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Note

1,4-Dioxane-2,5-dione-type monomers derived from L-ascorbic and D-isoascorbic acids. Synthesis and polymerisation

Manuel Bueno, Inmaculada Molina, Juan A. Galbis *

Departamento de Química Orgánica y Farmacéutica, Universidad de Sevilla, Facultad de Farmacia, 41012 Sevilla, Spain

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ABSTRACT

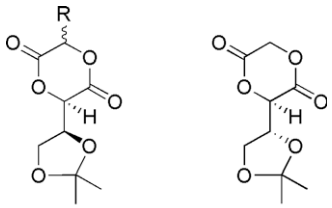
L-Ascorbic and D-isoascorbic acids have been used as the starting materials for the preparation of (3*R*,4′*S*)-3-(2′,2′-dimethyl-1′,3′-dioxolan-4′-yl)-1,4-dioxane-2,5-dione (**IPTA**), (3*R* and *S*, 4′*S*,6*R*)-3-methyl-6-(2′,2′-dimethyl-1′,3′-dioxolan-4′-yl)-1,4-dioxane-2,5-dione (**IPTP**) and (3*R*,4′*R*)-3-(2′,2′-dimethyl-1′,3′-dioxolan-4′-yl)-1,4-dioxane-2,5-dione (**IPEA**), three novel 1,4-dioxane-2,5-dione-type monomers. Ring-opening homopolymerisation and copolymerisation of the **IPTA** monomer, derived from L-ascorbic acid, with D,L-lactide have been performed. The polymers were characterised by elemental microanalysis, as well as IR and ^{1}H and ^{13}C NMR spectroscopies. GPC was used to estimate product molecular weights, and thermal studies (DSC and TGA) revealed that all the polymers were amorphous, being stable up to 250 °C under nitrogen.

There are numerous publications concerned with the use of degradable aliphatic polyesters for pharmacological, biomedical and environmental purposes.[1] Poly(α-hydroxy acids) such as poly(glycolic acid) (PGA), poly(lactic acid) (PLA) or their copolymers poly(lactic acid-*co*-glycolic acids) (PLAGA) are well known, and are routinely used as materials for sutures, bone prostheses or drug delivery systems.[2–4]

The interest in these materials is due to their degradability or biodegradability, mainly due to the presence of labile ester bonds along the main polymer chain, and to the fact that their degradation products are bioassimilable molecules. However, hydrophobicity and lack of functional groups could be a problem for some applications. One way to overcome these drawbacks is to synthesise aliphatic biorecyclable polyesters with functional side chains.[5–7] The preparation of novel carbohydrate-based polymers and copolymers is interesting for several reasons. First, we can take advantage of their natural occurrence and ready availability in great stereochemical diversity. Second, they come from natural, renewable resources. Third, the presence of hydroxyl groups along the polymer backbone would increase the hydrophilicity and provide multifunctionality and (fourth) improve some properties such as biodegradability and biocompatibility of the polymers.

Within the framework of the systematic investigation that we currently have under course to explore the potential of the sugar-based polymers,[8] a number of stereoregular[9,10] and non-stereoregular[10–14] sugar-based polyesters derived from O-protected carbohydrate monomers have been prepared and characterised. In this communication, we now present the synthesis and characterisation of three 1,4-dioxane-2,5-dione-type monomers: (3*R*,4′*S*)-3-(2′,2′-dimethyl-1′,3′-dioxolan-4′-yl)-1,4-dioxane-2,5-dione (**IPTA**), (3*R* and *S*, 4′*S*,6*R*)-3-methyl-6-(2′,2′-dimethyl-1′,3′-dioxolan-4′-yl)-1,4-dioxane-2,5-dione (**IPTP**) and (3*R*,4′*R*)-3-(2′,2′-dimethyl-1′,3′-dioxolan-4′-yl)-1,4-dioxane-2,5-dione (**IPEA**), which can be derived from L-ascorbic and D-isoascorbic acids (Fig. 1). We also report the homopolymerisation of the **IPTA** monomer and its copolymerisation with D,L-lactide.

The syntheses of **IPTA** and **IPTP** monomers were carried out from L-ascorbic acid in five steps as outlined in Scheme 1. Treatment[15] of L-ascorbic acid with 2,2-dimethoxypropane and anhydrous hydrogen chloride gave 5,6-*O*-isopropylidene-L-ascorbic acid (**2**). Oxidation of **2** with hydrogen peroxide in the presence of calcium carbonate yielded[16] calcium 3,4-*O*-isopropylidene-L-threonate (**3**) as a crystalline solid. Compound **3** was suspended



IPTA (R = H) **IPEA**

IPTP (R = CH_3)

Figure 1. Structure of monomers.

* Corresponding author.
E-mail address: jgalbis@us.es (J.A. Galbis).

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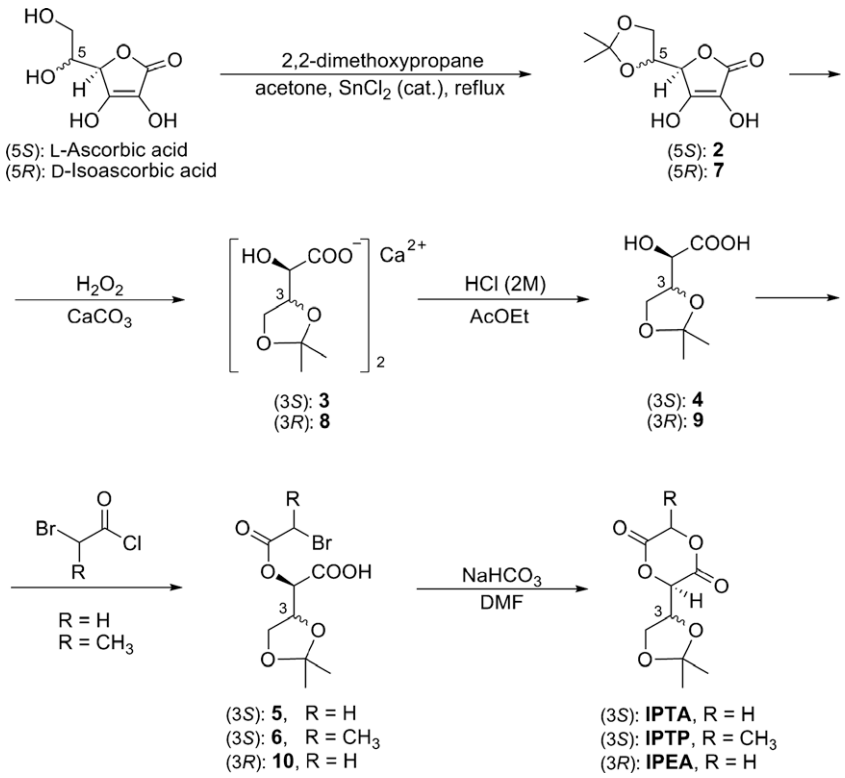


Scheme 1.

in cold water, acidified with HCl (2 M) and extracted several times with ethyl acetate to give, after evaporation, 3,4-*O*-isopropylidene-L-threonic acid (**4**) as an oil that crystallised on standing (73%). The reactions of **4** with bromoacetyl chloride or 2-bromopropanoyl chloride yielded 2-*O*-(2-bromoacetyl)-3,4-*O*-isopropylidene-L-threonic acid (**5**) and 2-*O*-(2-bromopropanoyl)-3,4-*O*-isopropylidene-L-threonic acid (**6**), respectively. Finally, **5** and **6** were converted to their corresponding 1,4-dioxane-2,5-diones, **IPTA** and **IPTP** monomers, by treatment with $NaHCO_3$ in DMF. Both monomers were obtained as solids, and were easily crystallisable from ethyl acetate and ethyl ether, respectively.

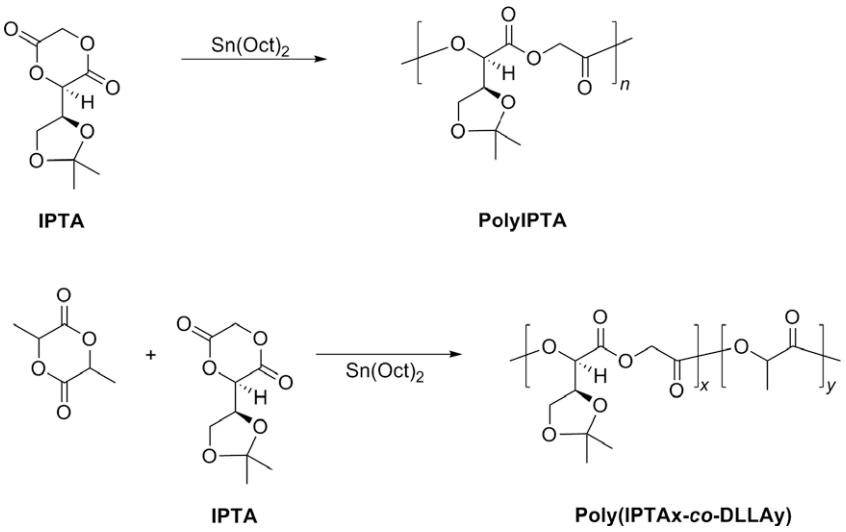
The **IPEA** monomer was prepared in a similar way, starting from D-isoascorbic acid (Scheme 1). Reaction of D-isoascorbic acid with 2,2-dimethoxypropane in acetone, using $SnCl_2$ as catalyst, gave 5,6-*O*-isopropylidene-D-isoascorbic acid[17] (**7**). Oxidation of **7** with hydrogen peroxide in the presence of calcium carbonate yielded calcium 3,4-*O*-isopropylidene-D-erythronate (**8**), which was suspended in cold water, acidified with HCl (2 M) and extracted several times with ethyl acetate to give, after evaporation, 3,4-*O*-isopropylidene-D-erythronic acid (**9**) as an oil that crystallised on standing (72%). The reaction of **9** with bromoacetyl chloride yielded 2-*O*-(2-bromoacetyl)-3,4-*O*-isopropylidene-D-erythronic acid (**10**), which was converted in the last step to its corresponding 1,4-dioxane-2,5-dione, **IPEA** monomer, by treatment with $NaHCO_3$ in DMF.

All the NMR data were consistent with the respective chemical constitutions. The cyclic structure of the **IPTA** monomer was confirmed by ^{1}H NMR spectroscopy. Thus, its ^{1}H NMR spectrum, in deuterochloroform (see Section 1), showed the characteristic signals of the glycolyl unit, detected at 5.11 and 4.85 ppm as two doublets. Similar signals had already been observed in other cyclic derivatives containing a glycolyl unit.[5,18] The presence of the 1,4-dioxane-2,5-dione ring in the **IPTA** monomer was confirmed by ^{13}C NMR spectroscopy (see Section 1). Thus, the signals appearing at 163.92, 163.29 and 65.32 ppm were assigned to the two carbonyls and to the methylene carbons of the ring, respectively. Two-dimensional ^{1}H–^{1}H homonuclear and ^{13}C–^{1}H heteronuclear shift correlation allowed us to make a complete assignment of the observed signals. The ^{1}H and ^{13}C NMR spectra of its C-3 epimer (IPEA) were also completely assigned in agreement with the proposed structure. While **IPEA** and **IPTA** both have a 1,4-dioxane-2,5-dione ring, differing only in the configuration of one centre of the sugar chain, in the **IPTP** monomer the glycolyl unit has been replaced by a lactyl one. In this case, we used racemic 2-bromopropanoyl chloride, giving **IPTP** as a mixture of diastereoisomers, as shown in Section 1.

We carried out the homopolymerisation and copolymerisation of **IPTA** monomer with D,L-lactide (Scheme 2). Some results of these polymerisations are displayed in Tables 1 and 2. The ring-opening polymerisation of this monomer was initiated with stannous octanoate. The initiator–monomer ratios used for the homo- and copolymerisation were different. While in the homopolymerisation the ratio was 1:113, in the copolymerisation we use a ratio of 1:600, to get higher molecular weights in the copolymers (Table 1).

The yield of **PolyIPTA** was low (50%) and, in general, it was observed that as the amount of sugar monomer increased in the copolymer chain the yield decreased. The copolymerisation of the **IPTA** monomer with D,L-lactide also significantly increased the molecular weight of the copolymers in comparison with **PolyIPTA**.

The structures of these polyesters were confirmed by both infrared and ^{1}H and ^{13}C NMR spectroscopies, as detailed in Section 1. The infrared spectra exhibited a carbonyl ester stretching vibration band appearing at 1762 cm^{-1} for **PolyIPTA** and, in both copolymers, this absorption band was observed at 1757 cm^{-1}. The NMR data were consistent with the chemical constitution anticipated for these polymers. In the case of **polyIPTA**, according to the pair addition mechanism of polymerisation of 1,4-dioxane-2,5-diones, in the absence of transesterification side reactions, the polymer chain should be composed of ascorbic–glycolic (Ag)



Scheme 2.

Table 1
GPC[a] and thermal analysis data of the polymers

Polymer	M_n	M_w	M_n/M_w	T_g[b] (°C)	T_{des}[c] (°C)
L-PLA[d]	19,600	64,800	3.3	54	242
D,L-PLA[d]	13,400	16,500	1.2	50	255
PolyIPTA	5300	9000	1.7	61	323
Poly(IPTA15-*co*-DLLA85)	24,100	47,200	2.0	51	349
Poly(IPTA5-*co*- DLLA 95)	51,900	79,000	1.5	45	342

[a] Determined by GPC analysis with polystyrene standards in chloroform.
[b] Measured by DSC, second heating after rapid cooling to room temperature.
[c] The onset-of-decomposition temperature was determined by TGA.
[d] Source: Ref. 19.

Table 2
Yield and composition of the polymers

Polymer	Yield (%)	IPTA:LA[a]	IPTA:LA[b]	Elemental analyses (C, H) Found[c]	
PolyIPTA	50	100:0	100:0	49.94	5.77
Poly(IPTA15-*co*-DLLA 85)	68	15:85	16:84	49.70	5.70
Poly(IPTA5-*co*-DLLA95)	89	5:95	4:96	49.95	5.76

[a] Monomer ratio in the feed.
[b] Copolymer composition determined from NMR spectroscopy.
[c] Elemental microanalysis, calculated for all the polymers: C, 50.00; H, 5.59. There is a coincidence in the calculated analyses of the three polymers because of the same elemental proportion in both IPTA and LA units in the polymeric chains.

or glycolic–ascorbic (gA) repeat unit pairs only, depending on the opened cyclic ester side (*O*-acyl glycolic or *O*-acyl ascorbic). These two possibilities of ring-opening reactions besides the asymmetry of the monomer led to different microstructures in the polymer chain as it is observed by the fine structure present in several signals of the ^{1}H and ^{13}C NMR spectra. Therefore, the homopolymer and copolymer chains lack regio- and stereo-regularity.

In accordance with the literature,[6] we could use H2 signal of **polyIPTA** to estimate the selectivity in the ring-opening of the monomer. Thus, H2 appeared as a broad triplet signal that led us to assume that the peaks corresponded to the ggA, AgA and Agg triads. The integral of the three H2 signals count for about 21%, 50% and 29%, respectively. These values are close to those calculated for the random (25%, 50% and 25%). The composition of the copolymers as determined by ^{1}H NMR was almost identical to that of the feed mixture (Table 2).

Thermal properties of the polyesters were studied by differential scanning calorimetry (DSC), and are reported in Table 1. In all cases, the polymers appeared to be amorphous. The thermograms did not show any melting transition but showed well-defined glass transition temperature between 45 and 61 °C. As deduced from the data of Table 1, the introduction of the sugar monomer (**IPTA**) along the **PLA** backbone significantly increased the glass transition temperature. Thermogravimetric analysis (TGA) indicated that the polyesters were stable, under nitrogen, up to 250 °C.

As they are chiral polymers, they show optical activity (Table 2), which increases with the amount of the sugar monomer in the chain of polyester. They were soluble in acetone, dimethyl sulphoxide, ethyl acetate or chloroform, but insoluble in water and alcohols (ethanol, methanol).

1. Experimental

1.1. General methods

Thin layer chromatography (TLC) was performed on Silica Gel 60 F254 (E. Merck) with detection by UV light or charring with H_2SO_4. Flash column chromatography was performed using E. Merck Silica Gel 60 (230–400 mesh). IR spectra (films or KBr discs) were recorded with a JASCO FT/IR-410 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker AMX-500 or Bruker AV300 spectrometers. Chemical shifts are reported as parts per million downfield from Me_4Si. Two-dimensional ^{1}H–^{1}H homonuclear and ^{13}C–^{1}H heteronuclear shift correlation spectra were recorded with COSY, HETCOR pulse sequences. Elemental analyses were determined in the Microanalysis Laboratories at the University of Seville (Seville, Spain). Optical rotations were measured at 20 ± 5 °C with a Perkin–Elmer 341 polarimeter. FABMS analyses were performed on a micromass Autospec spectrometer. Spectra were obtained using thioglycerol–NaI as a matrix. Melting points were determined by DSC using a Perkin–Elmer DSC-7, calibrated with indium. Samples of about 2–3 mg were heated at a rate of 10 °C min^{-1} and cooled to room temperature. The peak temperatures were taken as melting points. Thermogravimetric analysis (TGA) was performed with a Setaram (Caluire, France) Setsys 1200 system at a heating rate of 10 °C/min under nitrogen. GPC was performed at room temperature with a Waters apparatus equipped with a Waters 410 RI detector and a Millennium 2010

computerised data station. Three Waters styragel HR columns were placed in series, and the analysis was performed in chloroform at a flow rate of 1 mL min^{-1}. Calibration was performed using 12 polystyrene samples of narrow molecular-weight distribution.

1.2. Materials

D,L-Lactide was obtained from Aldrich and sublimed before polymerisation (45 °C, 10^{-3} mmHg). 5,6-*O*-Isopropylidene-L-ascorbic acid (**2**) and calcium 3,4-*O*-isopropylidene-L-threonate (**3**) were prepared as described by Wei[15] and Voeffray,[16] respectively. 5,6-*O*-Isopropylidene-D-isoascorbic acid (**7**) was prepared as described by Emons.[17]

1.3. 3,4-*O*-Isopropylidene-L-threonic acid (4)

To a suspension of calcium 3,4-*O*-isopropylidene-L-threonate[16] (**3**) (1 g, 2.56 mmol) in water (15 mL), cooled in an ice-water bath, HCl (2 M) was added up to pH 3–4. Immediately, the solution was extracted with EtOAc (9 × 25 mL). The pH of the aqueous solution was checked from time to time in order to keep it at about 3. The organic phase was dried over sodium sulfate and concentrated under reduced pressure to give **4** as an oil that crystallised on standing (0.65 g, 73%); mp 71–73 °C; IR (KBr): ν 1737 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$): δ 4.45 (ddd, 1H, $J_{2,3}$ = 2.9, $J_{3,4a}$ = $J_{3,4b}$ = 6.65 Hz, H-3), 4.18 (d, 1H, H-2), 4.13 (dd, 1H, $J_{4a,4b}$ = 8.45 Hz, H-4a), 4.03 (dd, 1H, H-4b), 1.44, 1.36 (2s, 6H, $2CH_3$); ^{13}C NMR ($CDCl_3$): δ 175.63 (CO), 110.31($C(CH_3)_2$), 76.00 (C-3), 70.11(C-2), 65.65 (C-4), 26.00, 25.13 ($C(CH_3)_2$). Anal. Calcd for $C_7H_{12}O_5$: C, 47.72; H, 6.87. Found: C, 47.49; H, 6.86.

1.3.1. 2-*O*-(2-Bromoacetyl)-3,4-*O*-isopropylidene-L-threonic acid (5)

To a solution of **4** (1.0 g, 5.67 mmol) in dry Et_2O (24.0 mL), bromoacetyl chloride (0.6 mL, 7.24 mmol) was added at 0 °C under argon. To this solution, stirred vigorously in an ice/salt bath, triethylamine (1.32 mL) dissolved in dry Et_2O (6.0 mL) was added dropwise over a period of 1 h. After this time, the mixture was stirred at 0 °C for a further 30 min, diluted with more Et_2O (10 mL), washed with water (2 × 2 mL) and dried over sodium sulfate. Concentration of the organic solution under vacuum gave a pale yellow viscous liquid (1.4 g, 83%). IR: ν 1749 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$): δ 8.72 (br s, 1H COOH), 5.15 (d, 1H, $J_{2,3}$ = 4.2 Hz, H-2), 4.61 (ddd, 1H, $J_{3,4a}$ = 5.7, $J_{3,4b}$ = 6.6 Hz, H-3), 4.13 (dd, 1H, $J_{4a,4b}$ = 8.9 Hz, H-4a), 3.97 (dd, 1H, H-4b), 3.96 and 3.95 (m, 2H, glyc), 1.45, 1.36 (2s, 6H, $2CH_3$); ^{13}C NMR ($CDCl_3$): δ 169.91, 166.78 (2 CO), 110.50 ($C(CH_3)_2$), 73.89, 72.73 (C-2,3), 65.00 (C-4), 26.00, 25.26 ($C(CH_3)_2$), 24.96 (CH_2Br). HRMS: *m*/*z* 320.977313 and 318.979444 (calcd for $[M+Na]^+$: 320.977273 and 318.979319).

1.3.2. IPTA monomer

A solution of **5** (0.614 mg, 2.07 mmol) in dimethylformamide (5.2 mL) was added to a vigorously stirred suspension of $NaHCO_3$ (0.295 g, 3.5 mmol) in dimethylformamide (73 mL) at 40 °C over 4 h. After the addition, the solution was stirred for 3 h more, and concentrated under reduced pressure to give a residue that was extracted with Et_2O (10 × 10 mL). The organic phase was washed with water (1 × 2 mL) and dried over sodium sulfate. Concentration of the organic solution under reduced pressure gave **IPTA** as a crystalline solid (0.251 g, 56%); mp 133–135 °C (recrystallised from EtOAc); $[\alpha]_D$ −94 (*c* 1.1, $CHCl_3$); IR: ν 1746 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$): δ 5.11 (d, 1H, *J* = 16.5 Hz, CH_2 glyc), 4.91 (d, 1H, $J_{2,3}$ = 1.5 Hz, H-2), 4.85 (d, 1H, CH_2 glyc), 4.61 (ddd, 1H, H-3), 4.17 (dd, 1H, $J_{3,4a}$ = 7.1 Hz, $J_{4a,4b}$ = 8.6 Hz, H-4a), 4.03 (dd, 1H, $J_{3,4b}$ = 7.0 Hz, H-4b), 1.38, 1.34 (2s, 6H, $2CH_3$); ^{13}C NMR ($CDCl_3$): δ 163.92, 163.29 (2 CO), 111.48 ($C(CH_3)_2$), 76.16 (C-3), 75.06 (C-2), 65.32 (CH_2 glyc), 64.72 (C-4), 25.19, 24.86 ($C(CH_3)_2$). Anal. Calcd for $C_9H_{12}O_6$: C, 50.00; H, 5.59. Found: C, 49.74; H, 5.40.

1.3.3. 2-*O*-(2-Bromopropanoyl)-3,4-*O*-isopropylidene-L-threonic acid (6)

Treatment of a solution of **4** in dry Et_2O with (±)-2-bromopropanoyl chloride as described for **5** gave, after concentration under reduced pressure, **6** as an oil (mixture of stereoisomers, 75%). IR: ν 1749 (CO) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 8.77 (br s, 1H COOH), 5.10 (m, 1H, H-2), 4.61 (m, 1H, H-3), 4.55–4.4 (m, 1H, CHBr), 4.11 (m, 1H, H-4a), 3.97 (m, 1H, H-4b), 1.90–1.82 (m, 3H, CH_3), 1.44, 1.35 (2s, 6H, $2CH_3$); ^{13}C NMR ($CDCl_3$): δ 171.38, 171.17, 169.82, 169.50 (CO), 110.57, 110.53 ($C(CH_3)_2$), 74.36, 74.19 (C-3), 73.04, 72.68 (C-2), 65.50, 65.38 (C-4), 39.58, 39.13 (CHBr), 26.10, 26.06, 25.44, 25.35 ($C(CH_3)_2$), 21.68, 21.55(CH_3). HRMS: *m*/*z* 334.992881 and 332.995306 (calcd for $[M+Na]^+$: 334.992923 and 332.994969).

1.3.4. IPTP monomer

Treatment of a solution of **6** in dimethylformamide as described for **IPTA** gave, after concentration under reduced pressure, **IPTP** (mixture of stereoisomers) as an oil, which crystallised from Et_2O (1.3 g, 30%). IR: ν 1756 (CO) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 5.27 and 5.08 (2q, 1H, $J_{H,CH3}$ = 7.0 Hz, CH propanoyl), 4.91 and 4.89 (2d, 1H, $J_{2,3}$ = 1.34 Hz and $J_{2,3}$ = 3.50 Hz, H-2), 4.63–4.56 (m, 1H, H-3), 4.22 and 4.16 (2 dd, 1H, $J_{4a,3}$ = 6.9 and 7.0 Hz, $J_{4a,4b}$ = 8.8 and 8.6 Hz, H-4a), 4.03 and 4.00 (2 dd, 1H, $J_{4b,3}$ = 6.7 and 7.2 Hz, H-4b), 1.72 and 1.65 (2d, 3H, CH_3 propanoyl), 1.40, 1.35 and 1.33 (3s, 6H, CH_3 isopropylidene); ^{13}C NMR ($CDCl_3$): δ 166.55, 165.66, 165.08, 163.85 (2CO), 111.41, 111.11 ($C(CH_3)_2$), 76.19, 75.88, 75.62, 74.67, 73.06, 72.56 (C-2,3 and CH propanoyl), 65.37, 64.79 (C-4), 25.85, 25.30, 25.11 (CH_3 isopropylidene), 18.15, 17.64 (CH_3 propanoyl). Anal. Calcd for $C_{10}H_{14}O_6$: C, 52.17; H, 6.13. Found: C, 52.18; H, 6.11.

1.3.5. Calcium 3,4-*O*-isopropylidene-D-erythronate (8)

To a suspension of calcium carbonate (16.0 g, 0.16 mol) in water (200 mL), 5,6-*O*-isopropylidene-D-isoascorbic acid[17] (**7**, 17.3 g, 0.08 mol) was added. The resulting mixture was cooled in an ice bath, and 30% aqueous hydrogen peroxide (33.0 mL) was added dropwise. Once the addition was complete, the mixture was warmed to room temperature, stirred for 1 h more and then heated at 40 °C for 30 min. After that, charcoal (4.3 g) was added, and the mixture was heated at 80 °C for 1 h. Then, the suspension was filtered over Celite and the filtrate was concentrated under vacuum to half volume; addition of acetone (200 mL) gave **8** as a solid (10.7 g, 70%); mp >250 °C; IR (KBr): ν 3410 (OH), 1602 cm^{-1} (CO); ^{1}H NMR (D_2O): δ 4.49 (ddd, 1H, $J_{2,3}$ = 1.8, $J_{3,4a}$ = $J_{3,4b}$ = 4.4 Hz, H-3), 4.27 (d, 1H, H-2), 4.00 (dd, 1H, $J_{4a,4b}$ = 8.3 Hz, H-4a), 3.92 (dd, 1H, H-4b), 1.43, 1.36 (2s, 6H, $2CH_3$); ^{13}C NMR (D_2O): δ 177.30 (CO), 109.96 ($C(CH_3)_2$), 76.93 (C-3), 71.49 (C-2), 63.59 (C-4), 25.11, 23.95 ($C(CH_3)_2$). Anal. Calcd for $C_{14}H_{22}O_{10}1/2H_2O$: C, 42.10; H, 5.80. Found: C, 41.80; H, 5.81.

1.3.6. 3,4-*O*-Isopropylidene-D-erythronic acid (9)

Treatment of a suspension of **8** in water as described for **4** gave, after concentration under reduced pressure, **9** as an oil which crystallised on standing (72%); mp 58–60 °C; IR (KBr): ν 1736 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$): δ 4.28 (m, 1H, H-3), 4.20 (d, 1H, $J_{2,3}$ = 5.6 Hz, H-2), 4.09–3.98 (m, 2H, H-4a,b), 1.14, 1.32 (2s, 6H, $2CH_3$); ^{13}C NMR ($CDCl_3$): δ 174.84 (CO), 110.54 ($C(CH_3)_2$), 76.24 (C-3), 70.54 (C-2), 65.27 (C-4), 26.25, 24.93 ($C(CH_3)_2$). Anal. Calcd for $C_7H_{12}O_5 1/4H_2O$: C, 46.53; H, 6.97. Found: C, 46.35; H, 6.69. HRMS: *m*/*z* 199.058831 (calcd for $[M+Na]^+$: 199.058243).

1.3.7. 2-*O*-(2-Bromoacetyl)-3,4-*O*-isopropylidene-D-erythronic acid (10)

Treatment of a solution of **9** in dry Et_2O as described for **5** gave **10** as a pale yellow viscous liquid (63%). IR: ν 1747 cm^{-1} (CO); ^{1}H

NMR ($CDCl_3$): δ 8.27 (br s, 1H COOH), 5.18 (d, 1H, $J_{2,3}$ = 4.7 Hz, H-2), 4.54 (m, 1H, H-3), 4.14 (dd, 1H, $J_{3,4a}$ = 6.4, $J_{4a,4b}$ = 8.9 Hz, H-4a), 4.09 (dd, 1H, $J_{3,4b}$ = 5.5 Hz, H-4b), 3.94 and 3.93 (m, 2H, glyc), 1.48, 1.40 (2s, 6H, $2CH_3$); ^{13}C NMR ($CDCl_3$): δ 171.25, 166.45 (2 CO), 110.80 ($C(CH_3)_2$), 74.24 (C-3), 73.06 (C-2), 65.29 (C-4), 26.27, 25.07 ($C(CH_3)_2$), 24.70 (CH_2Br). HRMS: m/z 320.977750 and 318.980021 (calcd for $[M+Na]^+$: 320.977273 and 318.979319).

1.3.8. IPEA monomer

A solution of **10** (3.7 g, 12.45 mmol) in dimethylformamide (40 mL) was added to a vigorously stirred suspension of $NaHCO_3$ (2.0 g, 3.5 mmol) in dimethylformamide (460 mL) at 40 °C over 4 h. After the addition, the solution was stirred for 3 h more, and concentrated under reduced pressure to give a residue that was treated with dichloromethane (100 mL). The resulting suspension was filtered through a plug of Celite on glass wool, and the residue was rinsed with dichloromethane (3 × 25 mL). The filtrate and rinses were combined, and dried over sodium sulfate. Concentration of the organic solution under reduced pressure gave **IPEA** as an oil that crystallised on standing in the refrigerator (1.17 g, 43%); mp 83–84 °C (recrystallised from EtOAc); $[\alpha]_D$ −143 (*c* 1.0, $CHCl_3$); IR: ν 1746 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$): δ 5.12 (d, 1H, $J_{6a,6b}$ = 16.5 Hz, H-6a), 4.95 (d, 1H, $J_{3,4'}$ = 2.1 Hz, H-3), 4.83 (d, 1H, H-6b), 4.58 (ddd, 1H, $J_{4',5'a} = J_{4',5'b}$ = 6.9 Hz, H-4′), 4.18 (dd, 1H, $J_{5'a,5'b}$ = 8.8 Hz, H-5′a), 4.12 (dd, 1H, H-5′b), 1.40, 1.34 (2s, 6H, $2CH_3$); ^{13}C NMR ($CDCl_3$): δ 163.34, 162.83 (2CO), 111.40 ($C(CH_3)_2$), 77.20 (C-3), 76.75 (C-4′), 65.46 (C-6), 64.90 (C-5′), 25.87, 24.85 ($C(CH_3)_2$). Anal. Calcd for $C_9H_{12}O_6$: C, 50.00; H, 5.59. Found: C, 49.78; H, 5.63.

1.3.9. Polymerisation

The monomers were introduced into round-bottomed flasks, and mixed with stannous octanoate. The mixtures were degassed through vacuum/argon cycles, and the flasks were sealed under vacuum. The polymerisation reactions were kept at 120 °C for 5 days. The polymers were purified by dissolving in acetone and pouring into a large volume of ethanol. The isolated yields and some characteristics of the polymers are given in Tables 1 and 2. We describe below their spectroscopic properties (IR and NMR).

1.3.10. PolyIPTA

$[\alpha]_D$ +36 (*c* 1.5, $CHCl_3$); IR: ν_{max} 1762 cm^{-1} (CO). ^{1}H NMR (DMSO-d_6; 333 K): δ 5.40–5.25 (H-2), 5.0–4.8 (CH_2, glyc), 4.65–4.35 (H-3), 4.2–4.0 (H-4a), 4.0–3.8 (H-4b), 1.5–1.2 (CH_3, isopropylidene); ^{13}C NMR (DMSO-d_6; 333 K): δ 167.0–165.2 (CO), 109.3 (quaternary C), 73.6 (C3), 72.6–72.0 (C2), 65.2–64.2 (C4), 61.0–60.2 (CH_2, glyc), 26.6–24.6 (CH_3, isopropylidene).

1.3.11. Poly(IPTA15-*co*-DLLA85)

$[\alpha]_D$ +8 (*c* 1.5, $CHCl_3$); IR: ν_{max} 1757 cm^{-1} (CO). ^{1}H NMR (DMSO-d_6; 333 K): δ 5.40–5.25 (H-2), 5.30–5.10 (CH, lac), 5.0–4.75 (CH_2, glyc), 4.60–4.43 (H-3), 4.15–4.00 (H-4a), 3.96–3.75 (H-4b), 1.53–1.40 (CH_3, lac), 1.40–1.24 (CH_3, isopropylidene); ^{13}C NMR (DMSO-d_6; 333 K): δ 169.70–168.50 (CO, lac), 166.90–165.70 (CO sugar, glyc), 109.30 (quaternary C), 73.7 (C-3), 72.57–71.70 (C-2), 69.51–67.50 (CH, lac), 65.20–64.53 (C-4), 61.00–60.25 (CH_2, glyc), 25.89–24.60 (CH_3, isopropylidene), 16.50–15.76 (CH_3, lac).

1.3.12. Poly(IPTA5-*co*-DLLA95)

$[\alpha]_D$ +3 (*c* 1.5, $CHCl_3$); IR: ν_{max} 1757 cm^{-1} (CO). ^{1}H NMR (DMSO-d_6; 333 K): δ 5.40–5.25 (H-2), 5.30–5.10 (CH, lac), 5.0–4.75 (CH_2, glyc), 4.60–4.43 (H-3), 4.15–4.00 (H-4a), 3.96–3.75 (H-4b), 1.53–1.40 (CH_3, lac), 1.40–1.24 (CH_3, isopropylidene); ^{13}C NMR (DMSO-d_6; 333 K): δ 169.70–168.50 (CO, lac), 166.90–165.70 (CO sugar, glyc), 109.30 (quaternary C), 73.7 (C-3), 72.57–71.70 (C-2), 69.51–67.50 (CH, lac), 65.20–64.53 (C-4), 61.00–60.25 (CH_2, glyc), 25.89–24.60 (CH_3, isopropylidene), 16.50–15.76 (CH_3, lac).

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