CO$_2$-Driven stereochemical inversion of sugars to create thymidine-based polycarbonates by ring-opening polymerisation†

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The development of biodegradable polymers from renewable resources is vital in addressing the dependence of plastics on petroleum-based feedstocks and growing ocean and landfill waste. Herein, both CO$_2$ and natural sugar diols are utilised as abundant, safe and renewable building blocks for the synthesis of degradable and biocompatible aliphatic polycarbonates. Despite a strong potential for advanced polymer properties, inspired by Nature’s supramolecular base-pairing, polycarbonates from the sugar components of DNA, 2′-deoxyribonucleosides have been limited by the inability of phosgene derivatives to form the cyclic carbonate monomers that would allow for controlled ring-opening polymerisation. CO$_2$ insertion at 1 atm pressure into methylated thymidine 2′-deoxyribonucleoside, facilitated by organic base 1,8-diazabicyclo-[5.4.0]-undec-7-ene, affected an intramolecular S$_\text{N}2$-like displacement of a tosyl leaving group to yield the cyclic carbonate by stereochemical inversion. Organocatalytic ring-opening polymerisation proceeded rapidly in solution resulting in high monomer conversions of 93% and number-average molecular weights, substantially greater and more controlled than via polycondensation routes. The thermodynamic parameters of the polymerisation ($\Delta H_p = -12.3 \pm 0.4 \text{ kJ mol}^{-1}$ and $\Delta S_p = -29 \pm 1.1 \text{ J mol}^{-1} \text{ K}^{-1}$) were determined from the equilibrium monomer conversions over a temperature range of 0 to 80 °C and pseudo-first order kinetics demonstrated. The amorphous thymidine-based polycarbonates exhibited high glass transition temperatures of 156 °C and were found to be highly degradable to constituent diol under basic aqueous conditions. Static water contact angle measurements and cell studies with MG-63 cell line indicated slightly hydrophilic and biocompatible materials, promising for tissue-engineering applications. The novel, CO$_2$-driven approach to cyclic carbonate synthesis represents a means of expanding the scope of sugar-based monomers for tailored material properties derived from natural products.

Introduction

Reliance on classical petroleum-derived materials and their lack of biodegradability has instigated a drive towards sustainable bio-based polymers from renewable resources.1 With an ever-growing population, the demand for commodity and engineering plastics is steadily increasing; in 2014, 311 mega-

†Electronic supplementary information (ESI) available: Experimental and computational details; spectroscopic and crystallographic data for 1 and 2; SEC traces, MALDI-ToF spectra, spectroscopic and thermal (TGA, DSC) data for polymers; DFT calculations data and associated digital repositories; tissue engineering protocol and results. CCDC 1523960 and 1523961. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c7py00118e
nucleobases into the backbone of synthetic polymers or as
pendent or terminal groups, either through direct polymerisation
or post-synthetic modification. Currently, there are several examples, albeit mainly oligomers, of 2′-deoxyribo-
nucleosides bearing carbonate, carbamate, ester, triazole, ether and silyl ether linkages. CO₂ is another abundant,
safe and renewable building block and its incorporation into
cyclic carbonate incorporating CO₂ at 1 atm pressure is
reported. Motivated by the work of Jessop et al. using 1,8-
diaza-bicyclo-[5.4.0]-undec-7-ene (DBU) reagent to capture CO₂
into alcohols, we employ the resulting carbonate as a nucleo-
phile to affect cyclisation via an intramolecular S_n2-type reaction.
We present DFT calculations that rationalise the
controlled ring-opening polymerisation (ROP) of typically 6-membered cyclic carbonates has emerged as an attractive choice in polycarbonate production and often proceeds under mild reaction conditions.

Both for polymer synthesis and various other applications (e.g. battery electrolytes), a growing research effort has focused on the improved synthesis of cyclic carbonates that avoids the use of phosgene or phosgene derivatives and directly incorporates CO₂ (ideally at ambient pressure and temperature).

Currently, sugar-based cyclic carbonates for ROP are limited to those derived from D-glucose, D-mannose and D-xylose (Fig. 1). Cyclocarbonation of trans-configured 1,3-diols in 5-membered furanoside sugars such as DNA 2′-deoxyribo-
nucleosides has never been achieved to the best of our knowledge. In 1972, Tittensor and Mellish reported the attempted synthesis of the 3′,5′-cyclic carbonate of thymidine and suggested the need for an active ester at the 3′-position rather than 5′-hydroxyl group for cyclisation to occur. Subsequently in 2011, Suzuki et al. selectively placed a carbonyldimidazole (CDI) component at the 3′-position of thymi-
dine and adenosine nucleosides. However, only polycondensa-
tion resulted, leading to thymidine-based polycarbonates of low M_n (4700 g mol⁻¹, D 1.86).

Herein, the synthesis and successful ROP of a thymidine-
based cyclic carbonate incorporating CO₂ at 1 atm pressure is
reported. Motivated by the work of Jessop et al. using 1,8-
diaza-bicyclo-[5.4.0]-undec-7-ene (DBU) reagent to capture CO₂
into alcohols, we employ the resulting carbonate as a nucleo-
phile to affect cyclisation via an intramolecular S_n2-type reaction.
We present DFT calculations that rationalise the
monomer synthesis and its ability to be polymerised. The
thermodynamic and kinetic parameters of the polymerisation
are reported, as well as the resulting new polymer microstructure and thermal properties. A preliminary tissue engineering study is finally presented.

Results and discussion

Monomer synthesis

Synthesis of the trans-3′,5′-cyclic carbonate of thymidine using our previously reported method (tosylation of a DBU-intro-
duced carbonate and cyclisation via an intramolecular nucleo-
philic addition-elimination mechanism, leading to stereo-
chemical retention), proved unsuccessful (trans-1, Fig. 2).

However, DFT calculations of the ring-closing kinetics (transition state ΔΔG‡ = +13.3 kcal mol⁻¹) and thermodynamic driving force (ΔΔG = −20.8 kcal mol⁻¹) suggested that this pathway should be accessible at ambient reaction conditions (Scheme S2†). Calculations also indicated that the ring-strain of the hypothetical monomer, consisting of a 6-membered
cyclic carbonate trans-fused to a furanose sugar ring, was much higher compared to when fused to the 6-membered pyranose ring in reported α-mannose and α-glucose based monomers (Schemes S4 and S5†). For example, ring-opening with methanol is thermodynamically favored with ΔΔ\(G\) = −6.7 kcal mol\(^{-1}\) compared to −0.9 and −0.2 kcal mol\(^{-1}\) for the mannose and glucose monomers, respectively. The calculated enthalpy of isodesmic ring-opening with dimethyl carbonate (Δ\(\Delta H\)) is also 5.5 kcal mol\(^{-1}\) more favorable for the trans-fused furanose monomer compared to the trans-fused α-mannopyranose cyclic carbonate. The pyranose ring can adopt a chair conformation that can accommodate a trans-fused ring whereas a furanose-monomer may be too highly strained to be isolated (especially in the presence of alcohol). The cis-3′,5′-thymidine analogue (cis-1, Fig. 2) however, lies 9.2 kcal mol\(^{-1}\) lower in energy compared to the trans- and shows a similar isodesmic ring-strain and in fact greater thermodynamic driving force for ring-opening compared to the \(\alpha\)-xylofuranose derived monomer prepared by Gross and co-workers.\(^25\) In that report, cyclocarbonation with ethylchloroformate in the presence of alcohol). The \(\alpha\)-xylofuranose cyclic carbonate synthesis from natural furanose sugars bearing the trans-fused \(\alpha\)-mannopyranose cyclic carbonate. The strategy represents a generally applicable method to cyclic carbonate synthesis from natural furanose sugars bearing a trans-1,3-diol. It extends the range of sugar-based cyclic carbonate monomers beyond those possible with known sugars and classical reagents such as phosgene and its derivatives, which require a nucleophilic addition-elimination mechanism. Although the need to protect the 3-N position of the nucleobase is somewhat limiting, the functionalisation potential of the pyrimidine arm is tremendous, ranging from Re(CO)\(_3\) complexes\(^31\) to alkyne functionalities for click chemistry.\(^35,32\)

As a further demonstration, we also prepared the 3-N-benzoyl derivative of 1 (1-Bz). Benzoylation could be carried out in tandem with the silylation and tosylation, reducing the number of overall synthetic steps (Scheme S1 and Fig. S12–S14†). Literature precedence has furthermore shown post-polymerisation removal of benzoyl protecting groups.\(^10\)

The structure of 1 was confirmed by \(^1\)H NMR (Fig. 6), \(^1\)C\(^{13}\)NMR and FTIR spectroscopies as well as electrospray ionisation mass spectrometry (ESI-MS), elemental analysis and single crystal X-ray diffraction. Full NMR assignment was aided by DEPT\(_{135}\), HSQC and COSY experiments (Fig. S1–S5). In the \(^1\)C NMR spectrum, further to the carbonyl environments of the nucleobase, an additional C=O resonance was observed at 147 ppm, typical of a 6-membered cyclic carbonate, and a vicinal \(^3\)J\(_{\text{C=O}}\) coupling constant in the \(^1\)H NMR spectrum of just 3.9 Hz was consistent with a cis-configuration. X-ray analysis of crystals of 1 grown from toluene (Fig. 3)

Fig. 3 ORTEP\(^{33}\) drawing of the crystal structure of 1 with thermal ellipsoids at the 50% probability level (see ESI†). Selected bond lengths (Å) and dihedral angles (°): (C(2)—O(2) 1.466 (2), O(2)—C(1) 1.326 (3), O(2) C(1) 1.202 (3), C(1)—O(3) 1.326 (4), O(3) C(6) 1.456 (3), C(4) C(5) C(2) C(5) 29.61 (19), C(5) C(2) O(4) 36.87 (19), C(2) C(5) O(4) C(4) 30.01 (2), C(5) O(4) C(4) C(3) 10.5 (2), O(4) C(4) C(3) C(2) 12.6 (2).
The ROP of Ring-opening polymerisation (ROP) monomer concentration, $[M]_0$. Further addition of monomer in the preceding furanose ring in the preceding to form the 3',5'-cis-cyclic carbonate in which the furanose ring adopts a strained 4'-endo-3'-exo twist ($^1T_2$) conformation. This is likely retained in solution as the ring-methylene H-2' protons display very different chemical shifts and $J$-coupling constants consistent with the Karplus equation. In contrast, the unconstrained furanose ring in the preceding trans-3',5'-dioxol 2 adopts a 2-endo ($^1E$) envelope conformation (see crystal structure in ESI†).

**Ring-opening polymerisation (ROP)**

The ROP of 1 was initially explored with bifunctional organocatalyst, 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) and 4-methyl benzyl alcohol initiator. Polymerisation proceeded rapidly at 25 °C in CH$_2$Cl$_2$, reaching a plateau at 80% monomer conversion (determined by $^1$H NMR spectroscopy) after 1 h for a monomer-to-initiator feed ratio of 100 and 1 mol L$^{-1}$ initial monomer concentration, $[M]_0$. Further addition of monomer after 24 h led to establishment of a new equilibrium monomer conversion indicating no catalyst deactivation and a concentration dependent equilibrium polymerisation. A higher monomer conversion of 90% was achieved at a higher $[M]_0$ of 2.5 mol L$^{-1}$ (Fig. 4).

A linear kinetic plot is consistent with pseudo-first order kinetics, typical for ROP, from which a $k_{app}$ of 1.39 ± 0.005 h$^{-1}$ was determined (inset Fig. 4 and S15†). The high melting point of the monomer (204–205 °C) and low thermal stability (178–205 °C, 88% mass loss, T$_{\text{max}}$ 248 °C) prevented polymerisation from being carried out in the melt. The temperature dependence of the equilibrium polymerization was also investigated at fixed $[M]_0$, catalyst loading and initiator concentration in 1,2-dichloroethane solvent to access a wider temperature range of 0–80 °C. A plot of ln$[M]_{eq}$ versus the reciprocal of the absolute temperature gave an estimate of the polymerisation thermodynamic parameters (Fig. 5): $\Delta H_p = -12.3 \pm 0.4$ kJ mol$^{-1}$ and $\Delta S_p = -29 \pm 1.1$ J mol$^{-1}$ K$^{-1}$. For comparison, Endo and co-workers$^{34}$ reported an enthalpic driving force of −26.4 kJ mol$^{-1}$ for the anionic polymerisation in THF of unsubstituted trimethylene carbonate and accompanying −44.8 J mol$^{-1}$ K$^{-1}$ entropy decrease ($[M]_0 = 1$ mol L$^{-1}$). A decrease in $\Delta H_p$ with increased steric bulk of substituted derivatives was attributed to distortion of the polymer backbone as opposed to a conformational effect on the monomer. Interestingly, for polymer recyclability, the polymerisation mixture at 0 °C, which showed a 72% conversion to polymer at equilibrium, resulted in near quantitative recovery of the monomer upon heating to 80 °C.

A linear increase in $M_n$ with percentage monomer conversion whilst maintaining narrow dispersities indicated that the polymerisation proceeded in a controlled fashion up to 60% monomer conversion (Fig. 6). Initially excellent agreement was observed between the calculated $M_n$ and those estimated by size exclusion chromatography (SEC) versus polystyrene standards with CHCl$_3$ eluent. For example, the polymer at 54% monomer conversion had a $M_n$ of 7210 g mol$^{-1}$ ($\bar{D}$ 1.12) as estimated by SEC (Fig. S17†), only slightly lower than the predicted$^{35}$ 7740 g mol$^{-1}$. Once the thermodynamic equilibrium was reached and with longer reaction times, a broadening of the polymer distribution was observed due to transesterification reactions.

Matrix-assisted laser desorption/ionisation time-of-flight (MALDI-ToF) mass spectrometry of this polymer showed a major linear polymer series of $M_m$ 7720 g mol$^{-1}$ and expected 4-methyl benzyl alcohol and O–H end groups (Fig. 7 and S19†). A minor (19%) cyclic species with $m/z$ consistent with no end-groups and an integer number of repeat units ($m/z$ ~282.25), was also observed due to backbiting of the polymer chain. As the polymer chain grows and monomer concen-

Fig. 4  ROP of 1 with 4-MeBnOH and TBD catalyst: conversion versus time for different $[M]_0$. Carried out at 25 °C in CH$_2$Cl$_2$ for $[M]_0$ : [TBD]$_0$ : 4-MeBnOH]$_0$ ratio of 100 : 1 : 1. Monomer conversion was determined by $^1$H NMR spectroscopy by relative integration of the anomic H-1' proton. (inset) Kinetic plot carried out under the same conditions for $[M]_0$ = 0.5 mol L$^{-1}$.

Fig. 5 ROP of 1 with 4-MeBnOH and TBD catalyst: calculation of the thermodynamic parameters from a plot of ln$[M]_{eq}$ as a function of 1/T, where $T$ is the absolute temperature. Carried out in 1,2-dichloroethane, over a temperature range of 0–80 °C for $[M]_0$ = 0.5 mol L$^{-1}$ and $[M]_0$ : [TBD]$_0$ : 4-MeBnOH]$_0$ = 100 : 1 : 1. Polymerisations were repeated three times at each temperature and an average taken.
tration decreases, a greater rate of chain backbiting relative to chain propagation may account for deviations observed between the calculated and SEC estimated \( M_n \) at higher monomer conversions. Dilution of the reaction conditions to 0.5 mol L\(^{-1}\) in an attempt to favour macrocycle formation resulted in lower \( M_n \) (Table 1, entry 1) and in more cyclic species observed by MALDI-ToF analysis (Fig. S21†). The lack of chain end in macrocycles should prevent reversion of the polymer to the monomer at elevated temperatures, however, difficulty in separating the cyclic and linear species prevented us from rigorously investigating the issue. Polymeric macrocycles are also interesting in their own right, including those derived from nucleosides, e.g. as supramolecular complexes with metal coordination characteristics.\(^{12}\)

The largest molecular weights, up to \( 17\,000 \text{ g mol}^{-1} (D \, 1.3) \) were achieved at 0 °C and \([M]_0\) of 2.5 mol L\(^{-1}\) (Table 1, entry 2). A greater disparity between the theoretical \( M_n \) and those determined by SEC was observed at higher \([M]_0/[I]_0\) ratios, most likely due to chain back-biting reactions. To explore the influence of the catalytic system on the control of \( M_n \), metal complexes were tested for the ROP of 1. Sn(Oct)\(_2\) catalyst with 4-MeBnOH initiator at 120 °C in toluene did not yield homopolymer. Y(OiPr)\(_3\) or Al(OTf)\(_3\) with BnOH initiator resulted in no control with only low \( M_n \) (1800–3910 g mol\(^{-1}\), \( D \, 1.35–1.39 \)) in DCM, dioxane and toluene solvents at 0, 25, 70 and 120 °C. Although highly active for lactide ROP in \( \text{CH}_2\text{Cl}_2 \) at rt, the zinc(II) alkoxide catalyst (L1ZnOEt) reported by Williams \textit{et al.}\(^{36}\) was slower compared to TBD for the ROP of 1, as was the (BDI-1)ZnEt catalyst\(^{37}\) with 4-MeBnOH initiator (Table 1, entries 3 and 4).

**Polycarbonate properties**

Initial insight into the structure of the thymidine-based polycarbonates was gained by NMR spectroscopy. Shown in Fig. 8, coalescence of the H-5′ and H-4′ proton environments in the \(^1\)H NMR spectrum of the polymer compared to the monomer

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**Table 1** ROP of 1

<table>
<thead>
<tr>
<th>Entry</th>
<th>Temp. (°C)</th>
<th>Cat.</th>
<th>([M]_0 : [C]_0 : [I]_0)</th>
<th>Conv. (%)</th>
<th>Time (h)</th>
<th>( M_n ) ( \times 10^3 )</th>
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<tr>
<td>1</td>
<td>0</td>
<td>TBD</td>
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<td>68</td>
<td>4</td>
<td>4260 [1.09]</td>
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<tr>
<td>2</td>
<td>0</td>
<td>TBD</td>
<td>150 : 1 : 1</td>
<td>90</td>
<td>3</td>
<td>17 000 [1.30]</td>
</tr>
<tr>
<td>3</td>
<td>25</td>
<td>L1ZnOEt</td>
<td>100 : 1</td>
<td>71</td>
<td>20</td>
<td>7250 [1.22]</td>
</tr>
<tr>
<td>4</td>
<td>25</td>
<td>(BDI-1)</td>
<td>60</td>
<td>24</td>
<td>5240 [1.15]</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>100 : 1 : 1</td>
<td>60</td>
<td>100 : 1 : 1</td>
<td>90</td>
<td>3</td>
<td>11 000 [1.27]</td>
</tr>
<tr>
<td>6</td>
<td>25</td>
<td>TBD</td>
<td>100 : 1 : 1</td>
<td>93</td>
<td>3</td>
<td>15 400 [1.28]</td>
</tr>
</tbody>
</table>

\(^{a}\) All polymerisations were carried out at \([M]_0 = 2.5 \text{ mol} \cdot \text{L}^{-1}\) in \( \text{CH}_2\text{Cl}_2 \) unless stated otherwise. \(^{b}\) Determined by \(^1\)H NMR spectroscopy in \( \text{CDCl}_3 \), \( \text{g mol}^{-1}\), calculated by SEC with \( \text{CHCl}_3 \) eluent versus polystyrene standards (RI detector). \(^{d}\)\([M]_0 = 0.25 \text{ mol} \cdot \text{L}^{-1}\). \(^{e}\) L1 = 2,4-di-tert-butyl-6-\(\text{[(2′-di-methylaminoethyl) methylamino]-methyl} \)-phenolate. \(^{f}\) BDI-1 = 2-\(\text{[(2,6-diisopropylphenyl)amido]-4-[(2,6-diisopropylphenyl) imino]-2-pentene} \).
was consistent with loss of constraint upon ring-opening of the cyclic carbonate moiety. In addition, retention of the distinct chemical environments of the furanose ring $2'$-methylene protons suggest that the sugar may adopt a similar puckered conformation in the polymer backbone to that observed in the monomer. $^{13}$C($^1$H) NMR analysis revealed three carbonate environments centered at 154.4, 153.6 and 152.8 ppm, consistent with tail–tail, head–tail and head–head linkages that would arise from the cleavage at either side of the asymmetric carbonate by either a free secondary or primary propagating alcohol chain. Relative assignments were suggested based on previous work$^{23a,24,25}$ and by the 1:2:1 integration ratio observed, which further suggested a regiorandom propagation of the chain (Fig. S9†). Further splitting observed within these three distinct environments is attributed to long range sequence effects as also reported for regiorandom glucose$^{23a}$ and xylose$^{25}$ derived polycarbonates. DFT calculations$^{28}$ of the initiation step in the ROP of 1 with 4-MeBnOH and TBD catalyst support this lack of preference for ring-opening to expose either a free primary ($\Delta \Delta G = -5.6$ kcal mol$^{-1}$) or secondary hydroxyl group ($\Delta \Delta G = -6.6$ kcal mol$^{-1}$) for chain propagation (Fig. S38†).

The thermal properties of the polycarbonates were investigated by thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC). The onset of thermal degradation occurred at relatively low temperatures of ~170 °C, reaching a maximum rate of mass loss ($T_{\text{max}}$) around 246 °C for polymers of $M_n$ 11 000 and 15 400 g mol$^{-1}$ (Table 1, entries 5 and 6). High mass losses of 91 and 94%, respectively were achieved by ~300 °C (Fig. S22†). Analysis of the gases evolved by tandem mass spectrometry confirmed the presence of m/z 44 attributed to the loss of CO$_2$ (Fig. S24†). The polymers exhibited high glass transition temperatures (Fig. S25–S27†); a $T_g$ of 156 °C was measured for polycarbonate of $M_n$ 15 400 g mol$^{-1}$ and is attributed to restricted rotation about the furanose ring backbone and to the bulky thymine group. For comparison, furanose-core isopropylidene-protected $\beta$-xylose polycarbonate exhibited a $T_g$ of 128 °C (for $M_n = 13 200$ g mol$^{-1}$)$^{23a}$ Pyranose backboned polycarbonates derived from isopropylidene-protected $\beta$-mannose and methyl protected $\beta$-glucose showed $T_g$ of 152 °C (13 600 g mol$^{-1}$)$^{23b}$ and 122 °C (14 700 g mol$^{-1}$), respectively. No transitions associated with a melting domain were observed implying an amorphous polymer, which was further confirmed by powder X-ray diffraction (Fig. S28†).

The hydrolytic stability of the water insoluble polymer was investigated at 0.25 wt% at rt in water, 1 mol L$^{-1}$ HCl and 1 mol L$^{-1}$ NaOH, as well as in PBS buffer at 37 °C in presence of Candida antartica lipase B. After 1 week, no dissolution or loss of mass by SEC was observed in the case of water and 1 mol L$^{-1}$ HCl. NMR analysis of the supernatant in D$_2$O revealed no environments. Under the alkali conditions, the polymer was observed to dissolve after 4 hours. $^1$H NMR spectroscopy in D$_2$O after 24 h at 4 wt% revealed proton environments consistent with the cis-diol of 3-N-methyl thymidine (Fig. S29 and S30†). Mass spectrometry (HR-MS ESI) after 24 h further confirmed the presence of the diol suggesting complete hydrolytic degradation of the polymer to its constituent components. In the case of lipase B, unknown degradation products were detected in solution after one week. Static water contact angle measurements of polymer thin films drop cast onto glass slides revealed an average contact angle of 48 ± 1°. This was more hydrophobic than the monomer but less hydrophilic compared to the glass control (Fig. S32†).

Cell attachment studies were carried out with a human osteoblast cancer cell line, MG-63, on polymer films drop cast onto glass slides. Cell attachment after a 1 h incubation period (37 °C, 5% CO$_2$) was comparable to the empty tissue culture polystyrene well-plate and glass controls, and indicated the possibility of thymidine-based materials to support cells (Fig. S33–S35†). After a longer 24 h incubation period, cell attachment dropped compared to the empty well-plate control suggesting further modifications to the polymer surface are required for it to serve as an effective tissue engineering scaffold. Nevertheless, the choice of the 3-N protecting group and general applicability of the strategy present wide-scope and future opportunities for novel biomaterials with applications in the tissue engineering and regenerative medicine fields. Other degradable polymers attractive in this area, such as PLA and PLGA, are notoriously difficult to functionalise.$^{28}$ Therefore, the successful preliminary ROP of benzoyl-protected monomer (1-Bz, see ESI†) offers promise for more elaborate functionality as well as post-polymerisation modifications, including self-assembly with base-paired nucleoside polycarbonates.

Conclusions

In summary, a novel strategy for the synthesis of challenging sugar-based cyclic carbonate monomers is presented that utilises CO$_2$ as a C1 resource at 1 atm pressure. Sugar-based
resources previously inaccessible for ROP such as 2′-deoxyribo-
nucleosides can thus be efficiently converted to cyclic carbon-
ate monomer. Here, novel polycarbonates derived from thymi-
dine are reported. DBU-facilitated CO$_2$ insertion into the
5′-hydroxyl group of 3-N-protected thymidine 2′-deoxyribo-
nucleoside sugar introduces a carbonate nucleophile to affect
an intramolecular displacement of a 3′-tosyl leaving group,
resulting in stereochemical inversion. The isolated cis-config-
ured 3,5′-cyclic carbonate undergoes ROP under mild reaction
conditions with organocatalyst TBD and 4-MeBnOH alcohol
initiator to yield novel thymidine-based polycarbonates. The
kinetic and thermodynamic parameters of the equilibrium
polymerisation were established and MALDI-ToF MS revealed
thymidine-based polycarbonates with both linear and cyclic
topologies. Thermal analysis revealed high glass transition
temperatures and a low onset of thermal degradation. Static
water contact angle measurements were carried out and cell
attachment studies with MG-63 cell line indicated promising
biocompatible materials. Work is ongoing to explore the func-
tionalisation of the 3′-N position of the thymine nucleobase
to impart specific properties for targeted applications.

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35 Calculated as $M_r(\text{4-MeBnOH}) + [M_r(1) \times [4-MeBnOH]]_{\text{conv.}}/100\%$.

