ABSTRACT: In this study we describe the synthesis of bis-pyrrolidone based dicarboxylic acids from itaconic acid and their application in 2-oxazoline resins for fully renewable thermoset materials. The monomers are obtained using a bulk aza-Michael addition of a diamine and two itaconic acid molecules using a catalytic amount of water. The monomers can be isolated in high purity after recrystallization, though their yield proved to be highly dependent on the selected diamine spacer length: In general, only the dicarboxylic acids containing diamines with an even number of methylene spacers are isolated in high yields. Through NMR, GPC, and FTIR analysis we demonstrate that these bis(pyrrolidone) based dicarboxylic acids exhibit significantly enhanced curing rates in 2-oxazoline resins compared to resins containing aliphatic dicarboxylic acids such as sebacic acid. Overall, we demonstrate that the rate of 2-oxazoline ring-opening addition with carboxylic acid functionalities is determined by the used dicarboxylic acid, whereas the ring-opening addition of the 2-oxazoline functionality with amide groups is determined by the used bis(2-oxazoline) compound. The thermosets obtained after curing proved to be readily plasticized by water, opening up possibilities for enzymatic degradation.

KEYWORDS: Bis(2-oxazoline), Itaconic acid, Pyrrolidone, Thermoset

INTRODUCTION

With the continuous growth of the plastic industry, an increasing amount of resources will be required for the production of polymeric materials in the future. To this end, both academia and industry have a strong focus to develop renewable, recyclable, and/or degradable polymer materials that can ensure the sustainability of the polymer industry. Particular monomers that contribute to this endeavor are the renewable 2,5-furandicarboxylic acid, and itaconic acid. 2,5-Furandicarboxylic acid, generally obtained from hydroxymethyl furfural or its derivatives, has proven to exhibit excellent gas permeability properties in thermoplastic materials and has also proven applicable for thermosetting resins. Itaconic acid, having two carboxylic functionalities combined with the presence of a vinyl group, has proven to be of interest for the synthesis of renewable polyesters, polyester resins, polyamides, and other polymers. One particularly interesting application of itaconic acid is its ability to undergo the aza-Michael addition reaction with amines, followed by ring closure and the generation of a carboxylic acid functionalized pyrrolidone ring. The resulting pyrrolidone based carboxylic acids are readily polymerized using conventional polycondensation methods, generally yielding amorphous and degradable polymer materials. In particular, the degradable nature of these carboxylic acids makes them interesting candidates for application in resins, as this opens up possibilities for chemical recycling or full biodegradation of thermoset materials.

Though 2-oxazoline chemistry is often used to develop polymers for (bio)medical applications, as is reported by the groups of Hoogenboom, Luxenhofer, and Nuyken, they are promising candidates for curing in resins for coatings or thermosets as they are highly reactive toward ring-opening addition with amines and carboxylic acid groups. One particular challenge in the field of 2-oxazolines is related to their sustainability, as most widely used synthesis routes to obtain the 2-oxazoline moiety require nitriles, haloalkylamides, or aziridines as starting materials. That being said, an eco-friendly synthesis route involving the bulk amidation and consecutive ring formation of a carboxylic acid with an amino alcohol is known, yielding the oxazoline functionality with only water as a reaction product.
Resins containing bis(2-oxazoline)s and dicarboxylic acids are known to undergo a thermal ring-opening addition polymerization reaction, generating poly(ester-amide)s, which has been earlier communicated by groups of Bohme, Sano, and others. In previous work we have demonstrated that the application of renewable monomers in 2-oxazoline resins (Scheme 1). In turn, the generated amide groups are participating in a ring-opening addition reaction with 2-oxazoline moieties, thereby forming tertiary amide bonds (k1 in Scheme 1). In fact, this mechanism is responsible for the cross-linking of the 2-oxazoline resins, where the cross-link density is controlled by the excess of bis(2-oxazoline) monomer. In previous work we have demonstrated that the application of renewable monomers in 2-oxazoline resins can be beneficial for the curing process: Besides being renewable in nature, the application of a 2,5-FDCA based bis(2-oxazoline) (FDCAox) was shown to be selectively enhancing this cross-linking reaction, thereby significantly suppressing the required curing time.

In the present study we evaluate the performance of itaconic acid based bis(pyrrolidone) dicarboxylic acid monomers in 2-oxazoline resins (Scheme 1). The effect of the dicarboxylic acids on the curing process is explored using NMR spectroscopy, FTIR spectroscopy, and GPC chromatography. Additionally, the thermal behavior of the developed thermosets is investigated while particular attention is paid to the plasticizing effect of water in these materials. Lastly, preliminary enzymatic degradation studies are performed to evaluate whether these thermosets can be depolymerized in nature.

**EXPERIMENTAL SECTION**

**Materials.** Itaconic acid, 1,2-diaminoethane, 1,3-diaminopropane, 1,4-diaminobutane, 1,5-diaminopentane, 1,6-diaminohexane, 1,7-diaminoheptane, 1,8-diaminoctane, 1,9-diaminononane, 1,10-diaminodecane, and 1,12-diaminododecane were purchased from Sigma-Aldrich. Sebacic acid (SeA), 2-chloroethylamine hydrochloride, triphenylphosphite (TPP), thionyl chloride, sodium hydroxide, and potassium phosphate (K3PO4) were purchased from Sigma. Itaconic acid (9.02 g, 0.069 mmol) and 1,8-diaminooctane (1.25 g, 0.003 mmol) were added to a 100 mL round-bottom flask. The mixture was heated to 130 °C and was allowed to stir for 18 h in the presence of a catalytic amount of distilled water to yield a yellow viscous liquid. The product was obtained as white crystals after recrystallization from a mixture of methanol and ethyl acetate, followed by filtration and drying in vacuo overnight at 50 °C. The yield of the synthesized monomer is shown in Table 1. The yield is measured gravimetrically, while the purity is traced with 1H NMR. 1H NMR analysis (CDCl3 + δ-D-TFA, 300 MHz): δ 3.80 (m, 4H), 3.44 (m, 4H), 3.31 (m, 2H), 2.99 (d, 2H, J = 7.9 Hz), 1.57 (m, 4H), 1.30 (m, 8H). 13C NMR (CDCl3 + δ-D-TFA, 300 MHz): δ 178.2 (C=O), 175.0 (NC=O), 49.7 (NCH2 ring), 43.4 (NCH2 spacer), 35.7 (CH ring), 33.8 (CH2 ring), 28.6 (CH2 spacer), 26.5 (CH2 spacer), 26.1 (CH2 spacer).

| Entry | Yield (%) | Tm (°C) | Tg (°C) | Td (°C) |
|-------|-----------|---------|---------|---------|
| BP-C2 | 95        | 238     | 48.5    | 272     |
| BP-C3 | 90        | 194     | 31.3    | 269     |
| BP-C4 | 85        | 196     | 24.1    | 274     |
| BP-C5 | 65        | 156     | 22.3    | 275     |
| BP-C6 | 75        | 181     | 18.7    | 272     |
| BP-C7 | 85        | 153     | 12.6    | 274     |
| BP-C8 | 30        | 81      | 4.9     | 271     |
| BP-C9 | 90        | 131     | 3.1     | 274     |
| BP-C10| 90        | 145     | 3.7     | 271     |

*Yield determined after purification by recrystallization. Determined from the DSC analysis, whereas the peak melting temperature (Tm) is determined from the first heating run and the glass transition temperature (Tg) is determined from the second heating run. Thermal degradation temperature determined from TGA analysis, where the Td denotes the onset point for degradation.*
For the detailed overview of the synthesis and NMR analysis of the BP-Cₙ monomers, we refer to the Supporting Information.

General Melt Polymerization Procedure. Reaction mixtures containing the desired molar ratio of BP-Cₙ and bis(2-oxazoline) were mixed using a mortar and pestle. When desired, 1 wt % of triphenyl phosphite (TPP) was added as catalyst. The obtained reaction mixtures were polymerized on small scale (10 mg in a HPLC vial) or were polymerized on a 3 g scale after loading into a 250 mL round-bottom flask fitted with a mechanical stirrer. The polymerizations were performed at 180 °C for 60 min to ensure full conversion. Regular sampling was performed to monitor the reaction over time.

Characterization Methods. ¹H NMR and ¹³C NMR spectroscopy was performed with a Bruker Ultrashield 300 spectrometer (300 MHz magnetic field). Samples were prepared by dissolving 10 mg of monomer or polymer in 0.5 mL of deuterated dimethyl sulfoxide (DMSO-d₆), in a mixture of deuterated chloroform (CDCl₃) and deuterated trifluoroacetic acid (TFA-d), or in deuterated dimethylformamide (DMF-d₇). All spectra were referenced against tetramethylsilane (TMS).

Molecular weight of the synthesized poly(ester amide)s was determined via gel permeation chromatography (GPC). The polymers (5.0 mg) were dissolved in 1.5 mL of 1,1,1,3,3,3-hexafluoropropanol (HFIP) containing 0.019% sodium trifluoroacetate. After full dissolution, the mixtures were filtered over a 0.2 μm PTFE syringe filter before injection. The GPC apparatus was calibrated with poly(methyl methacrylate) standards. Two PFG combination medium microcolumns with 7 μm particle size (4.6 mm × 250 mm, separation range 100–1,000,000 Da) and precolumn PFG combination medium with 7 μm particle size (4.6 mm × 30 mm) with refractive index detector (RI) were used in order to determine molecular weights and dispersities.

Thermal stability of the BP-Cₙ monomers and poly(ester amide)s synthesized in this study was evaluated using thermogravimetric analysis (TGA). Experiments were performed on a TA Instruments TGA Q500 in a nitrogen rich atmosphere. Samples were heated from 20 to 700 °C, at a heating rate of 10 °C/min. Differential scanning calorimetry (DSC) was performed to identify the thermal transitions of the developed materials using a TA Instruments DSC Q2000. Two heating and cooling runs were performed at heating and cooling rates of 10 °C/min. The melting temperature (T_m) was determined from the first heating run while the glass transition temperatures of the BP-Cₙ monomers were determined from the second heating run.

Enzymatic Depolymerization and Solubilization Procedures. The solubility and enzymatic degradation were evaluated on the developed thermosets obtained after curing of an equimolar mixture bis(2-oxazoline) and BP-Cₙ monomers for 1 h at 180 °C. In general, 30 mg of the thermoset was added to water or tris buffer solution (1 mL, 100 mM, pH 8), with or without Bacillus Sp (0.8 mL, 16 units/mL, Sigma-Aldrich) enzyme. The enzyme was added to the polymer

“For the detailed overview of the synthesis and NMR analysis of the BP-Cₙ monomers, we refer to the Supporting Information.”

“General Melt Polymerization Procedure. Reaction mixtures containing the desired molar ratio of BP-Cₙ and bis(2-oxazoline) were mixed using a mortar and pestle. When desired, 1 wt % of triphenyl phosphite (TPP) was added as catalyst. The obtained reaction mixtures were polymerized on small scale (10 mg in a HPLC vial) or were polymerized on a 3 g scale after loading into a 250 mL round-bottom flask fitted with a mechanical stirrer. The polymerizations were performed at 180 °C for 60 min to ensure full conversion. Regular sampling was performed to monitor the reaction over time.”

“Characterization Methods. ¹H NMR and ¹³C NMR spectroscopy was performed with a Bruker Ultrashield 300 spectrometer (300 MHz magnetic field). Samples were prepared by dissolving 10 mg of monomer or polymer in 0.5 mL of deuterated dimethyl sulfoxide (DMSO-d₆), in a mixture of deuterated chloroform (CDCl₃) and deuterated trifluoroacetic acid (TFA-d), or in deuterated dimethylformamide (DMF-d₇). All spectra were referenced against tetramethylsilane (TMS).”

“Molecular weight of the synthesized poly(ester amide)s was determined via gel permeation chromatography (GPC). The polymers (5.0 mg) were dissolved in 1.5 mL of 1,1,1,3,3,3-hexafluoropropanol (HFIP) containing 0.019% sodium trifluoroacetate. After full dissolution, the mixtures were filtered over a 0.2 μm PTFE syringe filter before injection. The GPC apparatus was calibrated with poly(methyl methacrylate) standards. Two PFG combination medium microcolumns with 7 μm particle size (4.6 mm × 250 mm, separation range 100–1,000,000 Da) and precolumn PFG combination medium with 7 μm particle size (4.6 mm × 30 mm) with refractive index detector (RI) were used in order to determine molecular weights and dispersities.”

“Thermal stability of the BP-Cₙ monomers and poly(ester amide)s synthesized in this study was evaluated using thermogravimetric analysis (TGA). Experiments were performed on a TA Instruments TGA Q500 in a nitrogen rich atmosphere. Samples were heated from 20 to 700 °C, at a heating rate of 10 °C/min. Differential scanning calorimetry (DSC) was performed to identify the thermal transitions of the developed materials using a TA Instruments DSC Q2000. Two heating and cooling runs were performed at heating and cooling rates of 10 °C/min. The melting temperature (T_m) was determined from the first heating run while the glass transition temperatures of the BP-Cₙ monomers were determined from the second heating run.”

“Enzymatic Depolymerization and Solubilization Procedures. The solubility and enzymatic degradation were evaluated on the developed thermosets obtained after curing of an equimolar mixture bis(2-oxazoline) and BP-Cₙ monomers for 1 h at 180 °C. In general, 30 mg of the thermoset was added to water or tris buffer solution (1 mL, 100 mM, pH 8), with or without Bacillus Sp (0.8 mL, 16 units/mL, Sigma-Aldrich) enzyme. The enzyme was added to the polymer.”
together with a CaCl₂ solution (0.01 M) at 50 °C in order to enforce depolymerization and dissolve the poly(ester amide) thermosets.58−60

RESULTS AND DISCUSSION

Bis(pyrrrolidone) Based Dicarboxylic Acid (BP-Cₓ) Synthesis. Previous reports on bis(pyrrrolidone) based dicarboxylic acids from itaconic acid and different aliphatic diamine spacers (Scheme 2) often involve synthesis from water as both reaction medium and catalyst.11,15 These dicarboxylic acids, generally obtained as viscous oily liquids, can be used directly for polymerization or are first isolated after several trituration steps.15 One potential problem with these methods is that residual unreacted primary or secondary amine groups may be present in the final product. The presence of such amine impurities is detrimental for thermal curing polymerizations with 2-oxazolines as they are known to negatively affect the reactivity of the mixture.61 Additionally, the presence of unreacted itaconic acid or amines will affect the stoichiometry and might hamper build-up of molecular weight. For this purpose, we have slightly modified the synthesis and purification methods provided in the literature.11,15 First the synthesis is performed in bulk at 130−180 °C in the presence of a catalytic amount of water. After reaction overnight, the formed oily yellow liquid is subjected to reduced pressure to remove the water generated during the reaction. Second, the monomers are dissolved and recrystallized from a methanol/ethyl acetate mixture to obtain them in high purity.

NMR spectroscopy analysis was used to confirm the structure and purity of the synthesized BP-Cₓ monomers. Figure 1 shows the HSQC and 1H NMR spectra for the BP-C₄ monomer as a representative example. In general, the signals of the methylene units between the pyrrolidone groups are found at 1.3, 1.7, and 3.3−3.4 ppm (signals 8, 7, and 6, respectively, in Figure 1) where the resonances 6′ and 6″ are split due to their interaction with the neighboring carbonyl of the pyrrolidone ring. Similarly, the presence of the pyrrolidone ring is detected by the resonances found around 3.3 ppm (signal 2), 3.0 ppm (signal 3), and 3.8 ppm (signal 5). Although the carbonyl signals in the pyrrolidone rings (signals 1 and 4) are not displayed in Figure 1 they are found at 178 and 175 ppm, respectively, in 13C NMR analysis. Overall, from NMR analysis we observe that the inclusion of recrystallization steps in our adapted synthesis and purification method yields the desired compounds with good purity as no traces of impurities were detected. For detailed NMR analysis of the other BP-Cₓ monomers, we refer to the Supporting Information.

With respect to the yield of the monomers after purification, we observe that the recrystallization process proceeds rapidly and results in high isolated yields for monomers with short (BP-C₂, BP-C₄, and BP-C₆) or long (BP-C₁₀ and BP-C₁₂) diamine spacers. However, recrystallization proved more challenging for the BP-Cₓ monomers having 5−9 methylene spacers between the pyrrolidone rings. Especially when using odd diamine spacers, recrystallization from solvent proved challenging, resulting in decreased isolated yields as is visible from Table 1. In fact, the BP-Cₓ monomer proved impossible to crystallize using the described purification procedure, even upon prolonged recrystallization times at −20 °C.

The obtained BP-Cₓ crystallites were tested for their thermal stability and melting behavior using TGA and DSC analysis. Overall, the monomers are stable up to temperatures well above their melting temperatures (Figure 2 and Table 1): In general, an onset of degradation is observed around 270 °C for all monomers, and no significant weight loss is detected below 250 °C. With respect to the thermal transitions prior to degradation, the BP-Cₓ monomers display distinct melting behavior (T_m) during the first heating run in DSC analysis. During the second DSC heating run, cold-crystallization and consecutive melting are observed only for the BP-C₂, BP-C₆, and BP-C₁₂ monomers, as is displayed in Figure 3A for BP-C₂. All other monomers do not crystallize within the time provided by the DSC analysis methods, but instead display a characteristic glass transition temperature (T_g). The presence of such a T_g likely originates from the hydrogen bonding between dicarboxylic acid groups, resulting in long-range order. Indeed, this seems to be the case as the T_g of the BP-Cₓ monomers (Figure 3B) decreases rather linearly with the hydrogen bonding density of the carboxylic acid groups, as is explained in the Supporting Information.

An overview of all the peak melting temperatures observed during the first heating run and the glass transition temperatures observed during the second heating run is depicted in Figure 3B. In general, the melting temperature of the BP-Cₓ monomers decreases with increasing methylene spacer length. For example, the BP-C₂ monomer exhibits a peak melting temperature at 238 °C, whereas the BP-C₁₂ monomer melts already at 145 °C. Additionally, a characteristic odd−even effect26,63 is observed: The BP-C₄ monomers with an odd amine spacer are displaying significantly lowered melting temperatures compared to those of the BP-Cₓ monomers containing even diamine spacers. This low melting temperature of BP-Cₓ monomers with odd amine spacers explains their previously observed low isolated yield: BP-Cₓ monomers with odd amine spacers can only form crystallites with defects and thus low melting temperatures during recrystallization from solvent. As a consequence, crystal growth is significantly hindered, thereby lowering the isolated yield after recrystallization.

Overall, on the basis of the synthesis procedure and the behavior of the synthesized BP-Cₓ monomers, we can conclude that the modified bulk synthesis allows for upsampling in good yield when using diamine spacers that generate high melting BP-Cₓ monomers.

Curing Performance of BP-Cₓ Monomer in 2-Oxazoline Resins. The BP-Cₓ monomers were used as dicarboxylic acid for the preparation of 2-oxazoline resins. To avoid the use of

Figure 2. Offset TGA thermograms depicting the thermal stability of the various BP-Cₓ monomers developed in this study. The applied heating rate for the TGA experiments was 10 °C/min.
solvents, the monomers were ground in the solid state and polymerized in bulk. In this study, the evaluated bis(2-oxazoline) monomers are 1,3-bis(4,5-dihydrooxazol-2-yl)benzene (IAox) and the renewable 2,5-bis(4,5-dihydrooxazol-2-yl)furan (FDCAox). An overview of the used monomers for polymerization reactions is provided in Scheme 3. The characteristic polymerization reaction of BP-C\textsubscript{x} monomers with FDCAox is depicted in Scheme 1. In general, the ring-opening polyaddition reaction between dicarboxylic acids and bis(2-oxazoline)s (k\textsubscript{1}) yields linear poly(ester-amide)s.\textsuperscript{57} However, the formed amide bond is susceptible to reaction with another 2-oxazoline moiety (k\textsubscript{2}), thereby providing the means to generate branched or cross-linked structures. In previous work we have demonstrated that the branching and cross-linking reaction is highly dependent on the selected bis(2-oxazoline spacer): To recall, the amorphous 2,5-furandicarboxylic acid based amide groups are highly susceptible to participation in a branching reaction with a 2-oxazoline.\textsuperscript{57}

The curing performance of the BP-C\textsubscript{x} monomers in 2-oxazoline resins was tested in equimolar systems containing either FDCAox or IAox. As reference, the reaction with sebacic acid as aliphatic dicarboxylic acid was performed. The equimolar systems were cured for 1 h at 180 °C under a nitrogen atmosphere. The conversion and molecular weights were determined through \textsuperscript{1}H NMR and GPC analysis of samples taken at regular time intervals. The conversion determination procedure from NMR analysis and representative NMR spectra are provided in the Supporting Information. Figure 4 depicts the conversion over time for the first 5 min of curing of the various 2-oxazoline resins at 180 °C. Characteristic NMR spectra and calculation method are provided in the Supporting Information.

Figure 3. (A) DSC thermogram of BP-C\textsubscript{8} depicting the characteristic melting behavior of purified BP-C\textsubscript{x} monomers. (B) Overview of the peak melting temperatures of the synthesized monomers observed during the first DSC heating run, and the glass transition temperature observed during the second DSC heating run. All heating and cooling rates were 10 °C/min. Note that the filled symbols depict the thermal transitions of the BP-C\textsubscript{x} monomers containing even amine spacers, whereas the open symbols depict the thermal transitions of the BP-C\textsubscript{x} monomers with odd amine spacers.

Scheme 3. Overview of the Used Monomers for Polymerization Reactions Performed in This Study

Figure 4. Conversion calculated from NMR analysis during the first 5 min of curing of the various 2-oxazoline resins at 180 °C. Characteristic NMR spectra and calculation method are provided in the Supporting Information.
To obtain more information on the molecular weight build-up at the start of the curing process, systems containing various BP-C_{x} monomers and IAox have been cured for 1 min at 180 °C, and their molecular weights were evaluated through HFIP-GPC. The results are shown in Figure 5. (A) GPC traces of equimolar systems containing dicarboxylic acid and IAox cured for 1 min at 180 °C. (B) Overview of corresponding molecular weights ($M_w$ and $M_n$) of the GPC traces shown in Figure 6A.

Figure 6. Molecular weight build-up according to GPC analysis during curing at 180 °C for an equimolar (A) BP-C_{8}:IAox and (B) sebacic acid:IAox resin. Parts C and D depict the increase in $M_w$ and PDH over time, respectively, for both systems.
analysis. Please note that we confine ourselves to IAox based systems for the determination of molecular weights given the high tendency of FDCAox based resins to undergo rapid cross-linking, thereby limiting their solubility. As is visible from Figure 5, the molecular weights (\(M_w\)) of the systems containing the BP-C\(_x\) monomers reach \(10^{-20}\) kg/mol within only 1 min of curing. In contrast, the system containing sebacic acid only yields a \(M_w\) of 4.5 kg/mol after the same reaction time. Additionally, the presence of monomers and oligomers can be detected in the GPC traces of all systems, confirming that no full conversion is yet achieved (Figure 5A). Furthermore, in all BP-C\(_x\) GPC traces a high molecular weight tail is observed, likely indicating the presence of branched structures.

To obtain more information on the polymerization proceeding over time, the IAox based resins containing sebacic acid and BP-C\(_8\) were cured for 1 h, and their molecular weight build-up was monitored over time using GPC analysis. As is shown in the GPC traces of the IAox:BP-C\(_8\) resin (Figure 6A), a rapid molecular weight build-up is achieved immediately upon melting. Over time, the residual monomers and oligomers continue to react, and the high molecular weight tail increases, but overall, no significant changes are observed in the GPC traces. This experiment confirms that systems with BP-C\(_8\) exhibit extremely high reactivity and rapidly build up molecular weight. Furthermore, after 60 min of curing, the sample proved to be only partially insoluble in the HFIP solvent, indicating that branching and cross-linking proceed over time.

In contrast, when looking at the GPC traces of the sebacic acid based resin (Figure 6B), we observe a more gradual increase in molecular weight over time. Such behavior is characteristic for the polycondensation type of polymerizations. Additionally, when the polymerization reaches high conversions, an increase in high molecular weight tail and \(M_w\) is observed together with a systematic increase in dispersity, indicating that branching also occurs in this system (Figure 6C,D). That being said, branching and cross-linking proceed significantly more slowly in the presence of sebacic acid compared to samples containing BP-C\(_8\).
as the system remains fully soluble in HFIP, even after 6 h of reaction time.

From previous observations we have strong indications that the BP-C₈ monomers significantly enhance the reaction rate of 2-oxazoline resins compared to aliphatic dicarboxylic acids. However, at this point it is not clear whether the presence of BP-C₈ selectively accelerates the $k_1$ (chain extension) or $k_2$ (branching) reaction constant as both processes seem to proceed simultaneously. In order to gain more information on this reactivity difference, online monitoring of the polymerization is performed using ATR-FTIR analysis. For these reactions a carboxylic acid:2-oxazoline ratio of 1:2 has been used to enforce cross-linking and to assess the $k_2$ reaction constant: The excess of 2-oxazoline moieties ensures a rapid conversion of the dicarboxylic acids into ester–amide bonds in the initial stage of polymerization, leaving the residual 2-oxazoline moieties only with the amide groups to react. The reaction of the 2-oxazoline moiety with the secondary amide yields a tertiary amide bond (Scheme 1), which exhibits a characteristic resonance in FTIR spectroscopy around 1417 cm⁻¹. Figure 7A,B depicts the characteristic FTIR spectra obtained during a polymerization of FDCAOx based resins containing BP-C₈ and sebacic acid as dicarboxylic acid, respectively. The FTIR spectra obtained during polymerization of systems containing IAox as bis(2-oxazoline) are provided in the Supporting Information. Three distinct vibrational bands are highlighted in Figure 7: I corresponds to the furan ring vibration (816 cm⁻¹), II corresponds to the 2-oxazoline ring vibration (922 cm⁻¹), and III corresponds to the tertiary amide bonds vibration (1412 cm⁻¹). In general for both systems we observe that peak area I remains constant during the curing process, indicating that no evaporation of the FDCAOx occurs over time. The fact that no components are evaporating over time allow us to use this vibration as internal standard. Signals II and III change over time as a result of the proceeding chemical reaction, as the 2-oxazoline ring is depleted during ring-opening (signal II) and tertiary amide bonds are formed upon cross-linking (signal III).

When qualitatively comparing the change in tertiary amide bond signal (III) over time for the four tested systems, we can identify two characteristic regimes in the polymerization (Figure 8). Regime 1 denotes the region where most melting of the mixture proceeds in combination with reaction of the 2-oxazoline moieties with carboxylic acid groups until a plateau value is observed. According to the NMR analysis depicted in Figure 4, this generally proceeds within the first minutes of polymerization. Regime 2 denotes the region where the remaining 2-oxazolines react with the generated amide bonds; hence, the cross-linking of the system is proceeding. Obviously, these regimes differ per reaction and depend on temperature, reaction rate, and the presence of a catalyst. For this reason, nonindicative lines separating the two regimes are added to guide the eye.

Interestingly, systems containing BP-C₈ tend to melt rapidly and reach a plateau value within seconds, as is visible from Figure 8A. However, the cross-linking of the reaction mixtures seems to depend mostly on the selected bis(2-oxazoline) spacer, as only the systems containing FDCAOx tend to rapidly cross-link over time. Systems containing IAox do exhibit cross-linking, but at a significantly decreased rate compared to those of FDCAOx based systems. The addition of triphenyl phosphite (TPP) as catalyst does facilitate the cross-linking reaction for all systems (Figure 8B), indicating that the $k_3$ reaction constant determined by either the selected bis(2-oxazoline) or catalyst, but not by the dicarboxylic acid. The FTIR spectra obtained during polymerization of systems containing 1 wt % TPP used for the generation of Figure 8B are provided in the Supporting Information.

To obtain quantitative insight on the effect of BP-C₈ monomers on the polymerization kinetics, data fitting using normalized resonance II (2-oxazoline ring vibration) as input has been performed for the systems containing FDCAOx. The reaction kinetics of the polymerization between bis(2-oxazoline)s and dicarboxylic acids can be described using differential equations (eqs 1–3):

$$\frac{\delta[\text{acid}]}{\delta t} = -\frac{\delta[\text{ester}]}{\delta t} = -\frac{\delta[\text{sec amide}]}{\delta t}$$

$$= -k_3[\text{acid}][\text{OX}]$$

$$\frac{\delta[\text{OX}]}{\delta t} = -k_3[\text{acid}][\text{OX}] - k_2[\text{sec amide}][\text{OX}]$$

$$\frac{\delta[\text{tert amide}]}{\delta t} = k_2[\text{sec amide}][\text{OX}]$$
In differential equations (eqs 1−3), the 2-oxazoline concentration is denoted as [OX] in mol/kg. Similarly, the concentrations of the ester groups, amide groups, and tertiary amide groups are denoted as [ester], [sec amide], and [tert amide], respectively (in mol/kg). After normalization of the area of resonance II by the area of resonance I, followed by conversion to concentration using a conversion factor, the 2-oxazoline concentration during polymerization is obtained. This data has been used as input to fit both $k_1$ and $k_2$ reaction constants using differential equations (eqs 1−3, Figure 9). For the data fitting we assumed that both reactions are second order and irreversible, and that both 2-oxazoline moieties in a bis(2-oxazoline) reactant are equireactive. Additionally, we assumed that the 2-oxazoline concentration is linearly dependent on the normalized resonance II peak area, thus ignoring contributions from potential evaporation or changes in density during polymerization.

From Figure 9 we can observe that the method used can fit the FTIR data rather well. Remarkably, the $k_2$ reaction constants of the two different resins are at the same order of magnitude, while the $k_1$ reaction constant increases with more than 1 order of magnitude when exchanging sebacic acid for BP-C$_8$. These findings indicate that the previously observed enhancement in reaction and cross-linking rate in BP-C$_8$ based systems can be attributed to the selective enhancement of the $k_1$ reaction constant only. The predicted molecular weight build-up during curing and the resulting decrease in cross-linking time as a function of the change in $k_1$ reaction constant is provided in the Supporting Information.

Please note, for the system containing BP-C$_8$, we expect that the $k_1$ reaction constant obtained from the fit depicted in Figure 9 is overestimated. This is a result from the rapid 2-oxazoline depletion immediately upon the melting of the mixture, thereby preventing the collection of sufficient data points, and at early stage of the polymerization. Nevertheless, despite the potential error in the $k_1$ value, we can clearly observe that the $k_1$ constant is significantly higher when using BP-C$_8$ as dicarboxylic acid. This behavior is consistently observed in systems containing other BP-C$_x$ monomers as is shown in the Supporting Information.

The observed enhancement in $k_1$ reaction constant in this work is rather comparable to the findings reported by Néry and co-workers for systems using a pyridine based bis(2-oxazoline). These authors attributed the enhanced reactivity to (1) the basic nature of the pyridine ring and (2) to the stabilization of the protonated 2-oxazoline moiety. Given the basic but non-reactive nature of N-alkylated pyrrolidone moieties, it is plausible that they promote the deprotonation of the carboxylic acid moiety and thereby enhance its reactivity toward electrophiles such as 2-oxazolines. Verification of this hypothesis is part of ongoing work and will be communicated in future publications.

**Thermal Behavior of the Developed Thermosets.** With an understanding of the effect of BP-C$_x$ monomers on the curing kinetics in 2-oxazoline resins, in this section we evaluate their effect on the thermal behavior of the fully renewable thermosets, being systems based on FDCAox. To this end, various resins containing FDCAox and several readily recrystallizable BP-C$_x$ monomers have been prepared in an equimolar ratio and were
cured for 1 h at 180 °C in the absence of catalyst. The obtained materials were analyzed for their thermal transitions using DSC analysis. The obtained materials are all amorphous in nature, as can be observed from the exemplary DSC heating and cooling traces for the FDCAox:BP-C₈ based thermoset (Figure 10A). As expected, the rigid nature of the pyrrolidone rings in the polymer...
backbone increases the \( T_g \) (70 °C for BP-C\textsubscript{8}) compared to the thermosets based on sebacic acid (52 °C). Furthermore, also in line with expectations, the \( T_g \) of the thermoset increases with a decreasing number of methylene spacers of the used BP-C\textsubscript{\textit{X}} monomer (Figure 10B).

One particular point for attention in these amorphous materials is that the presence of numerous free electron pairs on the oxygen and nitrogen atoms results in the significant absorption of water: As is visible from Figure 10A, exposure to water or moisture results in a plasticizing effect, thereby decreasing the glass transition temperature by roughly 30 °C. Such amorphous behavior combined with the plasticizing effect of water is observed for all FDCAoX:BP-C\textsubscript{\textit{X}} based thermosets, as is shown in Figure 10B. The introduction of water as plasticizer improves the deformability of the thermoset, but can also result in rapid hydrolysis of the ester groups present in these poly(ester-amide)s.\textsuperscript{11,17,54} Though such hydrolysis can hamper the structural integrity and lifetime of the materials, it also opens up possibilities for depolymerization and biodegradation of the thermosets.

To identify whether such depolymerization occurs in the presence of water, preliminary degradation studies were performed: In general, 30 mg of product was placed in 1 mL of demineralized water or tris(hydroxymethyl)aminomethane (tris) buffer (100 mM, pH 8). Optionally, protease enzyme from Bacillus \textit{Sp}\textsuperscript{58} (0.8 mL, 16 units/mL, Sigma-Aldrich) was added together with 200 \( \mu \)L of 0.01 M CaCl\textsubscript{2} solution. Please note that this enzyme is commonly present in soil and is generally responsible for the breakdown of amide bonds. Next, the vials were sealed and incubated for 72 h at 50 °C under constant shaking.

After incubation, the solutions were placed in a cuvette and analyzed using UV−vis spectrophotometry, together with a series of model compounds expected to form after hydrolysis of the ester bonds in the FDCAoX:BP-C\textsubscript{8} (1:1) polymers (Scheme 4). Directly after UV−vis analysis of the mixtures, 25 \( \mu \)L of a 1 wt % solution of 1,4,6-trinitrobenzenesulfonic acid (TNBS) sodium salt was added, mixed with a pipet, and placed back for UV−vis analysis. TNBS is a well-known indicator for primary amines\textsuperscript{64−68} which allows us to identify whether the used protease facilitates amide bond breakage. In general, TNBS (absorption maximum at 250−260 nm) reacts with primary amines to form a Meisenheimer complex (absorption maximum at 420 nm), which in turn can react further into a trinitrophenylamine (absorption maximum at 340 nm).\textsuperscript{59} In the absence of amines, partial hydrolysis of TNBS occurs yielding picric acid which displays an absorption maximum at 340 nm.\textsuperscript{65} Figure 11 displays the UV−vis spectra in the range between 250 and 600 nm for the various mixtures evaluated in this study.

In general we can observe from Figure 11A that both pure water and tris buffer do not absorb UV light in the evaluated range 250−600 nm. BHFD\textsubscript{A}, the compound expected to be formed after hydrolysis of the ester bonds in FDCAoX based thermosets (Scheme 4), does display a strong absorption peak around 280 nm. The other hydrolysis product, BP-C\textsubscript{8}, displays a minor absorption peak below 320 nm. Ethanolamine, a reaction product expected to be formed after hydrolysis of the furanidcarboxamide bonds displays an absorption maximum at 260 nm. Lastly, we observe also that the enzyme does not interfere with the TNBS activity as it only displays an absorption maximum below 300 nm.

As expected, the addition of TNBS to water only results in hydrolysis of the TNBS resulting in UV absorption correspond-
CONCLUSIONS

The synthesis of fully renewable bis(pyrrolidone) based dicarboxylic acids was shown to be readily achieved in bulk with only water as catalyst. Furthermore, these materials have shown to be excellent candidates for curing in 2-oxazoline based resins. Both GPC and NMR data indicate that the BP-C monomers improve the reaction rate, thus allowing for faster curing. Additionally, through FTIR characterization we observed that the reaction kinetics in 2-oxazoline based resins can be controlled by a judicious selection of the reactants; the $k_1$ reaction constant, responsible for chain extension, can be tailored by the choice of the dicarboxylic acid component, whereas the $k_2$ reaction constant, responsible for branching and cross-linking, can be controlled by the choice of the bis(2-oxazoline) reactant. Combined, these provide a toolbox for the development of fully renewable and highly reactive resins with tailored thermal properties. Furthermore, the developed thermosets in this study are readily plasticized by water and are promising candidates for biodegradation as they are susceptible for enzymatic depolymerization.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acssuschemeng.7b04716.

Information regarding the synthesis and NMR characterization of BP-C monomers, relation between glass transition temperature of BP-C monomers and the hydrogen bonding density, 2-oxazoline conversion determination procedure using NMR spectroscopy, FTIR analysis of 1Aox and/or TPP based systems, verification of enhanced $k_1$ reaction constant on the rate of cross-linking, and reaction kinetics of FDCAxox based systems containing various dicarboxylic acids (PDF)

AUTHOR INFORMATION

Corresponding Author

*E-mail: karel.wilsens@maastrichtuniversity.nl.

ORCID ©

Sanjay Rastogi: 0000-0002-7804-7349
Carolus H. R. M. Wilsens: 0000-0003-3063-9510

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This work is part of the research program and funded by Aachen Maastricht Institute of Biobased materials (AMIBM).

REFERENCES

(1) Gandini, A.; Belgaem, M. Furans in Polymer Chemistry. Prog. Polym. Sci. 1997, 22, 1203–1379.

(2) Robert, T.; Friebl, S. Itaconic acid—a versatile building block for renewable polyesters with enhanced functionality. Green Chem. 2016, 18 (10), 2922–2934.

(3) Winkler, M.; Lacerda, T. M.; Mack, F.; Meier, M. A. Renewable polyesters from itaconic acid by polycondensation and ring-openingmetathesis polymerization. Macromolecules 2015, 48 (5), 1398–1403.

(4) van Putten, R.-J.; van der Vaal, J. C.; de Jong, E.; Rasendra, C. B.; Heeres, H. J.; de Vries, J. G. Hydroxymethylfurural, A Versatile Platform Chemical Made from Renewable Resources. Chem. Rev. 2013, 113, 1499–1597.

(5) Wang, J.; Liu, X.; Zhang, Y.; Liu, F.; Zhu, J. Modification of poly(ethylene 2,5-furandicarboxylate) with 1,4-cyclohexanediol: Influence of composition on mechanical and barrier properties. Polymer 2016, 103, 1–8.

(6) Deng, J.; Liu, X.; Li, C.; Jiang, Y.; Zhu, J. Synthesis and properties of a bio-based epoxy resin from 2,5-furandicarboxylic acid (FDCA). RSC Adv. 2015, 5, 15930–15939.

(7) Dai, J.; Ma, S.; Wu, Y.; Han, L.; Zhang, L.; Zhu, J.; Liu, X. Polymers derived from itaconic acid for the properties and bio-based content enhancement of soybean oil-based thermosets. Green Chem. 2015, 17 (4), 2383–2392.

(8) Dai, J.; Ma, S.; Teng, N.; Dai, X.; Shen, X.; Wang, S.; Liu, X.; Zhu, J. 2,5-Furandicarboxylic Acid-and Itaconic Acid-Derived Fully Biobased Unsaturated Polymers and Their Cross-Linked Networks. Ind. Eng. Chem. Res. 2017, 56 (10), 2650–2657.

(9) Seppälä, J. V.; Helminen, A. O.; Korhonen, H. Degradeable polysteres through chain linking for packaging and biomedical applications. Macromol. Biosci. 2004, 4 (3), 208–217.

(10) Cowie, J. M.; Haq, Z. Poly (mono n-alkyl itaconic acid esters): Their preparation and some physical properties. Br. Polym. J. 1977, 9 (3), 241–245.

(11) Qi, P.; Chen, H.-L.; Nguyen, H. T. H.; Lin, C.-C.; Miller, S. A. Synthesis of biorenewable and water-degradable poly lactylactam esters from itaconic acid. Green Chem. 2016, 18 (15), 4170–4175.

(12) Dai, J.; Ma, S.; Liu, X.; Han, L.; Wu, Y.; Dai, X.; Zhu, J. Synthesis of bio-based unsaturated polyester resins and their application in waterborne UV-curable coatings. Prog. Org. Coat. 2015, 78, 49–54.

(13) Farmer, T. J.; Castle, R. L.; Clark, J. H.; Macquarrie, D. J. Synthesis of unsaturated polyester resins from various bio-derived platform molecules. Int. J. Mol. Sci. 2015, 16 (7), 14912–14932.

(14) Ali, M. A.; Tateyama, S.; Oka, Y.; Kaneko, D.; Okajima, M. K.; Kaneko, T. Syntheses of high-performance biopolymers derived from itaconic acid and their environmental corrosion. Macromolecules 2013, 46 (10), 3719–3725.

(15) Ayadi, F.; Mamzed, S.; Portella, C.; Dole, P. Synthesis of bis (pyrrolidone-4-carboxylic acid)-based polyamides derived from renewable itaconic acid-application as a compatibilizer in biopolymer blends. Polym. J. 2013, 45 (7), 766–774.

(16) Chau, N.; Matsuda, S.; Ikawara, Y. Synthesis of polyamides from esteramide-diamines. Makromol. Chem. 1979, 180 (6), 1435–1440.

(17) Wang, Z.; Wei, T.; Xue, X.; He, M.; Xue, J.; Song, M.; Wu, S.; Kang, H.; Zhang, L.; Jia, Q. Synthesis of fully bio-based polyamides with tunable properties by employing itaconic acid. Polymer 2014, 55 (19), 4846–4856.

(18) Lü, A.; Li, Z.-L.; Du, F.-S.; Li, Z.-C. Synthesis, functionalization, and controlled degradation of high molecular weight polyester from itaconic acid via ADMET polymerization. Macromolecules 2014, 47 (22), 7707–7716.

(19) Goerz, O.; Ritter, H. Polymers with shape memory effect from renewable resources: crosslinking of polyesters based on l-isosorbide, itaconic acid and succinic acid. Polym. Int. 2013, 62 (5), 709–712.

(20) Gao, C.; Wang, J.; Han, S.; Hu, Z.; Liu, Y. Copolymerization modification of poly (butylene itaconate). In AIP Conference Proceedings; AIP Publishing, 2017; p 020221. DOI: 10.1063/1.4993038.

(21) He, M.; Wang, Z.; Wang, R.; Zhang, L.; Jia, Q. Preparation of Bio-Based Polyamide Elastomer by Using Green Plasticizers. Polymers 2016, 8 (7), 257.

(22) Chen, K.-S.; Ku, Y.-A.; Lin, H.-R.; Yan, T.-R.; Sheu, D.-C.; Chen, T.-M.; Lin, F.-H. Preparation and characterization of pH sensitive poly (N-vinyl-2-pyrrolidone/itaconic acid) copolymer hydrogels. Mater. Chem. Phys. 2005, 91 (2), 484–489.

(23) Coşkun, R. Graft copolymerization of itaconic acid-methacrylaidemide comonomers onto poly (ethylene terephthalate) fibers. Eur. Polym. J. 2007, 43 (4), 1428–1435.

(24) Sabaa, M.; Mokhtar, S. Chemically induced graft copolymerization of itaconic acid onto cellulose fibers. Polym. Test. 2002, 21 (3), 337–343.
Adv. Technol. (ester amide) s of the AA+ BB type on the basis of 2-oxazolines. oxazolines from carboxylic acids using Deoxo-Fluor reagent. Lett. Polym. Chem. AB-type hydroxyphenyl-substituted 2-oxazolines. reactions of cyclic imino ethers. I. Ring-opening homopolyaddition of oxazolines, benzoxazoles, and oxadiazoles from carboxylic acids using polymerization of 2-substituted 2-oxazolines. Polym. Lett. polymerizations. I. Synthesis and polymerization of bis (dicarboxylic acids. J. Polym. Sci., Part A: Polym. Chem. 654−660. 660.−675.−6981.−6981.−713.−713.−723.−723.−744.−744.−767.−767.−786.−786.−800.−800.−817.−817.−837.−837.−857.−857.−877.−877.−897.−897.−917.−917.−937.−937.−957.−957.−977.−977.−997.−997.−1017.−1017.−1037.−1037.−1057.−1057.−1077.−1077.−1097.−1097.−1117.−1117.−1137.−1137.−1157.−1157.−1177.−1177.−1197.−1197.−1217.−1217.−1237.−1237.−1257.−1257.−1277.−1277.−1297.−1297.−1317.−1317.−1337.−1337.−1357.−1357.−1377.−1377.−1397.−1397.−1417.−1417.−1437.−1437.−1457.−1457.−1477.−1477.−1497.−1497.−1517.−1517.−1537.−1537.−1557.−1557.−1577.−1577.−1597.−1597.−1617.−1617.−1637.−1637.−1657.−1657.−1677.−1677.−1697.−1697.−1717.−1717.−1737.−1737.−1757.−1757.−1777.−1777.−1797.−1797.−1817.−1817.−1837.−1837.−1857.−1857.−1877.−1877.−1897.−1897.−1917.−1917.−1937.−1937.−1957.−1957.−1977.−1977.−1997.−1997.−2017.−2017.−2037.−2037.−2057.−2057.−2077.−2077.−2097.−2097.−2117.−2117.−2137.−2137.−2157.−2157.−2177.−2177.−2197.−2197.−2217.−2217.−2237.−2237.−2257.−2257.−2277.−2277.−2297.−2297.−2317.−2317.−2337.−2337.−2357.−2357.−2377.−2377.−2397.−2397.−2417.−2417.−2437.−2437.−2457.−2457.−2477.−2477.−2497.−2497.−2517.−2517.−2537.−2537.−2557.−2557.−2577.−2577.−2597.−2597.−2617.−2617.−2637.−2637.−2657.−2657.−2677.−2677.−2697.−2697.−2717.−2717.−2737.−2737.−2757.−2757.−2777.−2777.−2797.−2797.−2817.−2817.−2837.−2837.−2857.−2857.−2877.−2877.−2897.−2897.−2917.−2917.−2937.−2937.−2957.−2957.−2977.−2977.−2997.−2997.−3017.−3017.−3037.−3037.−3057.−3057.−3077.−3077.−3097.−3097.−3117.−3117.−3137.−3137.−3157.−3157.−3177.−3177.−3197.−3197.−3217.−3217.−3237.−3237.−3257.−3257.−3277.−3277.−3297.−3297.−3317.−3317.−3337.−3337.−3357.−3357.−3377.−3377.−3397.−3397.−3417.−3417.−3437.−3437.−3457.−3457.−3477.−3477.−3497.−3497.−3517.−3517.−3537.−3537.−3557.−3557.−3577.−3577.−3597.−3597.−3617.−3617.−3637.−3637.−3657.−3657.−3677.−3677.−3697.−3697.−3717.−3717.−3737.−3737.−3757.−3757.−3777.−3777.−3797.−3797.−3817.−3817.−3837.−3837.−3857.−3857.−3877.−3877.−3897.−3897.−3917.−3917.−3937.−3937.−3957.−3957.−3977.−3977.−3997.−3997.−4017.−4017.−4037.−4037.−4057.−4057.−4077.−4077.−4097.−4097.−4117.−4117.−4137.−4137.−4157.−4157.−4177.−4177.−4197.−4197.−4217.−4217.−4237.−4237.−4257.−4257.−4277.−4277.−4297.−4297.−4317.−4317.−4337.−4337.−4357.−4357.−4377.−4377.−4397.−4397.−4417.−4417.−4437.−4437.−4457.−4457.−4477.−4477.−4497.−4497.−4517.−4517.−4537.−4537.−4557.−4557.−4577.−4577.−4597.−4597.−4617.−4617.−4637.−4637.−4657.−4657.−4677.−4677.−4697.−4697.−4717.−4717.−4737.−4737.−4757.−4757.−4777.−4777.−4797.−4797.
(65) Cayot, P.; Tainturier, G. The Quantification of Protein Amino Groups by the Trinitrobenzenesulfonic Acid Method: A Reexamination. *Anal. Biochem.* 1997, 249, 184–200.

(66) Silva, C.; Cavaco-Paulo, A. Monitoring Biotransformations in Polyamide Fibres. *Biocatal. Biotransform.* 2004, 22, 357–360.

(67) Spadaro, A. C. C.; Draghetta, W.; Del Lama, S. N.; Camargo, A. C. M.; Greene, L. J. A Convenient Manual Trinitrobenzenesulfonic Acid Method for Monitoring Amino Acids and Peptides in Chromatographic Column Effluents. *Anal. Biochem.* 1979, 96, 317–321.

(68) Bubnis, W. A.; Ofner, C. M., III The Determination of ε-Amino Groups in Soluble and Poorly Soluble Proteinaceous Materials by a Spectrophotometric Method Using Trinitrobenzenesulfonic Acid. *Anal. Biochem.* 1992, 207, 129–133.

(69) Kiranas, E. R.; Tzouwara-Karayanni, S. M.; Karayannis, M. I. The reaction of glutamic acid and trinitrobenzenesulfonic acid kinetic study and analytical application. *Talanta* 1997, 44, 1113–1121.