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Synthesis and post-polymerisation modifications of aliphatic poly(carbonate)s prepared by ring-opening polymerisation

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Owing to their low toxicity, biocompatibility and biodegradability, aliphatic poly(carbonate)s have been widely studied as materials for biomedical application. Furthermore, the synthetic versatility of the six-membered cyclic carbonates for the realization of functional degradable polymers by ring-opening polymerisation has driven wider interest in this area. In this review, the synthesis and ring-opening polymerisation of functional cyclic carbonates that have been reported in the literature in the past decade are discussed. Finally, the post-polymerisation modification methods that have been applied to the resulting homopolymers and copolymers and the application of the materials are also discussed.

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Introduction

Alongside aliphatic poly(ester)s, aliphatic poly(carbonate)s are important biodegradable materials that have received considerable attention.[1–3] These materials are excellent candidates for pharmaceutical applications as a consequence of their low

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Sarah Tempelaar graduated from Utrecht University (The Netherlands) with a MSc in chemistry in 2008. During her studies she worked for six months in the laboratory of Prof. Dr Iztok Turel to study the interaction of metal ions with quinolone compounds and completed a research thesis under the supervision of Prof. Dr R. (Bert) J. M. Klein Gebbink and Prof. Dr Gerard van Koten on the synthesis of propargylamines via the aminoarenethiolato copper(I)-catalysed Mannich reaction. She then went to the University of Warwick (UK) to undertake a PhD in 2009 where she studied the synthesis and post-polymerisation functionalisations of aliphatic poly(carbonate)s under the supervision of Dr Andrew P. Dove. Sarah completed her PhD in 2012.

Laetitia Mespouille

Laetitia Mespouille received her MSc in chemistry in 2003 from the University of Mons (UMONS) in Belgium. She then obtained a PhD in 2007 from the same University under the supervision of Professor Ph. Dubois where she studied the preparation of controlled polymer conetworks by ATRP. During this period she performed a short stay in the laboratory of Dr James Hedrick at IBM Research Center (San Jose, CA) and in the laboratory of Professor Curt Franck (Chemical engineering department) from Stanford University. She then started a post-doctoral stay at IBM Almaden Research Center supervised by Dr J. L. Hedrick, focused on the preparation of functional cyclic carbonates and their metal-free ring-opening polymerization. She then returned to Belgium where she was appointed as an Assistant Professor at the University of Mons in 2008.

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toxicity, biocompatibility, and biodegradability. Copolymers of carbonates such as trimethylene carbonate (TMC) with other cyclic monomers such as lactide and glycolide have already found application as sutures and in other biomedical fields such as controlled drug delivery on account of the favourable materials properties that they bestow into the copolymers.[4,5] In addition, materials prepared from poly(trimethylene carbonate) (PTMC) are known to degrade *in vivo* by surface erosion in contrast to the bulk degradation behaviour shown by poly(ester)s. Furthermore, poly(ester) degradation products can lead to increased levels of acidity, which are not present during poly(carbonate) degradation, that may be hazardous to loaded drugs or living tissues.[6–9]

Poly(carbonate) synthesis is commonly realised either by the copolymerisation of epoxides with carbon dioxide or by the ring-opening polymerisation (ROP) of cyclic carbonate monomers.[1,3,10–13] The synthesis of poly(carbonate)s *via* CO_2/epoxide copolymerisation is a potentially useful method of utilising CO_2; however, the formation of five-membered cyclic carbonate by-products, the presence of ether linkages, and the use of air-sensitive coordination compounds make its application synthetically challenging. The ROP of cyclic carbonates has received significantly more attention and consequently provides an attractive and versatile methodology for the synthesis of functionalised poly(carbonate)s, despite the requirement to synthesise many of the monomers, and has been studied by many groups.[1,3,14] The ROP of cyclic carbonates can be realised using cationic, anionic, coordination-insertion, organocatalytic, and enzymatic methods and has resulted in high levels of control over polymer molecular weight, dispersity and end-group fidelity.[15–24]

For their use in biomedical applications, such as targeted drug delivery and tissue engineering, it is advantageous to be able to tailor the poly(carbonate) structure to enable specific interactions with cells or organs. The properties of poly(carbonate)s derived from TMC can be tuned by copolymerisation and blending with other biodegradable polymers (*i.e.* poly(lactide), poly(glycolide), poly(caprolactone)) and the introduction of functional end-groups.[25–32] Precise control over the physical properties or the addition of biologically active molecules to the poly(carbonate) structure however, is best achieved by post-derivatisation of pendant functionalities in the polymer backbone. Such pendant functionalities may be introduced *via* the ROP of cyclic carbonate monomers bearing the desired functionality however, not all functional groups are compatible with the ring-opening polymerisation process and in some cases the added functionality limits the polymerisation efficiency.[33] As a result, further modification of the polymer backbone following polymerisation is often required. While many further functionalisations of the pendant moieties in the poly(carbonate) backbone have been reported, modifications commonly involve many steps and typically only partial functionalisation is achieved.

Olivier Coulembier

Olivier Coulembier received his PhD degree from University of Mons-Hainaut (Belgium) in 2005 and joined the University of Stanford (United States) for his postdoctoral research in 2006. He is currently Research Associate by Belgian F.N.R.S. in the Laboratory of Polymeric and Composite Materials (LPCM) of Professor Philippe Dubois at University of Mons. His main activities are focused on the (non)organometallic ring-opening polymerization of cyclic monomers. He has (co)authored 56 scientific papers in international journals, 2 patents and 2 book chapters.

Philippe Dubois

Philippe Dubois, PhD in sciences, is full professor at University of Mons (UMONS, Belgium) and honorary senior research associate of the Belgian FNRS. He is currently director of the Center of Innovation and Research in Materials and Polymers (CIRMAP, ca. 150 persons). Prof. Dubois is Scientific Director at Materia Nova ASBL Research Center in Mons and Past-President of the Belgian Royal Chemical Society. His expertise covers organic chemistry, macromolecular chemistry, catalysis in polymer materials, melt (reactive) processing/engineering of nanocomposite and nanohybrid materials, incl. biodegradable and biosourced polymers. He has (co)authored more than 450 peer-reviewed scientific publications (h index: 57) and is inventor of 57 patents. Ph. Dubois is elected titular member of the Royal Academy of Sciences, Belgium.

Andrew P. Dove

Andrew P. Dove is an Associate Professor of Chemistry at the University of Warwick (UK). He graduated from the University of York with an MChem (Hons) degree in Chemistry in 1999 before studying for his PhD under the supervision of Prof. Vernon C. Gibson at Imperial College London, graduating in 2003. Andrew then moved to Stanford University, California and subsequently IBM Almaden research centre to undertake periods of postdoctoral research before returning to the UK in 2005. His current research is focused at the interface of chemistry, engineering and cell biology on the synthesis and application of degradable biomaterials. He has (co)authored over 40 scientific papers, patents and book chapters.

In recent years, however, post-polymerisation modifications of functional poly(carbonate)s using more efficient chemistries have been reported. In addition, many copolymerisations of functional cyclic carbonate monomers with simple cyclic esters (*i.e.* lactide or ε-caprolactone) have been reported to introduce functionality in the parent poly(ester) backbone in order to overcome the challenging nature of functional cyclic ester synthesis.[34–36]

Herein the synthesis and polymerisation of cyclic carbonates reported in the literature including post-polymerisation modifications of the resulting homo- and co-polymers are discussed with a focus on progress made in the area in the past decade.

Synthetic routes to functional poly(carbonate)s

Synthesis of cyclic carbonates can be achieved through a number of routes, commonly involving multiple steps using toxic phosgene derivatives for carbonate formation from a 1,3-diol (Fig. 1).[1,3] Alternative methods that do not involve the use of phosgene include the reaction of oxetane with CO_2, a two-step procedure using a pentafluorophenyl ester intermediate and the use of 1,1′-carbonyldiimidazole (CDI).[37,38] This section of this review article will focus on the specific methods for monomer synthesis centred on the most common feedstocks.

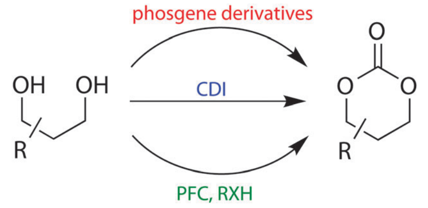
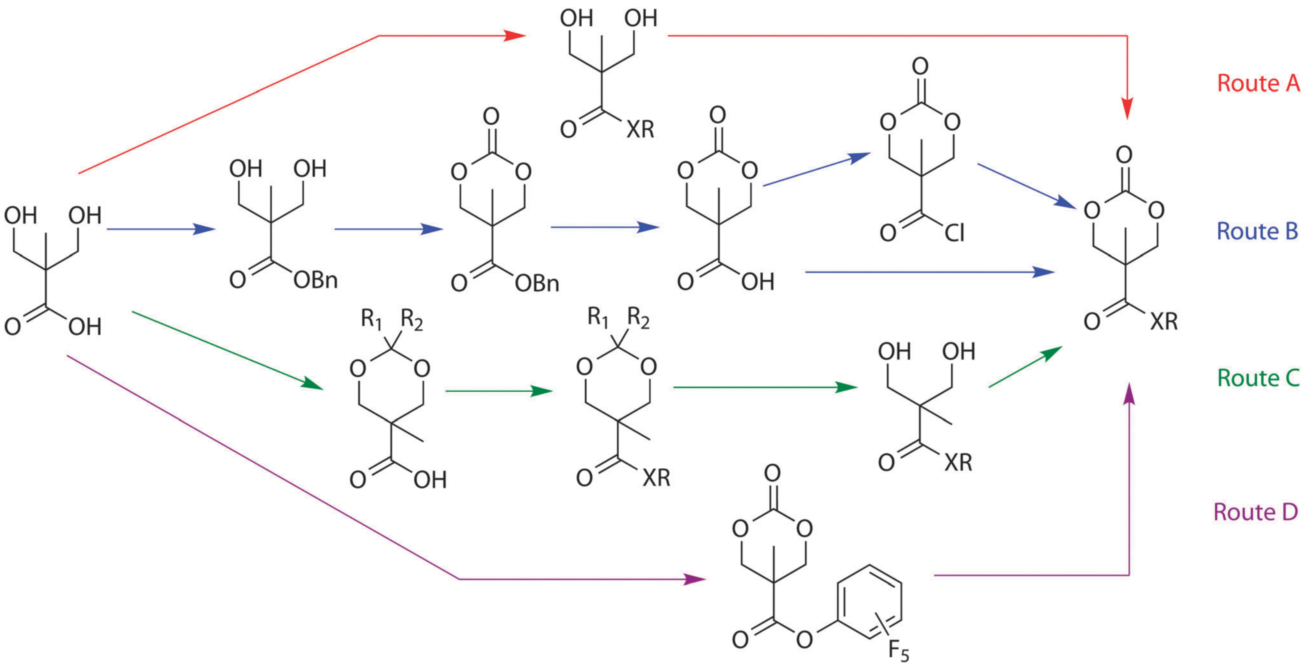


Fig. 1 Representative scheme for the synthesis of functional six-membered cyclic carbonates from 1,3-diols using phosgene derivatives, 1,1′-carbonyldiimidazole (CDI) or bis(pentafluorophenyl)carbonate (PFC) with an alcohol or amine (RXH).

Functional cyclic carbonate monomers derived from 2,2-bishydroxy(methyl)propionic acid (bis-MPA)

2,2-Bishydroxy(methyl)propionic acid (bis-MPA), also widely used in the preparation of biocompatible dendrimers,[39,40] and hydrogel materials,[41] was first used for the synthesis of cyclic carbonates by Bisht and coworkers in 1999.[42] The reported cyclic carbonate could be prepared by direct functionalisation of the acid group in bis-MPA under either acidic or basic conditions (Scheme 1A), before cyclisation to the carbonate using phosgene or a phosgene derivative such as ethyl chloroformate, di- or triphosgene.[42,43] Other possible synthetic pathways from the bis-MPA scaffold to provide functional cyclic carbonates have since been reported. Alternative pathways (Scheme 1, route B and C) are more suitable for the synthesis of monomers that have more sensitive substituents. In one example (Scheme 1, route B), cyclic carbonate synthesis involves protection of the acid functionality by conversion to a benzyl ester followed by the synthesis of benzyl functional cyclic carbonate, 5-methyl-5-benzyloxycarbonyl-1,3-dioxan-2-one (MBC, **15**). Subsequent deprotection of the acid functionality followed by activation of the free carboxylic acid, typically by the use of dicyclohexylcarbodiimide (DCC) or by conversion to the acyl chloride, allow reaction with an alcohol or an amine.[44] In a further alternative (Scheme 1, route C), the 1,3-diol is acetonide-protected before functionalisation of the carboxylic acid is carried out. Subsequent removal of the acetonide protecting group and formation of the functional

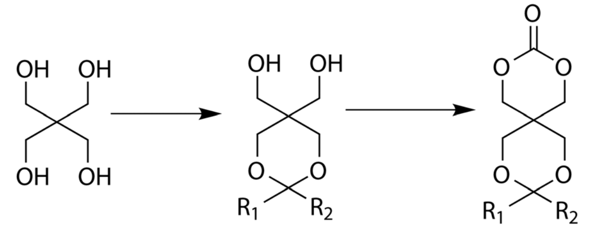


Scheme 1 Synthesis of functional cyclic carbonates derived from 2,2-bishydroxy(methyl)propionic acid (bis-MPA).

cyclic carbonate are realised in the last step. Finally, the use of bis(pentafluorophenyl)carbonate, as demonstrated recently by Hedrick and coworkers, provides an excellent alternative to the use of phosgene derivatives and multi-step procedures (Scheme 1, route D).[37] Here, the synthesis of a pentafluorophenyl-functionalised cyclic carbonate, 5-methyl-5-pentafluorophenyl-oxycarbonyl-1,3-dioxan-2-one, from bis-MPA is achieved in one step using bis(pentafluorophenyl)carbonate in the presence of caesium fluoride which followed by reaction of the pentafluorophenylester with amines or alcohols yields the desired monomers.[37] In summary, 2,2-bishydroxy(methyl)propionic acid (bis-MPA) is an excellent choice as biocompatible and versatile scaffold for the preparation of cyclic carbonate monomers with pendant ester and amide groups.

Functional cyclic carbonates derived from pentaerythritol, glycerol and trimethylolalkanes

The preparation of functional cyclic carbonates has also been reported in many cases using 1,3-diol containing compounds that have three or four hydroxyl groups in their molecular structure. Common precursors are pentaerythritol, glycerol and trimethylolalkanes which, apart from benzyl protection of the hydroxyl functionality (or functionalities) can also be used in the synthesis of other functional cyclic carbonates (Scheme 2).[45–50] A number of synthetic pathways are described in the literature that use glycerol or trimethylolalkanes as a scaffold to provide cyclic carbonates with a pendant functionality. In one example (Scheme 2, route A), two of the available hydroxyl groups are protected with acetonide or benzylidene groups before further reaction of the residual alcohol with an acid chloride or *via* DCC-coupling with a carboxylic acid-functional molecule. The deprotection of the diol and conversion to the cyclic carbonate yields the desired monomers. Alternatively, the precursor has been reacted with a dialkyl carbonate, mediated by immobilised *Candida antarctica lipase B*, to yield a hydroxyl-functional cyclic carbonate intermediate (Scheme 2, route B).



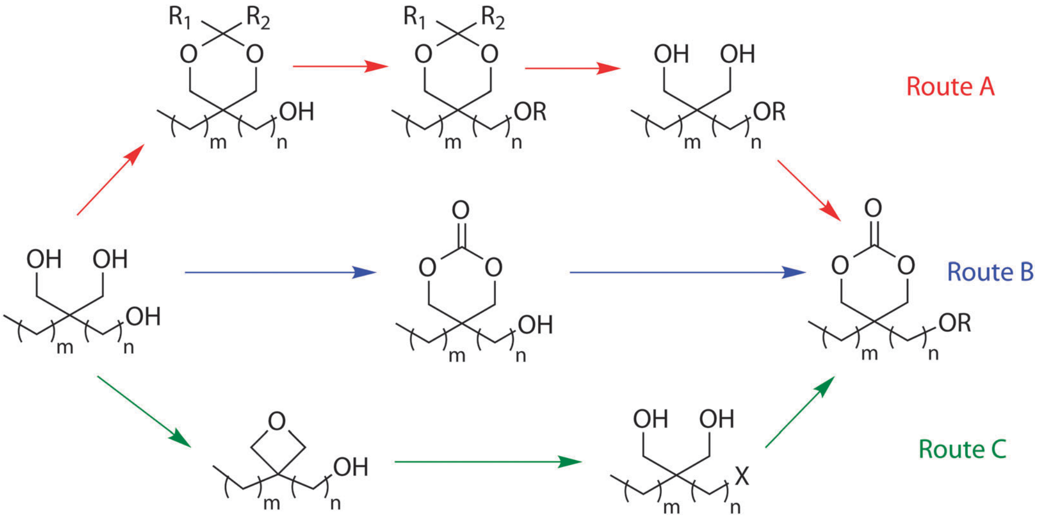
Scheme 3 Synthesis of functional cyclic carbonates derived from pentaerythritol.

The hydroxyl group was then further functionalised using the abovementioned chemistries. In a report by Hatti-Kaul and coworkers, the dialkyl carbonates were also used in the functionalisation of the hydroxyl group (Scheme 2, route B).[51] In a third pathway, under basic conditions, a dialkyl carbonate is used to form an oxetane by transesterification and subsequent decarboxylation. The oxetane can then be ring-opened by HX to give a 1,3-diol that can be converted to the corresponding halogen-containing carbonate (Scheme 2, route C).[37,38]

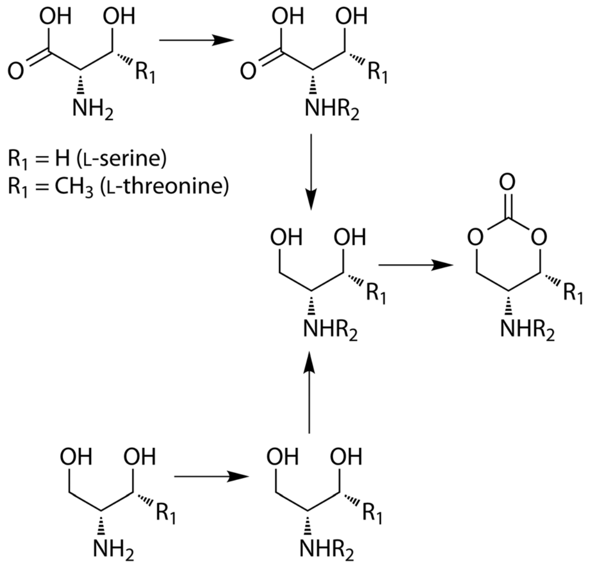
Synthesis of functional monomers derived from pentaerythritol is typically realised by partial functionalisation/protection of two of the hydroxyl functionalities leaving a 1,3-diol that can be cyclised using a phosgene derivative (Scheme 3).[50] In conclusion, glycerol and trimethylolalkanes are good alternatives to bis-MPA in the synthesis of functional cyclic carbonates with ether and halogen substituents, whilst pentaerythritol provides an excellent opportunity to introduce two hydroxyl groups per monomer unit into the poly(carbonate) backbone.

Functional cyclic carbonates derived from amino acids or sugars

Amino acids and sugars are natural products that are indispensable for life processes, hence poly(amino acid)s and poly(saccharide)s or sugar-based polymers are highly attractive biocompatible materials. In view of the biocompatibility of the resulting polymers and their degradation products, cyclic carbonates



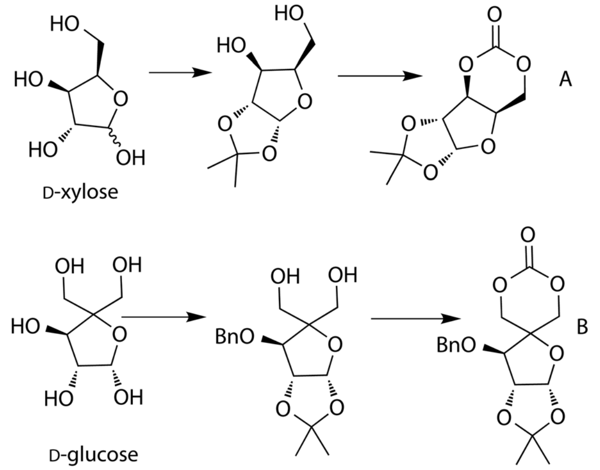
Scheme 2 Synthesis of functional cyclic carbonates derived from glycerol and trimethylolalkanes.



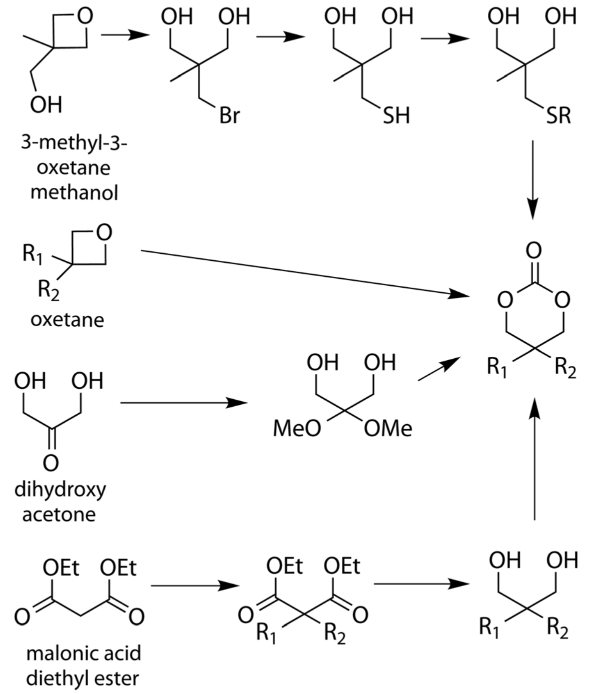
Scheme 4 Preparation of amino-acid derived cyclic carbonate monomers.

derived from amino acids and sugars have been reported by Sanda *et al.* and by Gross and coworkers, respectively.[52–54] The synthesis of cyclic carbonate monomers derived from L-serine and L-threonine was realised by protection of these amino acids *via* conversion of the amino groups to a carbamic acid benzyl esters (*Z*) or carbamic acid *tert*-butyl esters (Boc) followed by reduction and carbonate formation with triphosgene (Scheme 4).[52] In an alternative report, the serine-derived cyclic carbonate was prepared from the alcohol analogue of serine, serinol, instead.[55]

Sugar-derived cyclic carbonate monomers have been prepared from the furanose forms of D-xylose and D-glucose.[53,54,56] Synthesis from D-xylofuranose involves the acetonide protection of the two hydroxyl groups to form a 1,3-diol, which is commercially available (Scheme 5A). This 1,3-diol was converted to the cyclic carbonate using ethyl chloroformate. Monomer synthesis from D-glucofuranose involved protection (acetonide and benzyl ester) of three of the hydroxyl groups to give a 1,2-diol which was converted to a 1,3-diol (Scheme 5B) through a multi-step procedure. Carbonate formation was realised using a phosgene-derivative yielding the D-glucose-derived cyclic carbonate.



Scheme 5 Synthesis of cyclic carbonates from (A) D-xylofuranose and (B) D-glucofuranose.



Scheme 6 Synthesis of functional six-membered cyclic carbonates derived from oxetanes, malonic acid diethyl ester and dihydroxy acetone.

Synthesis of functional cyclic carbonates from other resources

Examples of other reported cyclic carbonate syntheses include those derived from commercially available diols, oxetanes, a malonic acid diethyl ester derivative, dihydroxy acetone and *N*-methyl diethanolamine (Scheme 6).[57–68] Direct synthesis of six-membered cyclic carbonates from oxetanes using CO_2 has been reported.[61] Alternatively ring-opening of 3-methyl-3-oxetanemethanol with HBr has also been reported and resulted in a bromo-functional diol. The bromide was then replaced with a thiol by reaction with NaSH, which was subsequently reacted with an alkene to generate the desired functional 1,3-diol. This diol was converted to the functional cyclic carbonate monomer by reaction with ethyl chloroformate.[64] A monomer prepared from dihydroxy acetone, a glycolytic metabolite, is converted to the dimethoxy acetal before ring-closure mediated with ethyl chloroformate.[62,63] In a final example, a functional malonic acid diethyl ester was functionalised with an alkyl halide in a first step followed by the reduction of the ethylesters to alcohols that enabled subsequent ring closure with diphosgene.[65]

Ring-opening polymerisation of functional cyclic carbonates

Cyclic carbonates with alkyl-containing functionalities

The introduction of a pendant functional group on a poly(carbonate) is desirable, but homopolymerisation of functional cyclic carbonates is not always necessary. Indeed, for some applications it is even advantageous to have a polymer backbone in which only a percentage of monomer units have a pendant functionality.[66,67] Furthermore, in cases in which the polymerisability of a functional monomer is not optimal, copolymerisation often enables a solution to be achieved.[33] In the preparation of functional poly(carbonate)s through copolymerisation, trimethylene carbonate (TMC) is often used as co-monomer, however other simple alkyl functional monomers have also been reported.[44,68] Hedrick and coworkers have recently reported copolymerisations of functional monomers with a simple ethyl functional monomer derived from bis-MPA, 5-methyl-5-ethyloxycarbonyl-1,3-dioxan-2-one (MEC, **7**), while Zhuo and coworkers report the use of dimethyl trimethylene carbonate, DTC, **1** (Table 1).[37,69–78] Only two examples of MEC homopolymerisations have been reported in the literature.[37,80] Using the sparteine/1-(3,5-bis(trifluoromethyl)-phenyl)-3-cyclohexyl-2-thiourea (TU) catalyst system in methylene chloride at room temperature, the polymerisation ([M]/[I] = 108) yielded a polymer with a molecular weight of 17 100 g mol^{-1} and a dispersity of 1.27, however application of a hexafluoroalcohol as a cocatalyst in place of the thiourea under comparable conditions resulted in polymers with decreased dispersity (1.13) and a lower molecular weight (3200 g mol^{-1}; ([M]/[I] = 88). In contrast, homopolymerisation of DTC has been reported using a number of catalysts.[79–84] The cationic ROP of DTC was reported in methylene chloride at room temperature using methyl trifluoromethane sulfonate (TfOMe) (<30% monomer conversion; M_n = 1800–2100 g mol^{-1}; $Đ_M$ = 1.30–1.38) or trifluoromethane sulfonic acid (<50% monomer conversion; M_n = 3000–3500 g mol^{-1}; $Đ_M$ = 1.10–1.11) or in nitrobenzene at 120 °C using methyl iodide (50% monomer conversion; M_n = 1100 g mol^{-1}; $Đ_M$ = 1.52). Homopolymerisation of DTC has also been reported, catalysed by tin octanoate under bulk conditions at 120 °C, and resulted in polymers with molecular weights ranging from 2900 to 8300 g mol^{-1} ($Đ_M$ = 1.52–1.58) or using rare earth catalysts at temperatures between 0 and 45 °C (M_n = 116 000–171 000 g mol^{-1}; $Đ_M$ = 2.28–2.79). Poly(DTC) is a hydrophobic, semi-crystalline material with reported melting points of 90–93 °C[78] and 122 °C[82] which consequently leads to decreased degradation rates of the homopolymer compared to poly(TMC) as well as for some of its copolymers.[85,79–83]

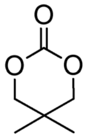
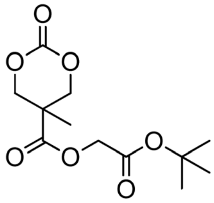
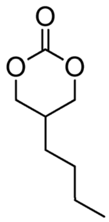
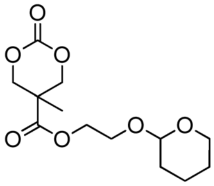
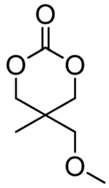
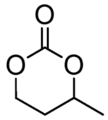
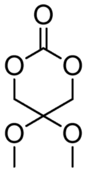
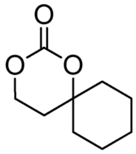
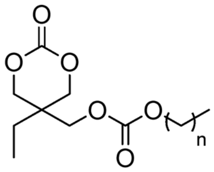
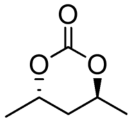
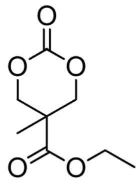
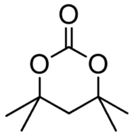
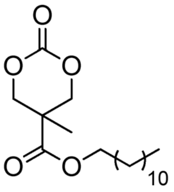
Many other alkyl-functional monomers have been reported (Table 1; **1–14**), however there are few reports on the properties of their resultant homopolymers.[37,51,61–63,70,74,81,86,87] Homopolymerisation of **2** in bulk using TfOMe as a catalyst (60–100 °C; M_n = 3500–5000 g mol^{-1}; $Đ_M$ = 1.67–2.58) or in chloro- or nitrobenzene at 120 °C initiated by methyl iodide (M_n = 600–800 g mol^{-1}; $Đ_M$ = 1.40–1.47)[81] has been reported whilst one example of the homopolymerisation of **10** using the organic catalyst 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in combination with the TU cocatalyst is reported in dichloromethane at room temperature ([M]/[I] = 99; M_n = 6600 g mol^{-1}; $Đ_M$ = 1.24).[37] Ring-opening of **4** using a range of metal-based and organic catalysts has recently received a lot of attention. Reported polymerisations were either carried out in bulk at elevated temperature (130 °C), or at temperatures between 60 and 110 °C in toluene.[76,86] ROP of **4** in bulk resulted in a polymer with M_n = 56 400 g mol^{-1} ($Đ_M$ = 1.44), whilst good results were obtained for both metal-based and the organic catalyst 4-dimethylaminopyridine (DMAP) in the solution polymerisation of **4** ([M]/[I] = 100; M_n = 6800–17 000 g mol^{-1}; $Đ_M$ = 1.18–1.25) as well. Poly(**4**) is a rigid, brittle, amorphous material with a glass transition temperature at 39–45 °C and a degradation temperature (225 °C) that is slightly lower than PTMC (230 °C).[62,86,88,89]

Other alkyl functional monomers that have a group at the alpha position on the carbonate ring are 1,3-dioxaspiro[5.5]undecan-2-one, **12**[81] and α-methyl trimethylene carbonate,[49,79,85,90,91] **11**. Endo and coworkers reported the cationic homopolymerisation of **11** in 2001, however only very low monomer conversions were observed and the resulting polymer was not isolated.[79] Higher monomer conversions have since been reported using rare earth initiators, aluminium triflate, β-diiminate zinc complexes and organic bases.[90,91] Good control was obtained using Al(OTf)$_3$ at 110 °C and 2-*tert*-butylimino-2-diethylamino-1,3-dimethylperhydro-1,3,2-diazaphosphorine (BEMP) and 1,4,7-triazabicyclodecene (TBD) resulting in poly(carbonate)s with molecular weights between 5700 and 10 000 g mol^{-1} and low dispersities. The substitution pattern of the carbonate ring can lead to two different propagating alcohols upon ring-opening which, in turn means that different microstructures can be expected depending on the regioselectivity of the catalysts applied in the ROP. Guillaume and coworkers investigated the regioselectivity of the resulting polymers using a range of catalytic systems.[90] Polymers with a high degree of regioregularity were obtained using β-diiminate zinc complexes, whereas organocatalysts showed poor regioselectivity. It was rationalised that this difference in regioselectivity was caused by the bulky nature of the β-diiminate ligand present in the zinc-catalysed reactions, but not in those catalysed by aluminium triflate or organic bases. The thermal properties of the poly(**11**) homopolymers reveal amorphous polymers with a glass transition temperature (T_g) between −18 and −10 °C, which is very similar to that of PTMC (−15 °C).[71] In addition, **11** was copolymerised with ε-caprolactone and lactide to form highly hydrophobic copolymers and was used in the synthesis of poly(butylene succinate-*co*-**11**) by a combination of ROP and condensation polymerisation.[49,91]

Cyclic carbonates with aryl-containing functionalities

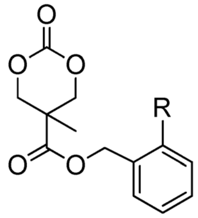
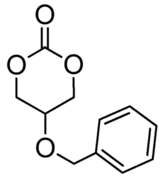
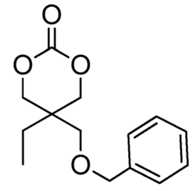
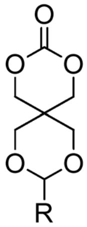
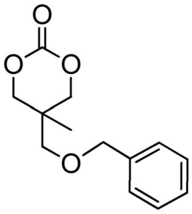
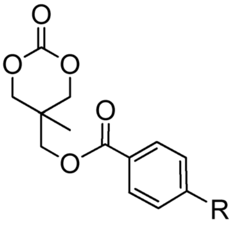
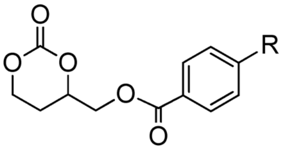
To date, many aryl-functional monomers and their respective polymers have been reported. Most commonly, those containing a benzyl group have been described. Monomers such as 5-methyl-5-benzyloxycarbonyl-1,3-dioxan-2-one, MBC **15** (Table 2) are readily polymerised and, moreover, the benzyl functionality can often be removed easily to yield hydrophilic materials or intermediates in the synthesis of carbonate monomers with more sensitive functionalities. For these reasons, benzyl-functional monomers have been used extensively in the preparation of functional aliphatic poly(carbonates) and poly(ester carbonate)s in recent years. MBC (**15**) and 5-benzyloxy-trimethylene carbonate (**17**), in particular have received much attention.[42,71,75,78,86,91–102] Homopolymerisation of

Table 1 Cyclic Carbonates with alkyl-containing functionalities

Monomer	Number	Ref.	Monomer	Number	Ref.
	**1 (DTC)**	75–85		**9**	87
	**2**	81		**10**	37 and 74
	**3**	61		**11**	49, 79, 85, 90 and 91
	**4**	62, 63 and 86		**12**	81
	**5** (n = 0) **6** (n = 1)	51		**13**	68
	**7 (MEC)**	37, 69–74 and 80		**14**	68
	**8**	70			

MBC was first reported by Bisht and coworkers in 1999 using enzymatic methods.[42] Polymerisation was studied using seven different commercially available lipases at 80 °C in bulk among which lipase AK (from *Pseudomonas fluorescens*) gave the highest monomer conversion (97%) and molecular weight (M_n) 6100 g mol^{-1} with no decarboxylation observed. Molecular weights remained low due to competitive initiation from water however higher molecular weights could be obtained when the lipase was dried extensively. Increasing molecular weight also led to significant broadening of the dispersities ($Đ_M \leq 7.5$). In order to control the incorporation of benzyl groups in the poly(carbonate) structures, copolymerisation with TMC was conducted

Table 2 Cyclic Carbonates with aryl-containing functionalities

Monomer	Number	Ref.
	**15 (MBC)** (R = H) **16** (R = NO_2)	42, 71 and 92–99
	**17**	49, 75, 78, 86 and 100–102
	**18**	49
	**19** (R = Ph) **20** (R = *p*OMePh) **21** (R = 2,4,6-OMe_3Ph)	50 and 103–105
	**22**	61
	**23** (R = H) **24** (R = OMe) **25** (R = NO_2)	79
	**26** (R = H) **27** (R = OMe) **28** (R = NO_2)	79

under the same conditions and led to statistical copolymers being isolated.[92] Organocatalytic ring-opening of MBC performed at room temperature with DBU as organocatalyst has resulted in well-defined homopolymers with controlled molecular weights (M_n = 4500–11 400 g mol^{-1}) and low dispersities ($Đ_M$ = 1.18–1.19).[99] The resulting poly(MBC) homopolymers are amorphous sticky polymers with a glass transition temperature (T_g) between 3 and 8 °C.[92,99] MBC has furthermore been reported in copolymerisations with lactide using tin- and zinc-based catalysts, mostly at elevated temperatures,[94–96] and in copolymerisations with MEC or lactide (LA) using organic catalysts (DBU or TU-amine) at room temperature.[71,98] In the latter case, reactivity ratios in the copolymerisation of lactide and MBC were found to be 1.1 for lactide and 0.072 for MBC. Micelles obtained from block copolymers prepared by the statistical copolymerisation of MBC with lactide, initiated from a poly(ethylene oxide), PEO, macroinitiator, demonstrated that the introduction of carbonate moieties did not only enhance solubilisation and drug loading of the hydrophobic drug bicalutamide, but also resulted in significant reductions in the value of critical micelle concentration (CMC) compared to micelles without MBC incorporated.[96]

Another frequently reported benzyl functional monomer is 5-benzyloxy-trimethylene carbonate (**17**). This monomer has been polymerised under bulk conditions at elevated temperatures using aluminium- and tin-based catalysts, a range of organic catalysts, porcine pancreas lipase immobilised on silica particles and under reduced pressure without added catalyst.[75,78,86,101,102] Reported poly(**17**) homopolymers displayed medium to large dispersities ($Đ_M$ = 1.41–1.92) and polymer molecular weights (M_n = 8800–22 400 g mol^{-1}) that are much lower than those expected for polymerisations with [M]/[I] = 1000. The resultant materials are rubbery at room temperature with T_g = 0–6 °C and no observed melting point.[100,101] Reported copolymerisations include random and block copolymers with DTC, lactide and PEO.[75,100,102] Another example is the combined ROP and polycondensation reaction of **17** or **18** with poly(butylene succinate) macromers.[49]

Other reported aryl-functional monomers, **19**, **22**, **23** and **26** have been studied to a lesser extent.[50,61,79,103,104] ROP of benzyl-functional monomer 9-phenyl-2,4,8,10-tetraoxaspiro-[5,5]-undecan-3-one (**19**) was investigated using diethyl zinc as initiator at 130 °C under bulk conditions for its homopolymerisation and its copolymerisation with both lactide and ε-caprolactone.[50,104] The resulting poly(**19**) homopolymers displayed a T_g = 124 °C, which is high compared to other poly(carbonate) homopolymers. Cationic ROP of **23** and **26** to form the respective homopolymers was reported at room temperature using a range of catalysts, however polymerisations were plagued by side reactions including backbiting and decarboxylation leading to poor control and low molecular weight products.[79] Suppression of decarboxylation was achieved using MeI as initiator, but increased reaction times and temperatures (120 °C) were required for the polymerisation to proceed.

Beyond simple benzyl-functional monomers, a number of monomers with methoxy- and nitro-substituted phenyl groups have been reported (Table 2).[79,105–107] The cationic ROP of **24**, **25**, **27** and **28** was reported by Endo and coworkers.[79] All four monomers were polymerised using methyl iodide at 120 °C to yield the respective homopolymers. Homopolymers were obtained with M_n = 10 000 g mol^{-1} ($Đ_M$ = 1.22) for poly(**24**), M_n = 3400 g mol^{-1} ($Đ_M$ = 1.88) for poly(**25**), M_n = 4400 g mol^{-1} ($Đ_M$ = 1.58) for poly(**27**) and M_n = 7100 g mol^{-1} ($Đ_M$ = 1.39) for poly(**28**). Polymerisation was also successfully conducted at room temperature in dichloromethane in case of **24** and **25** using TfOMe or TfOH as catalysts yielding polymers with M_n = 1300–3500 g mol^{-1} ($Đ_M$ = 1.13–1.24) and M_n = 3000 g mol^{-1} ($Đ_M$ = 1.16), respectively. Nitrobenzyl-functional monomer 5-methyl-5-(2-nitro-benzoxycarbonyl)-1,3-dioxan-2-one (**16**), methoxy functional monomers mono-2,4,6-trimethoxybenzylidene-pentaerythritol carbonate (**21**) and mono-4-methoxybenzylidene-pentaerythritol carbonate (**20**) have all been used in the synthesis of PEO block copolymers prepared by the homopolymerisation of the monomers or copolymerisation with lactide from methoxy-PEO macroinitiators.[105] Polymerisations were performed using tin octanoate as catalyst under bulk conditions at 110–120 °C (**16**) or using zinc bis[bis(trimethylsilyl)amide] in methylene chloride at 50 °C (**20** and **21**).[105–107]

Cyclic carbonates with alkene- and alkyne-containing functionalities

Alkene and alkyne functional groups participate in many organic reactions, including highly efficient and orthogonal reactions, as a consequence of their (double) unsaturation such as Michael addition, radical thylation, Huisgen 1,3-dipolar cycloaddition, epoxidation[120] and UV-cross-linking.[124,125] The introduction of such functionalities to the poly(carbonate) backbone leaves the resulting polymers open for further functionalisation.[108–112] Notably, there have been several reports of the synthesis and subsequent modification of (pendant) alkenes and alkyne groups in poly(ester)s.[113,114]

The introduction of pendant unsaturated groups in poly(carbonate)s prepared by the ring-opening of cyclic carbonate monomers has received increased attention in the past few years. The ROP of allyl ester-functional cyclic carbonate 5-methyl-5-allyloxycarbonyl-1,3-dioxan-2-one (MAC, **29**), for example, has been described in the preparation of a range of (co)polymers by Storey, Jing, Zhuo, Dove, Cui and their respective coworkers (Table 3).[76,115–122] Reported homopolymerisations of MAC were either performed without added catalyst at elevated temperature (at 115 °C; M_n = 13 700 g mol^{-1}; $Đ_M$ = 1.8), or in toluene at 95 °C using tin(II)-based poly(lactide) macroinitiator ([M]/[I] = 40; M_n = 9200 g mol^{-1}; $Đ_M$ = 2.5) and at 110 °C catalyzed by diethyl zinc ([M]/[I] = 200; M_n = 19 000 g mol^{-1}; $Đ_M$ = 1.6).[116,120] However, in all cases polymerisations showed relatively poor control and resulted in branched polymers in some cases. More recently Dove and coworkers demonstrated that the ROP of MAC using efficient organocatalysts led to a high level of control over the resulting polymer such that the application of the sparteine/TU catalyst system resulted in the isolation of PMAC with M_n up to *ca.* 13 000 g mol^{-1} ([M]/[I] = 100) and low dispersities ($Đ_M$ = 1.12).[121] Notably in this study, the polymer T_g was reported to be −26.4 °C, lower than that previously reported (T_g = −12 °C),[116,120] attributed to an absence of chain branching as a consequence of very low levels of transesterification. The ROP of MAC has also been reported in the synthesis of 3-armed star polymers initiated from triethanolamine using a *O*,*N*,*N*,*O*-tetradentate salan lutetium alkyl complex.[122] The resulting polymers displayed low dispersities ($Đ_M$ < 1.10) and molecular weights close to the predicted values from the monomer-to-initiator ratio. Furthermore, the polymerisation proceeded well with low catalyst loadings (compared to initiator) thus demonstrating its 'immortal' nature. Other studies involving MAC have mostly focused on its copolymerization with lactide,[116] including the formation of amphiphilic block copolymers composed of PMAC-*co*-PLA and poly(ethylene oxide) to form micelles[118] and polycations from poly(ethylenimine)-grafted polycarbonate.[119] While ROP of the related allyl-functional monomer 5-allyloxy-1,3-dioxan-2-one (**30**) has been reported, only the synthesis of 5-(2-propenyl)-5-propyl-1,3-dioxan-2-one (**33**) is known.[45,46,65] Homopolymerisation of **30** was reported by Parzuchowski *et al.*[45] and He *et al.*[46] Polymerisations were carried out in ethyl acetate at 65 °C using DMAP as catalyst or under bulk conditions at 120 °C using immobilised *porcine pancreas lipase* on silica or tin octanoate as catalyst. No evidence of decarboxylation was observed during the polymerisation and resulted in a semi-crystalline poly(**30**) that was characterized by a melting temperature around room temperature ($T_m = 24$ °C) and a low glass transition temperature ($T_g = -40$ °C). In an effort to improve the thermal properties of the poly(carbonate)s, while taking advantage of this lateral reactive groups, Gross and coworkers prepared the cyclohexene functional monomer 2,2-[2-pentene-1,5-diyl]-trimethylene carbonate (**31**).[60,68,123] It was hypothesised that the introduction of the cyclohexene substituent would yield poly(carbonate)s with a more rigid backbone and, as a consequence of this rigidity, a higher glass transition temperature. Indeed, polymers obtained by the metal-mediated (Al, Sn, Zn) ROP of **31** in bulk at 120 °C exhibited a $T_g = 30$ °C ([M]/[I] = 200; $M_n = 6000$–$255\,000$ g mol^{-1}; $Đ_M = 1.3$–3.4) which is significantly higher than those reported for allyl-functional poly(carbonate)s and TMC. In contrast, the homopolymer obtained from ROP of cinnamate-functional 5-methyl-5-cinnamoyloxymethyl-1,3-dioxan-2-one (**32**) with a molecular weight of 6000 g mol^{-1} ($Đ_M = 1.87$) had a T_g of 42 °C.[124] Both its homopolymerisation and copolymerisation with L-lactide were performed in bulk at 120 °C using diethyl zinc as catalyst.

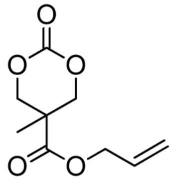
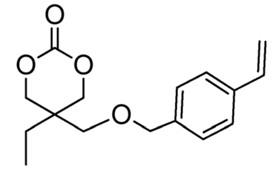
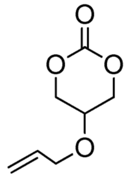
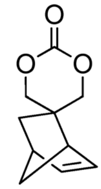
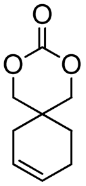
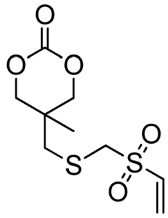
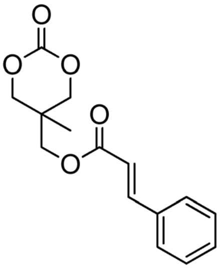
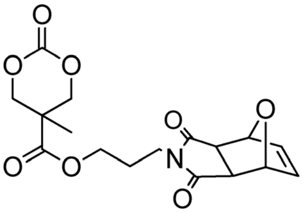
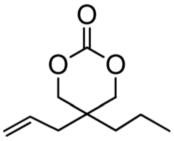
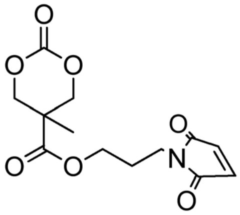
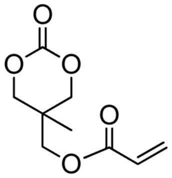
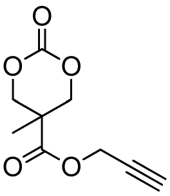
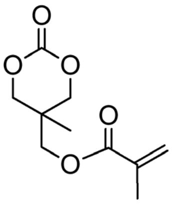
Acrylate-functional monomer **34** and methacrylate-functional monomer **35** were reported by Zhong and coworkers in copolymerisations with ε-caprolactone and lactide (incorporations lower than 33%) initiated from PEO to result in amphiphilic block copolymers.[47,126,127] The monomers were polymerised in toluene using tin octanoate at 110 °C or in methylene chloride at room temperature using bis[bis(trimethylsilyl)amido] zinc as a catalyst. Styrene-functional 5-ethyl-5-[(4-vinylphenyl)methoxymethyl]-1,3-dioxan-2-one (**36**), reported by Miyagawa *et al.*, was polymerised by anionic ROP in THF at 0 °C in the presence of potassium *tert*-butoxide (*t*-BuOK).[48] The resulting poly(**36**) homopolymer was characterised by a $M_n = 14\,000$ g mol^{-1} ($Đ_M = 1.44$) without polymerization of the pendant styrene groups.

Cyclic carbonate, 5,5-(bicyclo[2.2.1]hept-2-en-5,5-ylidene)-1,3-dioxan-2-one (**37**), with a pendant norbornene functionality was polymerised in bulk with a range of amine catalysts at 100–140 °C among which DBU proved to be the most active.[128] The resulting poly(**37**)s displayed high glass transition temperatures ($T_g = 108$ °C) as a consequence of the backbone rigidity resulting from the norbornene functionality. Copolymerisation of a vinyl sulfone-functional carbonate **38** was reported with TMC, caprolactone or lactide in toluene at 110 °C, using isopropanol as initiator and tin octanoate as catalyst has been reported.[64] The pendant vinyl sulfone remained intact during the polymerisation allowing subsequent modification of the polymer surface with thiol derivatives.[64] Onbulak *et al.* recently reported the synthesis and polymerisation of cyclic carbonate **39** which has a furan-protected maleimide as a pendant functionality.[129] The possibility to expose the maleimide functionality after polymerisation was demonstrated by the synthesis of **40** *via* deprotection in toluene at 110 °C. Homopolymerisation of **39** was carried out at room temperature using DBU as catalyst and benzyl alcohol as initiator. As polymerisations became severely retarded after 60% monomer conversion, polymerisations were stopped after 50% monomer conversion to avoid transesterification reactions resulting in poly(**39**)s with low dispersities ($Đ_M = 1.1$–1.2). In order to overcome poor polymerisability of **39**, its copolymerisation with LA was carried out, yielding well-defined copolymers with pendant furan-protected maleimides. Surprisingly, the only propargyl functional cyclic carbonate reported is 5-methyl-5-propargyloxycarbonyl-1,3-dioxan-2-one (MPC, **41**) and to date this monomer has only been copolymerised with lactide or trimethylene carbonate.[44,130–134] Copolymerisations were carried out in toluene or in bulk at 100–110 °C using diethyl zinc as catalyst/initiator[130–134] or in methylene chloride at room temperature using DBU/TU co-catalysts[44] resulting in copolymers with composition in MPC in agreement with the feed and ranging from 7 to 20%. In the latter study, it was found that MPC was incorporated preferentially to TMC at the beginning of the polymerisation.

Cyclic carbonates with halogen- and azide-containing functionalities

Cyclic carbonates carrying halogen groups are an attractive class of monomers as it allows subsequent nucleophilic substitution and introduction of novel functionalities even after polymerisation. Mindemark *et al.* recently reported the synthesis and polymerisation of four halide-containing monomers, **42–45** (Table 4).[38] The resulting homopolymers of these chloro- and bromo-functional monomers, obtained by ROP at elevated temperature (110 °C) in bulk using tin octanoate as a catalyst, yielded chloride-functional polymers with $M_n = 16\,000$–$38\,500$ g mol^{-1} and $Đ_M = 1.46$–1.81 and bromide functional polymers with $M_n = 8500$–$31\,900$ g mol^{-1} and $Đ_M = 1.41$–1.63, respectively. All polymers were semi-crystalline in nature with small variations of the measured melting points and glass transitions (**P42**: $T_g = 15$ °C, $T_m = 105$ °C; **P43**: $T_g = 10$–13 °C, $T_m = 131$–152 °C; **P44**: $T_g = 18$–23 °C, $T_m = 100$ °C; **P45**: $T_g = 15$–18 °C, $T_m = 121$–153 °C) However, a significant difference in solubility was observed between halide-containing polymers with a pendant methyl and an ethyl substituent. Indeed, whereas poly(**43**) and poly(**45**) are insoluble in most common organic solvents, poly(**42**) and poly(**44**) were found to be readily soluble in methylene chloride and tetrahydrofuran. Interestingly, copolymerisation of these monomers with TMC also resulted in semicrystalline poly(carbonate)s. A similar cyclic carbonate monomer with two

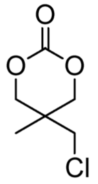
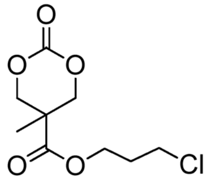
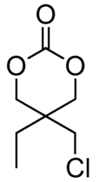
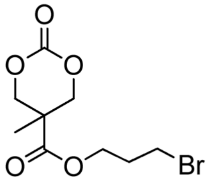
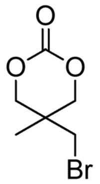
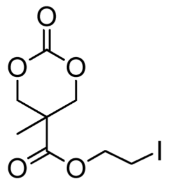
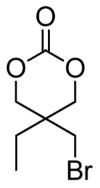
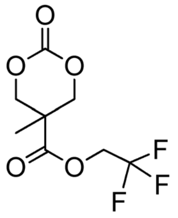
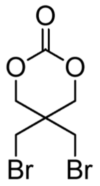
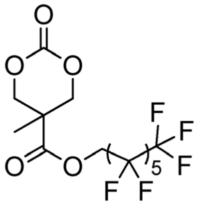
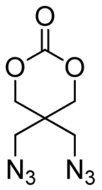
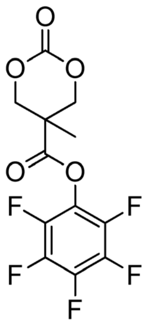
Table 3 Cyclic carbonates with alkene- and alkyne-containing functionalities

Monomer	Number	Ref.	Monomer	Number	Ref.
	**29 (MAC)**	76 and 115–122		**36**	48
	**30**	45 and 46		**37**	128
	**31**	60, 123 and 68		**38**	64
	**32**	124		**39**	129
	**33**	65		**40**	129
	**34**	47, 126 and 127		**41 (MPC)**	44 and 130–134
	**35**	47			

pendant bromide functionalities, 2,2-bis(bromomethyl)trimethylene carbonate (**46**), has also been reported.[57,58,135] Its homopolymerisation and its copolymerisation with ε-caprolactone were reported in bulk at 120 °C using tin octanoate as catalyst and the resulting polymers were subsequently modified with NaN_3 and used for the preparation of poly(carbonate) nanoparticles by the Huisgen 1,3-dipolar cycloaddition. The synthesis and polymerisation of halogen-functional cyclic carbonates derived from bis-MPA were also reported by Hedrick and coworkers (Table 4).[37,44,69,72,138,139] In a recent study, the pentafluorophenol pathway was exploited to form the cyclic carbonate **53** intermediate as outlined previously.

The synthesis of halogen-containing poly(**48**) ([M]/[I] = 55; M_n = 12 200 g mol^{-1}; $Đ_M$ = 1.17), poly(**49**) ([M]/[I] = 52; M_n = 11 700 g mol^{-1}; $Đ_M$ = 1.11), poly(**50**) ([M]/[I] = 51; M_n = 10 500 g mol^{-1}; $Đ_M$ = 1.22) and poly(**51**) ([M]/[I] = 54; M_n = 11 500 g mol^{-1}; $Đ_M$ = 1.26) was achieved *via* organocatalytic ROP at room temperature using the TU/DBU catalyst system.[37,72] Distribution of the pendant halogen functionalities in the poly(carbonate) backbone was achieved under these conditions

Table 4 Cyclic carbonates with halogen- and azide-containing functionalities

Monomer	Number	Ref.	Monomer	Number	Ref.
	**42**	38		**48**	37, 44, 69, 72 and 139
	**43**	38		**49**	37, 72 and 138
	**44**	38		**50**	72
	**45**	38		**51**	44
	**46**	57 and 58		**52**	37
	**47**	57, 58, 136 and 137		**53**	37

in copolymerisations with MEC (with **48**, **49**, **50**) or TMC (with **52**) and resulted in polymers with controlled molecular weights and low dispersities.[37,44,69,72,138,139]

Cyclic carbonates with lateral nitrogen-containing functionalities: amino-, amido, carbamate and urea functional cyclic carbonates

Nitrogen-containing cyclic carbonates include those with pendant amides and pendant amino, amido and urea functionalities.[37,52,55,59,87,140,141] Cyclic carbonates with pendant amides are those with pendant carbamic acid benzyl ester (Z) groups and carbamic acid *tert*-butyl ester (Boc) functional groups, which are used to protect functional groups that have primary amines during the polymerisation. Endo and coworkers reported the anionic ROP of **55**, **56** and **59** (Table 5) which was carried out in THF at temperatures between −78 and −30 °C using a range of initiators.[52] Molecular weights of the resulting poly(**55**) homopolymers ranged from 5600 g mol^{-1} to 20 000 g mol^{-1} with moderate dispersities being observed ($Đ_M$ = 1.20–1.46). Interestingly, poly(**56**) (M_n = 13 000–24 000 g mol^{-1}) and poly(**59**) (M_n = 5700–21 000 g mol^{-1}) showed inverse optical rotations compared to the respective cyclic carbonates and lower dispersities ($Đ_M$ = 1.18–1.24 and 1.11–1.20, respectively) than poly(**55**). Additionally, ROP of **56** and **59** showed a preference (9 : 1) for ring-opening at the least-hindered acyl bond. The bulk copolymerisation of **55** with lactide has also been reported at 120 °C using diethylzinc as catalyst and yielded poly(**55**) with comparable molecular weight and dispersity (M_n = 24 100 g mol^{-1}; $Đ_M$ = 1.51).[55] While the polymerisation of the Boc-protected-amine cyclic carbonate, **54**, has not been reported, the organocatalytic ROP of related monomer **57** has been reported with TMC.[37,44] The copolymerisation was performed using the TU/DBU catalytic system at room temperature in methylene chloride and resulted in copolymers of **57** and TMC with low dispersities ($Đ_M$ = 1.07). Synthesis of poly(**58**) homopolymers with low degrees of polymerisation (DP = 8–22) and copolymers of **58** with other cyclic carbonate monomers was realised using the TU/DBU catalyst system in CH_2Cl_2 at room temperature.[87,140] Homopolymers obtained from the organocatalytic ROP of **58** exhibited low dispersities ($Đ_M$ = 1.11–1.16) for molecular weights M_n ranging from 3800 to 10 000 g mol^{-1} and displayed excellent cellular uptake with longer oligomers being observed to mediate cell adhesion.[140] Furthermore, these homopolymers were also applied as components of non-covalent, degradable hydrogels.[87]

Although the synthesis of amido-functional cyclic carbonates **60** and **61** has been reported (Table 5),[44] no report was found describing their polymerisation. No other reports of the ROP of this type of amido-functional cyclic carbonate monomers were found, possibly as polymerisation could be complicated by the presence of the secondary amine. In contrast, homopolymerisation of **62**, with a tertiary amide pendant group, has been reported by Sanders *et al.* using the TU/DBU catalyst system at room temperature to yield poly(**62**) with M_n = 10 500 g mol^{-1} and $Đ_M$ = 1.32 ([M]/[I] = 63).[37] The homopolymerisations of the tertiary amine-containing 16-membered 6,14-dimethyl-1,3,9,11-tetraoxa-6,14-diaza-cyclohexadecane-2,10-dione (**64**), which contains two carbonate groups and two tertiary amines, was reported by Wang *et al.* in 2010.[59] ROP was attempted using both enzyme- and metal-based catalyst systems. Polymerisations performed in bulk at elevated temperatures (120 °C) using tin octanoate resulted in decarboxylation of the monomer whilst polymerisations performed in toluene at temperatures between 70 and 100 °C did not result in any polymerisation being observed. In contrast, the enzymatic ROP of **64** in toluene using Novozym-435 resulted in the formation of poly(**64**) both at 70 °C and at room temperature and displayed living characteristics. Poly(**64**) with a molecular weight of 8000 g mol^{-1} and a $Đ_M$ = 1.34 was obtained by the enzymatic process and were amorphous materials presenting excellent biocompatibility and fast degradability. Likewise, homopolymers obtained from the enzymatic ROP (60 °C; M_n = 4900 g mol^{-1}, $Đ_M$ = 1.40) of six-membered dimethylamine-functional cyclic carbonate, 2-dimethylaminotrimethylene carbonate (**63**), showed low toxicity and good degradability.[141] Finally, polymerisation of urea-functional monomers **65** and **66** were reported using the TU/(−)-sparteine catalyst system at room temperature in CH_2Cl_2. Poly(**66**) was obtained with M_n = 10 500 g mol^{-1} ([M]/[I] = 32; $Đ_M$ = 1.14) and displayed a T_g at approximately 15 °C.[142] The synthesis of block copolymers with a PEO block, a poly(TMC) and a poly(**66**) or poly(**65**) block have also been reported, as well as a block copolymer with a PEO block and a poly(MEC-*co*-**65**) sequence, was reported using the same mild conditions. These block copolymers were used for the formation of micelles that displayed low CMC's and increased stability of drug-loaded micelles due to the hydrogen-bonding interactions between the urea groups.[71,73] Strong H-bonding interaction arising from the urea-groups was also highlighted in semi-interpenetrating networks by a decrease of the overall degree of swelling.[142,143]

Cyclic carbonates with protected sugar functionalities

Beyond their degradable and biocompatible properties, carbohydrates display specific interactions with proteins (lectins) making them very desirable for targeted drug delivery systems.[144] Introduction of these groups on a poly(carbonate) backbone presents an attractive, non-toxic and biodegradable method to targeted drug delivery. As the hydroxyl groups in sugar-functional cyclic carbonates are incompatible with the ring-opening process, the hydroxyl groups require protection prior to the polymerisation of the cyclic carbonate. Gross and coworkers first prepared a cyclic carbonate monomer directly from xylose saccharide, 1,2-*O*-isopropylidene-D-xylofuranose-3,5-cyclic carbonate (**71**, Table 6).[54,145,146] This work was extended with the synthesis and polymerisation of glucose based 1,2-*O*-isopropylidene-3-benzyloxy-pentofuranose-4,4′-cyclic carbonate (**70**).[53] Monomers were homopolymerised as well as copolymerised with L-lactide under bulk conditions at elevated temperatures (120–180 °C) or in dioxane at 25–60 °C. The resulting poly(**70**) and poly(**71**) homopolymers were obtained with number-average molecular weights of 7900 g mol^{-1} ($Đ_M$ = 1.47),[145] and 2100–13 200 g mol^{-1} ($Đ_M$ = 1.22–1.92), respectively.[146] Thermal analysis of the polymers revealed that poly(**70**)

Table 5 Cyclic carbonates with lateral nitrogen-containing functionalities: amino-, amido, carbamate and urea functional cyclic carbonates

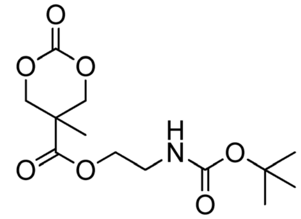
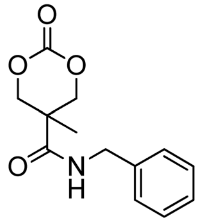
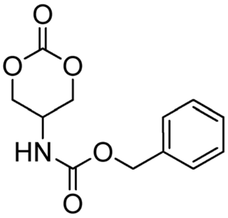
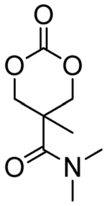
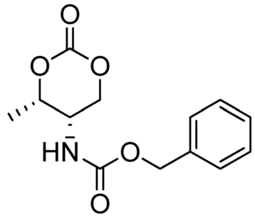
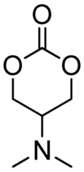
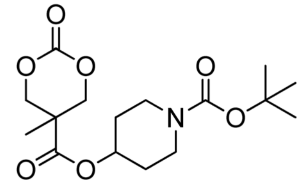
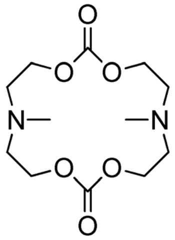
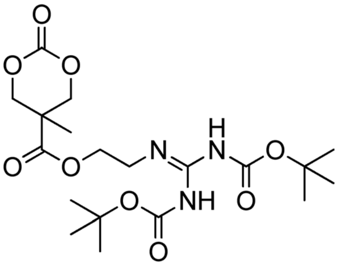
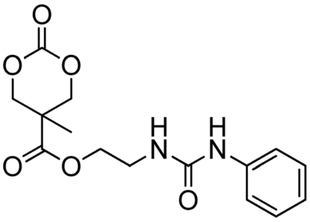
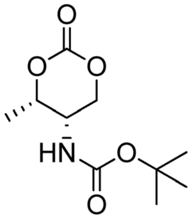
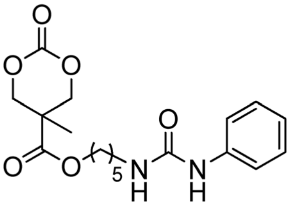
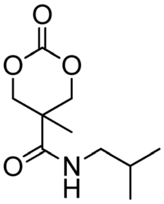
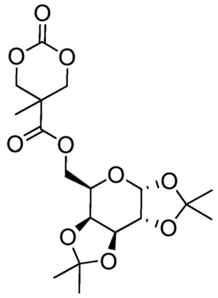
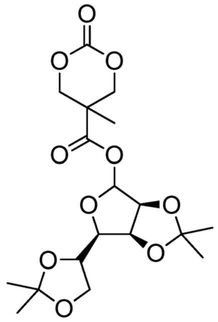
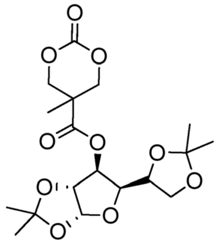
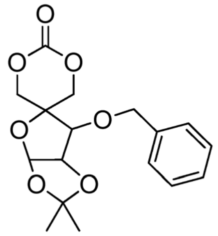
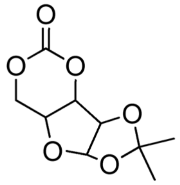
Monomer	Number	Ref.	Monomer	Number	Ref.
	**54**	37 and 44		**61**	44
	**55**	52 and 55		**62**	37
	**56**	52		**63**	141
	**57**	44		**64**	59
	**58**	87 and 140		**65**	71, 73 and 142
	**59**	52		**66**	71, 73 and 142
	**60**	44			

Table 6 Cyclic carbonates with protected sugar functionalities

Monomer	Number	Ref.
	67	147
	68	147
	69	147
	70	53 and 146
	71	54, 145 and 146

displayed a T_g = 128 °C[145] whereas poly(**71**) was also found to be semicrystalline and displayed a T_g = 128 °C.[146] Deprotection of ketal group of polymers containing monomer **71** was successfully achieved by using trifluoroacetic acid. Unfortunately however, deprotection resulted in some degradation due to the hydrolysis of the pendant ester bonds that link the carbohydrate to the carbonate. While deprotection of the homopolymer of **70** has not been reported to date, conversely, removal of a benzyl protecting group in copolymers containing monomer **70** can be achieved selectively by hydrogenation over palladium/carbon (90% removal) however again, acetonide deprotection resulted in some degradation. Deprotection of its copolymer with lactide showed a lowering in glass transition after both deprotection steps.

Homopolymerisation of cyclic carbonates **67**, **68** and **69** with pendant protected saccharides was carried out at room temperature using the TU/DBU organocatalytic system.[147] Homopolymers were obtained with molecular weights between 17 000 and 19 000 g mol^{-1} and dispersities of 1.20–1.28. Recovery of the hydroxyl groups was carried out by deprotection of the acetonide groups using formic acid solution. Interestingly, full deprotection was achieved and no degradation of the polycarbonate backbone was observed. Block copolymers of **67–69** with TMC were reported for the preparation of micelles in aqueous solutions, and were prepared by sequential addition of TMC to poly(**67**), poly(**68**) and poly(**69**).

Macromonomers, bis- and tris-carbonates

A number of cyclic carbonate-containing macromonomers and cross-linkers have been reported.[33,37,44,70,77,87,142] In particular those containing ethylene glycol moieties (**72–74**) have received increased interest in recent years (Table 7). PEO-functional cyclic carbonate macromonomer (**72**), prepared from methoxy poly(ethylene oxide)s, have been reported with molecular weights ranging from 350 g mol^{-1} to 1900 g mol^{-1} ($Đ_M$ = 1.03–1.14). While homopolymerisation of **72** in methylene chloride solution at room temperature using DBU as a catalyst was possible (with M_n = 1900 g mol^{-1} and $Đ_M$ = 1.03), the reaction showed a maximum at 55% monomer conversion.[33] The limited, low concentration of the cyclic carbonate (0.2 M), due to the large PEO pendant chain, was thought to cause the ring-chain equilibrium to dominate such that a high molecular weight polymers could not be obtained. To obtain higher molecular weight polymers, the cyclic carbonate concentration was increased by copolymerisation of **72** with TMC.[33,44] Random copolymerisation of **72** with dimethyltrimethylene carbonate (DTC) from a poly(ε-caprolactone) macroinitiator at 130 °C in bulk using tin octanoate as catalyst or with dodecyl-functional monomer **8** in CH_2Cl_2 at room temperature using organic catalysts were further reported.[70,77] The resulting block/graft copolymers could be self-assembled with the latter example displaying thermoresponsive behaviour owing to the combination of hydrophilic/hydrophobic groups in the second block. An organocatalytic approach to hydrogels was presented by Nederberg *et al.* by the synthesis of a bifunctional cyclic carbonate macromonomer from poly(ethylene oxide) diols.[33] Poly(ethylene oxide)-α,ω-methylcarboxytrimethylene carbonate crosslinkers, **74**, were prepared with M_n = 3400 g mol^{-1}, 8000 g mol^{-1} and 18 500 g mol^{-1} and copolymerised with TMC in CH_2Cl_2 at room temperature in the presence of DBU to form a poly(carbonate)/poly(ethylene oxide) cross-linked hydrogel. Hydrogels prepared with increased amounts of TMC showed hydrophobic PTMC domains which contribute to an increase of the toughness of the resulting hydrogels.[33,142] This led to further investigation by synthesis of telechelic, carbonate functional poly(ε-caprolactone), **75**, with a molecular weight of 8000 g mol^{-1} ($Đ_M$ = 1.40; DP = 70).

Copolymerisation of this hydrophobic crosslinker with **74** (8000 g mol^{-1}) and TMC to introduce hydrophobic segments resulted in particularly tough materials. Furthermore hydrogels prepared by copolymerisation from a poly(carbonate) macroinitiator bearing pendant urea functionalities (*i.e.* poly(**66**)) are presented as another method to strengthen the resulting network *via* hydrogen bonding with the poly(ethylene oxide) crosslinkers.[33,87,142] Very recently, Akashi *et al.* developed macromonomers based on oligo poly(ethylene oxide) connected to the cyclic carbonate by an ether linker (**73**).[148] Interestingly, the resulting homopolymers (M_n = 960–11 000 g mol^{-1}, $Đ_M$ = 1.06–1.42) displayed tunable thermoresponsive properties around body temperature.

The synthesis of a triazolium-based cyclic carbonate, **76**, that can act as an initiator for the anionic ROP of β-butyrolactone (BL) at elevated temperature was reported by Dubois and coworkers.[149] To prove that the carbene catalyst was selective for the polymerisation of BL, its polymerisation from **76** was carried out at 90 °C in bulk. The resulting poly(β-butyrolactone) PBL cyclic carbonate macromonomer (**77**) was characterised by low dispersity ($Đ_M$ = 1.21) and preservation of the cyclic carbonate end-group as attested by ^{1}H NMR spectroscopy. As an alternative, **76** was copolymerised with TMC at room temperature with a (−)-sparteine/4-chlorophenol cocatalyst system to give a co-poly(carbonate) with pendant triazolium groups (M_n = 4100 g mol^{-1}; $Đ_M$ = 1.19) which, in a subsequent step could then be used as initiator for the ROP of BL in the preparation of graft copolymers.

A range of other bis-cyclic carbonate cross-linkers and one tris-cyclic carbonate cross-linker have also been reported (**78–84**; Table 7) for the preparation of biodegradable cross-linked networks.[44,150] Monomer **81** exists in both the *trans*- and *cis*-isomers which could be separated by column chromatography and isolated in a 1 : 1 ratio. Cross-linked networks were obtained by copolymerisation of the bifunctional monomers with TMC and ε-caprolactone at 140 °C in bulk in the presence of tin octanoate. As expected and in agreement with Flory's theory,[151] the as-obtained cross-linked networks displayed increased glass transition temperatures with increased amount of cross-linker.

Other functional monomers

Several other six-membered cyclic carbonate monomers have been reported. Azidation of the 1,3-diol precursor to **46**, followed by carbonate formation using ethyl chloroformate yielded diazido-functional **85**. Poly(**85**) could be obtained at elevated temperatures under bulk conditions with tin-based catalysts (M_n = 10 700–57 900 g mol^{-1}; $Đ_M$ = 1.20–1.41) or using DBU in methylene chloride at room temperature resulting in polymers with low dispersities ($Đ_M$ < 1.1). Poly(**85**) was also shown to be a semicrystalline material with a melting temperature ranging from 50 to 100 °C and a glass transition temperature that is slightly below 0 °C.[136,137] Furthermore, **85** was reported in copolymerisations with DTC, lactide and in the preparation of block copolymers, by initiation from PEO macroinitiators. These copolymers were subsequently studied in hydrogel formation by "Click reaction".[57,58,136,137] In a comparable manner, Mindemark and Bowden described the azidation of **44** and **45** to yield the azide-functional analogues **86** and **87**. While the ROP of these monomers was not reported, a range of triazole-functional monomers (**88–97**; Table 8) were prepared by Cu(I)-catalysed Huisgen dipolar cycloaddition with terminal alkynes. ROP of **89**, **91**, **93** and **95** were reported (target DP = 50) using the TU/DBU organocatalyst system to yield polymers with low dispersities (1.13–1.25) and M_n between 2300 and 5600 g mol^{-1}.[152]

Other functional monomers reported include epoxide-functional cyclic carbonate, **98**, which was converted to bifunctional cyclic carbonate 5-(2-oxo-1,3-dioxolan-4-yl)methyl-5-propyl-1,3-dioxan-2-one (**99**, Table 8).[65] The selective polymerisation of the six-membered cyclic carbonate at 60 °C with DBU was achieved and the resulting homopolymer, with the pendant five-membered cyclic carbonate intact, was obtained in 50% yield (M_n = 14 900 g mol^{-1}; $Đ_M$ = 1.41). Hydroxyl-functional monomers **101** and **102** are incompatible for the controlled ROP process as the hydroxyl functionality acts as an initiating group. However, advantage was taken of this fact to prepare biodegradable, hydrophilic, hyperbranched hydroxyl-enriched aliphatic polycarbonates.[45,153,154] Attaching PEG arms onto the hyperbranched structure led to self-assembly into supramolecular micelles with excellent stability and good cell biocompatibility.[117]

In a recent report by Lee *et al.*, a cyclic carbonate with a pendant cholesterol group, cholesteryl-2-(5-methyl-2-oxo-1,3-dioxane-5-carboxyloyloxy) ethyl carbamate (**100**) was homopolymerised (DP 11) and copolymerised with TMC from a PEO macroinitiator using organic catalysts DBU and TU.[160] Micelles prepared from the abovementioned block copolymers showed increased loading of the anticancer drug paclitaxel. It was hypothesised that this excellent compatibility is a result of the rigid aromatic structure of cholesterol and its available stereocenters that may interact with those in paclitaxel. Sulphide and disulphide functional cyclic carbonates **103**, **104** and **105** (Table 8) have been reported, but their polymerisation has not yet been reported.[37,44] Other sulfur-containing monomers have been recently reported, including those containing pendant groups capable of acting as chain-transfer agents (CTAs) in reverse addition-fragmentation chain transfer (RAFT) polymerisations.[155,156] Mespouille *et al.* reported the synthesis of a bis-MPA-based cyclic carbonate bearing a 2-(benzylsulfanylthiocarbonylsulfanyl)ethyl ester, **106**.[155] ROP of **106** was investigated using both DBU and TU/(−)-sparteine catalysts with the latter system yielding polymers with lower dispersities ($Đ_M$ = 1.11–1.78). The polymerisation of *N*-isopropylacrylamide (NiPAAM) from the resulting polymers in a Z-group approach (in which the CTA remains bound to the backbone) in DMF at 70 °C for 8 h using AIBN as coinitiator resulted in successful chain grafting from the poly(carbonate) backbone. More recently, Williams, O'Reilly and Dove reported the synthesis of poly(carbonate) graft copolymers using ROP and an R-group RAFT approach in order that the CTA moiety be located at the graft chain termini.[156] Here, the ROP of an analogous dual-functional monomer, **107**, was undertaken simply using DBU as a catalyst to yield polymers with predictable molecular weights

Table 7 Macromonomers, bis- and tris-carbonates

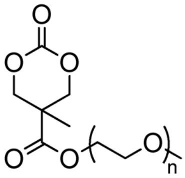
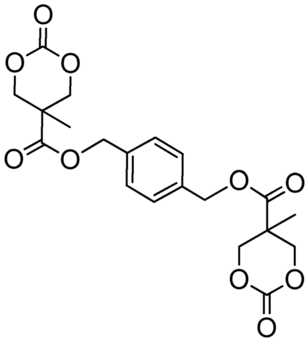
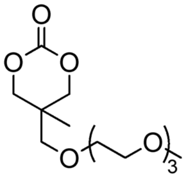
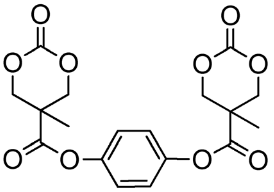
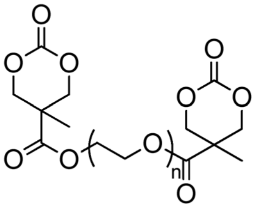
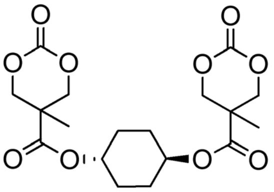
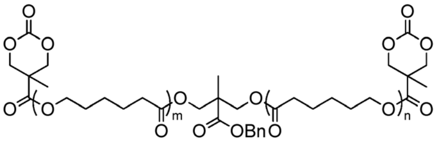
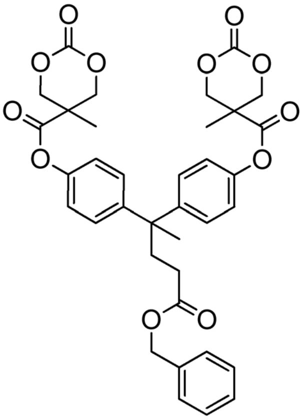
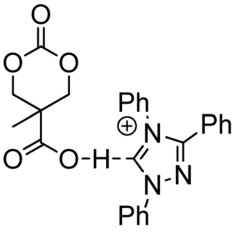
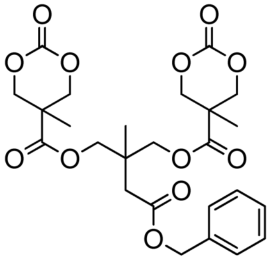
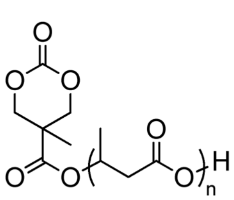
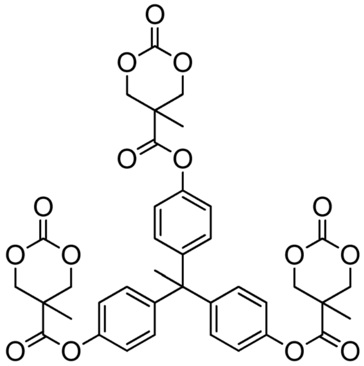
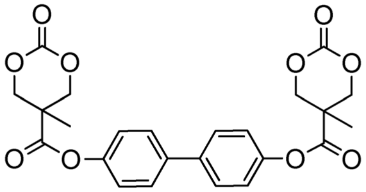
Monomer	Number	Ref.	Monomer	Number	Ref.
	**72**	33, 44, 70 and 77		**79**	44
	**73**	148		**80**	150
	**74**	150		**81**	150
	**75**	150		**82**	150
	**76**	149		**83**	150

Table 7 (*continued*)

Monomer	Number	Ref.	Monomer	Number	Ref.
	**77**	149		**84**	150
	**78**	150			

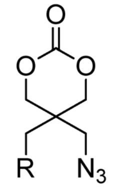
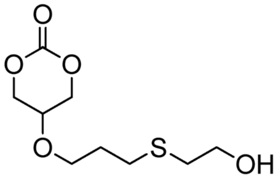
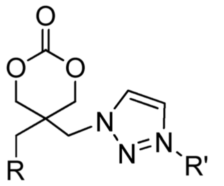
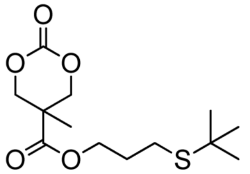
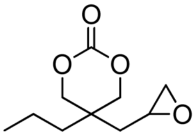
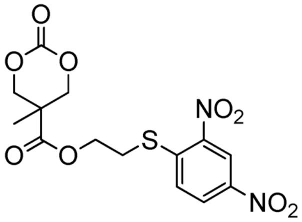
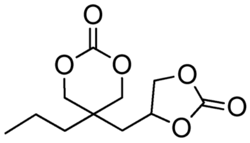
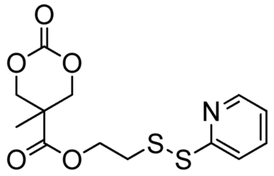
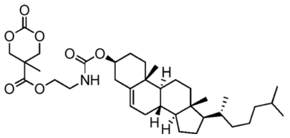
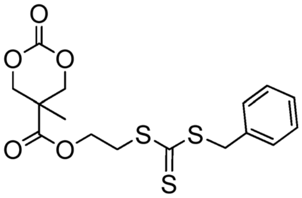
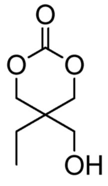
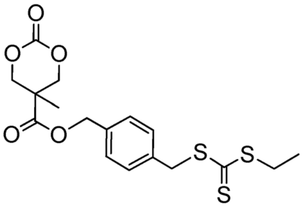
(in comparison to [M]/[I]) and low dispersities ($Đ_M < 1.16$). Graft copolymers with NiPAAM, styrene and methyl acrylate were prepared in $CHCl_3$ at 65 °C using AIBN as a coinitiator. Notably, the NiPAAM-grafted poly(carbonate)s displayed altered T_g's and lower critical solution temperatures that were in line with those expected based on their structure. Additionally, direct dissolution of these polymers in nanopure water at 3 °C resulted in the isolation of degradable nanoparticles.

Post-polymerisation modification of functional poly(carbonate)s

Deprotection of aryl- and alkyl-functional poly(carbonate)s

Alkyl- and aryl-functional groups are inert during most polymerisation conditions and are therefore often used to protect functional groups such as hydroxyl and carboxylic acid groups which may be incompatible in a ROP process. Aliphatic poly(carbonate)s containing pendant hydroxyl and carboxylic acid functions can be obtained by introducing benzyl ether or ester protecting groups respectively such that deprotection can be performed directly following the polymerisation process. Deprotection of the benzyl groups of poly(carbonate)s such as poly(MBC) and poly(**17**) has been reported by catalytic hydrogenolysis over palladium on carbon or palladium hydroxide on carbon to lead to carboxyl- and hydroxyl-functional poly(carbonate)s.[42,78,90,92,93,95–102,104,157–159] In both cases the reduction in the molecular weight was confirmed by a shift to higher retention time observed by GPC analysis. Poly(**17**) and poly(MBC) are highly hydrophobic materials before deprotection, but the resulting hydroxyl and carboxylic acid functional polymers are hydrophilic materials that show enhanced biocompatibility and hydrosolubility compared to the benzyl-containing material.[95,102] Homopolymers and copolymers of MBC also reveal a change in T_g after deprotection with poly(MBC) being isolated as a sticky amorphous polymer with T_g = *ca.* 3 °C. After deprotection, the polymer was isolated as a semicrystalline white powder with a higher T_g (47–60 °C) and a T_m = *ca.* 170 °C. Poly(**17**) homopolymers displayed an impressive 64-fold increase in water absorption after debenzylation. The bulk autodegradation process of poly(lactide) was increased in copolymers with **17** after benzyl deprotection due to the presence of the hydroxyl groups. The rate of degradation was found to be even faster under acidic conditions (pH = 4.4) than in neutral conditions (pH = 7.4).[100] In a similar manner, hydroxyl-functional polymers were obtained by removal of the benzylidene group in polymers prepared from **19**.[50] In contrast to poly(**17**), poly(**19**) reveals two hydroxyl groups per repeat unit due to the double hydroxyl protection of the benzylidene group. Although to date no thermal properties are reported for poly(**19**), copolymers of lactide with 10% incorporation of deprotected **19** already show a decrease in T_g of 14 °C due to the increased flexibility of the polymer chains after removal of the rigid benzylidene groups. Interestingly, these lactide copolymers showed surface degradation in contrast to pure poly(lactide) which usually displays a bulk degradation profile. Facile deprotection of the benzylidene group could be achieved under acidic conditions in case of block copolymers of PEO-*b*-P(**20**) or PEO-*b*-P(**21**). In poly(**20**) and poly(**21**) the benzylidene groups are substituted with methoxy groups at the *para*-position and the *ortho*- and *para*-positions, respectively.[105] Despite the high number of hydroxyl groups on the polymer, the deprotected poly(**20**/**21**) block is still insoluble in water and hence the block copolymers self-assemble into stable micelles at pH 7.4 and also show altered degradation profiles in slightly acidic conditions (pH 4–5). This polymer was successfully employed for the

Table 8 Miscellaneous functional cyclic carbonates

Monomer	Number	Ref.	Monomer	Number	Ref.
	**85** (R = N_3) **86** (R = H) **87** (R = Me)	57, 58, 136, 137 and 152		**102**	45
	**88** (R = H, R′ = Ph) **89** (R = Me, R′ = Ph) **90** (R = H, R′ = C_3H_5) **91** (R = Me, R′ = C_3H_5) **92** (R = H, R′ = C_3H_7) **93** (R = Me, R′ = C_3H_7) **94** (R = H, R′ = C(= CH_2)CH_3) **95** (R = Me, R′ = C(= CH_2)CH_3) **96** (R = H, R′ = C(OH)Me_2) **97** (R = Me, R′ = C(OH)Me_2)	152		**103**	44
	**98**	65		**104**	37
	**99**	65		**105**	37 and 44
	**100**	160		**106**	155
	**101**	153 and 154		**107**	156

encapsulation of anti-cancer drugs and their subsequent pH-controlled release.[105,161,162]

Fukushima *et al.*[74] reported another example of a poly(carbonate) that deprotects under acidic conditions. In this contribution, deprotection of tetrahydropyranyloxy protecting groups in poly(**10**) was carried out at 50 °C using an ion-exchange resin to reveal hydroxyl functional polymers. The hydroxyl functionalities then acted as initiating sites in further ROP of stereopure poly(lactide) to form graft-copolymers with a poly(carbonate) backbone and stereopure poly(lactide) grafts. After mixing these PEO-poly(carbonate) block-copolymers grafted with PLA of opposite chirality (PLLA and PDLA), micelles could be formed at extremely low concentrations owing to the stereocomplexation driving force between PDLA and PLLA in the core of the micelles.

Jing *et al.*[106,107] reported recently that the nitrobenzyl lateral groups in PEO-*b*-P(**16**) block copolymers could be deprotected under UV irradiation at 365 nm to convert the poly(carbonate) block from a hydrophobic block to a hydrophilic carboxylic acid-functional block. Micelles prepared from these PEO-*b*-P(**16**) block copolymers were shown to dissociate readily when irradiated due to the conversion of the amphiphilic block copolymers into hydrophilic copolymers.[106,107]

The newly available carboxylic acid and hydroxyl groups after deprotection are also open to further reactions. Further modification of carboxylic acid functional polymers were reported *via* *N*,*N*′-diisopropylcarbodiimide (DIC), 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC) or DCC couplings with free alcohol groups present in biologically active molecules or with *N*-hydroxysuccinimide (NHS) or hydroxybenzotriazole (HOBt) for further reaction with amines.[95,96,98–100] Conjugation using these methods is limited since quantitative conversion of the acid groups into esters is rarely observed and can be as low as 20% in some reported cases. Examples of post-polymerisation modifications of acid-functional polymers obtained after deprotection included conjugation with aliphatic amines in the formation of DNA/polymer nanoparticles, the grafting of PEO-amines[98] to form amphiphilic copolymers with a hydrophobic backbone and hydrophilic grafts that self-assemble in aqueous environments and conjugation with peptides[95] or drugs such as heparin,[93] docetaxel[95] and paclitaxel.[96] Further modifications of hydroxyl-functional monomers include reaction of the hydroxyl groups with acid chlorides (*e.g.* 4-isobutylmethylphenyl acetic acid).[100]

Post-polymerisation modifications of alkene-functional poly(carbonate)s

Alkenes participate in many reactions and are for that reason utilised extensively. In the post-polymerisation functionalisation of biodegradable polymers, the presence of carbon–carbon double bonds in the polymer chain[113] or as lateral group have been utilised in cross-linking reactions and in the addition of new pendant functional moieties.[44–48,60,65,68,71,76,115–134] Reported post-polymerisation functionalisations of alkenyl-functional poly(carbonate)s can divided into three general categories: cross-linking, thiol additions and epoxidations. Cross-linking of the hydrophobic core of micelles prepared from block copolymers with hydrophilic PEO blocks and hydrophobic poly(ester-carbonate) blocks with pendant allyl- or acryloyl-groups was realised by heating in the presence of azobisisobutyronitrile (AIBN) at 60 °C and by UV irradiation of the micelles in the presence of a biocompatible photoinitiator respectively.[115,116,126] Micelles with cross-linked poly(ester-carbonate) cores, loaded with anti-cancer drug paclitaxel and with galactose groups at the micelle surface for specific targeting displayed enhanced antitumor efficacy in *in vivo* studies. The acroyl-functional monomer, **34**, has also been copolymerised to form triblock PEG-*b*-Poly(**34**)-*b*-PLA copolymers.[163] Here, the micellization in the presence of paclitaxel was followed by irradiation with UV light to crosslink the acroyl groups and stabilize the particle to prevent premature release of drug. In an extension to this work, synthesis of PEG-initiated statistical copolymers of **34** with **21** enabled the synthesis of crosslinked nanoparticles that were able to be deprotected upon lowering of the pH to enable a triggered release of the cargo.[164] In another example, the radical cross-linking of a poly(carbonate) homopolymer with pendant styrene groups (poly(**36**)) was realised in the presence of the radical initiator benzoyl peroxide.[48] The cross-linking was carried out in the presence of styrene to yield a poly(carbonate)/poly(styrene) network. Notably, the resulting cross-linked networks could be unlinked in the presence of *t*-BuOK, resulting in poly(styrene) with pendant six-membered cyclic carbonates. Photo-cross-linking of poly(ester-carbonates) (copolymers of L-lactide and **32**) with pendant cinnamate functionalities could be cross-linked by UV irradiation at 365 nm providing biodegradable networks.[124] This type of cross-linking occurs *via* dimerisation through the [2+2] cycloaddition reaction of two cinnamate moieties upon irradiation with UV light.

The reaction of thiols and alkenes ('thiol–ene') has been utilised extensively as an efficient method in the preparation of functional polymers. Reactions proceed either *via* the free-radical addition of thiols to carbon–carbon double bonds or *via* the Michael-addition of thiols to electron-deficient carbon–carbon double bonds.[111] Radical-type addition of thiols to the poly(carbonate) backbone has been reported for polymers containing pendant allyl functionalities.[45,116,118,121] Homopolymers of MAC (**29**) were readily functionalized under radical 'thiol–ene' conditions (>2 eq. thiol, 90 °C, 24 h) in 1,4-dioxane with a range of thiol-containing species including some with functional groups that are not compatible with ring-opening polymerization such as alcohol and carboxylic acid groups.[121] As expected the changes to the side-chain led to changes in the polymer T_g being observed, although the thermal degradation behaviour was largely unchanged. Copolymers prepared *via* the ROP of lactide and allyl-functional monomers (MAC, **29**) could be functionalised with a number of thiols by UV irradiation at 254 nm in the presence of 1-hydroxycyclohexylphenyl ketone as radical initiator or without radical initiator.[45,118] Although the reaction proceeds to high conversion at equimolar ene-thiol ratios, again an excess was necessary to achieve full conversion (5 : 1). Functionalisation of poly(ester-carbonates) with folic acid *via* radical thiol addition resulted in polymers which displayed increased cell affinity.[116] Similarly, a range of alkene functional poly(carbonate)s could be modified with thiols *via* Michael-addition.[47] PLA- or PCL-based polymers with low contents of acryloyl or methacryloyl functional cyclic carbonate monomers (**34** and **35**), were further functionalised in dimethylformamide at room temperature with a number of thiols.[47] Quantitative conversions (using 10 equivalents of thiol) of the pendant (meth)acrylates was obtained for functionalisation with mercaptoethanol, cysteine and 2-mercaptoethylamine, but conjugation with a peptide only proceeded to 58% conversion whilst mercaptopropanoic acid only displayed a conversion of 30%. Conjugation of block copolymers composed of PEO and a small acryloyl-functional poly(carbonate) blocks (DP < 20) was performed with thiolated chitosan that led to *in situ* hydrogel formation.[127] Such methodology was also extended to functionalise statistical copolymers of **34** with ε-caprolactone with cysteamine that was subsequently converted into a CTA for the RAFT polymerisation of hydroxyethylmethacrylate. In turn, these copolymers were assembled into graft copolymer micelles that showed pH-responsive release of doxorubicin.[165] Vinyl sulfone-functional copoly(carbonate)s and poly(ester-carbonate)s, obtained from the copolymerisation of **38** with other cyclic monomers, could also be quantitatively functionalised *via* the Michael addition of thiols to the vinyl group without catalyst and under aqueous conditions.[64] Another example of functionalisation of poly(carbonate)s and poly(ester-carbonate)s *via* Michael-addition of thiols was presented by Onbulak *et al.*[129] Polymers with pendant furan-protected maleimides were deprotected *via* thermal *retro*-Diels Alder to give maleimide functional polymers that were further functionalised with the thiol-containing molecules, 6-(ferrocenyl)-hexanethiol and 1-hexanethiol, in the presence of triethylamine. Notably, both deprotection and thiol addition proceeded without degradation of the polymer backbone.

Finally, alkene functional poly(carbonate)s could also be epoxidised using *meta*-chloroperoxybenzoic acid (*m*-CPBA). Epoxidation of functional aliphatic poly(carbonate)s and poly(ester-carbonate)s was reported for pendant allyl groups and pendant cyclohexenyl groups with efficiencies ranging from 35 to 99%. Hydrolysis of the epoxide groups was noted to occur in some cases.[46,76,119–123] In case of epoxidation of PMAC homopolymers an increase in glass transition temperature from −12 °C to 14 °C was observed. The introduction of this new reactive functionality was applied in the grafting of poly(ethylene imine) to the poly(carbonate) backbone in the formation of biodegradable polycations and polycation/DNA polyplexes by Zhuo and coworkers.[119]

Post-polymerisation modifications of poly(carbonate)s *via* dipolar cycloadditions

Alkyne- and azide-functional poly(carbonate)s or poly(ester-carbonate)s were successfully functionalised *via* 1,3-dipolar cycloaddition reactions.[57,58,69,73,150,126–129] Modifications of poly(ester-carbonates) obtained from copolymerisation of MPC (**41**) with lactide were successfully functionalised with azido-containing molecules using copper(II) sulfate pentahydrate and sodium ascorbate in water–DMSO mixtures.[130,133,134] Modifications with glucose and galactose azides were shown to lead to increased biocompatibility and enhanced hydrophilicity and cellular affinity of the resulting polymers.[134] Similarly, some polymers were also modified with CO-protected hemoglobin and proteins including Testis-specific protease 50 (TSP50), a breast cancer sensitive protease, and bovine serum albumin (BSA). The latter achieved only low grafting efficiencies of 0.7–1.6 mol%.[130,133] Alternatively, azide-functional poly(carbonate)s could be obtained *via* polymerisation of azide functional cyclic carbonates or *via* modification of bromide functional poly(carbonate)s with sodium azide in DMF at various temperatures.[57,58] The latter method, however, has limitations as azidation of bromide-functional polymers did not exceed 25% for homopolymers and degradation of the poly(carbonate) backbone was observed in both bromide functional homopolymers and copolymers.[57,58] Successful cycloaddition of alkyne-functional molecules to azido-functional poly(carbonate)s *via* copper catalysed methods (CuAAC) and *via* strain-promoted methods (SPAAC) was reported by Song and coworkers and was used in the preparation of hydrogels by cross-linking of poly(carbonate)s with DABCO-terminated poly(ethylene oxide)s.[136,137]

Quaternisation of halogen-functional poly(carbonate)s

A range of polymers containing quaternary amines have shown to exhibit antimicrobial activity. These polymers are, however, often not degradable which limits their use. The quaternisation of amines by reaction with halogen-containing compounds enables poly(carbonate) homopolymers and copolymers bearing pendant halogen functionalities to be reacted with tertiary amines such as trimethylamine or *N*,*N*,*N*′,*N*′-tetramethylethylenediamine. Recently, Yang and coworkers reported the first example of quaternised poly(carbonate) nanoparticles prepared from block copolymers of PTMC and a chloro-functional poly(carbonate) prepared from monomer **48**.[139] Investigation of quaternisation conditions revealed a dependence on the halogen substituent on the pendant chain. While chloro-functional poly(carbonate)s required heating at 90 °C, bromo- and iodo-functional poly(carbonate)s could be fully converted at room temperature. Another application for these cationic poly(carbonate)s was found in the synthesis of poly(carbonate)/DNA complexes.[69,72,138,139]

Deprotection of carbamate-functional poly(carbonate)s

Poly(carbonate)s with pendant primary amines can be prepared *via* the ROP of monomers in which the primary amines are protected by conversion to benzyl- or *tert*-butyl-carbamate groups. Deprotection of the benzyl carbamate (Z) groups is carried out *via* hydrogenation catalysed by palladium while the *tert*-butyl-carbamate (Boc) groups can easily be removed using trifluoroacetic acid.[52,55] Resulting primary amine-functional poly(carbonate)s and poly(ester-*co*-carbonate)s have been obtained whilst retaining low dispersities. As expected, a reduction in molecular weight was observed after deprotection and polymers were highly hydrophilic in contrast to the protected polymers. Primary amine functional poly(ester-carbonate)s could be further modified by reaction with peptides in the presence of CDI. Films of the resulting polymers displayed increased cell adhesion and multiplication.[55] In another report, two Boc-protecting groups were removed to reveal pendant guanidinium groups. Hydrogels prepared from bis(carbonate) poly(ethylene oxide) cross-linker, Boc protected guanidinium functional cyclic carbonate and *tert*-butoxy protected carboxylic acid functional cyclic carbonate revealed additional stabilisation of the hydrogel network after removal of the protecting groups with trifluoroacetic acid as a result of the hydrogen bonding between the free guanidinium and carboxylic acid groups.[87]

Other post-polymerisation modifications of functional poly(carbonate)s

Putnam and coworkers has reported a post-polymerisation conversion of dimethoxy-functional poly(carbonate), poly(**4**), and its copolymers into dihydroxy acetone-based poly(carbonate)s.[63] The conversion to dihydroxyacetone functional poly(carbonate)s was accomplished by refluxing poly(**4**) with iodine in acetone. The resulting polymer presents an increase in glass transition temperature compared to the precursor from 45 to 68 °C. In addition, the resulting polymers showed very low solubility in common organic solvents. Moreover, copolymers composed of lactide and dihydroxyacetone-functional carbonate showed increasing degradation kinetics in copolymers enriched in functional carbonate.

Conclusions

The combination of the many versatile methods reported for the synthesis of functional cyclic carbonate monomers from a range of biocompatible scaffolds and the excellent control in their ring-opening polymerisation, have led to preparation of a multitude of functional poly(carbonate)s with controlled molecular weights, low dispersities and high end-group fidelity. Despite the development of the large range of functional aliphatic poly(carbonate)s, their specific design to achieve better-controlled drug release and advanced tissue engineering scaffolds is very rare. Further development of controlled poly(carbonate) synthesis in combination with efficient post-polymerisation modifications with a specific focus on application could open up new ways to achieve their widespread biomedical application.

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