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Organocatalytic Synthesis of Poly(hydroxymethylfuroate) via Ring-Opening Polymerization of 5-Hydroxymethylfurfural-Based Cyclic Oligoesters

Daniele Ragno,*[a] Graziano Di Carmine,[a] Micaela Vannini,[b] Olga Bortolini,[c] Daniela Perrone,[c] Sara Buoso,[d] Monica Bertoldo,[a] and Alessandro Massi*[a]

In memory of Professor Giancarlo Fantin

The synthesis of hydroxymethylfuroate macrocyclic oligoesters ***c*(HMF)$_n$** promoted by an N-heterocyclic carbene (NHC) organocatalyst is herein presented together with the subsequent organocatalytic, entropically-driven ring-opening polymerization (ED-ROP) leading to the fully furan-based poly(hydroxymethylfuroate) (**PHMF**). The target macrocycles (mostly trimer and tetramer species) have been obtained directly from the platform chemical **HMF** (77% isolated yield) under high dilution conditions using a quinone as the external oxidant and the green solvent Me-THF. The ED-ROP of ***c*(HMF)$_n$** has been optimized at 160 °C (melt condensation technique) with the couple triazabicyclodecene (TBD)/n-octanol (1:1) as catalyst/initiator of the polymerization process in the presence of commercial antioxidants Irganox 1010 (0.1% w/w) and Irgafos 126 (0.3% w/w) to suppress degradation side reactions. Under these conditions, the bio-based **PHMF** (poly-HMF) was obtained as a color-free polymer with number-average molecular weight up to 48600 g mol^{-1} and dispersity between 1.5 and 1.9 as determined by NMR and GPC analyses. The thermal behavior of the novel furan-based polyester **PHMF** was investigated (TGA and DSC analyses) observing a good thermal stability (onset temperature of degradation ~310°C) and a semicrystalline structure with melting temperature above 160°C when processed from solvent, thus making **PHMF** a promising material for processing as others commercial polyesters.

Introduction

In recent years, depletion of crude oil resources and environmental concerns have driven extensive research on polymers from renewable feedstocks and greener polymerization strategies.[1] Linear polyesters (PEs) represent one of the main classes of polymers with diversified applications in the packaging, clothing, electronic, and biomedical fields.[2] Common methods for the synthesis of PEs include the step-growth polymerization of hydroxy acids or diol/diacid pairs, and the ring-opening polymerization (ROP) of lactones.[3] Among bio-based PEs,[4] polyfuranoates are of particular interest as sustainable alternatives to industrial PEs derived from terephthalic acid such as poly(ethylene terephthalate) (PET) and poly(butylene terephthalate) (PBT).[5] Indeed, poly(ethylene furanoate) (PEF) and poly(butylene furanoate) (PBF) are going to be produced on a large scale due to their favorable mechanical and barrier properties, recyclability, and integration within the context of a circular economy.[6] Renewable monomers typically employed to access furan-based polyesters and copolyesters are 5-hydroxymethyl-2-furancarboxylic acid (**HMFCA**), 2,5-dihydroxymethylfuran (**DHMF**), and furan-2,5-dicarboxylic acid (**FDCA**), which are synthesized from the platform chemical 5-hydroxymethyl furfural (**HMF**) in some steps (Figure 1).[6] Furanic PEs are usually produced by melt polycondensation or polytransesterification;[4a,5,7] however, the severe reaction conditions (eventually causing polymer discoloration/degradation), the need for by-product removal, and the moderate molecular weights may represent important limitations of those approaches in some occasions. Very recently, thanks to the pioneering studies of Morbidelli[8] and Muñoz-Guerra groups,[9] the entropically driven ring-opening polymerization (ED-ROP)[10] of furan-based macrocyclic oligoesters (MCOs) has emerged as an alternative strategy to access a variety of poly(alkylene 2,5-furandicarboxylate)s with high efficiency. While the ROP of small-to-medium size cyclic oligoesters takes place by the relief of the ring strain, the ROP of MCOs proceeds without enthalpy exchange and it is mainly driven by entropy. Advantages of this methodology are usually those deriving from a living polymerization mechanism and include a more precise control of the structure and molecular weight of the polymer, minimization of side reactions, and utilization of milder reaction conditions, this latter aspect being particularly relevant for polyfuranoates due to the intrinsic thermal instability of the furanic unit. Therefore, considerable efforts have been devoted to the synthesis of furanic MCOs, but limited to the class of alkylene 2,5-furandicarboxylates until now.[11] Current approaches towards this type MCOs involve the (pseudo)high dilution condensation (HDC)[12] of diols and the acyl dichloride derivative of **FDCA**,[11] and cyclodepolymerizations (CDPs) at high temperatures of furan-based polymers (Figure 1).[8b,9a,11,13] The former methodology relies on the Ziegler-Ruggli dilution principle;[14] accordingly, condensations are carried out at low concentration of reactants to maximize the rate of intramolecular reactions and favor the

formation of cyclic over linear oligomers. Very recently, the enzymatic condensation of diols with the dimethyl ester of **FDCA** catalyzed by environmentally benign enzyme catalysts has proven to be an effective strategy as well (Figure 1).[11,15]

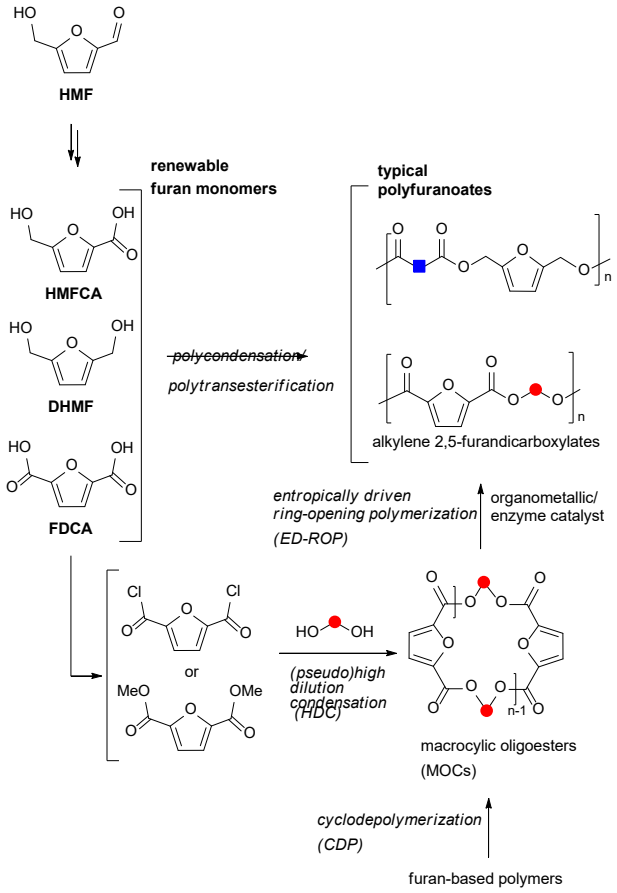


Figure 1. Main routes to typical polyfuranoates.

Organocatalysis also plays a prominent role in green polymer chemistry for promoting polymerization processes by the polycondensation and ROP techniques.[16] To the best of our knowledge, however, the application of non-toxic, metal-free organocatalysts to the synthesis of furanic MCOs is unreported in the literature. In the present study, we describe the first synthesis of hydroxymethylfuroate macrocyclic oligoesters ***c*(HMF)$_n$** by application of an N-heterocyclic carbene (NHC) organocatalyst[17] under high dilution conditions (Figure 2). Main advantage of the proposed methodology is the direct access to the target MCOs from the platform chemical **HMF**, which is catalytically activated as acyl azolium intermediate in the presence of an external oxidant.[18] The straightforward and efficient entry to ***c*(HMF)$_n$** (mostly trimer and tetramer species) paved the way to the unprecedented synthesis of the high molecular weight (HMW) poly(hydroxymethylfuroate) (**PHMF**) by organocatalytic ED-ROP using triazabicyclodecene (TBD) as the promoter.[10,16] Actually, the production of the fully furan-based polyester **PHMF** (poly-HMF) was previously attempted with little success by high temperature transesterification polymerization of the methyl ester of **HMFCA** catalyzed by a mixture of calcium acetate and antimony oxide.[19] By this strategy, however, **PHMF** was obtained as a brown powder in low yield and with modest molecular weight. The milder conditions of the herein disclosed approach to **PHMF** allowed, instead, to obtain a color-free HMW polymer, whose thermal properties were also evaluated to establish its potential in the field of bio-based materials.

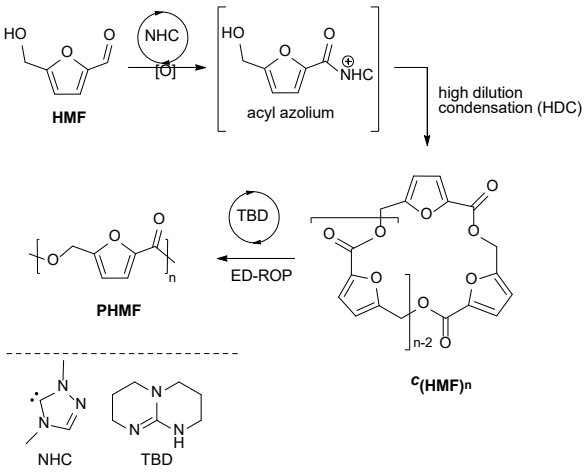
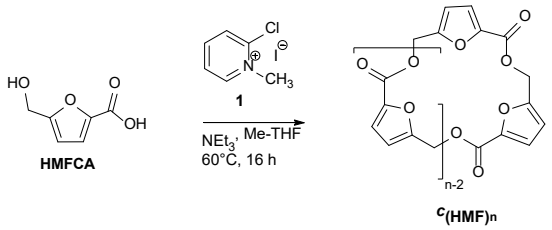


Figure 2. Fully-organocatalytic synthesis of poly(hydroxymethylfuroate) (**PHMF**) from 5-hydroxymethyl furfural (**HMF**).

Results and discussion

The feasibility of our synthetic plan toward **PHMF** was initially investigated by considering the previous synthesis of hydroxymethylfuroate macrocyclic oligoesters ***c*(HMF)$_n$** reported by Hirai and co-workers via polycondensation of **HMFCA**.[19b,c] By a slight modification of the original procedure aimed at improving process sustainability,[20] ***c*(HMF)$_n$** were prepared in the biomass-derived Me-THF at 60 °C using 2-chloro-1-methylpyridinium iodide **1** (2.5 equiv.) as condensing agent and Et_3N (3 equiv.) as the base (Scheme 1). Under these conditions, ***c*(HMF)$_n$** were isolated in 69% yield by chromatography and then fully characterized by NMR, ESI-MS, and HPLC analyses to determine the size and distribution of cycles.



Scheme 1. Synthesis of hydroxymethylfuroate macrocyclic oligoesters ***c*(HMF)$_n$** from **HMFCA**.

In agreement with Hirai study,[19b,c] the ^{1}H NMR spectrum of ***c*(HMF)$_n$** (Figure 3a) showed four cyclic species with different abundance (***c*(HMF)$_3$** = 42%, ***c*(HMF)$_4$** = 35%, ***c*(HMF)$_5$** = 14%, ***c*(HMF)$_6$** = 9%) and the absence of linear species. The ESI-MS analysis (Figure 3b) further confirmed the presence of cyclic trimers, tetramers, pentamers, and hexamers with a peak-to-peak mass increment of 124 Da corresponding to the methylfuran-2-carboxylate repeating unit (see ESI for full ESI-MS peak assignments and HPLC chromatogram).

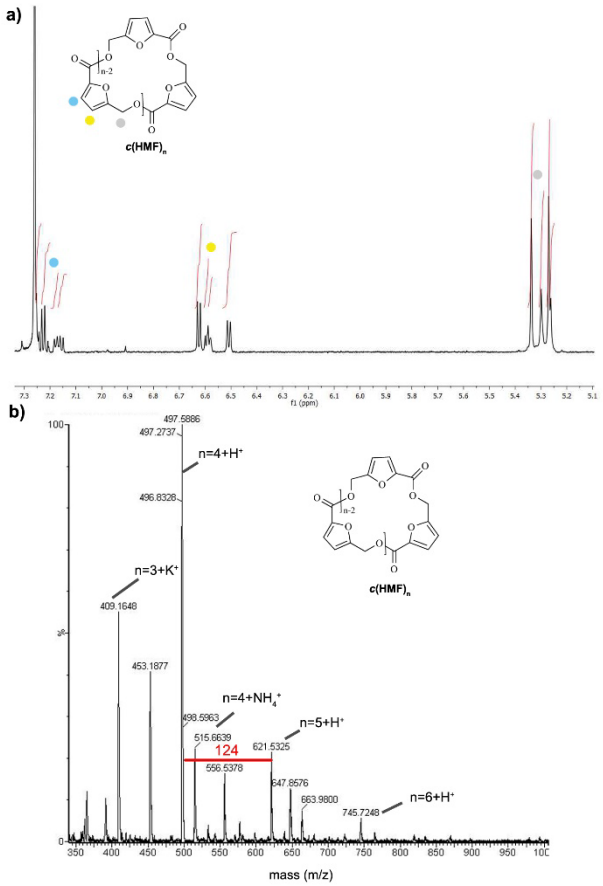
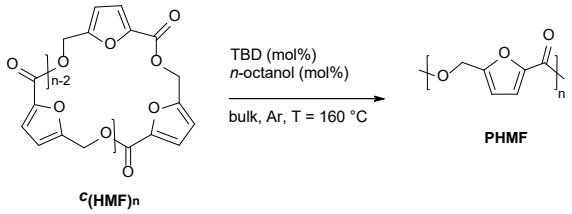


Figure 3. Characterization of hydroxymethylfuroate macrocyclic oligoesters ***c*(HMF)$_n$**: a) ^{1}H NMR spectrum (300 MHz, $CDCl_3$); b) ESI-MS spectrum (positive ion mode).

The thermal stability of ***c*(HMF)$_n$** was also evaluated by thermal gravimetric analysis (TGA; see the ESI), observing that the mixture of cycles was stable under nitrogen atmosphere up to 320 °C (onset temperature of degradation). Once established the promising thermal behavior of ***c*(HMF)$_n$**, the ED-ROP process was then investigated by the melt condensation technique. Actually, ED-ROPs are typically performed in solution at high concentration or solventless with melt MOCs, this latter method being more efficient in terms of polymer growth and reduction of reaction times.[10] We were aware, however, that processing ***c*(HMF)$_n$** at high temperatures could be troublesome due to the well-known thermal instability of the (hydroxymethyl)furan unit under acidic and/or oxidative conditions resulting in polymer discoloration and resinification.[6d-g] Indeed, although no weight loss was detected by TGA analysis up to 320°C (except the loss of trapped solvents and moisture), side reactions that do not result in mass decrease may occur. Hence, in a control experiment, the gradual heating (10 °C min^{-1}) of ***c*(HMF)$_n$** was evaluated in the reaction flask (inert atmosphere, Argon) observing a visible melting at 160 °C and no discoloration over 16 h with almost complete mass recovery of cycles after cooling. Afterwards, inspired by the work of Pinaud and co-workers on the use of TBD for the ROP of butylene terephthalate cyclic oligomers,[21] we examined the ROP of melt ***c*(HMF)$_n$** with this organocatalyst (2 mol%) and n-octanol (2 mol%) as the initiator (Table 1). All experiments run at temperatures higher than 160 °C (Argon atmosphere) led to partial discoloration after 30 minutes and formation of a hard black solid within 2 hours. To our delight, 160 °C was confirmed as the optimal polymerization temperature, observing complete conversion of ***c*(HMF)** in 15 h with slight discoloration of the polymer. Under these conditions, **PHMF** (hereafter referred to as **PHMF$_{E1}$**) was recovered as a beige solid in 88% yield after trituration with ethyl acetate (entry 1). The number-average molecular weight (M_n) of **PHMF$_{E1}$** was determined by ^{1}H NMR analysis ($M_{n(NMR)}$ = 5100 g mol^{-1}) and GPC ($M_{n(GPC)}$ = 5600 g mol^{-1}); the chain length dispersity (D = 1.6) was measured by GPC as well. Reduction of reaction time to 2 hours led to a partial decrease of conversion (86%) and yield (80%) accompanied by M_n increase (**PHMF$_{E2}$**: $M_{n(NMR)}$ = 6200 g mol^{-1}, $M_{n(GPC)}$ = 6600 g mol^{-1}) and no discoloration (entry 2). A further increment of polymer length (**PHMF$_{E3}$**: $M_{n(NMR)}$ = 9200 g mol^{-1}, $M_{n(GPC)}$ = 8400 g mol^{-1}) with comparable conversion (85%) was achieved after 4 h by halving the amount of catalyst and initiator (1 mol%; entry 3).

Application of a longer reaction time (6 h) in combination with 0.6 mol% of TBD/octanol couple gave **PHMF$_{E4}$** with higher molecular weight ($M_{n(NMR)}$ = 10400 g mol^{-1}, $M_{n(GPC)}$ = 9900 g mol^{-1}) but still as a beige material (entry 4). Hence, addition of the commercial antioxidants Irganox 1010 (0.1% w/w) and Irgafos 126 (0.3% w/w) was investigated with the aim to suppress the oxidative radical degradation of **PHMF**, which was likely triggered by the presence of residual oxygen in the reaction mixture.[22] Gratifyingly, full conversion of ***c*(HMF)** was observed after 6 h with no discoloration (see ESI) and increase in yield (95 %) and molecular weight (**PHMF$_{E5}$**: $M_{n(NMR)}$ = 13400 g mol^{-1}, $M_{n(GPC)}$ = 14400 g mol^{-1}; entry 5). Next, chain elongation was achieved with loss of conversion efficiency (77%) by decreasing the loading (0.25 mol%) of catalyst and initiator (**PHMF$_{E6}$**: $M_{n(NMR)}$ = 38000 g mol^{-1}, $M_{n(GPC)}$ = 18800 g mol^{-1}; entry 6). Looking at the M_n values of **PHMF$_{E6}$,** it appeared evident to us the discrepancy between the results provided by NMR and GPC analysis. After some experimentation, we concluded that the different outcome was attributable to polymer solubility. Indeed, GPC analysis of **PHMF** with different $M_{n(NMR)}$ (e.g. **PHMF$_{E1}$** and **PHMF$_{E6}$**) gave different UV-Vis response at the same concentration (w/v), although the two samples contained the same number of furanic units (see the ESI). This experimental evidence could be mainly explained by either incomplete polymer dissolution in the preparation of samples ($CHCl_3$:HFIP = 9:1) or precipitation during elution ($CHCl_3$:HFIP = 9.5:0.5). By contrast, NMR samples were fully solubilized in $CDCl_3$/trifluoroacetic acid (TFA) (1:1) solutions within 15 minutes. Nevertheless, the presence of minor amount of high molecular weight cyclic polyesters cannot be excluded.[23] In any case, only NMR analysis was considered for molecular weight determination of **PHMF** with M_n > 15000 g mol^{-1}. The optimization study was concluded without significant improvements considering the further reduction of TBD/octanol loading (0.12 mol%. **PHMF$_{E7}$**: $M_{n(NMR)}$ = 48600 g mol^{-1}, 38 % yield; entry 7) and the variation of catalyst/initiator ratio (1:2. **PHMF$_{E8}$**: $M_{n(NMR)}$ = 25000 g mol^{-1}, 70 % yield; entry 8), which also led to oligomer formation as detected by GPC analysis (see the ESI). Overall, the optimized conditions of entries 5-6 furnished **PHMF** with a level of efficiency comparable to that observed in previous studies on the synthesis of polyfuranoates by the ED-ROP strategy.[9b] Notably, the dispersities of synthetized **PHMF** (entries 1-8) ranged between 1.5 and 1.9 in accordance with expected *D* values for ED-ROP processes.[10]

Table 1. Optimization study for the synthesis of **PHMF** through organocatalyzed ED-ROP of ***c*(HMF)$_n$**.[a]



Entry	**PHMF**[b]	TBD : n-octanol (mol% : mol%)	Time (h)	Conv.[c] (%)	Yield[d] (%)	$M_{n(NMR)}$[e] (g mol^{-1})	$M_{n(GPC)}$[f] (g mol^{-1})	*D*[f]	Color
1	**$PHMF_{E1}$**	2 : 2	15	>95	88	5100	5600	1.6	Beige
2	**$PHMF_{E2}$**	2 : 2	2	86	80	6200	6600	1.7	White
3	**$PHMF_{E3}$**	1 : 1	4	85	74	9200	8400	1.6	Beige
4	**$PHMF_{E4}$**	0.6 : 0.6	6	89	85	10400	9900	1.5	Beige
5[g]	**$PHMF_{E5}$**	**0.6 : 0.6**	**6**	**>95**	**95**	**13400**	**14400**	**1.6**	**White**
6[g]	**$PHMF_{E6}$**	**0.25 : 0.25**	**7**	**77**	**75**	**38000**	**18800**	**1.6**	**White**
7[g]	**$PHMF_{E7}$**	0.12 : 0.12	16	46	38	48600	12500	1.6	White
8[g]	**$PHMF_{E8}$**	0.6 : 0.12	7	78	70	25000	13200	1.9	White

[a]***c*(HMF)$_2$** (100 mg, 0.8 mmol of furanic units), Ar atmosphere. [b]**$PHMF_{En}$** is related to **PHMF** synthetized in the corresponding entry. [c]Calculated from recovered ***c*(HMF)$_n$**. [d]Isolated yield. [e]Determined by ^{1}H NMR ($CDCl_3$:TFA = 1:1). [f]Determined by GPC. [g]Addition of Irganox 1010 (0.1% w/w) and Irgafos 126 (0.3% w/w).

The structure of **PHMF** was elucidated by one- and two- dimensional NMR spectroscopy (Figure 4 and ESI). The ^{1}H NMR spectrum of model **$PHMF_{E6}$** clearly showed high intensity peaks of the repeat unit (5.38, 6.68, 7.31 ppm) accompanied by weak signals of the terminal hydroxymethyl (4.80 ppm) and octyl (4.40, 1.60, 1.29, 0.88 ppm) groups (Figure 4a, zoom), thus confirming the role of n-octanol in the ring opening mechanism as initiator. The $M_{n(NMR)}$ values of **PHMF** reported in Table 1 were obtained from the integral ratios of peaks corresponding to the repeating (furan-2-yl)methylene and terminal hydroxymethyl groups (5.38 and 4.80 ppm, respectively). The ^{13}C NMR analysis further established the integrity of the (hydroxymethyl)furan moiety of **$PHMF_{E6}$** and, consequently, the important presence of antioxidant additives (Irganox 1010 and Irgafos 126) in the polymerization mixture. The newly synthesized HMW **PHMF** exhibited good thermal stability as confirmed by TGA analysis of **$PHMF_{E5}$**, whose onset temperature of degradation was at 310°C, close to the one of ***c*(HMF)$_n$**(ESI). Differential scanning calorimetric (DSC) analysis of **$PHMF_{E5}$** showed two endothermic peaks in the first heating scan (Figure 5) with maximum temperature at 165 and 194°C, thus suggesting a semi-crystalline structure. The peaks were not detectable anymore in the second heating scan up to 220 °C (Figure 5a), where only a baseline step was observed at 86° C. In addition, no exothermic peak was detected on cooling. After solubilization with HFIP and drying at room temperature, the sample showed again the endothermic peak on heating (ESI), with no peak on cooling and on further heating, thus excluding extended degradation as cause of the absence of crystallization. Furthermore, if the first heating scan is stopped at 200°C instead of 220°C, that is just after the melting peak, in the subsequent heating, a cold crystallization process followed by melting was observed (Figure 5b), suggesting a self-nucleation capability due to a memory effect.[24] This behavior clearly indicates that **PHMF** is a semi-crystalline polymer that easily crystallizes from solution, while it does not from the melt unless nucleated. In this case, it behaves as an amorphous polymer with Tg at 86°C. The semi-crystalline structure was confirmed also by X-ray diffraction analysis (XRD) of **$PHMF_{E5}$** after solubilization with HFIP and drying at room temperature (ESI).

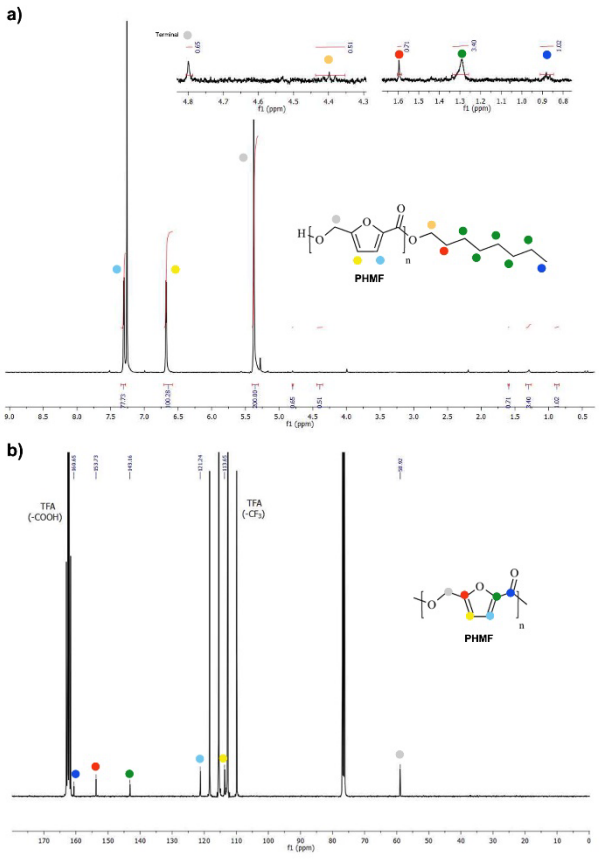


Figure 4. a) ^{1}H NMR spectrum of **PHMF$_{E6}$** (300 MHz, $CDCl_3$:TFA = 1:1). b) ^{13}C NMR spectrum of **PHMF$_{E6}$** (101 MHz, $CDCl_3$: TFA = 1:1).

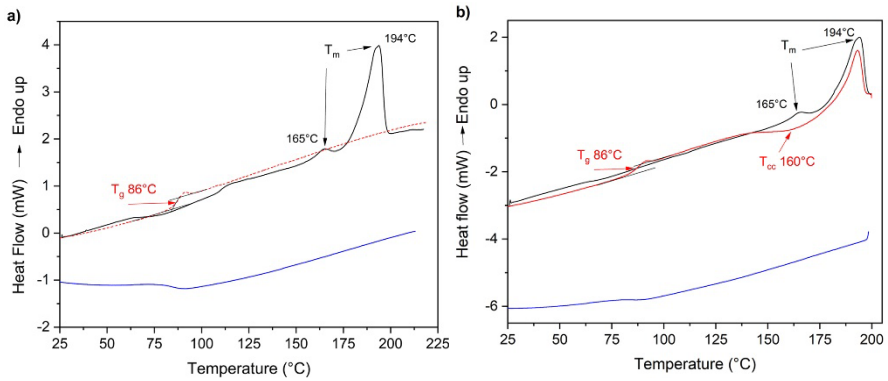
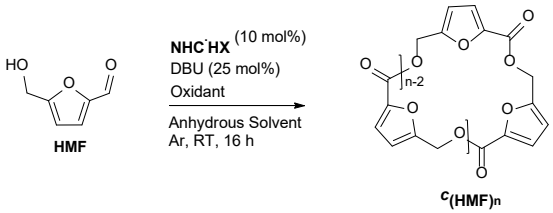


Figure 5: Differential scanning calorimetric (DSC) analysis of **PHMF$_{E5}$** with maximum heating temperature of 220°C (a) and 200°C (b): first heating scan (solid black line), cooling scan (solid blue line), and second heating scan (dash red line).

At this stage of our study we were interested in the development of a more sustainable and straightforward route to valuable ***c*(HMF)$_n$** starting from the platform chemical **HMF**. Based on our experience in the application of oxidative NHC catalysis as synthetic platform to access bio-based furan polyesters/polyamides[3c,25] and HMF upgraded products,[26] we commenced our investigation by considering the polycondensation of **HMF** (0.13 M, THF) promoted by the triazolium pre-catalyst **A** (10 mol%) in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU; 0.25 mol%) and a stoichiometric amount (1.0 equiv.) of the quinone oxidant **2** (Table 2, entry 1). After reaching full **HMF** conversion (16 h), the reaction mixture was triturated in ethyl acetate (EtOAc), filtrated to remove insoluble linear oligomers, and submitted to flash chromatography to obtain ***c*(HMF)$_n$** in 24% yield (see the Experimental Section for details). As expected on the basis of the Ziegler-Ruggli principle,[14] a 10-fold dilution (**HMF**: 0.013 M, THF) led to an important improvement in terms of selectivity (cyclic vs. linear oligomers) allowing for the isolation of

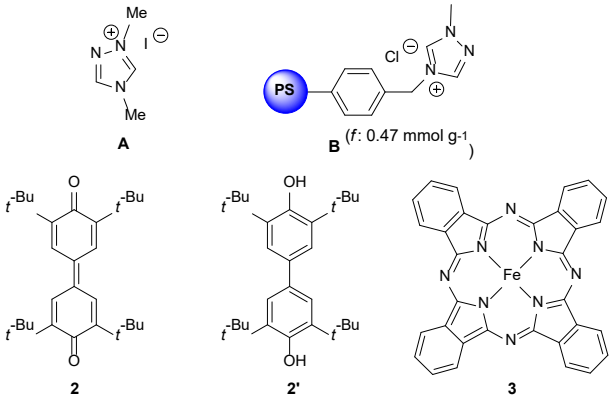
***c*(HMF)$_n$** in satisfactory 73% yield (entry 2). Next, the use of air as the terminal oxidant was investigated under diluted conditions by applying the biomimetic system of electron-transfer mediators (ETMs) developed by Bäckvall[27] and Sundén[28] groups. By this strategy, catalytic quinone **2** (10 mol%) is first reduced to the corresponding diol **2'** during acyl azolium formation, and then reoxidized by atmospheric oxygen in the presence of catalytic iron(II) phthalocyanine **3**.[26b] Unfortunately, under these conditions **HMF** was only partially converted (80%) and ***c*(HMF)$_n$** were isolated in modest 56% yield (entry 3). Heterogeneous high dilution conditions were also tested using the polystyrene-supported triazolium pre-catalyst **B**, which proved to be a highly active promoter of this type of catalysis in our previous investigations.[26] Disappointingly, application of both oxidation systems (stoichiometric **2** and aerial oxygen) with heterogeneous **B** led to good HMF conversions but low selectivities toward ***c*(HMF)$_n$** (25% and 13% isolated yield, entries 4-5). Additionally, the best conditions of entry 2 were tested using the biomass-derived Me-THF as the solvent observing a comparable reaction outcome by the recovery of ***c*(HMF)$_n$** in 74% yield (entry 6). Remarkably, the optimized process could be scaled up to 6.5 mmol of **HMF** affording ***c*(HMF)$_n$** in 77% yield (entry 7), this value being in line with previous HDC studies.[8a,9,15a,15b] In this gram-scale experiment, Me-THF was easily recovered by distillation and the diol **2'** separated and reoxidized to **2** with air in the presence of catalytic phthalocyanine (see the Experimental Section).

Table 2. Optimization study of the NHC-catalyzed synthesis of ***c*(HMF)$_n$**.[a]



Entry	**NHC·HX**	Oxidant (mol %)	Solvent	Conv. (%)[b]	***c*(HMF)$_n$** (%)[c]
1	**A**	**2** (100)	THF	>95	24
2[d]	**A**	**2** (100)	THF	>95	73
3[d]	**A**	Air, **2**/**3**[e]	THF	80	56
4[d]	**B**	**2** (100)	THF	>95	25
5[d]	**B**	Air, **2**/**3**[e]	THF	72	13
6[d]	**A**	**2** (100)	**Me-THF**	**>95**	**74**
7[f]	**A**	**2** (100)	Me-THF	>95	77

[a]**HMF** (1.60 mmol), anhydrous solvent (12 mL). [b]Detected by 1H NMR analysis of the crude reaction mixture (durene as internal standard). [c]Isolated yield. [d]Anhydrous solvent (120.0 mL). [e]**2** (10 mol%), **3** (5 mol%), atmospheric air (balloon technique). [f]**HMF** (6.50 mmol), **A** (0.65 mmol), DBU (1.6 mmol), Me-THF (480 mL).



Size and distribution values of HMF-derived ***c*(HMF)$_n$** (Table 2) were totally comparable with those of HMFCA-derived ***c*(HMF)$_n$** (Scheme 1), in details ***c*(HMF)$_3$** = 47%, ***c*(HMF)$_4$** = 36%, ***c*(HMF)$_5$** = 10%, ***c*(HMF)$_6$** = 7% (see the ESI for NMR and HPLC analyses). Analogously, the TBD-promoted ROP of ***c*(HMF)$_n$** from Table 2-entry 5 gave **PHMF** as a withe solid with conversion (92%), yield (90%), molecular weight ($M_{n(NMR)}$ = 12400 g mol^{-1}, $M_{n(GPC)}$ = 14300 g mol^{-1}), and dispersity (*D* = 1.8) values very similar to those registered for **PHMF$_{E5}$** under the same polymerization conditions (see the ESI).

Conclusions

In summary, we have described the unprecedented synthesis of hydroxymethylfuroate macrocyclic oligoesters ***c*(HMF)$_n$** (trimer to hexamer species) starting from the bio-based aldehyde **HMF** mediated by an N-heterocyclic carbene (NHC) catalyst under high dilution oxidative conditions using Me-THF as recyclable solvent. Macrocyclic oligoesters ***c*(HMF)$_n$** proved to be suitable substrates for subsequent ED-ROP promoted by TBD affording, for the first time, high molecular weight poly(hydroxymethylfuroate) (**PHMF**) with number-average molecular weight up to 48600 g mol^{-1} and dispersity between 1.5 and 1.9. Polymer discoloration and undesired side reactions were suppressed under the optimized reaction conditions, allowing for the production of a color-free polymer with excellent yields. The new bio-based polyester **PHMF** is a semicrystalline polymer with melting temperature above 160°C when processed from solvent. It does not crystalize easily from the melt giving an amorphous solid with glass transition temperature of 86°C. However, if nucleated, **PHMF** crystallizes also on heating in the absence of solvents. Its thermal stability is very good starting to degrade at ~310°C under nitrogen atmosphere, thus looking promising for processing as others commercial polyesters such as PBT or PET. Further investigations aimed at evaluating reaction kinetics, process scale-up, rheological and mechanical properties of **PHMF** are currently under way in our laboratories and results will be reported in due course.

Experimental section

Moisture-sensitive reactions were performed under an argon atmosphere using oven-dried glassware. Anhydrous solvents were freshly distilled and dried over standard drying agents prior to use. Reactions were monitored by TLC on silica gel 60 F_{254} with detection with phosphomolybdic acid. Flash chromatography was conducted on silica gel 60 (230-400 mesh). ^{1}H (300 MHz), ^{13}C (101 MHz) NMR spectra were recorded at room temperature in $CDCl_3$ and mixtures of $CDCl_3$: TFA (1 : 1 v/v). The chemical shifts in ^{1}H and ^{13}C NMR spectra were referenced to tetramethylsilane (TMS). Peak assignment was aided by gradient-HMQC experiments. ESI MS (LTQ-XL Linear Trap from Thermo Scientific) analyses were performed in positive ion mode with samples dissolved in a 10 mM solution of HCO_2NH_4 in 1:1 MeCN-H_2O. HPLC was performed using a Prep Nova-Pak HR SILICA column (60 Å, 6 µm, 3.9 x 300 mm), *n*-hexane/dioxane 70/30 (v/v) as eluent with a 1.0 mL/min flow and an Ultra-Violet detector (254 nm). GPC samples were prepared as follows: 1.5 mg of every sample were dissolved in 1 mL of 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) and kept in this solvent for 2 days, to ensure their complete dissolution. Then, 9 mL of $CHCl_3$ were added, allowing to reach 90/10, $CHCl_3$/HFIP (v/v) as solvent mixture ratio, and 0.15 mg/mL as solution concentration. The obtained solutions were filtered through a Teflon syringe filter with a pore size of 0.45 mm to remove possible insoluble fractions. Insoluble portions were not visible during sample solubilisation; nevertheless, solutions did not pass through the syringe filter smoothly during filtration. GPC

measurements were performed at 30°C on Hewlett Packard Series 1100 liquid chromatography (Milan, Italy) using a PL gel 5 mm Minimixed-C column and a mixture of $CHCl_3$/HFIP 95/5 (v/v) as eluent with a 0.3 mL/min flow; an Ultra-Violet detector was used and a calibration plot was constructed with monodisperse polystyrene standards. Elemental analyses were performed using a FLASH 2000 Series CHNS/O analyzer (ThermoFisher Scientific). Pre-catalysts **A**, 2-chloro-1-methylpyridinium iodide **1**, durene, Iron(II) phthalocyanine **3**, **HMF**, **HMFCA**, TBD, *n*-octanol, Irganox 1010 and Irgafos 126 were purchased from commercial source and used as received. DBU and Et_3N were freshly distilled before their utilization. Quinone oxidant **2** was synthetized according to a literature procedure.[29] Supported pre-catalysts **B** was synthetized according to a literature procedure[26a] and the relative degree of functionalization was detected via elemental analysis (*f*: 0.47 mmol g^{-1}). Differential scanning calorimetry (DSC) was performed with a PerkinElmer DSC 8000 equipped with intracooler II cooling device and Software Pyris for data acquisition and analysis. Analyses were accomplished under nitrogen atmosphere (30 ml/min) on 6-12 mg of sample in open aluminum pan. Program temperature was: heating from 25 to 200°C or 220°C, cooling back to -20°C and heating to 200-220°C (second scan). Heating and cooling steps were performed at 10°C/min as scanning rate. Instrument was calibrated with Indium and lead as standards. Thermogravimetric analysis was performed with PerkinElmer TGA4000 equipped with software Pyris for data acquisition and analysis. 6-7 mg of sample in alumina pan was analysed in the 25-900 °C temperature range under nitrogen atmosphere (50 ml/min) at 10°C/min as heating rate. Powder XRD data were obtained at room temperature on a Bruker AXS D8 Advance by using Cu Kα radiation (λ = 1.5406) with an applied operating voltage 40 kV and current 40 mA, over a 2θ range of 3-70°.

Synthesis of *c*(HMF)$_n$ from HMFCA (Scheme 1)

A mixture of **HMFCA** (1 g, 7 mmol), 2-chloro-1-methylpyridinium iodide **1** (4.5 g, 17.6 mmol) and Et_3N (3 mL, 21 mmol) in anhydrous Me-THF (60 mL) was stirred at 60 °C under an argon atmosphere. After solvent removal under reduced pressure, reaction mixture was dissolved in EtOAc (40 mL) and washed with water (2 × 20 mL). The organic layer was dried (Na_2SO_4), concentrated and eluted from a column of silica gel with heptane / EtOAc = 1 : 2 to afford a mixture of ***c*(HMF)$_n$** as a white amorphous solid (604 mg, 69%). Cycles composition was determined by NMR. ***c*(HMF)$_3$** (42 mol%); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.25 (d, *J* = 3.5 Hz, 3H, Ar), 6.50 (d, *J* = 3.5 Hz, 3H, Ar), 5.34 (s, 6H, CH_2). ***c*(HMF)$_4$** (35 mol%); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.22 (d, *J* = 3.5 Hz, 4H, Ar), 6.62 (d, *J* = 3.5 Hz, 4H, Ar), 5.27 (s, 8H, CH_2). ***c*(HMF)$_5$** (14 mol%); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.18(d, *J* = 3.5 Hz, 5H, Ar), 6.58 (d, *J* = 3.5 Hz, 5H, Ar), 5.30 (s, 10H, CH_2). ***c*(HMF)$_6$** (9 mol%); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.16 (d, *J* = 3.5 Hz, 6H, Ar), 6.60 (d, *J* = 3.5 Hz, 6H, Ar), 5.26 (s, 12H, CH_2).

Synthesis of *c*(HMF)$_n$ from HMF (Table 2, entry 6)

A mixture of **HMF** (162 µL, 1.60 mmol), quinone oxidant **2** (654 mg, 1.60 mmol), and pre-catalyst **A** (36 mg, 0.16 mmol) in anhydrous Me-THF (120 mL) was degassed under vacuum and saturated with argon (by using an Ar-filled balloon) three times. DBU was then added (60 µL, 0.4 mmol), and the reaction was stirred at RT for 16 h. The mixture was concentrated, triturated in EtOAc, filtrated (to remove insoluble linear polyesters) and submitted to flash chromatography. Reduced form of quinone oxidant **2'** was first recovered using heptane : EtOAc = 2 : 1 as elution system and submitted to recycle process (see above). Next, cycles mixture ***c*(HMF)$_n$** was isolated as a white amorphous solid (147 mg, 74%) using heptane : EtOAc = 1 : 2 as elution system. Cycles composition was determined by NMR: ***c*(HMF)$_3$** = 47mol%, ***c*(HMF)$_4$** = 36 mol%, ***c*(HMF)$_5$** = 10 mol%, ***c*(HMF)$_6$** = 7 mol%.

Procedure for quinone oxidant 2 recycle (Table 2, entry 7)

The quantitative oxidation of the recovered **2'** to quinone **2** was performed stirring **2'** (2.4 g, 5.85 mmol) with **3** (330 mg, 0.58 mmol) in THF (40 mL) under air atmosphere (1 atm, balloon) for 16 h. Filtration over a celite pad and concentration under reduced pressure afforded **2** as a red amorphous solid (2.30 g, 86%).

General procedure for the synthesis of PHMF

***c*(HMF)$_n$** (100 mg, 0.8 mmol of furanic units) was transferred in a reaction flask and dissolved in EtOAc (5 mL). Then, a mixture containing the required amounts (according to Table 1) of TBD, *n*-octanol and antioxidants (Irganox 1010 and Irgafos 126, when required) in EtOAc was added to cycles solution and stirred for 30 minutes. After this period, solvent was removed under reduced pressure and the reaction flask was connected to a glass oven (Büchi GKR-50) and dried under vacuum for 30 minutes. The mixture was degassed under vacuum and saturated with argon (by using an Ar-filled balloon) three times to remove residual oxygen, then heated at T = 160 °C under mechanical rotation for the requested time at atmospheric pressure. After cooling, the resulting product was triturated with EtOAc (10 mL). The soluble

fraction contained unreacted cycles while the precipitate corresponded to **PHMF** which was then analyzed by GPC and NMR. ^{1}H NMR (300 MHz, $CDCl_3$: TFA = 1 : 1) δ = 7.31 (d, J = 3.5 Hz, 1H, Ar), 6.68 (d, J = 3.5 Hz, 1H, Ar), 5.38 (s, 2H, CH_2), 4.80 (s, 2H, terminal $C\underline{H}_2OH$), 4.40 (t, J = 6.8 Hz, 2H, terminal $OC\underline{H}_2C_7H_{15}$), 1.60 (m, 2H, terminal $OCH_2C\underline{H}_2C_6H_{13}$), 1.29 (m, 10H, terminal $OCH_2CH_2C_5\underline{H}_{10}CH_3$), 0.88 (t, J = 7.1 Hz, 3H, terminal CH_3). ^{13}C NMR (101 MHz, $CDCl_3$: TFA = 1 : 1) δ = 160.6 (CO), 153.7 (C-5), 143.2 (C-2), 121.2 (CH-3), 113.6 (CH-4), 58.9 (CH_2O).

Conflicts of interest

There are no conflicts to declare.

Author contributions

Daniele Ragno: conceptualization, supervision, writing, investigation, methodology. Graziano Di Carmine: investigation, methodology. Micaela Vannini: investigation, methodology. Olga Bortolini: investigation, methodology. Daniela Perrone: investigation, methodology. Sara Buoso: investigation, methodology. Monica Bertoldo: conceptualization, supervision, writing. Alessandro Massi: conceptualization, supervision, writing.

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