined by $^1$H NMR; $^c$Values determined using SEC against PMMA standards in HFIP.

7.3.2 Conformational analysis of the copolymers by solid-state NMR and quantum-chemical calculations.

Compared to other step-growth polymers, e.g. polyesters, PAs often have higher melting temperatures mainly due to the strong interchain hydrogen bonds formed between the recurring amide groups. In the solid-state form, the crystal packing of the polymer chain fragments is highly related to the construction of a hydrogen-bonded network. As shown previously, the introduction of DAII or DAIS into the linear polyamides PA 4.10 or PA 4.13
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affects the ordered crystal packing and therefore lowers the melting temperatures of the co-PAs. The solution \textsuperscript{1}H NMR spectroscopy, as described above, has been effective in elucidating the molecular structure of the synthesized PAs. In order to study the effect of IIDMA incorporation on the hydrogen-bonding network of the obtained co-PAs, we have employed variable-temperature (VT) \textsuperscript{13}C\textsuperscript{[\textsuperscript{1}H]} cross-polarization/magic-angle spinning (CP/MAS) NMR spectroscopy. Upon heating from 40 °C to the temperatures close to their corresponding melting points, the hydrogen bonding density of the polyamides can be affected, which will be reflected in a change of the NMR resonance signals. Moreover, through careful examination of the resonance signal changes over a wide range of temperatures, additional information concerning the distribution of isohexide-based monomers over crystalline and amorphous phases of the PAs, as well as on the mobility of the polymer chain fragments can be identified. In this work, by using solid-state NMR spectroscopy techniques, particular emphasis is given to the investigation of the existence of different potential IIDMA conformers and their influences on the formation and/or regularity of hydrogen bonding structures. Subsequent quantum-chemical calculations to reveal the most energetically stable IIDMA conformations. Two co-PAs samples, PA3 and PA8 based on SA and BrA, respectively and both having approximately 50/50 IIDMA/1,6-HDA molar ratio, were analyzed for this purpose.

During the heating course of PA3, the resonances from the IIDMA moieties appear as well resolved, albeit broad signals at 86.4, 71.6 and 48.2 ppm for $\beta_{\text{IIDMA}}$, $\beta'_{\text{IIDMA}}$ and $\gamma_{\text{IIDMA}}$, respectively (Figure 7-2a, Table 7-2, see Figure 7-1 for signal assignment). The resonance signals of the methylene proton from the cyclic skeleton ($\alpha_{\text{IIDMA}}$) are difficult to recognize due to overlapping with signals of the alkylene protons from 1,6-DAH units ($\alpha_{\text{N}}$). All the $\beta'_{\text{IIDMA}}$, $\beta_{\text{IIDMA}}$ and $\gamma_{\text{IIDMA}}$ signals show additional minor shoulders that gradually disappear with the increasing of temperature, i.e., above ~150 °C these signals have disappeared. Meanwhile, the remaining major signals from the IIDMA groups become narrower and shift only slightly to lower frequency even when going to the molten state compared to the situation at low temperature. This shows that the IIDMA groups adopt similar conformations over the whole temperature range. At high temperature the reduced \textsuperscript{13}C line width suggests a decrease in hydrogen bonding density of the polyamides upon heating. Furthermore, the characteristic carbonyl resonances located at ~173 ppm also appear as a rather broad signal, which gradually decreases in intensity with increasing temperature. In the melt two carbonyl signals with similar intensity appear that can be assigned to the different monomer parts of the copolymer. As reported for the PAs synthesized from DAII and DAIS the broad and bimodal C=O resonance signals may indicate that the carbonyl groups are involved in two types of hydrogen-bonding environments, and most probably referring to the hydrogen bonding occurring in the crystalline and amorphous regions of the sample.
However, for PA3, it is not possible to make such an assignment due to the similar degree of intensity decay of the both types of signals (Figure 2a), as well as and the presence of carbonyl signals in the melt at the same position.\textsuperscript{18,19} Moreover, over the investigated temperature range, the $\alpha_N$ and $\alpha_C$ methylene groups attached to each side of the amide bonds are present as well-defined and narrow signals at 40.5 ppm and 36.7 ppm, respectively, without any visible shoulders (see Figure 7-2a, Table 7-2 and Figure 7-1 for assignment). Interestingly, based on the chemical shift for $\alpha_N$ and $\alpha_C$ below and above the melting temperature, and a comparison to our previous work on PAs synthesized from DAIII and DAIS, the number of trans conformers in the linear chain fragments of the copolymer PA3 appears to be very limited, i.e., the signals from trans conformers should be visible as well resolved resonances at higher frequency.\textsuperscript{18,19} Thus, the (VT) $^{13}$C\{H\} CP/MAS NMR spectra of the PA3 in Figure 7-2a illustrate that the incorporation of IIDMA significantly increases the transition between trans and gauche conformers in the methylene moieties of SA and 1,6-HDA, causing the appearance of more gauche conformations and a visible reduction in the fraction of trans conformers. These observations are in line with FT-IR analysis of PA3 where signals of gauche CH$_2$ scissor vibrations were emphasized (see below). Further information about the local organization of polymer chains in PA3 can be achieved from the 2D NMR correlation spectra shown in Figures 2b and c. From the 2D $^{13}$C\{H\} FSLG-HETCOR spectrum in Figure 7-2b, the presence of two different hydrogen bond environments can be identified via the correlations of the amide groups to the aliphatic moieties. The non-hydrogen bonded fraction does not show any correlation to the carbonyl groups whereas the hydrogen bonded does. This observation combined with the isotropic chemical shift position of the amide protons at ~8.3 ppm and its correlations to the aliphatic moieties in Figure 2c show that the formed hydrogen bonds in PA3 based on IIDMA are stronger than in PAs synthesized from DAIII and DAIS. A possible explanation for the increase in chemical shift, and thereby an increase in hydrogen bond strength,\textsuperscript{41} could be that the incorporation of a methylene segment in between the isohexide group and the amide groups enables the hydrogen bonds formation to become organized more perfectly due to improved spatial arrangements, although this occurs at the expense of the occurrence of more gauche conformers in the methylene segments as discussed above. The increases in hydrogen bonding strength in turn also explain the higher melting temperatures for the samples studied in this work.

An enhanced mobility of the polymer chain fragments, caused by the increase in gauche conformers, is also visible for PA8 synthesized from BrA, 1,6-HDA and IIDMA. As shown in Figure 3a, the $\alpha_N$ and $\alpha_C$ resonances associated with gauche conformers of the linear methylene groups attached to NH and CO motifs at 40.3 ppm and 37.0 ppm are clearly visible throughout the whole temperature range. As also observed for PA3, the intensity of these signals upon heating decreases with only minor displacements visible. Meanwhile, a gradual shift of the
relatively broad carbonyl resonance at 173.4 ppm to higher ppm values is observed throughout the temperature range in Figure 3a. This is most likely caused by a reduction in hydrogen bonding efficiency leading to an enhanced mobility of the non-hydrogen bonded amide domains during the course of heating. The $^{13}$C [$^1$H] CP/MAS NMR spectra of PA8 also includes broad $\gamma$IIDMA, $\beta$IIDMA and $\beta'$IIDMA signals between 47–90 ppm and the $\alpha$IIDMA resonance located at 40.3 ppm, overlapping with the $\alpha$N signal. Again, the narrow $^{13}$C line widths of the IIDMA resonances point toward a reduced number of IIDMA conformers over the whole temperature range. From the 2D NMR correlation spectra shown in Figures 7-3b and c similar conclusions about the polymer chain organization can be derived for PA8 as for PA3. This includes that the non-hydrogen bonded fraction does not show any correlation to the carbonyl groups and that strong hydrogen bonds are formed, since the amide protons resonate at ~8.6 ppm.

The IIDMA moiety in both PA3 and PA8 show quite narrow $^{13}$C resonances suggesting that only a single IIDMA conformer is present. To reveal if this is the case we have performed a 1D Potential Energy Scan (PES). In our previous study on DAIII and DAII fragments we have shown that the cheaper DFT method B97-D reproduces the potential energy curve obtained by the more expensive MP2 method. For this reason, we have chosen to perform the current study of the conformational profile for the dihedral angle between the amide group and the isohexide fragment in IIDMA at the B97-D level of theory. From the 1D PES it is clear that three conformational minima exist with comparable energies (see Appendix F, Figure F-4). Based on this result a full set of possible conformations have been generated and further optimized at the same level of theory. Contrary to our previous studies of other isohexide derivatives (DAIS and DAIII), which showed a large spread of conformers, the incorporation of a methylene segment in between the isohexide and amide groups enables the isohexide fragment to adopt a unique conformation as illustrated in Figure 7-4a. This conformation is ~10 kJ/mol lower in energy compared to the second most abundant conformer found. In Figure 7-4a the most abundant conformers of DAIII and DAIS fragments are also shown for comparison with the current IIDMA unit. Inspection of these conformers show that the stability of the IIDMA and DAIII moieties is due to a pronounced “boat” conformation, which is distorted into the “chair” conformation for DAIS. These conformational differences come as a result of the specific stereo configuration of the different isohexide groups. To compare the NMR spectroscopic signatures of all three isohexides we have performed $^{13}$C chemical shift calculations at the B97-D/6-311G** level of theory and summarized these as shown in Figure 4b. For the IIDMA unit studied in this work the calculated $^{13}$C chemical shifts are in good agreement with the experimental results in Figures 7-2 and 7-3. Clearly, the different isohexide units can be distinguished by their characteristic signals for the anchoring carbons. These carbons are inherently sensitive to a
specific conformation of the isohexide moiety ("boat" or "chair"), resulting in a $$^{13}C$$ chemical shift spread of 14 ppm in the region from 45-65 ppm.

**Figure 7-2.** (a) Variable-temperature solid-state $$^{13}C$$[$$^1H$$] CP/MAS NMR spectra recorded at 11.75 T (500 MHz for 1H) of copolyamide PA3 synthesized from SA, IIDMA, 1,6-HDA with a IIDMA/1,6-DAH molar ratio of 49/51. (b) 2D $$^{13}C$$[$$^1H$$] FSLG-HETCOR spectrum acquired using a 2.0 ms CP step and five FLSG blocks per t1 increment to improve the 1H resolution. (c) 2D 1H-1H DQ-SQ spectrum recorded using a BaBa recoupling period of 67.2 μs. Both 2D spectra were recorded at 20.0 T corresponding to 850.27 MHz for 1H. The dashed lines in (b) and (c) illustrate selected cross-peaks and autocorrelation peaks, including hydrogen bonded (HB) and non-hydrogen bonded (non-HB) amide fragments. Assignment of the signals is performed according to Figure 7-1 and the asterisk in (a) indicates the position of a spinning side band (ssb) from the carbonyl resonance.
Figure 7-3. (a) Variable-temperature solid-state $^{13}$C{1H} CP/MAS NMR spectra recorded at 11.75 T (500 MHz for 1H) of copolyamide PA8 synthesized from BrA, IIDMA, 1,6-HDA with a IIDMA/1,6-DAH molar ratio of 42/58. (b) 2D $^{13}$C{1H} FSLG-HETCOR and (c) 2D 1H-1H DQ-SQ spectra recorded as described in the caption of Figure 2. The dashed lines in (b) and (c) illustrate selected cross-peaks and autocorrelation peaks, including hydrogen bonded (HB) and non-hydrogen bonded (non-HB) amide fragments. Assignment of the signals is performed according to Figure 1 and the asterisk indicates the position of a spinning side band (ssb) from the carbonyl resonance.
Figure 7-4. (a) Top and side views of the most stable conformers for the primary diamine (IIDMA) studied in this work, and the diaminoisosorbide (DAIS or exo-endo oriented diamine) and diaminoisoidide (DAII, exo-exo oriented diamine) studied in our previous work\textsuperscript{17-19} All conformers were found via gas phase MP2/6-311G** level of theory (see Supporting Information for details). (b) Graphical representation of the calculated $^{13}$C chemical shifts for all three conformers shown in (a). Note that we have used the nomenclature 4-6 to assign the $^{13}$C resonances for non-symmetric isohexide fragments as shown for DAII in (a).
Table 7-2. Chemical shifts (ppm) of the $^{13}$C CP/MAS NMR signals for the copolyamides PA3 and PA8. The position of the signals is given for the spectra recorded at 41.0 °C, 173.6 °C and 164.1 °C.

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<td>22.3–35.0</td>
<td>22.3–35.0</td>
<td>22.3–35.0</td>
<td>48.4</td>
<td>87.2</td>
<td>71.6</td>
<td>41.0</td>
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</table>
7.3.3 FT-IR Investigation of the polyamides upon Heating.

The hydrogen bonding between the amide moieties of the IIDMA-based polyamides was further investigated by temperature-dependent Fourier transformed infrared (FT-IR) spectroscopy. The applied temperature ranges from 30 °C to slightly above the melting point of the PAs. Three polyamides samples were characterized for this purpose, viz. PA3, PA8, and PA6.13 (PA6). Their respective FT-IR spectra are presented in Figure 7-5 to Figure 7-7.

Special attention was given to analyzing the intensities of the signals appearing around 3300 cm\(^{-1}\) for all three PAs, which are assigned as the signals caused by N-H stretching vibrations. At elevated temperatures, these signals were observed to broaden and their intensities significantly decreased as well. As pointed out by Schroeder\(^\text{43}\) and Skrovanek\(^\text{44,45}\) for even- and odd-type nylonas, the number of such bands reflects the average absorptive strength of the hydrogen-bonded N–H groups. The broadening and weakening of these signals upon heating are related to the reduction of the hydrogen bond density and the formation of non-hydrogen bonded N-H groups. As can be seen from the FT-IR spectra recorded above 180 °C in Figure 7-5 to Figure 7-7, additional signals can be observed around 3444 cm\(^{-1}\). They are the typical indication of the presence of the non-hydrogen bonded N-H groups.

Interesting information about the population of trans and gauche conformers in the backbone of the polyamides is provided by the signals of the C-H vibration from the methylene units attached to each side of the amide groups (-HN-C(O)-). According to literature and our previous findings on the DAII/DAIS-based copolyamides, the C-H vibration from the trans-methylene units attached to amine (NH) and carbonyl (C=O) groups shows absorptions at wave numbers of 1475 cm\(^{-1}\) and 1417–1419 cm\(^{-1}\), respectively.\(^\text{46,47}\) In the case of PA 6.13, given the pronounced absorptions at 1474 cm\(^{-1}\) and 1419 cm\(^{-1}\), both the methylene units attached to each side of the amide groups (-HN-C(O)-) are believed to adopt trans-conformations (Figure 7-6b). When IIDMA is incorporated, as shown in Figure 7-5b for the BrA-based PA8, the presence of the absorption at 1419 cm\(^{-1}\) indicates the trans-type of methylene units next to C=O; while the methylene units next to N-H in contrast adopt gauche-conformation by showing absorptions at around 1430–1460 cm\(^{-1}\) instead of 1475 cm\(^{-1}\). According to Yoshioka et al.,\(^\text{46}\) due to the lower torsion energy barrier, the conformational changes of the methylene groups next to the CH2-NH motifs can possibly be easier compared to those attached to the carbonyl group. The SA-based PA3 should also adopt gauche conformation, as shown in Figure 7-5.
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Figure 7-5. Variable-temperature FT-IR spectra of the copolyamide PA 3 recorded on heating from 30 °C to above the melting point. The copolymer was synthesized from SA, IIDMA, 1,6-DAH with IIDMA/1,6-DAH molar ratio 0.49/0.51.

Figure 7-6. Variable-temperature FT-IR spectra of the copolyamide PA 8 recorded on heating from 30 °C to above the melting point. The copolymer was synthesized from BrA, IIDMA, 1,6-DAH with IIDMA/1,6-DAH molar ratio 0.42/0.58.

Figure 7-7. Variable-temperature FT-IR spectra of the homopolyamide PA 6 recorded on heating from 30 °C to above the melting point. The polyamide was synthesized from BrA and 1,6-DAH.

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Interestingly, as we reported for the DAII-based polyamides, the presence of exo-exo oriented isohexide diamines in the backbone of the macromolecules more readily enhances the molecular motion and the induction of gauche type conformers in the linear fragments compared to their exo-endo oriented analogues. Although IIDMA is a one-carbon extended isohexide diamine on both sides of the molecule, because of a similar configuration as present in DAII the vanishing of the bands corresponding to CH2 scissoring next to the N-H and C=O groups with trans conformation is already observed for the copolyamides containing around 20 mol % of the bicyclic comonomer (see Appendix F, Figure F-2 and Figure F-3).

With regard to the resonances from the isohexide bicyclic skeleton, the FT-IR bands located at 1093 cm⁻¹, 1055–1057 cm⁻¹ and 907–910 cm⁻¹ are assigned to the asymmetric C-O-C stretching, skeletal C-C stretching and C-CO stretching signals, respectively. It was noticed that these bands exhibit lower intensity when the applied temperatures are close to the melting points, indicating that IIDMA motifs distribute over both the crystalline and the amorphous phases of the materials. Similar phenomena have also been observed for DAII and DAIS-derived polyamides. Moreover, the signals at 1552 cm⁻¹ and 1537 cm⁻¹ represent the Amide II in-plane N-H deformation with CN and C=O stretch vibration; while the signals corresponding to Amide III and Amide II+III coupled with the hydrocarbon skeleton appear at 1360–1370 cm⁻¹ and 1180–1190 cm⁻¹, respectively. Since the latter vibrations display a significant degree of decay in their intensity when the recorded temperatures are close to the melting points of the materials, they should originate from the temperature-sensitive crystalline phase. Besides, the FT-IR bands corresponding to the methylene motifs of the PAs, related to CH2 wagging or twisting and skeletal C-C stretch vibrations are found at 1280–1290 cm⁻¹, 1230–1250 cm⁻¹, 1218 cm⁻¹, 1050–1060 cm⁻¹, and 1019 cm⁻¹, respectively. These modes, excluding signals at 1055–1057 cm⁻¹, display significant changes in their line width at elevated temperature and can therefore also be assigned to the crystalline phase of the polyamides.

7.3.4 Thermal properties of the polyamides

The thermal stability of the polyamides was investigated by thermogravimetric analysis (TGA). As presented in Table 7-3, it is evident that the thermal stability of these new bio-based materials is dependent on the chemical composition, viz. the molar ratio of IIDMA and 1,6-HDA of the copolyamide, as well as the molecular weight. For the SA or BrA-based PAs containing less than 50 mol % of IIDMA, the 5% weight loss temperatures are in the range of 390–410 °C, which are comparable to those of the reference polyamides PA 6.10 or PA 6.13. However, for the PAs having IIDMA contents exceeding 50 mol%, as indicated for
the SA-based series, the thermal stability decreased significantly. Especially the 5% of weight loss temperature of the SA/IIDMA-derived homopolyamide is very low (323 °C, entry 5, Table 7-3). A similar trend has been observed by Jasinska et al. when proportionally introducing diaminoisoidide (DAII) into PA4,10,17 as well as when introducing diaminoisosorbide (DAIS) into PA4.13,18 Such an adverse effect on the thermal stability of IIDMA incorporation into the copolyamides is assumed to be caused by the generation of the crystal structural irregularity. Introduction of the isohexide-cyclic moiety into the original linear chains may cause a reduction of the hydrogen bonding density, as shown earlier by the solid-state NMR and FT-IR analyses. Moreover, the relatively low molecular weight of the PA5 (Mₙ= 3,900 g/mol) can also be a factor contributing to the observed poor thermal stability of this material.

Table 7-3. Thermal stability of the polyamides, glass transition temperatures (Tₙ), melt and crystallization temperatures (Tₜ, Tₜ₈), and enthalpy of the transitions upon heating/melting (m) and cooling (c) of the novel IIDMA-based polyamides.

<table>
<thead>
<tr>
<th>entry</th>
<th>T₃% (°C)</th>
<th>Tₘ₉ (°C)</th>
<th>Tₜ (°C)</th>
<th>Tₜ₈ (°C)</th>
<th>ΔHₘ (J/g)</th>
<th>Tₙ (°C)</th>
<th>ΔHₙ (J/g)</th>
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<td></td>
<td></td>
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<tr>
<td>PA1</td>
<td>399.6</td>
<td>456.7</td>
<td>-</td>
<td>222.6</td>
<td>63.1</td>
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<td>390.2</td>
<td>460.5</td>
<td>-</td>
<td>210.4</td>
<td>49.5</td>
<td>174.4</td>
<td>52.2</td>
</tr>
<tr>
<td>PA3</td>
<td>403.1</td>
<td>449.7</td>
<td>59.5</td>
<td>204.9</td>
<td>36.7</td>
<td>160.4</td>
<td>40.9</td>
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<td>PA4</td>
<td>356.7</td>
<td>446.5</td>
<td>66.8</td>
<td>181.6</td>
<td>33.7</td>
<td>123.4</td>
<td>14.1</td>
</tr>
<tr>
<td>PA5</td>
<td>323.6</td>
<td>443.8</td>
<td>62.6</td>
<td>157.7</td>
<td>26.1</td>
<td>120.7</td>
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<tr>
<td>BrA/IIDMA/1,6-DAH</td>
<td></td>
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<tr>
<td>PA6</td>
<td>408.7</td>
<td>460.8</td>
<td>-</td>
<td>206.7</td>
<td>71.6</td>
<td>184.3</td>
<td>59.7</td>
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<tr>
<td>PA7</td>
<td>413.1</td>
<td>455.3</td>
<td>-</td>
<td>201.8</td>
<td>53.8</td>
<td>175.3</td>
<td>45.5</td>
</tr>
<tr>
<td>PA8</td>
<td>401.8</td>
<td>450.9</td>
<td>-</td>
<td>197.1</td>
<td>54.1</td>
<td>173.9</td>
<td>37.3</td>
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</table>

T₃% = temperature of 5% mass loss, Tₘ₉ = temperature of maximal rate of decomposition, Tₜ = glass transition temperature, Tₜ₈ = melting point, Tₙ = crystallization temperature, ΔHₘ = enthalpy of the transition during melting (m) and crystallization (c).

To study the melting (Tₘ), glass transition (Tₙ) and crystallization (Tₜ) temperatures of the synthesized polyamides, differential scanning calorimetry (DSC) analysis was conducted. According to the data presented in Table 7-3, the presence of IIDMA in the linear PA 4.10 and PA 4.13 also affect the corresponding melting points of the investigated materials. As the IIDMA content increases from 0 to 100 mol %, the Tₘ values of the SA-based polyamides progressively decrease from 223 °C to 158 °C (PA1–5, Table 7-3, Figure 7-8). A similar trend was also observed for the BrA-based polyamides (PA6–8, Table 7-3, Figure 7-8). An
approximate 10 °C reduction of the $T_m$ was observed when 42% of 1,6-HDA was replaced by IIDMA (PA8, Table 7-3). In the meanwhile, upon increasing of the IIDMA content, the melting enthalpies of both series of the copolyamides were reduced accordingly. Compared to PA 6.10 (PA 1, Table 7-3), the melting enthalpy of the PA IIDMA.10 (PA 5, Table 7-3) was reduced by more than half. Such trend is in agreement with our previous observation for DAlI- and DAIS-derived homo- and copolyamides.17-19 Such phenomena were previously ascribed to the formation of a less perfect chain packing as well as to the reduction of the hydrogen bond density of these isohexide-based copolyamides.17,48 Additionally, bimodal melting endotherms combined with the presence of cold crystallization exotherms were observed for the copolyamides synthesized from BrA. This is a typical indication of the existence of imperfect crystals (low melting temperature peak), their melting upon heating and recrystallization into more perfect crystals (high melting temperature peak). Similar bimodal melting endotherms have also been observed for the DAlI-based copolyamides containing more than 40 mol% of DAlI, as well as for all the copolyamides based on DAIS and BrA-derived copolyamides.17,18 In contrast, the shapes of the second DSC melting peaks of the SA-based (co)polyamides containing similar percentages of IIDMA appear to be unimodal. This may imply that the crystal structure of SA-based copolyamides is more perfectly formed from the melt than the crystal structure of the BrA-based copolyamides. Concerning the number of carbon atoms present in the used comonomers, it is speculated that the combination of brassylic acid and IIDMA/1,6-DAH, viz. the combination of an odd (=13) and an even (=6) number of carbon atoms in the two monomeric residues, is less favorable for a regular crystal packing than the combination of two monomers both with an even number of carbon atoms, viz. SA (10 carbons) and IIDMA/1,6-DAH (6 carbons).

**Figure 7-8.** DSC thermograms of the homopolyamides PA 6.10 (PA1), PA IIDMA.10 (PA5), PA 6.13 (PA6), SA,1,6-DAH,IIDMA-based copolyamides PA2, PA3, PA4 and BrA,1,6-DAH,IIDMA-based copolyamides PA7, PA8. The graph shows the second DSC heating runs employing the heating rate of 10 °C/min.
Closely related to the decrease of $T_m$ and the melting enthalpies, the crystallization temperatures ($T_c$) and crystallization enthalpies were reduced as well as with increasing percentage of IIDMA in the copolyamides. Nevertheless, when the IIDMA content was below 50 mol %, such adverse effect on $T_c$ and crystallization enthalpy is considerably less pronounced than in the cases where the IIDMA content exceeds 50%.

In addition, during the cooling DSC runs at a cooling rate of 10 °C/min (Table 7-3), pronounced glass transitions were observed for the SA-based copolyamides containing more than 50 mol% IIDMA. From PA3 to PA5, the glass transition temperature of the (co)polyamides increases with the percentage of IIDMA. Compared to the commercialized PA6,10 ($T_g = 50$ °C), the introduction of IIDMA into PA6,10 raises the $T_g$ by 10–17 °C. As extensively shown for other types of isohexide-derived monomers, such a $T_g$-enhancing effect can be understood by the intrinsic rigidity of the bicyclic cis-fused tetrahydrofuran rings in IIDMA.

### 7.3.5 WAXD analysis of the polyamides

Wide-angle X-ray scattering measurements were conducted on all the obtained (co)polyamides. As presented in Figure 7-9, all the synthesized SA-based polyamides are semicrystalline materials, as evidenced by the sharp scattering signals appearing in their diffractograms recorded at room temperature. The crystallographic structure of these polyamides show a strong dependence on the chemical compositions, viz. the molar ratio of IIDMA/1,6-HDA in the copolyamides. When a relatively low content of IIDMA ($<50$ mol %, PA2 and PA3) is incorporated, the diffraction profiles of these copolyamides are rather similar to that of the linear PA 6.10 (PA1, Figure 7-9). Given the presence of four characteristic reflections in the 20 ranges of 3–7°, 10–12° and 18–25° corresponding to the crystallographic planes 001, 002, 100 and 010/110 (Figure 7-9, Table 7-4), the crystallographic structures of these polyamides are believed to adopt triclinic forms. The 100 diffraction peak corresponds to the interchain distance, i.e., the distance between two polymer chains lying within the same hydrogen-bonded β-sheet, while the 010/110 peak corresponds to the intersheet distance, i.e., the distance between two adjacent hydrogen-bonded β-sheets. The 001 and 002 diffraction peaks give information on the length of the chemical repeat unit.

With increasing content of IIDMA in the copolyamides, different trends for the four types of diffraction signals are observed: the 001 and 002 diffraction peaks tend to move towards a region with lower 20 values, meaning an increase of the $c$-axis dimension of the copolymers due to cocrystallization phenomenon of the comonomers in the same crystallographic lattice; 100 diffraction peaks move towards higher 20 regions, meaning a decrease of the interchain distance within the same hydrogen-bonded sheets; the 010/110 diffraction peaks move...
Investigation of polyamides based on isoidide-2,5- dimethyleneamine

towards lower 2θ regions, indicating an increase of the inter-sheet spacing. Additionally, in the diffractogram of PA 6.10 (PA1) shown in Figure 7-9, we can observe a weak signal with a 2θ value of 21.6°, which is indicative of the presence of a small amount of the pseudo-hexagonal type of crystals. Comparing PA1 to PA3, further increasing the the IIDMA content to above 50 mol % in the SA-based copolymer leads to significant changes of the diffractograms. The diffraction profile of PA4 containing about 68% IIDMA (PA4) displays a comparable diffraction pattern as that of PA IIDMA.10 (PA5). In both cases, there are only two major strong scattering signals appearing in the 2θ regions of 3–7° and 18–25°, respectively. Thus, with increasing IDMA content in the (co)polymides, the crystal structures transform from triclinic (when IIDMA% ≤ 50 mol%, PA1, PA2 and PA3) to a close to hexagonal form (PA4 and PA5). Moreover, as a result of overlapping of the signals coming from different potential crystallographic phases, the scattering signals of PA4 and PA5 in the 2θ range of 3–7° appear to be asymmetric. Hence, two data are given in Table 7-4 by deconvolution using WAXSFit software to indicate the possible positions of these two peaks for samples PA5 and PA4. In addition, a few low intensity signals were observed to be present at 2θ values of 18°, 22.5° and 23.6°, respectively, which together with the previous phenomena may indicate the presence of a small percentage of triclinic crystals as well. In comparison with PA5, the scattering signals of the 001 and 100 reflections in the diffraction profile of PA4 were observed to be located at regions of slightly higher 2θ values, suggesting slightly smaller intersheet and interplane spacings. Nevertheless, given the potential displacements that may exist for the reflection signals of the triclinic phase in terms of 2θ values, and in view of the low content of this crystallographic form, determining the precise location and displacement scope s of these signals is difficult.

![Figure 7-9. X-ray powder diffraction profiles of 1,6-hexamethylene diamine-, isoidide-2,5-dimethylamine-, and sebacic acid-based polyamides.](image_url)
Table 7-4. X-ray diffraction spacings of the polyamides based on 1,6-hexamethylene diamine (1,6-HAD), iodide-2,5-dimethylenamine (IIDMA) and sebacic acid (SA).

<table>
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<th>2θ (°)</th>
<th>X-ray diffraction (nm)</th>
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<tbody>
<tr>
<td></td>
<td>001</td>
<td>002</td>
</tr>
<tr>
<td>PA1</td>
<td>5.15</td>
<td>10.33</td>
</tr>
<tr>
<td>PA2</td>
<td>4.88</td>
<td>9.89</td>
</tr>
<tr>
<td>PA3</td>
<td>4.83</td>
<td>9.62</td>
</tr>
<tr>
<td>PA4</td>
<td>4.78, 5.13</td>
<td>–</td>
</tr>
<tr>
<td>PA5</td>
<td>4.32, 5.03(*)</td>
<td>–</td>
</tr>
</tbody>
</table>

(*)Due to overlapping of the signals coming from different crystallographic phases, data were derived by deconvolution using WAXSFit software to indicate the possible positions of the diffraction signals.

Little knowledge is available concerning the crystallographic structure of the BrA-based polyamides, e.g. PA6.13 (PA6). As shown in Figure 7-10, the diffraction profile of PA 6.13 shows a reflection signal of medium intensity in the 2θ range of 3–7°, as well as two strong reflections in the 2θ range of 18–25°. Such a diffraction pattern resembles those of several linear aliphatic PAs, such as PA 6.10,49–52 PA 4.13,18 PA 6.1249,51 or PA 6.18.49 Therefore, we assume that indexing of individual signals of the BrA-based polyamides should be the same as in the case of SA-based analogous polyamides. In this regard, we assume that the reflection signal located in the 2θ range of 3–7° arises from the 001 plane, while the signals appearing in the 2θ range of 18–25° coming from the 100 and 010/110 planes of the triclinic crystallographic form.49 To indicate the mentioned uncertainty regarding the assigned planes for further discussion, individual signals of BrA-based polyamides are marked in asterisks (*) as shown in Figure 7-10. In the diffractogram of PA6, several weak signals in the 2θ range of 6–14° were observed for all three PAs, PA6, 7 and 8, which might represent the crystallographic planes indexed as 00l. Again, the presence of IIDMA strongly influences the crystallographic structures of the BrA-based polyamides (PA7, PA8). When 18 mol % 1,6-HDA is replaced by IIDMA (PA7, Figure 7-10), the diffraction signal indexed as 010/110* planes was observed to shift from 24° to a significantly lower 2θ value of 21.8°, suggesting an increase of the inter-sheet distance (Table 7-5). Incorporation of 42 mol % of IIDMA completely changed the diffractogram, as evidenced by the diminishing of the 010/110* signal (in case of the SA-based polyamides, the complete change of the crystallographic structure has taken place only when the IIDMA content exceeds 49 mol %). Therefore, we observe a single reflection in the 2θ range of 18–25° meaning that the material had crystallized into a close to hexagonal form. Furthermore, upon introduction of IIDMA into PA 6.13, the 100* signals show a slightly increase of the 2θ values, which indicates a decrease of the interchain distance within one hydrogen-bonded β-sheet. Most probably the high IIDMA content disturbs the hydrogen-bonding to such a degree that the chains can approach one another.
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Figure 7-10. X-ray powder diffraction profiles of 1,6-hexamethylene diamine-, isoidide-2,5-dimethylamine-, and brassyllic acid-based polyamides.

Table 7-5. X-ray diffraction spacings of 1,6-hexamethylene diamine-, isoidide-2,5-dimethylamine-, and brassyllic acid-based polyamides.

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<th></th>
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<th>X-ray diffraction (°)</th>
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<tr>
<td></td>
<td>001*</td>
<td>100*</td>
</tr>
<tr>
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<td>3.67</td>
<td>20.57</td>
</tr>
<tr>
<td>PA7</td>
<td>3.61</td>
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</tr>
<tr>
<td>PA8</td>
<td>3.68</td>
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</table>

7.4 Conclusions

A combination of melt polymerization and solid state post-condensation (SSPC) has been used as a suitable route to synthesize two novel series of homo- and copolyamides based on the newly developed biobased isoidide-2,5-dimethyleneamine (IIDMA), 1,6-hexamethylenediamine (1,6-DAH), and the renewable sebacic acid (SA) or brassyllic acid (BA). The number-average molecular weights (Mn) of the synthesized polyamides are in the range of 3,900–49,000 g/mol. 1D and 2D NMR spectroscopy confirmed the exo-exo configuration of the IIDMA moieties in the resulting polyamides. Moreover, the combination of (VT) 13C[1H] CP/MAS NMR experiments with temperature dependent FT-IR analyses revealed that, as a result of the presence of isohexide building blocks in the backbone of the polyamides, the hydrogen bonding of these semicrystalline materials changed significantly compared to the linear PA 6.10 and PA 6.13. Due to less regular crystal
structures of the IIDMA-containing polyamides, enhanced thermal transitions between trans and gauche conformations of the alkyene moieties of the SA/BrA and 1,6-DAH were observed. Moreover, it was noticed that the IIDMA moieties are present in both the crystalline and amorphous phases of the copolyamides. Incorporation of the new isohexide-based diamine IIDMA in the linear PA 6.10 or PA 6.13, but on the one hand, enhances the glass transition temperature of the polyamides; on the other hand, lowers the melting temperatures by forming a less regular hydrogen bonded structure. Computational calculations revealed that contrary to our previous studies on DAIs- and DAII-based polyamides, where bicyclic diamines revealed several different conformers, the presence of methylene units between the isohexide and amide groups in IIDMA favors one stable “boat” conformation of the isohexide fragment. WAXD analysis showed that all the IIDMA-based homo- and copolyamides are semicrystalline materials. The crystallographic structures of the SA-based polyamides are dependent on the molar ratio of the IIDMA moieties. As an increasing incorporation of IIDMA, the crystallographic structures of the copolyamides transform from the triclinic form, as in the cases of PA 6.10, PA 6.13 and the co-PAs containing low contents of IIDMA, to a close to hexagonal form for copolyamides containing over 50 mol % of IIDMA units. This observation combined with a pronounced increase of the c-axis dimension of the copolymers proved the cocrystallization phenomenon of the comonomers in the same crystallographic lattice.

REFERENCES

Chapter 7

Epilogue

8.1 Highlights

Despite the various benefits of utilizing rigid isohexides as building blocks for step-growth polymers, the intrinsically low reactivity of the secondary hydroxyl groups is currently restricting their industrial application. The main target of this work is to try to overcome this drawback by developing new isohexide-based building blocks with combined rigidity and enhanced reactivity, which are suitable for step-growth polymer synthesis. Therefore, the contents of this thesis can be categorized into two aspects: firstly, the exploration of synthetic routes to prepare novel isohexide-based building blocks and secondly, the exploration of the polymerization of these new building blocks. Furthermore, their advantages/disadvantages with respect to the parent isohexides and the corresponding polymers have been investigated. Highlights of the major achievements and conclusions are summarized as follows:

1) By one-carbon-extension on the C2 and C5 carbon atoms of the isohexide skeleton, a new family of isohexide-based building blocks was developed from a key dinitrile intermediate, viz. isoididedinitrile (IIDN). The new IIDN-derived monomers are: isoidide-2,5-dicarboxylic acid (IIDCA) and its dimethyl ester (IIDMC), isoidide-2,5-dimethanol (IIDML) and isoidide-2,5-dimethyleneamine (IIDMA). After optimization of the respective synthetic routes, these building blocks can be obtained at a sufficient scale (>20 g/batch) and in high purity (>99.5%) suitable for polymerizations.

2) Three isomeric isohexide dinitriles were synthesized by base-induced epimerization. The strong non-nucleophilic organic base 1,8-Diazabicycloundec-7-ene (DBU) was found to be a suitable catalyst for such type of isomerization. A kinetic study on the epimerization of three dinitrile isomers revealed an equilibrium between the three possible isomers in THF. Single crystal X-ray diffraction studies demonstrated several structural characters of these
molecules regarding the symmetry and linearity. Density Functional Theory (DFT) calculations further supported the base-induced epimerization mechanism.

3) Three series of polyesters based on the novel 1-carbon extended isohexides were synthesized. The first series of polyesters is based on isoidide dicarboxylic acid (IIDCA) and linear alkylene diols with $M_n$ values between 7,000 g/mol and 14,000 g/mol. Unexpectedly, they have rather low $T_m$ (60–100 °C) values whereas the recorded low $T_g$ values (~30–18 °C) were more or less expected. The second series of polyesters is fully based on renewable, isohexide-derived monomers with $M_n$ values around 2,000–5,000 g/mol. Combination of both isohexide-based AA/BB monomers gave significantly higher $T_g$ values (45–85 °C) than the partially linear aliphatic polyesters of the first series. Importantly, this part of the project revealed the promising characteristics (reactivity, rigidity and thermal stability) of isoidide-2,5-dimethanol (IIDML) for potential applications in performance polymers with high $T_g$ and $T_m$. Therefore, the third series of polyesters was entirely focused on IIDML-based semi-aromatic systems. The $T_g$ and $T_m$ values of these polyesters were found to exceed even those of the conventional PET and PBT polyesters, confirming our expectation that IIDML is a promising rigid cyclic diol for engineering plastic applications.

4) Two series of semi-crystalline (co)polyamides were synthesized from the new isoidide 2,5-dimethyleneamine (IIDMA) or from a mixture of IIDMA and 1,6-hexamethylene diamine with the biobased dicarboxylic acids sebacic acid or brassylic acid. A combination of melt polymerization on nylon salts with solid-state polycondensation (SSPC) processes afforded the desired copolyamides with the highest number average molecular weight ($M_n$) of 49,000 g/mol. Analysis by temperature dependent solid state NMR and FT-IR spectroscopies revealed that the new diamine IIDMA exsit in both the crystalline and amorphous phases of the copolyamides. Given the sufficient high $T_m$ values (~200 °C) of the copolyamides containing less than 50% of IIDMA, these bio-based semicrystalline copolyamides can be useful for engineering plastic applications.

5) By comparing the thermal properties of the polymers based on the new isohexide-based building blocks, i.e. IIDCA, IIDML and IIDMA, with relevant reference polymers, systematic structure-thermal properties studies of each series of polymers were conducted. This work objectively evaluated the relative rigidities, as well as reactivities and thermal stabilities of these new building blocks with respect to those of the parent isohexides, as well as with respect to their linear, cyclic aliphatic and aromatic analogues.

6) Both the experimental (i.e., single crystal X-ray diffraction) and computational-aided methods (i.e., Density Functional Theory (DFT)) were employed to elucidate the structural characteristics of the isohexide-based building blocks, as well as to understand the specific thermal properties of the polymers based thereon.
This work concerns a pioneering study of deoxy-1-carbon-extended iso-hexide-based building blocks. All the monomers and polymers synthesized, characterized and evaluated in this thesis are entirely new. Suitable synthetic laboratory-scale protocols were developed for all the monomers and polymers. The reported study of the structure-thermal properties relations, as well as the crystal structure elucidation by single crystal X-ray diffraction and DFT, are also of high importance concerning the field of iso-hexide-based polymers and will certainly prove to be very useful for drawing conclusions on the industrial feasibility of such bio-based materials.

8.2 Technology assessment

A significant part of the commercialized synthetic polymers are step-growth polymers derived from various AA or AB types of monomers. Given that most of the research interest regarding iso-hexides in the field of polymer chemistry is concentrated on step-growth polymers, it is obvious that the novel iso-hexide-based AA monomers and the step-growth polymers based thereon, and disclosed in this thesis, may have a certain industrial relevance.

Concerning the synthetic route of the 1-carbon extended iso-hexides, several stoichiometric steps were adopted in this thesis, which are obviously not viable for industrial applications. For this pioneering study, considering the rather high requirements of achieving, respectively retaining regio- and stereo-selectivity during the synthesis of these compounds, it is believed that the protocol involved in this study is a fast and efficient method for supplying the desired monomers in sufficient quantities and purities in short term on laboratory scale. Exploration of more sustainable and industrially-applicable catalytic routes towards these C2 and C5 carbon extended iso-hexides can be conducted in the future, particularly for the molecules showing sufficient commercial potential. In addition, some key steps of atom-efficient catalytic routes have been investigated by our collaborators from the University of Amsterdam. More progress regarding this issue will most likely be revealed in the future.

With regard to the polymerization methods, we particularly focused on industrially relevant melt polymerization and solid state post-condensation (SSPC). All of the polymers obtained in this work were synthesized by such methods instead of using methods with less industrial applicability, such as solution or interfacial polymerizations. Moreover, for all the polymerizations careful attention was payed to color formation and thermal decomposition of the monomers and polymers. These issues could be crucial factors limiting the industrialization of these monomers and step-growth polymers. Therefore, most of the selected polymerization methods are rather mild to ensure that most of the important polymers can be obtained with low discoloration and minimal thermal decomposition.
Poly(alkylene isoidide dicarboxylate)s (PE-nIIDCs, Chapter 4) have rather low $T_m$ (60–100 °C) and $T_g$ (~30–20 °C) values, which does not make them very suitable to be used as engineering and high-performance plastics. The potential applications of these polymers might be in the compostable packaging or biomedical field, comparable to e.g. the commercial polycaprolactone (PCL) which also has a rather low $T_m$ (60–70 °C) and $T_g$ (~60°C). A second relevant commercial reference is poly(butylene succinate) (PBS, Bionolle®, Showa Denko). Despite the relatively low $T_g$ (~32 °C) and $T_m$ (113 °C) values, PBS is been widely used in packaging, agricultural and biomedical products. Poly(alkylene isoidide dicarboxylate)s are expected to be suitable for similar applications, but for the time being it is difficult to indicate advantages of the poly(alkylene isoidide dicarboxylate)s over the mentioned commercial counterparts.

The fully isohexide-based polyesters developed in Chapter 5 display rather high $T_g$ values (48–86 °C), which are within the required range of powder coating resins. The fully aliphatic character of these polyesters predicts good UV-resistance properties for outdoor applications. Moreover, given the high water uptake tendency of isohexide moieties, the fully isohexide-based polyesters are expected to be easily dispersible in water. This is interesting, since currently water-borne coatings exhibit an enormous growth at the expense of solvent-based coatings. The expected favorable water dispersion performance implies that relatively low amounts of external surfactants will be required for obtaining stable emulsions, which is an advantage since surfactants tend to deteriorate the physical and mechanical properties of water-borne coatings. Therefore water-borne coating systems might also be a possible application area for these polyesters. Whether the hygroscopic nature of the fully isohexide-based materials negatively influences the properties in humid environments remains to be seen. If the applied cross-linking chemistry is very efficient the problems might be limited.

For the series of semi-aromatic polyesters described in Chapter 6, given the high $T_g$ (~95°C) and $T_m$ (~250°C) of the fully bio-based polyester derived from furan-2,5-dicarboxylic acid (2,5-FDA), as well as the promising thermal characteristics of the terephthalic acid (TA)-based polyester, a broad range of engineering plastics applications should be well within reach. In view of the comparable crystallization window of IIDML-based semi-aromatic polyesters ($T_m-T_g = 185$ °C for poly(isoidide 2,5-methylene terephthalate; 155 °C for poly(isoidide 2,5-methylene furan-2,5-dicarboxylate) to that of the commercialized PET ($T_m-T_g = -175$ °C), heterogeneous nucleation can be considered to facilitate the crystallization from the melt of these polymers if necessary.

Proportional incorporation of isoidide-2,5-dimethylene amine (IIDMA) into the known nylon 6,10 and nylon 6,13 yielded two series of predominantly bio-based polyamides. Given the relatively high molecular weights, $T_g$ (up to 67 °C) and $T_m$ (approximately 200 °C) values
of the polyamides derived from IIDMA, a broad range of engineering plastics applications should be within reach, especially for those copolyamides containing ≤ 50 molar % IIDMA. The decrease of melting temperatures with respect to those of nylon 6,10 and 6,13 by 20 °C can have advantages in lowering the processing temperature, minimizing thermal degradation, as well as saving energy during the industrial processing of such type of polymers. Moreover, the possible improved water uptake character of IIDMA-based (co)polyamides with respect to the very non-polar 6,10 and (especially) 6,13 can be beneficial for providing a higher wearing comfort of clothes based thereon.

### 8.3 Outlook

The major contribution of this thesis to isohexide chemistry is the exploration of a new area by developing a family of 2/5 carbon-extended building blocks. According to the preliminary results elucidated in this thesis, different types of polymers derived from these new building blocks have shown diverse thermal properties, some of which might be promising for certain industrial applications. However, this work is basically only the starting point of such an exciting area. There are various remaining questions with regard to the work presented in this thesis, such as the thermal degradation mechanism of IIDCA/IIDMC-based polyesters and polyamides, and (bio)degradability as well as mechanical properties of the synthesized polymers. For future work, among all the newly developed building blocks, the 2,5-methylene-extended diol, i.e. isoidide-2,5-dimethanol (IIDML), is certainly the most promising monomer deserving subsequent detailed investigations within the scope of engineering plastic applications well as other possible areas. With respect to the well-known isosorbide and isoidide building blocks this molecule combines a good balance between improved reactivity and structural rigidity with sufficient thermal stability, and therefore is believed to be a successful example showing how to rationally design and develop novel types of bio-based building blocks. Further investigations on the synthesis and thermo-mechanical properties of various potential IIDML-based polymers might open up additional valuable findings. Given the infinite possibilities of the combination of all these new renewable building blocks with others, numerous bio-based homo- or co-polymers can be the potential targets for future research, even possibly outperforming their petro-based counterparts. Last but not least, exploration of more sustainable and industrially relevant catalytic routes to produce the monomers is certainly a crucial issue which needs to be solved before their commercialization can be turned from a dream into reality.
Chapter 8
Appendix A
-Supporting Information of Chapter 1-

Scheme A-1. Synthetic routes of diaminoisoidide (DAII).
**Scheme A-2.** Schematic presentation of the synthesis of diisocyanatoisoidide (IIDI) from diaminoisoidide HCl salt (DAII HCl salt) and diaminoisoidide (DAII).109

**Scheme A-3.** Schematic representation for the synthesis of 5-deoxy-5-isocyano-isoidide.110
Scheme A-4. Preparation of diisocyanatoisoidide (IIDI) via non-isocyanate route.¹⁰⁹
Appendix B
-Supporting Information of Chapter 2-

Table A-1. Methanolic hydrolysis of 3

![Chemical structure diagram](image)

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<td>trace</td>
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<td>trace</td>
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[a] All the reactions were conducted in methanol at reflux temperature. Detailed reaction conditions: 1. H₂SO₄ (10 equiv., 98 %); 2. H₂SO₄ (10 equiv., 98 %), H₂O (4.6 equiv.). 3. H₂SO₄ (20 equiv., 98 %). 4. Methanolic HCl (3N, 20 mL). 5. HCl (37 %)/MeOH = 1:1 mixture. [b] Data derived from GLC analysis.

Figure B-1. Packing pattern and hydrogen bonding of isoididie dicarboxylic acid (IIDCA).
Table B-2. Structures and cartesian coordinates (in Å) of optimized structures at the BP86/TZ2P level.

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<th>side and top view</th>
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Appendix C

-Supporting Information of Chapter 3-
Figure C-1. 2D-COSY NMR spectra of isohexide dinitriles.

Figure C-2. Anion of ISDN shown from the side (left) and top (right) in the gas phase. Negatively charged carbon atom is highlighted. (BP86/TZ2P).
Table C-1 Atomic charges (in electrons) of the three isohexide dintrile isomers and the anions thereof.

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<th>Idide</th>
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*Atomic Voronoi Deformation Density (VDD) Charges have been computed at the BP86/TZ2P level of theory using COSMO to estimate the solvent effects by THF. See Ref 69 for the (VDD) charges.*
Table C-2 Cartesian coordinates of the three isohexide dinitrile isomers computed at BP86/TZ2P.

A) Cartesian coordinates of IIDN

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B) Cartesian coordinates of the anion of IIDN

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D) Cartesian coordinates of the anion of ISDN

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Appendix D
-Supporting Information of Chapter 4-

Figure D-1. TGA derivative curves versus temperature ranging from 30–600 °C. (a) TGA curves of the poly(alkylene isoididedicarboxylate)s; (b) TGA curves of the poly(alkylene adipate)s.
Figure D-2. Energy barrier (kcal/mol) of rotation around the ester bond of IIDCA and Galx (C–C bond is shown in red).
Figure E-1. $^{13}$C NMR and 2D COSY spectra of poly(isosorbide isoididedicarboxylate).
Figure E-2. $^{13}$C and $^1$H NMR spectra of poly(isoididedimethlyene adipate) (PleA).
**Figure E-3.** First DSC cooling curves of the fully isohexide-based polyesters recorded from –50 °C to 180 °C at the heating rate of 10 °C/min.
Appendix F

-Supporting information of Chapter 7-

Figure F-1. 2D COSY spectrum of the polyamide derived from IIDMA and SA (PA5).
Figure F-3. Variable-temperature FT-IR spectra of the copolyamide PA 2 recorded on heating from 30 °C to above the melting point. The copolymer was synthesized from SA, IIDMA, 1,6-DAH with IIDMA/1,6-DAH molar ratio 0.26/0.74.

Figure F-2. Variable-temperature FT-IR spectra of the copolyamide PA 7 recorded on heating from 30 °C to above the melting point. The copolymer was synthesized from BrA, IIDMA, 1,6-DAH with IIDMA/1,6-DAH molar ratio 0.16/0.84.
Conformational Analysis and NMR chemical shifts calculation

In order to interpret the experimental $^1$H and $^{13}$C chemical shifts of the IIDMA fragment, the NMR calculations were carried out for a simplified model with Pr-CO-NH-CH$_2$- groups terminating the IIDMA fragment from both sides. In addition, we have replaced the propyl groups by methyl groups in the initial conformational search procedure.

In general, the conformational diversity of the IIDMA moiety itself is similar to the chair/boat-like conformations of cyclohexane$^1$ and was already discussed in our previous work.$^{2,3}$ Analogously to the previous work,$^{2,3}$ we have defined UU and DD as the conformations of a normal boat and an inverted boat, whereas both CH$_2$ groups are bent either up or down with respect to the protons 5 and 5a, which are, in turn, pointing down in all cases. Consequently, UD and DU conformations do represent the mirrored chair-conformations. Fixing the possible conformations of the IIDMA unit to one of the conformations (DD, DU, UD, or UU) by varying the torsional angle $\phi_1$ (see Figure F-4), the energy profiles of IIDMA were obtained, which were summarized in Fig. S4. The variation of the torsional angle $\phi_1$ was performed in counter-clockwise steps of 15° where, during energy minimizations, the conformation of the IIDMA core was fixed, while the rest of the fragment was unrestricted to relaxation. The sampled energy points were further used to plot 1D-PES curves (Figure F-4, right), i.e. for each geometry and angle $\phi_1$ the lowest energy conformation was selected. An extensive quantum-chemical conformational analysis (via B97-D functional with Grimme dispersion correction$^4$ and 3ζ basis set 6-311G**) revealed only one most abundant conformer (as depicted in Figure F-4), which was further submitted to the NMR chemical shifts calculation at the B97-D/6-311G** level of theory. All other found conformers were lying higher in energy by roughly 10 kJ/mol and above.
Figure F-4. Conformational search scheme for the different boat and chair conformations (DD, DU, UD, and UU) of the isohexide unit (left) and corresponding 1D potential energy plots (right). For clarity only methyl groups have been attached. Since, the torsional angle variation \( \phi_1 \) and \( \phi_2 \) do not affect each other, for a simplicity reason, only \( \phi_1 \) was varied.

References
Acknowledgment

It took me long time to start this part. Every scene of the last four years keeps floating through my mind like playing a movie. I tried my best to keep the rest of thesis as rational as possible. For this part, I would like to express my sincere feelings to all the people that I appreciate.

I must thank my promoter Cor Koning, without whom this thesis would definitely not become completion. Cor, to me you are a great “boss” and a nice friend. Although most of the molecules involved in this project were not as “friendly” as the project name (GREENER), I was so touched by your endless understanding and trust, motivating me to be strong and confident. You offered me not only enlightening suggestions, but also a lot of freedom to carry out my rational/absurd ideas, as well as unconditional support. You are happy that I am now a polymer chemist, thank you for bringing me to this wonderful field. I deeply know this is a just starting point and I still have a long way to go. Cor, thank you for everything.

Secondly, my sincerest gratitude goes to my co-promoter Daan van Es from FBR. Daan, I still remember the first day you picked me up at Schiphol and carried my 30 kg suitcase to my room, very warm scenario. I enjoyed so much of our discussions and daily communications. You are such a great coach, always being kind and optimistic. Never complained but only wanted to help. Discussion with you is always inspiring, and I learned a lot about how to critically and creatively think (at least still trying). Thanks for all the efforts and time spent for manuscript and thesis writing.

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Jing Wu
乌婧
2012/9
Curriculum Vitae

Jing Wu was born on the 27th of May 1984 in Chifeng, China. After finishing her high school education in 2001, she started her bachelor studies on Pharmaceutical Science at the faculty of Pharmaceutical Science and Technology of the Tianjin University in China. In June 2005, she graduated within the group ‘medicinal chemistry’ of Prof. Jian Song on the research entitled: ‘Optimization of the synthetic route of Iohexol by varying synthetic methods and reaction conditions’. In September 2005, she started her master studies at the college of Chemistry of the Nankai University in Tianjin, China. From January 2006 to June 2008, she worked as a researcher on her master dissertation entitled ‘Design, synthesis and biological Study of novel ketol-acid reductoisomerase (KARI)’ within the group ‘pesticide chemistry’ under the supervision of Prof. Zheng-ming Li and Dr. Bao-lei Wang at the State Key laboratory of Elemento-organic chemistry of Nankai University.

In September 2008, she started her PhD project under the supervision of Prof.dr. Cor E. Koning at the Laboratory of Polymer Chemistry (SPC, now renamed as Laboratory of Polymer Materials, SPM) of the Eindhoven University of Technology (TU/e). The research was sponsored by the Dutch Polymer Institute (DPI), and was carried out in collaboration with the Food & Biobased Research (FBR, part of the Wageningen University and Research Center, WUR). From September 2008 to April 2011, she worked at FBR for developing the novel bio-based building blocks as well as the preliminary investigation of polymerizations. Dr. Daan. S. van Es was her coach during this period. In April 2011, she moved to Eindhoven and started to work in SPC focusing on polymer development. Dr. Bart A.J. Noordover and Dr. Lidia Jasinska-Walc were her coaches in SPC. The most important results of the studies obtained at both FBR and SPC are described in this thesis.
List of Publications

Scientific papers:


5. S. Thiyagarajan, J. Wu, D. S. van Es, J. van Haveren. Rigid bicyclic AB-type monomers for fully isohexide based aliphatic polyesters. to be submitted.


Patents


2. J. Wu, P. Eduard, D. S. van Es. Polymer, process for producing such polymer and composition comprising such polymer. DPI 12.002 1C to the Dutch Polymer Institute (filed in October 2012)
Conference proceedings


5. L. Jasinska, M. Villani, **J. Wu**, D. S. van Es, S. Rastogi, C. E. Koning. Diaminoisoidide as a renewable monomer for the synthesis of polyamides with natural origin. *Polycondensation 2010* proceeding, 82-83
