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Enzymatic polymerization of various biobased and biodegradable BHMTHF-based (co)polyesters

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2,5-Bishydroxymethyltetrahydrofuran (BHMTHF), also known as 2,5-tetrahydrofurandimethanol (THFDM), is a sugar-derived monomer containing a rigid alicyclic tetrahydrofuran structure. In this study, three series of BHMTHF-based (co)polyesters were enzymatically synthesized using various aliphatic comonomers and the furanic comonomers 2,5-bishydroxymethylfuran (BHMF) and 2,5-furandicarboxylic acid (FDCA). The length of the aliphatic comonomers had a significant effect on the T_g and complex viscosity. Similarly, a higher furan content, either BHMF or FDCA, in the copolyesters increased the T_g values and complex viscosities. Biodegradation experiments in activated sludge demonstrated that all aliphatic-BHMTHF-based polyesters were biodegradable, with rates ranging from 60 to 89% in 28 days. In addition, the furan-BHMTHF-based copolyesters also demonstrated a biodegradable behavior over time, without a significant influence of either the BHMF or FDCA content. Finally, the greenness of the enzymatic synthesis process was assessed based on atom economy (AE), reaction mass efficiency (RME), overall efficiency (OE), E-factor, and EcoScale. This work supports the tuneability of the thermal and rheological properties of BHMTHF-based (co)polyesters and reveals the biodegradability of these materials. This emphasizes that BHMTHF is a very promising biobased rigid monomer for the production of sustainable (co)polyesters.

Green foundation

1. The conventional plastic economy relies largely on fossil-based polymers, bio-based polymers are renewable and more sustainable alternatives. Sugar-derived monomers, including BHMTHF, are considered key materials for the development of green polymers.

2. The design and application of biodegradable polymers are important to reduce (micro)plastic pollution and accumulation in the environment. BHMTHF-based (co)polyesters are demonstrated to be biodegradable and have tunable properties, which makes BHMTHF a promising monomer for the production of environmentally friendly polyesters.

3. The traditional synthesis process of polyesters involves high temperature and toxic metal-based catalysts. Enzymatic polymerization is an efficient, selective, and low-temperature synthesis process, and is suitable for a wide range of monomers. BHMTHF-based (co)polyesters could be successfully synthesized *via* a sustainable enzymatic bulk polymerization process in relatively high molecular weight.

Introduction

Sugar-derived monomers are key materials for producing renewable polymers due to their sustainable character, inexpensiveness, abundance and chemical diversity, and align with the principles of Green Chemistry.[1] An important sugar-based intermediate is the biobased platform chemical 5-(hydroxymethyl)furfural (HMF), which can be converted into numerous different monomers that can be used for the synthesis of polyesters, polyamides and polyurethanes.[2] The most famous HMF-derived monomer is the oxidized product 2,5-furandicarboxylic acid (FDCA), which is close to being produced at a large scale by the Dutch company Avantium.[3]

Furthermore, HMF can also be reduced to yield monomers such as 2,5-bishydroxymethylfuran (BHMF), 2,5-bishydroxymethyltetrahydrofuran (BHMTHF), 1,6-hexanediol (HDO), and 1,2,6-hexanetriol (HT).[4] Among these, BHMTHF, also reported as 2,5-tetrahydrofurandimethanol (THFDM) and 2,5-dihydroxymethyltetrahydrofuran (DHMTHF), is particularly attractive. Its alicyclic tetrahydrofuran structure in combination with two primary hydroxyl groups makes it structurally similar to BHMF, while providing the additional benefit of a remarkably higher thermal stability compared to its furan-based counterpart.[5]

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This makes BHMTHF, in contrast to BHMF, suitable for high temperature bulk polymerization for the synthesis of diverse polyesters with unique properties. The group of Wei synthesized a variety of BHMTHF-based (co)polyesters *via* melt polymerization using an L-scale reactor. They synthesized poly (ethylene-*co*-tetrahydrofurandimethanol terephthalate) (PETT) wherein BHMTHF (THFDM) was demonstrated to be a suitable alternative to replace 1,4-cyclohexanedimethanol (CHDM), which is currently used in the industrial production of poly (ethylene terephthalate-*co*-cyclohexanedimethanol terephthalate) (PETG).[6] In addition, they (co)polymerized BHMTHF with terephthalic acid (TA), FDCA, succinic acid, and adipic acid, which resulted in a polymeric material with a wide range of properties.[7–9] The copolyester PETT is popular for fiber applications and was also synthesized by other groups to study melt spinning, electrospinning, crystallization behavior and mechanical performances.[10–12] In general, the incorporation of BHMTHF units in copolyesters results in reduced crystallinity or even fully amorphous materials, relatively high T_g values and increased hydrophilicity.[13–15] These features are attributed to the rigid tetrahydrofuran ring structure, which contains an electronegative ether group. These unique characteristics of the BHMTHF ring are also recognized in polyurethanes, which demonstrated self-healing behavior due to strong hydrogen bonding between the urethane groups and the oxygen functionality in the BHMTHF units.[16–18]

Although BHMTHF-based polymers are not extensively studied, it is mainly (co)polymerized with either FDCA or TA, while only succinic acid and adipic acid are used as aliphatic comonomers. Hence, it is important to polymerize BHMTHF with biobased aliphatic comonomers of various sizes to expand the library. In addition, conventional melt polycondensation is currently the only reported synthesis route. Enzymatic polymerization is demonstrated to be a sustainable, efficient and selective tool to produce various biobased polyesters.[19–22] In addition, the use of toxic metal-based catalysts and high temperatures are avoided, which follows the Green Chemistry principles about efficient catalysis and less hazardous chemical syntheses. Due to BHMTHF's structural similarity to BHMF, it is expected that enzymatic polymerization could be a viable synthesis route as well.[23,24] Furthermore, poly(butylene-*co*-tetrahydrofurandimethylene succinate) is shown to be prone to enzymatic degradation, which is another indication that enzymatic polymerization might be a promising alternative.[9] These results indicate that BHMTHF-based polyesters are prone to biodegradation. Although enzymatic degradation is not the same as biodegradation, where polymers degrade by microorganisms to water, minerals, biomass, and CO_2.[25] The produced CO_2 returns in the carbon cycle, or can be a valuable input for the chemical industry.[26]

In this work, BHMTHF is enzymatically polymerized with aliphatic comonomers that contain a varying number of methylene units. In addition, the polyester derived from BHMTHF and dimethyl adipate (poly(tetrahydrofurandimethylene adipate)) was copolymerized with either BHMF or diethyl FDCA in varying ratios. The impact of aliphatic spacer length and the furanic content (BHMF or FDCA) on the thermal characteristics, rheology and biodegradability are studied. The results give a broad perspective on the structure–property relationship of BHMTHF units in (co)polyesters.

Experimental

Materials

2,5-Bishydroxymethyltetrahydrofuran (BHMTHF, >98%, 90.6% *cis*, 9.4% *trans*) was purchased from AKOS GmbH (Germany). 2,5-Bis(hydroxymethyl)furan (BHMF, >97%) and 2,5-furan dicarboxylic acid (FDCA, >97%) were both obtained from Apollo Scientific. Dimethyl succinate (DMSuc, 98%), dimethyl glutarate (DMGlu, 99%), dimethyl adipate (DMAd, >99%), dimethyl pimelate (DMPim, 99%), dimethyl suberate (DMSub, 99%), chloroform (amylene stabilized, HPLC grade, >99.8%), and lipase acrylic resin (*Candida antartica* lipase B (iCALB), 5000 U g^{-1}, recombinant, expressed in *Aspergillus niger*) were all purchased from Sigma-Aldrich. Dimethyl azelate (DMAze, >98%) and dimethyl sebacate (DMSeb, >98%) were both obtained from TCI EUROPE. Diethyl ether was purchased from Honeywell Research Chemicals and ethanol (absolute) was obtained from J.T. Baker. Ethyl acetate was purchased from Macron Fine Chemicals and sulfuric acid (96–98%) was obtained from Boom B.V. All chemicals were used as received. The wastewater treatment facility in Glimmen (the Netherlands) kindly supplied the activated sludge.

Synthesis of diethyl furan-2,5-dicarboxylate

FDCA was converted into diethyl furan-2,5-dicarboxylate (DEFDCA) *via* esterification with ethanol.[27] A round bottom flask was filled with 10.0 g (64 mmol) FDCA, 300 mL of ethanol and 0.8 mL concentrated sulfuric acid as a catalyst. The mixture was allowed to reflux for 24 h by using an oil bath. Then, the ethanol was removed under reduced pressure, and 200 mL of ethyl acetate was added to the reaction product. The organic layer was washed several times with water and once with concentrated $NaHCO_3$. Anhydrous $MgSO_4$ was used to remove water traces and the ethyl acetate was removed under reduced pressure. The obtained DEFDCA appeared as white crystals in a yield of 81% and its structure was confirmed by ^{1}H-NMR: (600 MHz, DMSO-d$_6$), δ (ppm): 7.39 (s, 2H, **CH**-furan), 4.32 (m, 4H, **CH$_2$**-ethyl group), 1.29 (t, 6H, **CH$_3$**-ethyl group).

Synthesis of BHMTHF-based (co)polyesters

All polyesters were synthesized *via* the same procedure, only the ratios and type of monomers varied. The reactions were performed in a 25 mL three-necked round bottom flask, which was magnetically stirred and connected to a distillation setup and Schlenk line. The BHMTHF-aliphatic polyesters were produced on a 2.50 g scale, at a BHMTHF : dimethyl ester molar ratio of 1.00 : 1.00, and 10% w/w iCALB was added as a catalyst (Fig. 1). The same scale and catalyst loadings were used for the
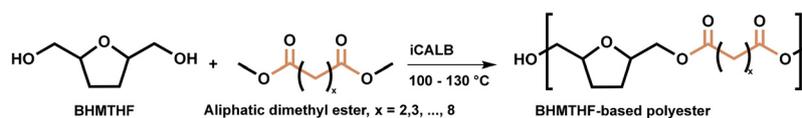
Fig. 1 Enzymatic bulk polymerization of BHMTHF and aliphatic dimethyl esters with a varying number of methylene units x.

synthesis of the copolyesters poly(tetrahydrofurandimethylene adipate-co-tetrahydrofurandimethylene 2,5-furandicarboxylate) (PTAd-TF) and poly(tetrahydrofurandimethylene adipate-co-2,5-furandimethylene adipate) (PTAd-FAd)(Fig. 2), and the feed ratios are provided in Table 2.

The reaction mixture was first maintained at 100 °C for 24 h under a mild argon flow. Then, the temperature was increased to 120 °C, and the system was gently switched to vacuum (2×10^{-2} mbar) and maintained for another 24 h. Finally, the temperature was increased to 130 °C for the last 7 h of the experiment. The obtained polymer was dissolved in chloroform, separated from the enzyme using a needle and syringe, precipitated in diethyl ether, centrifuged (10 min, 4500 rpm) and dried in the vacuum oven at 80 °C for 24 h. Organic solvents were required for purification and product recovery, but could be eliminated at larger scales, where polymers can be directly extruded from the reactor. All synthesized polyesters appeared as a viscous colorless liquid except PTAd-FAd_100, which appeared as a solid. The detailed NMR data of all synthesized polyesters are provided in the SI Fig. S1–S19.

Structural characterization

A Bruker AVANCE NEO 600 MHz NMR spectrometer, equipped with a BBFO probe and DMSO-d_6 as the solvent, was used for proton nuclear magnetic resonance (^{1}H-NMR) measurements. Carbon-13 nuclear magnetic resonance (^{13}C-NMR), Heteronuclear Single Quantum Coherence (HSQC), Heteronuclear Multiple Bond Correlation (HMBC) and Correlated Spectroscopy (COSY) were performed at the same device and used to identify all signals of BHMTHF and its derived polymers.

The number average molecular weight ($\overline{M_n}$) and weight average molecular weight ($\overline{M_w}$) were determined *via* gel permeation chromatography (GPC). The analyses were performed on a Hewlett Packard 1100 device with three MIXED-E columns (Agilent Technologies PL, 300 × 7.5 mm 3 µm) equipped with a GBC 1240 refractive index detector. THF, stabilized with BHT, served as the solvent and eluent at a flow rate of 1 mL min^{-1} at 40 °C. The polymer samples were prepared at a concentration of 5 mg mL^{-1}, and toluene acted as an internal standard. A conventional calibration curve based on monodispersed polystyrene (PS) standards was used to calculate the relative molecular weights.

The degree of polymerization (DP) of the copolyesters was determined as follows:

$$ \text{DP} = \frac{\overline{M_n}}{M_{0,\text{BHMTHF}} \times f_{\text{BHMTHF}} + M_{0,\text{furan}} \times f_{\text{Furan}}} \tag{1} $$

wherein f_{BHMTHF} and f_{Furan} represent the molar fractions, obtained from ^{1}H-NMR analysis, of the BHMTHF and furan units (*i.e.*, BHMF or FDCA) in the copolyester, respectively. $M_{0,\text{BHMTHF}}$ and $M_{0,\text{furan}}$ represent the masses of the repeating units of the corresponding segments.

Thermal stability analysis

The thermal stability of the (co)polyesters was investigated *via* thermogravimetric analysis (TGA) on a TA-Instruments Discovery TGA 5500. To eliminate solvent residues, the samples were first heated to 80 °C for 1 h in a nitrogen environment. The samples were then heated from room temperature to 700 °C at a steady rate of 10 °C min^{-1}.

The glass transition temperatures (T_g) and the melting points (T_m) of the polymers were determined by modulated differential scanning calorimetry (mDSC) analysis. A TA-Instruments Q1000 DSC was used to subject the samples (5–6 mg) to a heat-cool-heating cycle ranging from −70 to 150 °C under a nitrogen atmosphere. The average heating rate
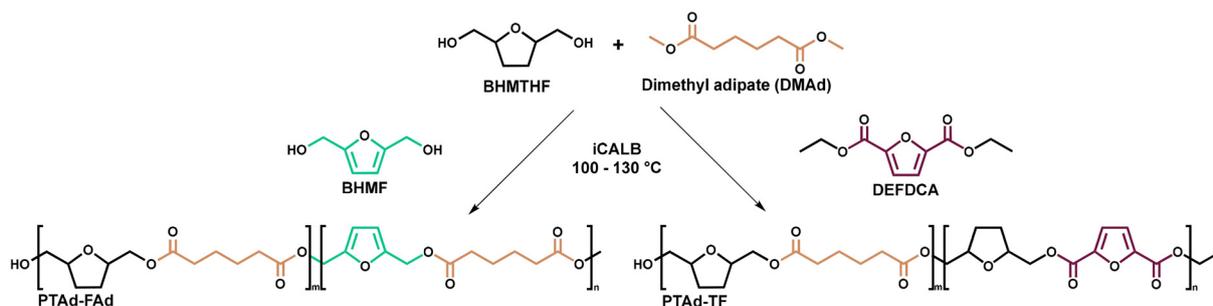

Fig. 2 Overview of the enzymatic bulk polymerization of the copolyesters poly(tetrahydrofurandimethylene adipate-*co*-2,5-furandimethylene adipate) (PTAd-FAd) (left) and poly(tetrahydrofurandimethylene adipate-*co*-tetrahydrofurandimethylene 2,5-furandicarboxylate) (PTAd-TF) (right).

was set to 3 °C min⁻¹ with a temperature modulation period of 60 s and an amplitude of 0.50 °C.

Rheological analysis

The rheology of the polyesters was analyzed on a TA-Instruments HDR20 rheometer, equipped with an 8 mm plate–plate geometry. The experiments were performed at 40 °C, well above all T_g values, under a nitrogen atmosphere and a constant gap size, ranging from 0.5 to 1.0 mm between the different samples. A dynamic strain sweep experiment was conducted to determine the linear viscoelastic regime at a constant oscillation frequency (100 rad s⁻¹), while the strain ranged from 0.1 to 10%. Subsequently, a dynamic frequency sweep was performed at a constant strain of 1%, well within the linear viscoelastic regime, while the frequency ranged from 0.01–100 rad s⁻¹.

Biodegradability examination

A Lovibond® Water testing BOD-System BD 600 setup was used to study the biodegradability of the BHMTHF-based polyesters in activated sludge. The method was based on the OECD 301F manometric respirometry test guidelines and is described in detail in our previous work.[28,29] Briefly, the experiments are based on the biochemical oxygen demand (BOD) and the theoretical oxygen demand (ThOD) of the tested sample. The BOD ranges from 0 to 400 mg L⁻¹ oxygen and the ThOD is used to determine the mass of each sample that is required to reach the theoretical maximum BOD value of 400 mg L⁻¹ oxygen. The activated sludge, obtained from a wastewater facility, was aerated for 3 days prior to use, diluted with water and provided with nutrient salts. The experiments were performed for 28 days and each sample was measured in duplicate. A reference (sodium acetate) and a control (no sample) were also included in duplicate to verify the activity of the sludge and the measurement range. The percentage of biodegradation was based on the averaged values and corrected for the average BOD value of the control experiment:

$$\text{Biodegradation (\%)} = \frac{\text{BOD}_{\text{test sample}} - \text{BOD}_{\text{control}}}{400} \times 100 \quad (2)$$

Green metrics calculations

The greenness of the polymerization protocols was evaluated using a set of complementary green metrics, namely atom economy (AE), reaction mass efficiency (RME), overall efficiency (OE), E-factor, and EcoScale.[30,31] These metrics were calculated at the level of the polymerization step, from diester and diol to isolated (co)polyester, following established definitions used for synthetic organic and polymer chemistry.[32]

AE was determined from the reaction stoichiometry as the ratio between the molecular weight of the ideal repeating unit and the total molecular weight of all reactants entering the polymer backbone, assuming methanol or ethanol to be the only stoichiometric by-products (eqn (3)). RME was obtained by dividing the mass of the isolated polymer by the total mass of all reactants, and incorporates, therefore, the yield and non-

stoichiometric excess of BHMTHF or diester(eqn (4)). OE is defined as the ratio between RME and AE and was used as an integrated measure of the transformation efficiency (eqn (5)).

$$\text{AE (\%)} = \frac{\text{molecular weight of repeating unit}}{\text{total molecular weight of reactants}} \times 100 \quad (3)$$

$$\text{RME (\%)} = \frac{\text{mass of isolated product}}{\text{total mass of reactants}} \times 100 \quad (4)$$

$$\text{OE (\%)} = \frac{\text{RME}}{\text{AE}} \times 100 \quad (5)$$

The E-factor was calculated as the mass ratio of all waste generated to the mass of isolated (co)polyester (eqn (6)). In accordance with common practice, water was excluded from the E-factor calculations, whereas all organic solvents, immobilized enzyme, and other auxiliaries used during the polymerization and work-up were counted as waste.[33] Hence, the reported E-factors represent conservative laboratory-scale values that do not account for solvent recycling or enzyme reuse.

$$\text{E-factor (kg/kg)} = \frac{\text{total mass of waste}}{\text{mass of isolated product}} \quad (6)$$

EcoScale scores were determined using the semi-quantitative methodology proposed by Van Aken *et al.*, in which an ideal score of 100 is reduced by penalty points associated with low yields, hazardous or expensive reagents and catalysts, non-preferred solvents, high temperatures, long reaction times, and demanding work-up.[31] The input parameters for the EcoScale calculations (yields, reagents, solvent types, temperature, and reaction time) were taken directly from the experimental procedures used for each polymerization.

Results and discussion

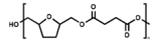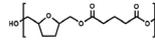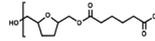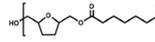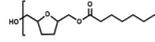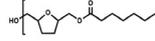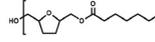### Synthesis and structural confirmation

Three different series of BHMTHF-based polyesters were successfully polymerized in bulk by using the enzyme iCALB as a catalyst. In the first series, BHMTHF was reacted with aliphatic dimethyl esters of various sizes, and the results are provided in Table 1. The use of diesters instead of dicarboxylic acids violates the principles of Green Chemistry about atom economy and reducing derivatives. However, the reaction kinetics of dimethyl esters are higher, which improves the efficiency and reduces overall energy consumption, while the produced methanol could be recycled.

The number average molecular weight ($\overline{M_n}$) ranged from 5500 to 11 200 g mol⁻¹, corresponding to a degree of polymerization (DP) ranging from 26 to 41. The use of DMSuc and DMPim as comonomers resulted in slightly lower $\overline{M_n}$ and DP values, expected due to lower reaction kinetics, which was also observed in our previous work about BHMF-based polyesters.[29]

The second series involves copolyesters consisting of BHMTHF, BHMF, and DMAd, wherein the BHMTHF content

Table 1 Structural and thermal characteristics of the polyesters obtained from BHMTHF and aliphatic comonomers. Number average molecular weight ($\overline{M_n}$), weight average molecular weight ($\overline{M_w}$), polydispersity (Đ), degree of polymerization (DP), glass transition temperature (T_g), and 5% and 50% decomposition temperatures ($T_{d5\%}$, $T_{d50\%}$)

Polymer	Structure	$(CH_2)_x$	$\overline{M_n}$ (g mol^{-1})	$\overline{M_w}$ (g mol^{-1})	Đ	DP	T_g (°C)	$T_{d5\%}$ (°C)	$T_{d50\%}$ (°C)
PTSuc		2	5500	9100	1.7	26	−7.7	324	404
PTGlu		3	8200	14 800	1.8	36	−26.2	342	417
PTAd		4	10 500	17 900	1.7	43	−32.8	326	387
PTPim		5	7500	14 700	2.0	29	−37.9	302	409
PTSub		6	11 200	17 900	1.6	41	−42.6	331	418
PTAze		7	7300	17 400	2.4	26	−47.2	299	420
PTSeb		8	9000	21 200	2.3	30	−48.7	285	421

was gradually increased at the cost of BHMF content (Table 2a). The $\overline{M_n}$ values varied from 6600 to 11 000 g mol^{-1} and there was no significant effect of the BHMTHF/BHMF content on the molecular weight of the copolyesters. This implies a similar reactivity of BHMTHF and BHMF toward DMAd during enzymatic polymerization with iCALB. However, the polyester consisting of only BHMF (PTAd-FAd_100) demonstrated a lower $\overline{M_n}$ compared to the pure polyester from BHMTHF and DMAd (PTAd-FAd_00, or PTAd). Noteworthily, the polymerization reactions started at 100 °C, while the synthesis of BHMF-based homopolyesters was initiated at 70 °C in our previous work due to BHMF's limited thermal stability.[29,34] The possibility of starting the polymerization at a higher temperature was attributed to a higher purity of the BHMF used in this study. BHMF is commonly derived from the thermally less stable intermediate HMF, and trace amounts might influence the overall thermal stability.[35]

A different phenomenon was observed in the third series, which covered copolyesters based on BHMTHF, DEFDCA, and DMAd (Table 2b). The $\overline{M_n}$ values decreased significantly for higher contents of DEFDCA in the feed. In addition, the enzymatic polymerization of only BHMTHF and DEFDCA was unsuccessful since only oligomer formation was observed. This is attributed to the limited enzymatic activity towards polymerization of two cyclic monomers, e.g., FDCA and BHMTHF. This substrate limitation effect of the active site of iCALB was also observed for copolyesters based on dimethyl FDCA, BHMF, and aliphatic diols.[21]

It is worth noticing that iCALB easily polymerizes BHMTHF with DMAd, but FDCA with BHMTHF does not even result in oligomers under the same conditions, while BHMTFH and FDCA contain both a five-membered ring structure. This lipase consists of a Ser-His-Asp catalytic triad, which is surrounded by a relatively large hydrophobic pocket to allow absorption on hydrophobic surfaces, a mechanism called interfacial activation.[36,37] The catalytic transesterification mechanism involves first the incorporation and activation of the carbonyl group in the active site and subsequently the liberation of the

alcohol group, as described in detail by Hevilla et al. (2021).[38] This is followed by the nucleophilic attack of another primary alcohol group and the release of the product with the newly formed ester bond.[20,22] This means that the chemical structure and bulkiness of the diacid, dimethyl, or diethyl ester is key to interacting and fitting in the active site and thus the possibility of polymerization. In addition, the results in this work demonstrate that the bulkiness of the diol, i.e., BHMTHF or BHMF, has no significant limitation.

Although iCALB has difficulties with polymerization of two cyclic monomers, it proved to be a very selective and efficient catalyst at relatively low temperature, which makes it an advantageous tool for monomers with limited thermal and chemical stability, such as BHMF, and avoids the use of toxic metal-based catalysts and solvents. This aligns with the principles of Green Chemistry related to less hazardous chemical syntheses, designing safer chemicals, and efficient catalysis.

The polymer structures were confirmed by NMR analysis. The ^{1}H-NMR spectrum of PTAd, named as PTAd-TF_00 and PTAd-FAd_00 in the two copolyester series, is provided as a representative example and depicted in Fig. 3. The spectra of the other BHMTHF-based polyesters are provided in the SI (Fig. S1–S6). The ^{13}C-NMR, COSY, HSQC, and HMBC spectra (SI, Fig. S7–S10) were used to assign all protons to their corresponding signals in the ^{1}H-NMR spectrum, due to overlapping signals of the protons "3" and "4" of the tetrahydrofuran ring, caused by the presence of the chiral carbons. The polymerization was confirmed by the substantial decrease of BHMTHF hydroxyl groups ("1") and methoxy groups of DMAd ("7"), and the appearance of the protons next to the formed BHMTHF ester group ("3" and "4").

The furan content of the copolyesters, either BHMF or FDCA content, was derived from ^{1}H-NMR spectra as well, which are provided in the SI (Fig. S11–S19). In case of the BHMF-based copolyesters, the integrated signals of the CH_2 groups of the furan next to the ester bond ("8") and the similar peaks of BHMTHF units ("3" and "4") were used to determine the actual furan content in the copolymers (eqn (7)). The

Table 2 (a) Structural and thermal characteristics of the copolyesters poly(tetrahydrofurandimethylene adipate-co-2,5-furandimethylene adipate) (PTAd-FAd_X) with varying BHMF content (X) and (b) the copolyesters poly(tetrahydrofurandimethylene adipate-co-tetrahydrofurandimethylene 2,5-furandicarboxylate) (PTAd-TF_Y) with varying FDCA content (Y). Molar furan feed ratio, molar furan content in the copolyester based on ^{1}H-NMR analysis, number average molecular weight ($\overline{M}_n$), weight average molecular weight ($\overline{M}_w$), polydispersity ($Đ$), degree of polymerization (DP), glass transition temperature (T_g), melting temperature (T_m), and 5% and 50% decomposition temperatures ($T_{d5\%}$, $T_{d50\%}$)

(a) Polymer	BHMF feed (%)	BHMF polymer (%)	$\overline{M}_n$ (g mol^{-1})	$\overline{M}_w$ (g mol^{-1})	$Đ$	DP	T_g (°C)	T_m (°C)	$T_{d5\%}$ (°C)	$T_{d50\%}$ (°C)
PTAd-FAd_100	100	100	6600	10 800	1.6	28	−18.8	65.5	271	293
PTAd-FAd_75	75	74	9800	15 200	1.5	41	−22.0	43.6	276	305
PTAd-FAd_50	50	50	10 500	17 500	1.7	44	−23.3	—	276	370
PTAd-FAd_25	25	24	8600	16 600	1.9	36	−24.8	—	298	375
PTAd-FAd_00	0	0	11 000	17 900	1.6	45	−27.5	—	303	365

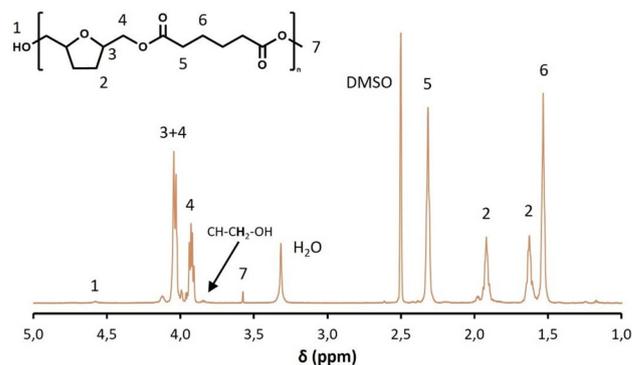| (b) Polymer	FDCA feed (%)	FDCA polymer (%)	$\overline{M}_n$ (g mol^{-1})	$\overline{M}_w$ (g mol^{-1})	$Đ$	DP	T_g (°C)	T_m (°C)	$T_{d5\%}$ (°C)	$T_{d50\%}$ (°C)
PTAd-TF_100	100	—	<500	<500	—	—	—	—	—	—
PTAd-TF_75	75	69	1000	1300	1.3	4	−3.0	—	267	385
PTAd-TF_50	50	53	4600	7100	1.6	18	−4.5	—	332	392
PTAd-TF_25	25	29	8500	15 100	1.8	35	−9.0	—	338	394
PTAd-TF_00	0	0	9100	17 200	1.9	38	−29.9	—	322	393

Fig. 3 ^{1}H-NMR spectrum of poly(tetrahydrofurandimethylene adipate) (PTAd, PTAd-TF_00, PTAd-FAd_00) in DMSO-d$_6$.

FDCA content was derived from the integrated BHMTHF peaks "3" and "4" for the BHMTHF-DMAd segments, and similar signals at slightly higher ppm for the BHMTHF-FDCA segments ("8" and "9") (eqn (8)).

The results are provided in Table 2a and b, and reveal that the feed ratios are similar to the final ratios in the case of the BHMF-BHMTHF-based and FDCA-BHMTHF-based copolyesters. The oligomer PTAd-TF_75 yielded a furan ratio of 69%, however this value is underestimated due to the presence of relatively large DEFDCA end groups that overlap with the BHMTHF ester bonds.

$$\text{BHMF content polymer } (\%) = \frac{I_{\text{BHMF "8"}}/4}{I_{\text{BHMF "8"}}/4 + I_{\text{BHMTHF "3+4"}}/6} \times 100 \quad (7)$$

$$\text{FDCA content polymer } (\%) = \frac{I_{\text{FDCA "8+9"}}}{I_{\text{FDCA "8+9"}} + I_{\text{BHMTHF "3+4"}}} \times 100 \quad (8)$$

Thermal behavior

The thermal stability of the BHMTHF-based polyesters was determined by TGA analysis and the results of the first series are given in Table 1, while the curves are depicted in the SI (Fig. S20). All polyesters demonstrated a high thermal stability with $T_{d5\%}$ and $T_{d50\%}$ values ranging from 285 to 342 °C and 387 to 420 °C, respectively. This illustrates that BHMTHF-based polyesters have enhanced thermal stability compared to their BHMF-based polyester counterparts.[24,29] The size of the aliphatic spacer had no significant influence on the thermal degradation behavior, attributed to their chemical similarities.

The thermal behavior of the polyesters was analyzed by modulated DSC experiments. The T_g values of the BHMTHF-based polyesters from the first series were obtained from the second reversing heating ramp to prevent interference with the relaxation enthalpy. Fig. 4 demonstrates the decreasing quadratic behavior of the T_g values as a function of the aliphatic spacer, *i.e.*, the number of methylene units in the aliphatic comonomer. A longer aliphatic spacer length increases chain
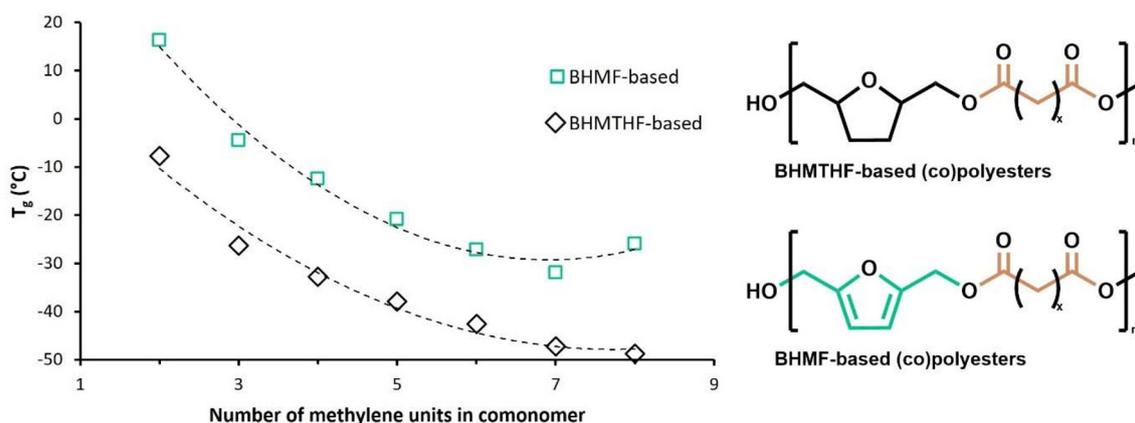
Fig. 4 T_g values of BHMTHF- and BHMF-based polyesters containing different numbers of methylene units in the comonomer segment, and the structural representations of the polyesters. Data of the BHMF-based polyesters is obtained from previous work.[29]

flexibility and mobility, while steric hindrance decreases due to the relatively lower BHMTHF content for a higher number of methylene units. This thermal behavior is very similar to the BHMF-based polyesters that are synthesized with the same aliphatic comonomers; only the absolute T_g values of the BHMF-based polyesters are approximately 20 °C higher. This difference is attributed to the planar and aromatic structure of BHMF, which is absent for BHMTHF.

All BHMTHF-based polymers from the first series lack a melting endotherm and are therefore completely amorphous. This corresponds well with the literature, for PTSuc and PTAd, respectively, and their appearance as a viscous liquid.[8] The lack of crystallinity was attributed to the rigidity of the ring structure of BHMTHF, which disrupts interactions between the chains.[15]

The $T_{d5\%}$ and $T_{d50\%}$ of the two series of copolyesters are given in Table 2a and b for the BHMF and FDCA-based copolyesters, respectively. The thermal stability of the BHMF-based copolyesters (PTAd-FAd) increased for higher BHMTHF content, as represented by the $T_{d5\%}$ values. In addition, these copolyesters demonstrated a twostep degradation profile (Fig. S21), which corresponded well with the degradation profiles of the pure polyesters and could be linked to the composition of the copolyesters.

The thermal stabilities of the FDCA-based copolyesters were all relatively high and similar in magnitude. However, the oligomer PTAd-TF_75 demonstrated a lower $T_{d5\%}$ value, which is attributed to its significantly lower molecular weight.

The thermal behavior of the two series of BHMTHF-based copolyesters are depicted in Fig. 5. The T_g values of the BHMF-BHMTHF-based copolyesters increased linearly with a higher furan content as a result of increased structural rigidity. In other words, the T_g values of the copolyesters align well between the values of the two homopolyesters PTAd-FAd_100 (−19 °C) and PTAd-FAd_00 (−28 °C), and correspond well with literature values of the same homopolyesters, −13 and −33 °C, respectively.[8,29]

The T_g values of the FDCA-BHMTHF-based copolyesters increased more drastically for a higher furan content. This behavior is expected due to the high T_g value of the homopolyester PTAd-TF_100 (poly(2,5-tetrahydrofurandimethanol 2,5-furandicarboxylate) (PTF)), which could not be enzymatically synthesized, but literature reported values around 75 °C.[7,13] The T_g value of the oligomer PTAd-TF_75 is included, however, is expected to be on the low side due to the limited molecular weight.

The BHMF-based polyester PFAd, synthesized in our previous work, is known to be a semicrystalline material with a relatively low T_m (63 °C).[29] This T_m (65 °C) was also observed in the first heating ramp of the same polyester (PTAd-FAd_00) in this work (Fig. S26). In addition, the copolyester PTAd-FAd_25 also demonstrated a T_m (44 °C), and was considerably lower in magnitude, which indicated a significant reduction in degree of crystallinity. None of the other copolyesters, from both series, demonstrated a melting endotherm, attributed to BHMTHF's ability to hinder crystallization.[7]

The modulated DSC curves of the second reversing heating ramps of all BHMTHF-based (co)polyesters are provided in the SI (Fig. S23–S25).

Rheology

The mechanical behavior of the BHMTHF-based polyesters was analyzed by rheology. A strain sweep was initially performed to determine the linear viscoelastic behavior at 40 °C, well above all T_g values. Subsequently, a frequency sweep was applied to study the behavior at various shear stresses and the results of the complex viscosity *versus* frequency of the first series BHMTHF-based homopolyesters are shown in Fig. 6a. In all cases, the amorphous polyesters behaved like low viscous Newtonian fluids, since the complex viscosity was hardly influenced by the frequency. Only a minor shear-thinning behavior was observed for the polymers PTPim, PTSub, PTAze, and PTSeb at higher frequencies. The low frequency complex viscosity (1 rad s^{-1}) of each polyester was plotted *versus* the
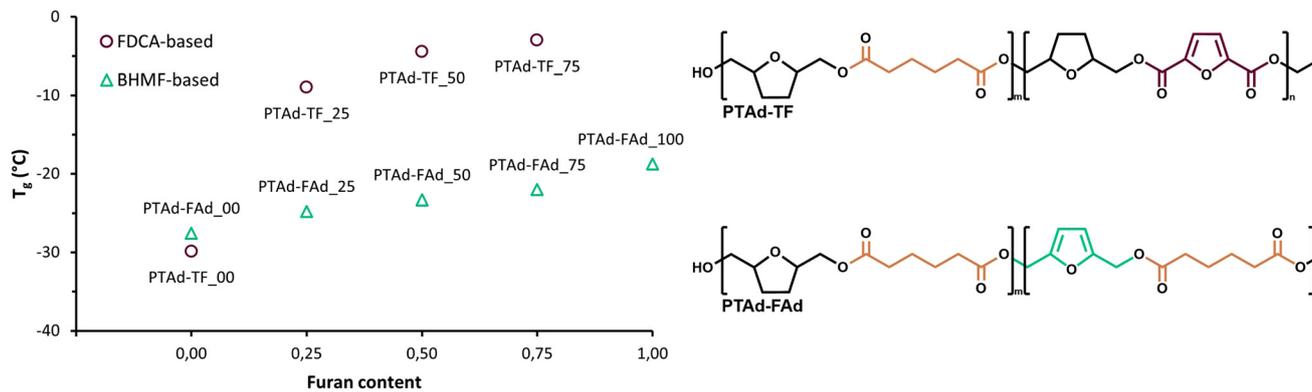
Fig. 5 T_g values *versus* the furan content of the copolyesters (PTAd-FAd_X) with varying BHMF contents (X) and the copolyesters (PTAd-TF_Y) with varying FDCA contents (Y), and the structural representations of the copolyesters.

number of methylene units in the aliphatic comonomer (Fig. 6b). This demonstrated a decreasing viscosity for BHMTHF-based polyesters containing a longer aliphatic segment. This phenomenon was also observed for BHMF-based polyesters obtained from the same aliphatic comonomers.[29]

The same rheology experiments were performed on the two series of copolyesters. The low frequency complex viscosities were derived from the frequency sweeps (Fig. S27 and S28), and are plotted here *versus* the furan content, either BHMF or FDCA. Fig. 6c visualizes that the incorporation of FDCA results generally in higher strength materials with respect to the BHMF-based copolyesters, which aligns with the T_g results. In addition, in both cases, a higher furan content resulted in higher viscosities. The copolyester PTAd-TF_75 is an outlier in this trend; however, the low strength was attributed to its low molecular weight ($\overline{M_n} = 1000\,\mathrm{g\,mol}^{-1}$). The polymers PTAd-TF_100 and PTAd-FAd_100 demonstrated a very similar viscosity, which is expected given that they are structurally identical polyesters (PTAd) with similar $\overline{M_n}$. The polymer PTAd-FAd_100 was not subjected to the rheology measurements, since its T_m (65 °C) is higher than the experimental temperature (40 °C). PTAd-FAd_75 was also observed as a semi-crystalline material (T_m = 44 °C), but its melting endotherm was very low in magnitude and the material behaved like a viscoelastic material during the strain and frequency sweeps. Therefore, this data point is still included in Fig. 6c, but could have been influenced by minor crystalline phases in the material during the measurement.

In summary, the rheological behavior of the BHMTHF-based (co)polyesters was demonstrated to be tunable by varying the number of methylene units or the furan content. In addition, it indicates their behavior during (re)processing and confirms their recyclability to prevent waste and increase their sustainability.

Biodegradation

The biodegradability of the BHMTHF-based polyesters was tested in activated sludge, which consists of various naturally occurring microorganisms, and is the most common inoculum, and is seen as a reliable method to study the biological degradation of polymers.[39] Although the biodegradability of polymers is dependent on multiple parameters, for example, environmental conditions and the type of microorganisms, the polymeric properties play an important role as well. First of all, the amorphous parts of semi-crystalline polymers are more prone to biodegradation than the crystalline phases.[40] Furthermore, aliphatic polyesters generally have a higher rate of biodegradation compared to aliphatic–aromatic polyesters.[41,42]

Fig. 7a demonstrates the percentage of biodegradation *versus* time for the first series of BHMTHF-based polyesters, and supports this theory. All these polyesters demonstrated a clear biodegradation behavior over time in activated sludge. The percentage of biodegradation of days ranged from 60 to 89%, while there was no discernible relationship observed between the chemical structure and degree of biodegradation.

The biodegradation behavior of the BHMF-BHMTHF-based copolyesters is depicted in Fig. 7b. All copolyesters were partially degraded in the active sludge, and the percentage of biodegradation ranged from 60 to 78%. Similar results are obtained from the FDCA-BHMTHF-based polyesters, which resulted in biodegradation rates ranging from 44 to 81% (Fig. 7c). In both series, the copolyester composition did not influence the biodegradation performances significantly. This is attributed to the amorphous morphology and low T_g values of all these copolymers, implying a similar physical appearance.

The pure BHMF-based polyester PTAd-FAd_100 (PFAd) demonstrated a remarkably lower degree of biodegradation (8%) compared to the copolyesters, while the biodegradation result of the same polyester in our previous work was also higher (22%).[29] The difference regarding the BHMF-BHMTHF-based copolyesters is attributed to the differences in crystallinity. PTAd-FAd_100 demonstrated a clear melting peak, while PTAd-FAd_75 showed only a small melting endotherm and the other copolyesters were completely amorphous (Table 2). The lower percentage of biodegradation with respect to our pre-
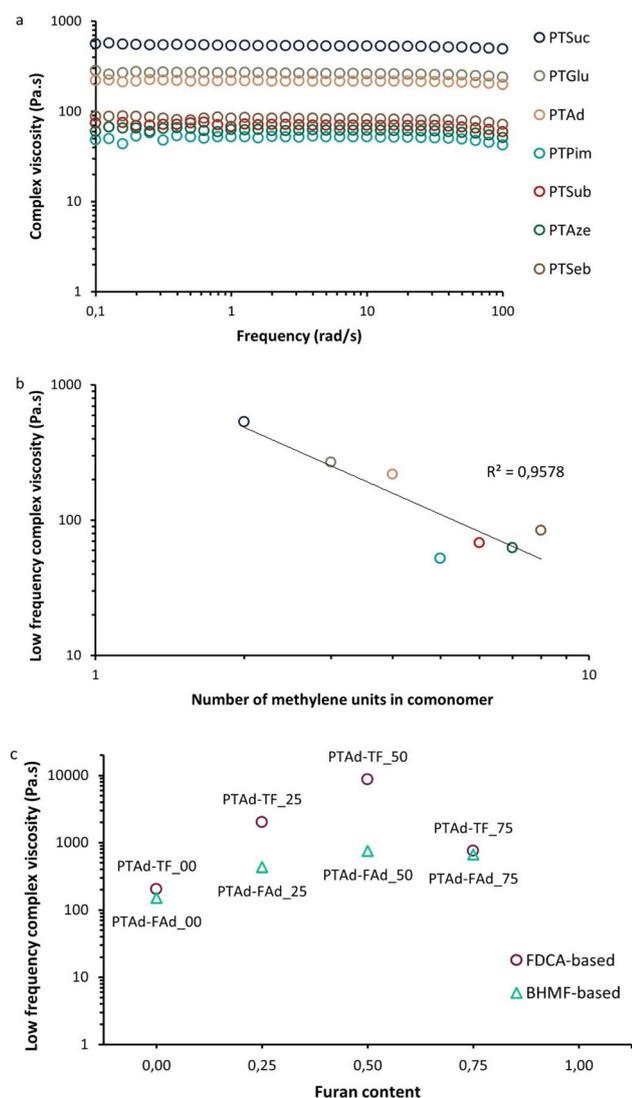
Fig. 6 (a) Complex viscosity *versus* angular frequency of the polyesters obtained from BHMTHF and aliphatic comonomers. (b) Low shear viscosity (1 rad s^{-1}) *versus* the number of methylene units in the comonomer of the BHMTHF-based polyesters. (c) Low shear viscosity *versus* furan content of the copolyesters (PTAd-FAd_*X*) with varying BHMF content (*X*) and the copolyesters (PTAd-TF_*Y*) with varying FDCA content (*Y*). All rheology measurements were performed at a constant temperature of 40 °C.

vious result of the same polyester is explained by a difference in surface area. In this work, all viscous polymers were attached to the stirring bar at the start of the experiments, while PTAd-FAd_100 was first melted and subsequently also attached to the stirring bar for consistency in surface area. In our previous work, all polyesters were added as a fine powder, implying a higher surface area and enhanced biodegradation.

All polymers are measured in duplicate, except for the polymers highlighted (*) due to technical failure of the setup. However, the simplex data of these polymers are in line with expectations and the other polymers tested in duplicate, and

are therefore still considered to give a good estimation of the biodegradation behavior. The minor fluctuations in the obtained BOD values and calculated percentages of biodegradation are attributed to relatively small variations in the surrounding temperature during the experiments.

In summary, the percentage of biodegradation after 28 days ranged from 44 to 89% for all BHMTHF-based (co)polyesters, and can therefore be considered biodegradable. This is in line with expectations due to their similarities with biodegradable BHMF-based polyesters and their amorphous morphology.[29] The biodegradability of these polymers prevents the formation and accumulation of microplastics, which aligns with the principles of Green Chemistry about waste prevention, safer chemicals, design of degradation, and pollution prevention.

Green characteristic analysis

The greenness of the enzymatic bulk polymerizations was quantified using AE, RME, OE, *E*-factor and EcoScale (Table 3) in line with recent recommendations on multi-metric assessment of green chemistry processes.[43] For the BHMTHF homopolyesters (PTSuc–PTSeb), AE values are in a narrow range of approximately 77 to 82%, reflecting the favorable stoichiometry of diester–diol polycondensation with only methanol as byproduct. RME values between roughly 48 and 60% and OE values between about 60 and 77% indicate that the mass efficiency of these bulk polymerizations is mainly limited by the isolated yield rather than by intrinsic stoichiometric constraints. The corresponding *E*-factors (67–84) are in the range of pharmaceuticals at an industrial scale, due to the use of solvent for purification and product collection.[33] However, the use of solvents could be limited or eliminated in the case of upscaling, where the polymer product is commonly extruded directly from the reactor, which would drastically reduce the *E*-factor for all synthesized polymers. EcoScale scores (63–75) place all BHMTHF-based homopolyester syntheses firmly in the "acceptable" region (75–50), with PTGlu and PTSeb approaching the threshold for "excellent" protocols (>75), mainly attributed to their higher yields.

A similar picture emerges for the BHMF-BHMTHF-based copolyesters (PTAd-FAd series). Introduction of BHMF resulted in similar AE (79%) relative to the purely aliphatic PTAd, as expected from the similarities in molecular weight between BHMF and BHMTHF. In addition, RME (48–56%) and OE (61–71%) remain comparable to those of the homopolyesters due to similarities in yield. The *E*-factors ranged from 72 to 84 and were of similar magnitude as the aliphatic homopolymers due to an identical experimental procedure. EcoScale scores of 66 to 72 again classify these syntheses as "acceptable", with no significant influence of the BHMF content.

For the FDCA-BHMTHF-based copolyesters (PTAd-TF series), the metrics highlight both strengths and clear opportunities for further improvement. In the case of the FDCA-BHMTHF polymer (PTAd-TF_100), only the AE is presented since the enzymatic polymerization was unsuccessful for these two cyclic monomers, and the obtained oligomers would represent unrealistic values for the other green metrics.
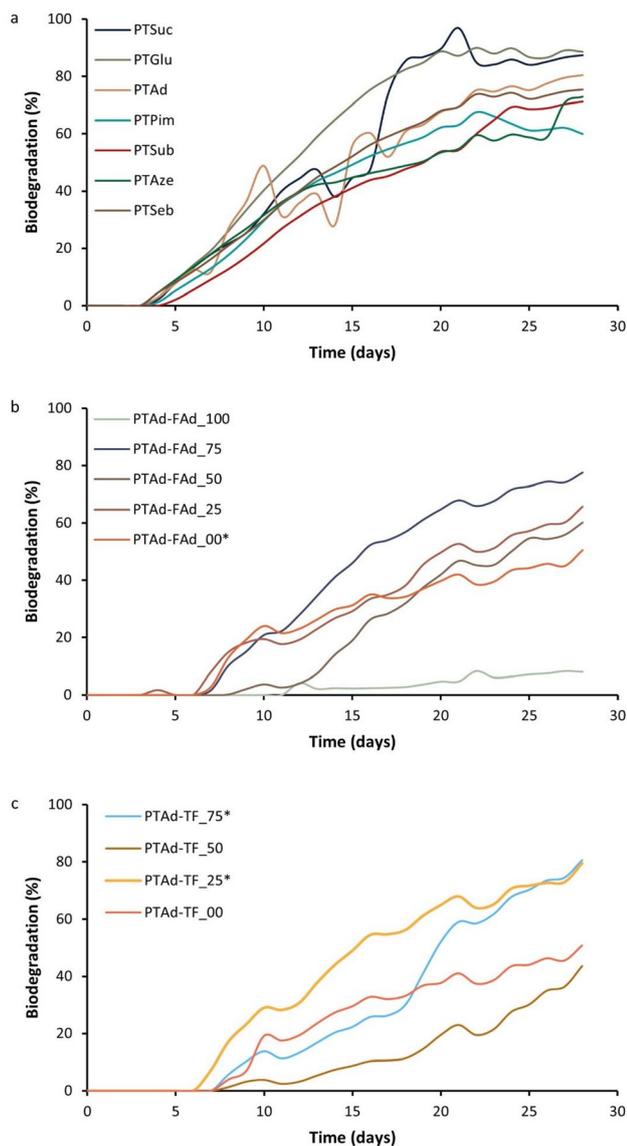
Fig. 7 Percentage of biodegradability in active sludge *versus* time of (a) the polyesters obtained from BHMTHF and aliphatic comonomers, (b) the BHMF-BHMTHF-based copolyesters, and (c) the FDCA-BHMTHF-based copolyesters. All samples are averaged based on duplicates, except the polymers denoted with *, which are simplex data points.

Table 3 Overall quantitative greenness metrics of the BHMTHF-based homopolyesters (a), BHMF-BHMTHF-based copolyesters (b), and FDCA-BHMTHF-based copolyesters (c), based on atom economy (AE), reaction mass efficiency (REM), overall efficiency (OE), *E*-factor, and EcoScale

Polymer	AE (%)	RME (%)	OE (%)	*E*-factor (kg/kg)	EcoScale
(a)					
PTSuc	77	48	62	84	67
PTGlu	78	60	77	67	75
PTAd	79	58	73	69	73
PTPim	80	50	62	81	64
PTSub	81	49	61	82	64
PTAze	82	49	60	82	63
PTSeb	82	54	66	74	69
(b)					
PTAd-FAd_100	79	56	71	73	72
PTAd-FAd_75	79	56	71	73	71
PTAd-FAd_50	79	56	71	72	72
PTAd-FAd_25	79	48	61	85	66
PTAd-FAd_00	79	55	70	74	71
(c)					
PTAd-TF_100	73	—	—	—	—
PTAd-TF_75	75	49	66	82	61
PTAd-TF_50	76	49	64	83	60
PTAd-TF_25	78	53	69	76	65
PTAd-TF_00	79	59	74	69	68

the BHMTHF homopolyesters. This underlines that the entire BHMTHF-based (co)polyester family can be accessed *via* protocols that are consistently in the "acceptable" EcoScale range and comparable in performance.

These values are in line with, and in several cases slightly better than, those reported recently for enzymatic bulk polycondensation of BHMF-based polyesters using the same immobilized CALB catalyst and very similar work-up procedures. This resulted in AE values around 77 to 82%, *E*-factors on the order of 98 to 161 and EcoScale scores between 62 and 73 for the synthesis of BHMF-based polyesters.[29]

A meaningful benchmark for the green advance of the present work is provided by the state-of-the-art preparation of BHMTHF-based polyesters *via* conventional melt polycondensation. Jin and co-workers demonstrated the synthesis of various BHMTHF-based polyesters at the kilogram scale using a titanium catalyst up to 240 °C under high vacuum and with multiple steps for pre-polymer formation and removal of low-molecular-weight by-products.[8] Although green metrics were not reported, the use of metal catalysts, high reaction temperatures, extended reaction times, and additional purification steps inherently increases energy consumption and the mass of auxiliaries, and would be expected to result in significantly higher *E*-factors and lower EcoScale scores than those obtained for the mild enzymatic bulk polymerizations described here.[45] In contrast, the present method operates at substantially lower temperatures, avoids any metal catalyst, and relies on a recyclable biocatalyst in a solvent-free reaction medium, which directly addresses several of the "Measuring Green Chemistry:

All other copolyesters in this series (PTAd-TF_75–PTAd-TF_00) show AE values of roughly 75 to 79%, RME values of 49 to 59% and OE in the range of 64 to 74%, with *E*-factors of 69 to 83 and EcoScale scores of 60 to 68. This shows that partial substitution of adipate by FDCA, enabling higher glass transition temperatures, complex viscosities, and expected improved barrier properties as reported for related furanic copolyesters,[44] can be achieved without a significant penalty in the reaction-level green metrics.

This highlights that the distribution of AE, RME, OE, *E*-factors, and EcoScale values across the PTAd-TF and PTAd-FAd series becomes essentially indistinguishable from that of

Methods, Models, and Metrics" criteria highlighted for greener polymer syntheses.[43]

At the same time, the metrics analysis clearly identifies the main hotspots of the current laboratory procedure. Across all polymerizations, the *E*-factor is dominated by the organic solvents used for precipitation, washing, and enzyme removal, rather than by the reagents themselves. This is consistent with quantitative studies showing that solvent use and work-up typically contribute the majority of the mass intensity and environmental burden in polymer synthesis.[29] In an industrial context, replacing chlorinated solvents with greener alternatives, minimizing the number of work-up steps and implementing solvent recycling or direct melt processing (for example, *via* extrusion of the crude polymer) would therefore be expected to reduce the effective *E*-factor by approximately an order of magnitude and move the EcoScale scores towards the "excellent" regime.

This work aligns with key Green Chemistry principles: the use of renewable feedstocks (7) such as sugar-derived monomers BHMTHF, BHMF, and FDCA; enzymatic catalysis (9) replacing metal catalysts; and energy-efficient, solvent-free bulk polymerization (6) under mild conditions. The resulting biodegradable materials (10) support circularity and environmental compatibility. Minor deviations occur in atom economy (2) due to methanol/ethanol release from ester monomers and in auxiliaries (5) through limited use of chloroform and diethyl ether for purification. Overall, the study exemplifies a renewable, catalytic, and degradable polymer synthesis consistent with the Green Chemistry framework.

Conclusion

BHMTHF, a rigid biobased building block containing a ring structure, was used in a *cis* : *trans* ratio of 90.6 : 9.4 for the enzymatic polymerization of various (co)polyesters. In the first series, BHMTHF was reacted with various aliphatic comonomers to obtain amorphous materials with a relatively high molecular weight, having a $\overline{M_n}$ ranging from 5500 to 11 200 g mol^{-1}. The second series consisted of copolyesters derived from BHMTHF, DMAd, and BHMF, wherein the BHMF-BHMTHF ratio was varied. Similarly, the third series consisted of copolyesters derived from BHMTHF, DMAd, and FDCA units, wherein the DMAd-FDCA ratio was altered. The BHMF-based copolyesters reached relatively high $\overline{M_n}$ values (6600–11 000 g mol^{-1}), while the enzyme iCALB had difficulties catalyzing the high FDCA content copolyesters, leading to lower $\overline{M_n}$ ranging from 1000–9100 g mol^{-1}.

DSC analysis demonstrated that a higher aliphatic spacer length in the first series resulted in a quadratic decrease in T_g values from −8 to −49 °C. Furthermore, a higher BHMF or FDCA content increased the T_g values of the copolyesters, this phenomenon was more pronounced in the FDCA-BHMTHF-based copolyesters.

Rheological analysis demonstrated that polyesters from the first series behave like Newtonian fluids, and the low shear viscosity decreased with an increase in aliphatic spacer length. The low shear viscosity increased with a higher furan content, which indicated that both BHMF and FDCA increased the strength of these materials.

Finally, biodegradation tests revealed that all BHMTHF-based (co)polyesters are prone to biodegradation in activated sludge. The aliphatic spacing length, BHMF, or FDCA content had no significant influence on the biodegradation performances due to their amorphous morphology and chemical similarities.

The greenness of the enzymatic synthesis of all BHMTHF-based (co)polyesters was evaluated based on AE, RME, OE, *E*-factor, and EcoScale. The polymer composition had no significant effect on the green characteristic metrics of these copolyesters, which were all assessed as "acceptable" according to the EcoScale criteria.

This study demonstrates the compatibility of BHMTHF to be used for various (co)polyesters featuring unique and tunable thermal and rheological properties. This paves the way for BHMTHF to be further explored and utilized as a renewable, rigid biobased monomer in a sustainable plastic economy.

Author contributions

C. Post: investigation, conceptualization, methodology, formal analysis, data curation, visualization, writing – original draft. G. Karchilakis: investigation, formal analysis, data curation, writing – review & editing. D. Maniar: supervision, writing – review & editing. V. S. D. Voet, R. Folkersma: supervision, funding acquisition, writing – review & editing. K. Loos: supervision, resources, project administration, funding acquisition, writing – review & editing.

Conflicts of interest

There are no conflicts to declare.

Data availability

The data supporting this article have been included as part of the supplementary information (SI). Supplementary Information: ^{1}H-NMR data and spectra, 2D-NMR spectra, TGA curves, DSC curves, and frequency sweeps of the BHMTHF-based (co)polyesters. Supplementary information is available. See DOI: https://doi.org/10.1039/d5gc06368j.

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