Review

Ring opening polymerization of macrocyclic oligoesters derived from renewable resources

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

Antxon Martínez de Ilarduya,*[a] and Sebastián Muñoz Guerra*[a]

Macrocyclic oligoesters (MCOs) derived from biomass such as those made of alkylene alkanedioates and 2,5-furandicarboxylates are suitable compounds for ring opening polymerization (ROP) to produce high molecular weight bio-based polyesters. The synthetic procedures that have been recently developed to obtain these MCOs in good yields, their ROP either alone or together with other cyclic compounds, as well as their recovery by cyclodepolymerization of final polyesters, are the main topics covered in this review. Both organometallic compounds and enzymes such as *Candida antarctica* lipase B are the catalytic systems used for all reactions. This synthetic approach based on ROP of MCOs coming from renewable sources opens a green pathway for a circular economy in plastics.

1 Introduction

Linear polyesters stand out today as one of the main classes of polymers because of their exceptional properties and a wide diversity of applications that go from packaging to smart materials.[1] They derive either from hydroxyacids or from diol/diacid pairs and embrace both aliphatic and aromatic compounds. Most of polyesters used today are built up from petrochemical monomers. Poly(ethylene terephthalate) (PET), poly(butylene terephthalate) (PBT) and poly(butylene succinate) (PBS), are paradigmatic examples of commercial polyesters that are currently consumed in big amounts but still mostly produced from fossil feedstocks. The increasing environmental consciousness worldwide is motivating the growing interest for bio-based polyesters and also fostering new greener polymerization technologies that allow the development of more sustainable manufacturing strategies.[2]

Condensation polymerization (PC) and ring-opening polymerization (ROP) are the two main tools applied for linear polyester synthesis. PC is the method commonly used for the condensation of diols with either diacids or their methyl ester whereas ROP of lactones is the method preferentially chosen when polyesters derived from hydroxyacids are wanted. The PC technology was settled a long time ago and has remained substantially unmodified despite it is applied for the fabrication of the most important polyesters.[3] PC for polyesters is a two-stages bulk process consisting of an oligocondensation reaction leading to a prepolymer that is then converted into the final polyester by transesterification. PC generally requires high temperatures and low pressures to achieve satisfactory molecular weights, and metallic or organometallic catalysts are mostly used. ROP of cyclic esters is a much more dynamic technology that is continuously expanding to cover novel bio-based compounds emerging as promising options for the synthesis of greener polyesters. ROP requires less severe reaction conditions than PC because no volatile by-products have to be removed from the viscous polymerization media and therefore higher molecular weights can be usually achieved.[4]

Small to medium size cyclic oligoesters, i.e. those with a number of skeletal ring atoms between 3 and 12, are more or less strained cycles that readily polymerized by ROP involving an enthalpy output.[5] These include lactones of high commercial impact and technical relevance as glycolide, lactides, and ε-caprolactone. This subject has been review on several occasions and updating reports dealing with last advances in the field have recently appeared.[6] Macrocyclic esters, *i.e.* those containing 14 skeletal atoms at least, cover the macrocycles derived from long ω-hydroxyacids (macrolactones) as well as the macrocyclic oligoesters (MCOs) containing enough number of ester monomeric units. Since macrocycles are strainless rings, their ROP takes place without enthalpy exchange so that entropy is essentially the only polymerization driving factor. Entropically-driven ROP of MCOs exploits the occurrence of ring–chain equilibria between polyester chains and MOCs in the presence of a suitable catalyst. This issue has been extensively studied by different authors[7-9] and recently authoritatively reviewed by Hodge in 2014 in a comprehensive manner.[10] Nevertheless, this field is very active and continues growing with notable advances being achieved in these five last years in both cycle synthesis and ROP.[11-13]

This review is focussed on MCOs, in particular on those that have recently received exceptional attention for their impact on polyester sustainability, i.e. cyclic oligo(alkylene

[a] *Department d'Enginyeria Química, Universitat Politècnica de Catalunya, ETSEIB, Diagonal 647, 8028 Barcelona, Spain. E-mail: antxon.martinez.de.ilarduia@upc.edu; sebastian.munoz@upc.edu*

alkanedioate)s and oligofuranoates intended for the synthesis of bio-based polyesters by ROP. Novel compounds and synthetic routes, as well as those advances achieved in reaction procedures with special attention devoted to those concerning enzymatic catalysis, are surveyed. Macrolactones are not included in this review because they have been reviewed in detail last year by Heise et al.[14] Poly(alkanodioate)s and polyfuranoates are two distinguished classes of polyesters that are reaching a forward position in green polymer chemistry because their well-proven accessibility from renewable sources at large scale.[15, 16] Furthermore, the possibility of recycling these polyesters by thermal cyclodepolymerization to generate their respective MCOs adds invaluable merits to their preparation by ROP methods regarding their integration in a sustainable circular economy.

2 Synthesis and ROP of macrocyclic oligoesters

MCOs to be used for ROP may be extracted from their homolog polyesters or chemically produced by cyclization reactions. It is known that polyesters synthesized by the classical melt polycondensation process invariably contain small amounts (0.5-3.0 mol-%) of MCOs which can be recovered by solvent extraction from the crude polymer.[17] This method is particularly attractive when the production of MCOs derived from certain commercial polyesters is pursued at the industrial scale. On the other hand, various methods of general application have been used for the synthesis of MCOs, i.e. pseudo-high dilution condensation (HDC), cyclodepolymerization of the preformed polymer (CDP), and enzymatic cyclization (EC).[10]

2.1 Methods for the synthesis of MCOs.

2.1.1 Pseudo-high dilution condensation (HDC). This method was first used by Brunelle et al. for the preparation of MCOs derived from poly(butylene terephthalate) (PBT). The reaction is carried out by slow and simultaneous mixing of the diacid chloride and the diol at high dilution, usually below 0.2 M. Key factors for having high yields in cyclics are the presence of unhindered tertiary amines such as 1,4-diazabicyclo[2.2.2]octane (DABCO), which provides complete reactions in minutes, and the use of anhydrous solvents.[18] Cyclics have to be separated from linear oligomers by filtration and flash chromatography. This methodology has been applied for the preparation of several cyclic oligoesters derived from biobased monomers such as adipic[19] or 2,5-furandicarboxylic acids[20, 21] (Figure 1).

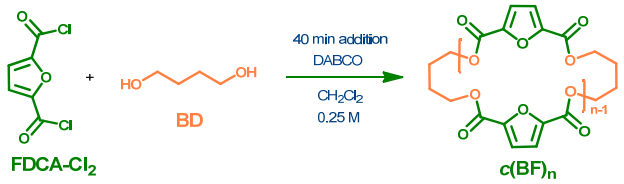

Fig 1. Synthesis of $c(BF)_n$ by HDC. Adapted from reference 20 with permission from Elsevier, copyright [2016].

2.1.2 Cyclodepolymerization. This method was discovered by Carothers et al.,[22] who observed that linear polyesters could be depolymerized by thermal treatment to cyclic oligomers using different metal catalysts. The procedure is based on the chemical equilibrium that takes place between linear chains and cyclic oligomers at high temperatures. This equilibrium is shifted to the formation of cycles if they are continuously removed from the reaction mixture by high vacuum distillation or if the reaction is carried out at high dilution (Figure 2).[23, 24] As this method provides MCOs that can be polymerized again to produce the same original polymer, it has been also termed as "ring chain recycling" (RCR).[25] The method has been applied for the preparation of biobased MCOs derived from succinic,[26, 27] fumaric,[28] adipic[29, 30] and 2,5-furandicarboxylic acids.[20, 31, 32]

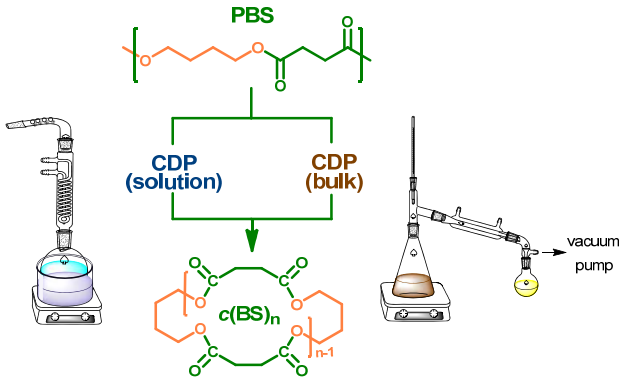

Fig 2. Different CDP routes for the synthesis of $c(BS)_n$ from poly(butylene succinate) (PBS).

2.1.3 Enzymatic cyclization/depolymerisation (EC/ED). In this method the MCOs are generated from monomers or condensation polymers dissolved in organic solvents and with the concourse of non-toxic and eco-friendly enzyme catalysts, the most widely used being *Candida antarctica* lipase B (CALB).[33]

High dilution is a required condition to get high yields in MCOs production otherwise concentrated solutions shifts the equilibrium to the formation of the polymer (Figure 3). This methodology has been applied for the synthesis of several biobased MCOs derived from succinic,[34-45] adipic[34, 40, 41, 43] or 2,5-furandicarboxylic acids.[46]

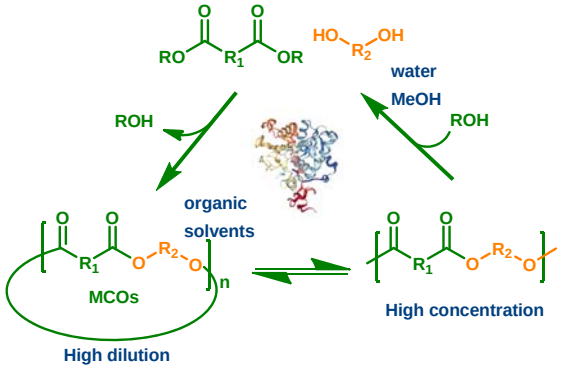

Fig 3. Different routes for the enzymatic synthesis of MCOs.

2.2 Alkylene alkanedioate MCOs

Succinic acid and adipic acids are two aliphatic diacids that can be produced by petrochemical or by renewable resources using different fermentation processes.[47] They have been used for the production of aliphatic polyesters and copolyesters that find applications in packaging or in the biomedical fields.[48-50] These polyesters are usually obtained by melt polycondensation of an aliphatic dicarboxylic acid or its dimethyl ester and the corresponding alkanediol. However, the molecular weights usually achieved by this method are low, and chain extension with diisocyanates is sometimes required for attaining high molecular weight polymers able to display good mechanical properties.[51] ROP of cyclic alkylene alkanedioate oligoesters has been proposed as an alternative to overcome this problem with the additional advantages that no side products are generated during the reaction. Since MCOs could be recovered in high yields from polyesters, this methodology is promising as a green route for polymer recycling.[25, 34, 37, 40, 52]

2.2.1 Butylene succinate MCOs. Poly(butylene succinate) (PBS) is after poly(lactic acid) (PLA) the commercial aliphatic polyester most used for green packaging applications. PBS is classified as a biobased polymer due to the fact that both the diacid and the diol used for its synthesis can be obtained from renewable resources. Interestingly, butylene succinate *c*(BS)$_n$ are generated as side products in equilibrium with the linear chains during the PBS synthesis carried out by the classical two steps melt polycondensation process. Great amounts of these cycles are picked up in the condensation vessel due to their volatilization taking place at the high temperature and vacuum usually applied for the polymerization reaction. Labruyere et al.[27] took advantage of such fact to producing butylene succinate MCOs (*c*(BS)$_n$) by pyrolysis of oligomeric PBS in a glass oven at 290 ºC under 10 mBar vacuum and using different metallic and organic catalysts (Figure 4). The most efficient one was stannous octoate, that after several purification steps allowed producing *c*(BS)$_n$ with a yield in the cyclic dimer of 12.1 wt-%.

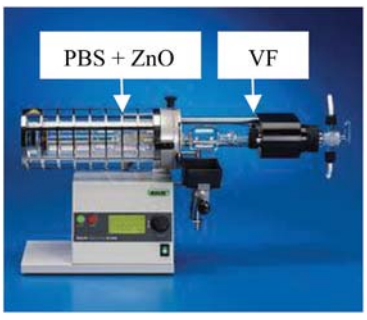

Fig 4. Glass Oven B-585 Kugelrohr used for thermal depolymerisation of PBS and recovery of *c*(BS)$_n$. Taken from reference 27 with permission from the Royal Society of Chemistry [2014].

Higher yields (50 wt-%) in *c*(BS)$_n$ were achieved by HDC of succinic acid and butanediol carried out in refluxing toluene and catalysed by *p*-toluene-sulfonic acid.[53] The use of enzymes as catalysts for the synthesis of MCOs constitutes a recent alternative that has been exploited on several occasions. The enzymatic processes avoid the presence of metallic or organic catalysts, require milder reaction conditions and produce these cycles almost quantitatively. Thus, *c*(BS)$_n$ have been prepared by high dilution enzymatic condensation of BD and succinic acid[36] or dimethyl succinate[35, 37-39] and also by enzymatic depolymerization of PBS.[34, 40] Among the different lipases used, CALB has been the most widely studied due to its high catalytic activity and selectivity.[33] Mixtures of BS cycles of different sizes were usually obtained with the dimer being in all cases the predominant specie. On the other hand, it is observed that the BS cyclic monomer is barely produced, which is most probably due to the high ring strain supported by this small cycle or to the size specificity required for cyclization taking place in the catalytic triad and oxyanion hole residues.[35] The composition of these mixtures could be accurately estimated by different techniques such as GPC,[34] HPLC,[35, 36, 39] MALDI-TOF[34, 35, 37, 38, 40, 53] or ^{13}C NMR (Figure 5).[38]

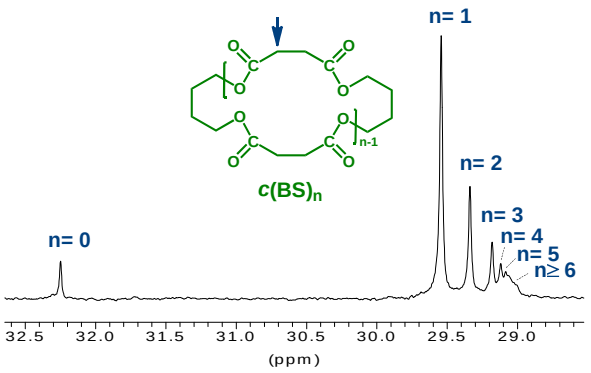

Fig 5. Quantitative ^{13}C NMR spectrum of *c*(BS)$_n$ in the region of the succinate methylene carbon (indicated with an arrow). n= 0 represents the cyclic monomer. Adapted from ref. 38 with permission from Elsevier [2017].

ROP of *c*(BS)$_n$ both in solution and in bulk provided PBS of high molecular weight. As these cycles possess low ring strain, the enthalpic contribution to the Gibbs energy is very low and is the entropic term, therefore, the main responsible for shifting the thermodynamic equilibrium towards the formation of the linear polymer.[10] Both, high temperatures and high concentrations are required in order to attain high conversions and high molecular weight polymers.

Different catalysts have been screened for the preparation of PBS from *c*(BS)$_n$ by ROP. It has been observed that rare earth metallic catalyst such as Nd(BH$_3$)(THF)$_3$ and Nd(O^{i}Pr)$_3$ are very active in producing PBS of high molecular weight (M_n ~ 7500-25,000 g·mol^{-1}) in both bulk and solution at moderate temperatures, and in good yields.[53] In order to check the effect of the ring size on polymerizability, the ROP reaction was

carried out using isolated $c(BS)_2$ as monomer. This cyclic diester gave a polymer with M_n of about 38,000 g·mol^{-1}, a value comparable to the one obtained by melt polycondensation followed by chain extension. Stannous octoate catalyst was also essayed for ROP of this cyclic diester and shown to give a polymer with M_n = 29,500 g·mol^{-1}.[27] An optimization of the reaction using the same tin catalyst provided a polymer with M_n = 95,000.[54] As it is expected for an entropically driven ROP, an increase of the reaction temperature from 140 ºC to 200 ºC improved significantly both conversion and molecular weight and gave a polymer with a dispersity of 2.1. On the other hand, the use of enzymes for ROP of $c(BS)_n$ has been also explored. As well as in the synthesis of the MCOs precursors, the most studied enzyme has been CALB lipase due to its thermal stability and high catalytic activity. The polymerization of $c(BS)_n$ under azeotropic dehydration conditions in toluene at 60 ºC gave a polymer with M_w of 21,000 g·mol^{-1} and dispersity of 1.7 in good yields. It was observed as well, that reactions carried out in bulk or in toluene solution at higher temperatures led to polymers with much higher molecular weights (M_w = 68,000-130,000 g·mol^{-1}),[35] which were very influenced by reaction conditions such as the $c(BS)_n$ concentration and added amount of CALB lipase. As it is inferred from entropically driven ROP, the molecular weight increased with MCOs concentration up to a limit of 50 mg·mL^{-1}. Higher concentrations resulted in adverse effects due to an increase in the viscosity of the polymer solution which reduced the mobility of both polymer and MCOs. On the other hand, an increase in the CALB concentration increased both reaction rate and molecular weight. Above 40 wt-% of enzyme content, a small decrease in the molecular weight was however observed which was ascribed to the ending of growing chains by the water bound to the enzyme.[30]

Copolymerization is a good method to improve the thermal and mechanical properties as well as to enhance its hydrolytic or enzymatic degradability.[48] Copolyesters with a random microstructure are usually obtained by melt polycondensation of mixtures of diols or diacids, and the final properties can be tuned by a control of the copolymer composition. The use of $c(BS)_n$ for the synthesis of block copolymers has been recently explored. Thus, PBS diblock and triblock copolymers with amphiphilic properties were prepared by ROP of $c(BS)_n$ initiated by mono- and di-hydroxyl functionalized poly(ethylene glycol) macro-initiators and using a tin catalyst.[54] On the other hand, the use of enzymatic catalysts, such as CALB lipase, produced random copolymers. In these systems, the crystallinity of the copolymers is very affected by the copolymer composition. Copolyesters obtained by ROP of $c(BS)_n$ and alkylthiosuccinate MCOs, were observed to be semicrystalline, with the degree of crystallinity reduced to the half for PBS contents of around 20 mol-%.[37] A similar behaviour has been observed for copolyesters obtained by enzymatic ROP of $c(BS)_n$ and ε-caprolactone. In this series, all copolymers were observed to have a random microstructure but all of them were semicrystalline, and interestingly isodimorphic for intermediate compositions.[38]

2.2.2 Other alkylene succinate MCOs. Poly(ethylene succinate) (PES), poly(1,3-trimethylene succinate) (PTS), poly(hexamethylene succinate) and poly(octamethylene succinate) (POS) are also interesting aliphatic polyesters because, as well as PBS, they are biodegradable and biocompatible and most of their monomers can be produced from renewable resources.[44, 55, 56]

The synthesis of these MCO_S has been performed by enzymatic cyclization of ethylene succinate $c(ES)_n$,[42] hexamethylene succinate $c(HS)_n$, octamethylene succinate $c(OS)_n$ and other longer alkylene succinates MCOs[44, 45] or by extraction of the cyclics from PTS polymer subjected to thermal treatments for ring-chain equilibration (trimethylene succinate, $c(TS)_n$).[57] MCOs from dimer to hexamer were obtained for the former and from monomer to heptamer for the other MCOs (Figure 6), which sizes distributions being quite different for the different series. Thus, the cyclic dimer was the predominant specie in $c(TS)_n$, $c(HS)_n$ and $c(OS)_n$ whereas trimer and tetramer were the most important cycles found in $c(ES)_n$. Such differences could be ascribed to the number of skeletal bonds that are present in each cyclic species.

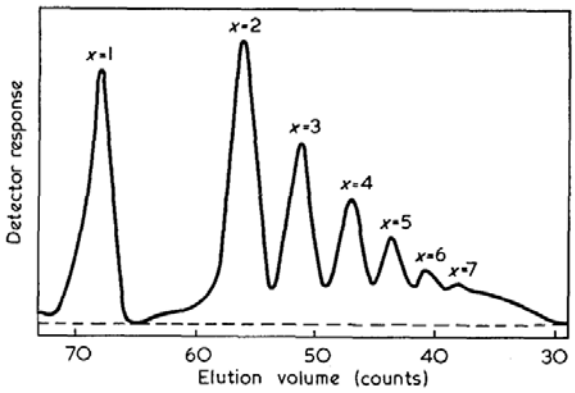

Fig 6. GPC chromatogram of $c(TS)_n$ extracted from PTS equilibrium in the melt at 150 ºC. Reproduced from ref. 57 with permission from Elsevier [1974].

ROP in bulk of $c(ES)_n$ assisted by stannous octoate or CALB lipase provided PES homopolymers with M_w around 50,000 and 65,000 g·mol^{-1}, respectively after 24 hours of reaction.[42] On the other hand, copolymerization in bulk of these MCOs with smaller size lactones,[42] such as ε-caprolactone or L-lactide as well as with other MCOs[39] was successfully achieved using similar ROP conditions catalysts. Random copolyesters with high molecular weight were attained in all cases.

2.2.3 Alkylene adipate MCOs. Although in less extension than for the case of succinate derivatives, the MCOs derived from adipic acid and alkanediols have also attracted considerable attention regarding their suitability to produce poly(alkylene adipate)s by ROP. Among them, ethylene, butylene and decamethylene adipates have been mostly studied. Cyclic ethylene adipate $c(EA)_n$ could be successfully

prepared in high yields by pseudo-high dilution condensation of adipoyl chloride and ethylene glycol using different organic bases[19] or by CDP of poly(ethylene adipate) in chlorobenzene solution using di-*n*-butyl tin oxide catalyst.[29, 58] The last method was also applied for the synthesis of cyclic decamethylene adipate $c(DA)_n$.[30, 59] $c(DA)_n$ from monomer to heptamer were well resolved by GPC, being the first one the predominant species observed after 5 days of CDP. Similar results were achieved by extraction of these MCOs from poly(decamethylene adipate) thermally treated in bulk at 150 ºC after 3 days of ring-chain equilibration.[57] The content distribution of cycle sizes agrees very well with the values predicted by the Jacobson and Stockmayer cyclization theory for MCOs containing three or more repeating units.[60] On the other hand, the use of an eco-friendly lipase catalyst for CDP was claimed as a sustainable route for cyclodepolymerization of poly(butylene adipate).[34, 40, 41] Butylene adipate cycles $c(BA)_n$ from monomer to tetramer were recovered almost quantitatively, and interestingly it was observed that the composition in cyclic species could be modulated either by the lipase concentration (Figure 7) or by the flow rate of the polymer solution run through an enzyme packed column.[40]

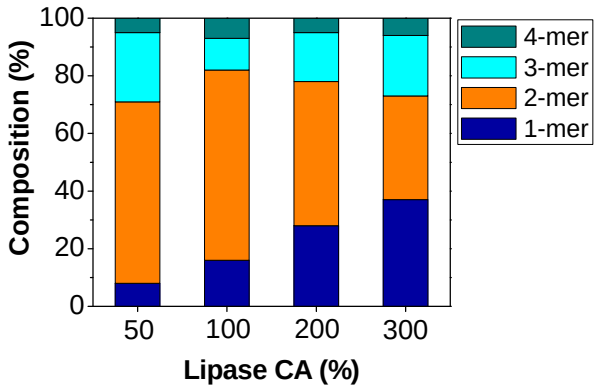

Fig 7. Composition of $c(BA)_n$ as a function of lipase concentration. Adapted from ref. 40 with permission from ACS [2008].

All reported alkylene adipate MCOs, whichever was the synthesis route used for their synthesis, have been successfully polymerized by ROP to their corresponding polyester or derived copolyesters. For instance, $c(EA)_n$ were polymerized in bulk at 200 ºC using different metallic catalysts such as tetra-butyl-titanate (TBT)[19] or di-*n*-butyl tin oxide[29] to give high molecular weight PEAs. Polymerization of $c(BA)_n$ was achieved by lipase enzymatic polymerization.[34, 41] Kondo et al. studied the effect of ring size on the rate of the reaction and molecular weight of the resulting PBA. These authors reported that molecular weight decreased with the increase in ring size so that the highest value (M_w = 173,000) was achieved in the polymerization of the cyclic monomer. On the other hand, the reaction rate increased with ring size, a result that authors attributed to the increase of initiating species.[41]

Copolymerization of $c(EA)_n$ with ethylene terephthalate MCOs produced random copolyesters with thermoplastic elastomeric properties.[29] The low viscosity of the MCOs feed allowed its polymerization in the presence of porous hydroxyapatite templates able to generate composites with *in vitro* bioactivity suitable for mimicking naturally occurring bone systems.[58]

2.2.4 Other alkylene alkanedioates and alkenedioates MCOs. Bio-based MCOs others than those made of succinate or adipate units have been considered in much less extent. In fact, MCOs made of hexamethylene and decamethylene fumarate/adipate oligomers reported by Mezoul et al.[61] and Heath et al.,[28] respectively, and MCOs of isosorbide suberate reported by Kricheldorf et al.[62] constitute the only examples found in the accessible literature. The enzymatic reaction of 1,6-hexanediol and the mixture of the two geometrical isomeric dimethyl alkenedioates produced high amounts of MCOs of the maleate derivative with the cyclic dimer being the main component. Almost no cyclic fumarate compounds were detected, which was interpreted as being due to the *trans* configuration of the double bond and the specificity of the enzyme. Cyclodepolymerization of poly(decamethylene alkenedioate)s using a tin catalyst was found to produce MCOs from dimer to heptamer as assessed by ESI-MS and GPC.[28] The contents of different cycle sizes in the cyclic fractions were compared with the theoretical values determined by Rotational Isomeric State and Monte Carlo Metropolis calculations. The double bonds present in these cycles were made to react with alkyl thiols to produce alkyltiosuccinate MCOs that were then copolymerized with $c(BS)_n$ oligomers to give elastomeric copolymers.[37]

2.3 2,5-Furandicaboxylate MCOs

2,5-Furandicarboxylic acid (FDCA) is a renewable aromatic compound that has been extensively explored in recent years as building-block for the synthesis of bio-based polyesters and other polymers produced by polycondensation.[16, 63-65] FDCA has close similarities with terephthalic acid (TPA), a petrochemical aromatic benzendicarboxylic acid widely used in the manufacture of extremely important commercial polyesters, such as PET and PBT. The replacement of TPA by FDCA provides aromatic polyesters and copolyesters that not only are more sustainable but also display lower permeability to oxygen and carbon dioxide without significant detriment of their basic properties.[66] As a matter of fact, poly(ethylene furanoate) (PEF) and poly(butylene furanoate) (PBF) are emerging polymers that are displacing poly(terephthalate)s in some of their traditional applications at accelerating rates.

The furanoate polyesters are usually synthesized using the same polymerization methodology that is firmly established for the preparation of poly(terephthalate)s *i.e.* the two-stage melt polycondensation of 2,5-furandicarboxylic acid,[67] or dimethyl 2,5-furandicarboxylate[68] with the corresponding alkanediol catalysed by either organometallic compounds[69] or lipases.[70, 71] An enormous amount of efforts has been devoted to study in detail the polycondensation of FDCA with both ethylene glycol (EG) and 1,4-butanediol (BD). The influence of pressure, temperature, and catalyst on yield, molecular weight, and colour of PEF and PBF has been carefully assessed and their production optimized.[72] Nevertheless, the increase in viscosity of the reaction melt with conversion is a characteristic inherent to polycondensation that makes difficult the removal of volatile byproducts. As a consequence high molecular weight polymers are difficult to obtain unless severe reaction conditions are applied with the adverse consequence that polymer discoloration is enhanced. This limitation is particularly harmful in the polycondensation of FDCA due to the lower thermal stability of furanic compounds.

2.3.1 Alkylene 2,5-Furandicaboxylate MCOs. The application of ROP to the preparation of poly(alkylene 2,5-furandicarboxylate)s has been reported for the first time in these last years as a promising alternative to polycondensation. The preparation of cyclic (butylene 2,5-furandicarboxylate) oligomers, abbreviated as *c*(BF)$_n$, has been carried out independently by Morbidelli et al. and Muñoz-Guerra et al. a few years ago by using the high dilution condensation method described by Brunelle. *c*(BF)$_n$ were obtained as mixtures contaminated with a minor fraction of linear oligomers that could be removed by chromatography. The cyclic fraction consisted of a mixture of species with sizes ranging from dimer to heptamer with dimer, trimer, and tetramer being the main components in a quantity distribution that apparently varied with the experimental conditions used for the synthesis. The polymerization of the *c*(BF)$_n$ mixture carried out in an aluminium crucible inside a DSC furnace and catalysed by tetrakis(2-ethylhexyl)-titanate afforded a PBF with a M_n of around 6,000-8,000 g·mol^{-1}.[21] In the study carried out by Morales-Huerta et al., the individual dimer, trimer and tetramer species were isolated by preparative HPLC of the *c*(BF)$_n$ mixture and individually polymerized by applying the usual melt ROP procedure catalysed by Sn(Oct)$_2$ (Figure 8). The PBFs coming from the three different cyclic species were obtained in similar yields with weight-average molecular weights in the 55,000-65,000 g·mol^{-1} range indicating that the influence of cycle size on polymerization was not very significant.[20] A parallel work with similar results was carried out by these authors using EG instead of BDO to prepare cyclic (ethylene 2,5-furandicarboxylate) oligomers, abbreviated as *c*(EF)$_n$. In this case, the trimer was by far the predominant specie (about 75% of the mixture) in the *c*(EF)$_n$ unresolved fraction which upon ROP afforded a PEF with a M_w = 55,000 and $Đ$ = 1.4.

Morales-Huerta et al. also reported the preparation of both *c*(EF)$_n$ and *c*(BF)$_n$ by thermal cyclodepolymerization.[20] Reactions were carried out in dichlorobenzene at 180 ºC in the presence of dibutyl tin dioctanoate affording cyclic mixtures in 60-70 % yields. The compositions of these mixtures were less heterogeneous than those obtained by high-dilution condensation although dimer and trimer continued being the predominant species.

Fig 8. ^{1}H NMR spectra of isolated cyclic oligo(butylene 2,5-furandicarboxylate)s and their mixture. Reproduced from ref. 20 with permission from Elsevier [2016].

More recently Fleckenstein et al.[31] optimized the production of *c*(EF)$_n$ by thermal cyclodepolymerization of a short molecular weight PEF (M_w < 5,000 g·mol^{-1}) by testing different solvents such as polar aprotic solvents, aromatic solvents and ionic liquids. 2-Methylnaphthalene was found to be the most suitable solvent due to the high solubility of PEF in this medium and the high yields therein attained. The depolymerized product was composed of cyclic oligomers from dimer to heptamer together with linear species in relative amounts according to the ring-chain thermodynamic equilibrium model of Jacobson and Stockmayer.[60] These authors developed a kinetic model that allows predicting the timescale of the cyclodepolymerization reaction for every involved oligomeric species. Combination of thermal behaviour with selective precipitation was claimed to be a reliable tool for the synthesis of *c*(EF)$_n$ appropriate for being then used in ROP. Thus, a *c*(EF)$_n$ fraction composed of cycles with n = 2, 3 and 4 and largely enriched in the dimer species was prepared by cyclodepolymerization under optimal conditions. The fraction was then polymerized at temperatures below 300 ºC with a tin catalyst in less than 30 min to give PEF of M_n > 30.000 g·mol^{-1} and free of colour, a feature required for bottle grade applications.[32] To reduce the ROP temperature, an inert liquid plasticizer, which could be then removed, was added in order to depress the melting temperature of the pristine cyclic dimer, which was above 370 ºC.

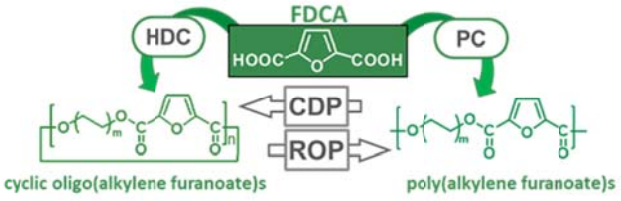

Fig 9. Chemical routes for the synthesis of sustainable poly(alkylene 2,5-furandicarboxylate)s from bio-based FDCA including ROP of MCOs obtained by either high-dilution condensation (HDC) or cyclodepolymerization (CDP), and polycondensation (PC) of FDCA with alkanediols. Reproduced from ref. 20 with permission from Elsevier [2016].

The synthesis of cyclic alkylene 2,5-furandicarboxylates was later extended to comprise structures containing long polymethylene segments. Flores et al.[46] recently reported the synthesis of cyclic (hexamethylene 2,5-furandicarboxylate) oligomers, abbreviated as *c*(HF)$_n$, by enzymatic cyclization method using dimethyl 2,5-furandicarboxylate and 1,6-hexanediol with toluene as solvent and CALB as catalyst. The cyclic fraction obtained after seven days of reaction at 90 ºC consisted of a mixture of dimer to hexamer species highly enriched in the smaller size ones. The high flexibility inherent to the hexamethylene segments rendered much less strained cycles which are able to polymerize through a process exclusively driven by the increasing entropy. In fact, the enzymatically ROP of *c*(HF)$_n$ to produce poly(hexamethylene 2,5-furandicarboxylate) (PHF) was carried out in a high monomer concentration solution. Furthermore, an exceptionally low polymerization temperature compatible with the activity of CALB (around 100 ºC) could be used. Interestingly, PHF was found to be able to degrade enzymatically to give the corresponding cyclic oligomers, which stands for a novel biosynthetic route for the recycling of this kind of polymers.

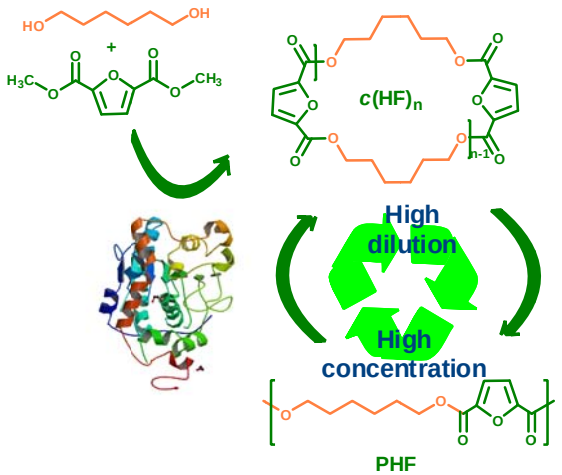

Fig 10. Scheme of the fully enzyme-mediated route applied for the synthesis of PHF by ROP and its recycling by CDP to recover the MCOs. Adapted from reference 46 with permission from the American Chemical Society [2019].

2.3.2 2,5-furandicarboxylate copolyesters. Property modulation of polymers is frequently attained by copolymerization. 2,5-furandicarboxylate stands out as a particularly convenient comonomeric unit to be inserted in polyesters in which glass temperature and sustainability are wanted to be preserved or even simultaneously increased. Thus, a series of copolyesters derived from PBT with Mw in the 55,000-80,000 g·mol^{-1} range and the butylene terephthalate units (BT) partially or totally replaced by BF units have been recently reported. These *co*PBF$_x$T$_y$ copolyesters were obtained by melt ROP of cyclic fractions *c*(BF)$_n$ and *c*(BT)$_n$ using Sn(Oct)$_2$ catalyst. The two cyclic fractions had similar cycle size compositions consisting of a mixture of dimer, trimer and tetramer species and also displayed similar relative reactivities. The resulting random copolyesters were semicrystalline for the full range of compositions with glass transition temperatures comprised within the 30-50 ºC interval.[73] Similar polymerization results were obtained in the ROP copolymerization of *c*(BF)$_n$ with *c*(BI)$_n$ (cyclic oligo(butylene isophthalate)s) for the synthesis of *co*PBF$_x$I$_y$ although in this case the crystallinity of the PBF homopolyester was drastically repressed upon the insertion of isophthalate units.[74]

ROP copolymerization of *c*(BF)$_n$ with aliphatic MCOs in bulk has been demonstrated to be a suitable route for the production of biodegradable aliphatic-aromatic copolyesters with properties similar to those displayed by their analogues obtained by the traditional two-stage melt polycondensation method. Thus, poly(butylene 2,5-furandicarboxylate-*co*-succinate) copolyesters with a random microstructure were prepared by ROP of mixtures of the corresponding cyclic oligoesters catalysed by either Sn(Oct)$_2$ or CALB.[75] The copolyesters had weight average molecular weights in the 50,000-65,000 g·mol^{-1} or 15,000-45,000 g·mol^{-1} ranges according to what catalyst, organometallic or enzymatic, was used. The thermal behaviour of these copolyesters was almost identical to that displayed when they were obtained by polycondensation of mixtures of the dimethyl esters of succinic and 2,5-furandicarboxylic acids with BD. All copolyesters were semicrystalline with glass transition temperatures between the two corresponding homopolymers (-40 and 42 ºC respectively). Both hydrolytic and enzymatic degradations were favoured by the presence of butylene succinate units in the copolyester.

c(BF)$_n$ have been demonstrated to be able also to copolymerize successfully by ROP with medium size lactones. Copolyesters made of butylene 2,5-furandicarboxylate and butylene 6-oxyhexanoate units were prepared by ROP of mixtures of *c*(BF)$_n$ and ε-caprolactone at 130 ºC using CALB catalyst.[76] In this case, relative reactivities should be significantly over one since copolyesters with a rather heterogeneous blocky microstructure were obtained. These copolyesters had weight average molecular weights between 20,000 and 50,000 g·mol^{-1} and were semicrystalline within the full range of compositions. The glass transition temperature of poly(ε-caprolactone), which is about -60 ºC, increased steadily with the content in BF units to reach 20 ºC for the copolyester containing 80% of these units.

With the purpose of extending the copolymerization by ROP to the preparation of furanic copolyesters with higher contents in sugar-based units, the synthesis of MCOs made of 2,5-furandicarboxylic acid and isohexides has been attempted by high dilution condensation (Figure 11).[77] Cyclization failed when isosorbide was the tried diol whereas cyclic (isomannide 2,5-furandicarboxylate) oligomers, $c(\mathrm{ImF})_n$, mainly consisting of dimer species were obtained in 60% yield. The opposite behaviour observed for these two isohexides was predicted by molecular simulation to be due to the different relative spatial orientation (*endo-endo* and *exo-endo*, respectively) displayed by the two hydroxyl groups. Unfortunately no study was made with isoidide (*exo-exo*) the which would have added further support to such predictions. $c(\mathrm{ImF})_n$ were copolymerized with $c(\mathrm{BF})_n$ in the melt at 220 ºC with $Sn(Oct)_2$ as a catalyst to produce random copolyesters $co\mathrm{PBIm}_x\mathrm{F}_y$ containing up to 50% of ImF units. These copolyesters had molecular weights between 30,000 and 50,000 $g{\cdot}mol^{-1}$, were semicrystalline and displayed glass transition temperatures increasing from 40 ºC up to 100 ºC with the content in ImF units. They degraded noticeably by water and this degradability was enhanced in the presence of enzymes.

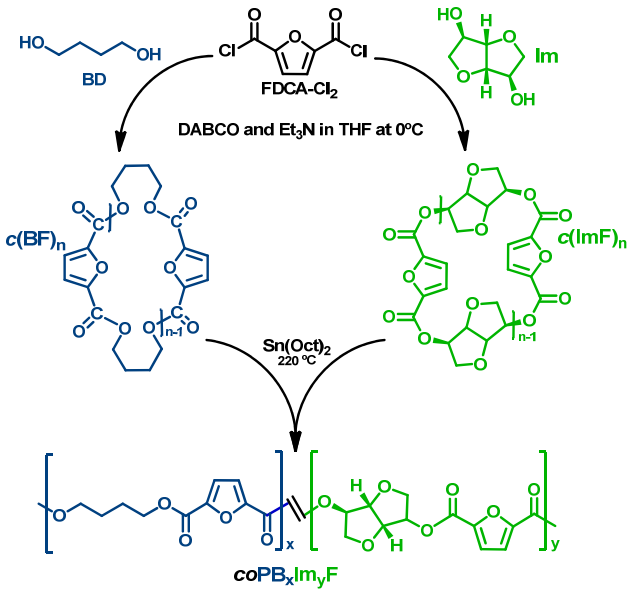

Fig 11. ROP synthetic route for furanic copolyesters containing isomannide units. Adapted from reference 77 with permission from the American Chemical Society [2018].

The last example of the application of ROP of MCOs to the synthesis of copolyesters showing outstanding properties is provided by the terpolymers obtained by ROP of mixtures of the $c(\mathrm{BS})_n$ or $c(\mathrm{ES})_n$ aliphatic macrocycles and a fraction of cyclic oligoesters prepared from FDCA and di-*O*-2-(hydroxyethyl) resorcinol (HER) (Figure 12).[39] These cycles are abbreviated as $c(\mathrm{RF})_n$ and are made of 2,5-furandicarboxylate and 1,3-dioxyphenylene groups linked by an ethylene spacer. They are composed essentially of dimer, trimer and tetramer species with the trimer being the predominant one. The combination of the two aromatic moieties in the RF unit provided a highly rigid structure that upon random insertion in PES or PBS renders copolyesters that are amorphous and display largely enhanced T_g (15ºC and 30 ºC respectively for copolyesters containing 50% of RF units). Both $co\mathrm{PE}_x\mathrm{R}_y\mathrm{F}$ and $co\mathrm{PB}_x\mathrm{R}_y\mathrm{F}$ continue being fully biobased and their biodegradability is not only preserved but even increased in the case of the PBS derived copolyesters.

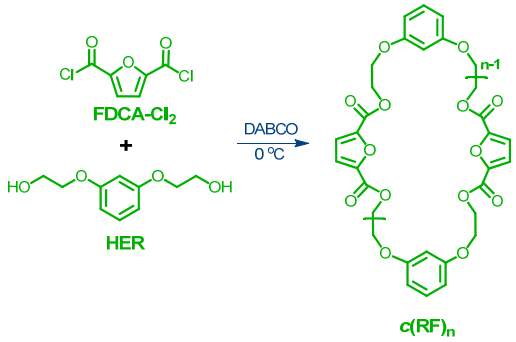

Fig 12. Synthesis of $c(\mathrm{RF})_n$ by high-dilution condensation. Adapted from reference 39 with permission from the MDPI [2017].

Summary

ROP of macrocycles is a well-settled polymerization technique that was initiated at the end of the last century and that has not ceased of expanding thenceforth. A considerable number of reviews have been published covering practically all the significant aspects of this polymerization procedure. In this review, the recent advances produced in the ROP of MCOs made of poly(alkanedioate)s or polyfuranoates have been surveyed. The more relevant information brought up in this study can be summarized as follows:

a) Enzymatic catalysis has increased in importance for both macrocycle synthesis and ROP of MCOs. In spite that longer reaction times are required and lower molecular weights are produced when reactions are enzymatically assisted, the biocatalytic option is increasingly considered. Avoiding metals or toxic organic compounds together with the capacity of new supported enzymes for retaining activity at high temperatures are the main reasons for explaining such a trend.

b) The synthesis of MCOs from biobased aliphatic dicarboxylic acids, such as succinic or adipic acids and alkanediols is favoured by the flexibility of the polymethylenic segments that allow obtaining them in high yields using different organometallic or enzymatic catalysts. Their ROP provide aliphatic polyesters and copolyesters with very high molecular weight that in some cases are not achievable by melt polycondensation.

c) The synthesis of MCOs from FDCA and a diversity of alkanediols has been carried out, which has allowed the preparation by ROP of polyfuranoates, both homopolyesters and copolyesters, almost exactly identical to those prepared by polycondensation. The synthesis of cyclic oligo(ethylene

2,5-furandicarboxylate)s has been optimized with the aim at using them at industrial scale for the production of poly(ethylene 2,5-furandicarboxylate), a fully bio-based aromatic polyester that is replacing traditional PET in an increasing number of applications. Macrocycles made from FDCA and other cyclic diols coming from vegetal sources have been also synthesized and used for the preparation of bio-based polyesters with high contents in cyclic structures.

d) Cyclodepolymerization of polyesters leading to MCOs is widely considered a crucial procedure for hastening the expansion of the ROP technique. Both solution and bulk CDP processes have been demonstrated to work with both polysuccinates and polyfuranoates. Combination of CDP with ROP makes a synthetic loop that meets all the requirements for the sustainable circular economy is satisfied. In the last decade, new CDP processes have been implemented using novel catalysts including supported lipases. Interestingly the MCOs fraction invariably generated as a by-product in the industrial production of PBS by polycondensation represents an example for the viability of ROP as a complementing technique for polycondensation. PBS with tailored properties could be produced by taking benefit of the application of ROP to the residual butylene succinate MCOs fraction.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

Financial support for this research was given by Ministerio de Ciencia, Innovación y Universidades (MCIU/AEI/FEDER, UE) with grant RTI2018-095041-B-C33. The three-dimensional image of *Candida antarctica* lipase B (CALB) was taken from the Protein Data Bank (PDB 4K6G).

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