

Synthesis and characterization of copolyesters based on tartaric acid derivatives

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Abstract A series of aliphatic copolyesters based on naturally occurring L-tartaric acid amenable to facile post-polymer modification have been synthesized and characterized. The hydroxyl groups of the tartaric acid were protected and copolyesters were synthesized by taking different feed molar ratio of dimethyl 2,3-*O*-isopropylidene tartarate and dimethyl succinate with 1,6-hexanediol. Then, a series of copolyesters were synthesized by taking equal feed molar ratio of dimethyl 2,3-*O*-isopropylidene tartrate and dimethyl succinate or dimethyl adipate with different alkane diols. The acetal protecting groups were then selectively hydrolyzed to prepare a new series of copolyesters with pendant hydroxyl groups along the copolymer chain. The number average molecular weights (M_n) of the copolymers were found to vary in the range of $3.7\text{--}8.4 \times 10^3 \text{ g mol}^{-1}$. The hydroxy copolyesters show higher glass transition (T_g) and melting (T_m) temperatures as compared to isopropylidene copolyesters and the T_g varies from -8.0 to -48.2 °C depending on the feed ratio of the comonomers. The hydrolytic degradation studies of copolyesters revealed that hydroxyl copolyesters degrade faster than isopropylidene copolyesters.

Keywords Aliphatic copolyesters · Hydroxyl-functionalized copolyesters · Step polymerization · L-Tartaric acid

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Introduction

Among the synthetic polymers, aliphatic polyesters have attracted considerable attention as a useful material for biomedical and pharmaceutical applications, since they combine the features of biodegradability and biocompatibility [1–3]. Aliphatic polyesters, such as poly(lactide) (PLA), poly(glycolide) (PGA), poly(β -hydroxy butyrate) (PHB), and poly(ϵ -caprolactone) (PCL) have been extensively investigated as biodegradable polyesters, and biomedical applications of these polyesters as bioadsorbable surgical sutures, absorbable bone plates, surgical fixation devices, and carriers for the controlled release of drugs have been well documented [3–6]. Although these aliphatic polyesters are suitable in several biomedical and pharmaceutical applications, their hydrophobic nature and lack of functional groups prevent them from many other biomedical and pharmaceutical applications. Therefore, the need for synthesis of functional aliphatic polyesters having hydrophilic reactive pendant groups like hydroxyl, carboxyl, and amino has attracted a great deal of interest in recent years [7–12]. The functional polymers having reactive pendant groups can possibly be applied to prepare comb-type and grafted structural polymers through post-polymer modification [13]. The reactive functional groups and tunable biodegradability can enable these functional polyesters to be new biomaterials useful in the construction of novel controlled drug delivery systems and functional vectors. For example, polyesters in general, degrade over a long time period which is disadvantageous when the drug needs to be released for only a few days or even weeks and hence there is interest in developing polymers which degrade faster and allow controlled release of drugs exclusively by polymer erosion [2, 14].

Tartaric acid has attracted a great deal of interest as a substrate for the synthesis of functional polymers, since it is widely available from relatively inexpensive natural resources and has been used in the synthesis of polyesters [15–18], polyamides [19, 20], poly(ester amide)s [21, 22], and polycarbonates [23, 24] etc. Tartaric acid-based copolyesters [25] have also been synthesized, however, these copolyesters have low molecular weight and mostly insoluble since crosslinking occurred through pendant hydroxyl groups also during the polycondensation reaction. Tartaric acid-based polyesters and copolyesters can be used as drug carriers and controlled release agents in controlled drug delivery. The ability of poly(alkylene tartarates) and its copolyesters as controlled release agents has been shown by Huang et al. [25] where they reported on the effect of various chemical modifications of poly(alkylene tartarates) on the release of two model compounds, methylene blue and bovine pancreatic insulin. Similarly, Walch et al. [26] also demonstrated the suitability of polytartarates for controlled release applications. Recently, we reported on the synthesis of tartaric acid-derived polyesters and facile post-polymer modification to generate hydroxyl-functionalized polyesters [15]. Here, we report on the synthesis and characterization of aliphatic copolyesters based on protected tartaric acid derivatives synthesized by bulk polycondensation method using titanium tetrakisopropoxide as a catalyst. We also demonstrate that the protecting groups can be easily removed under mild conditions to generate hydroxyl-functionalized aliphatic copolyesters.

Experimental

Materials

L-Tartaric acid, *p*-toluenesulfonic acid, 1,4-butanediol, 1,6-hexanediol, 1,8-octanediol, and 2,2-dimethoxypropane were purchased from Spectrochem Chemicals and used as received. Titanium tetraisopropoxide was purchased from Aldrich. Solvents were dried and purified, when necessary, by appropriate standard procedures.

Measurements

^1H and ^{13}C NMR spectra were recorded on a Bruker DPX-300 spectrometer at 25 °C operating at 300 and 75.5 MHz, respectively. The copolyesters were dissolved in deuterated chloroform, and spectra were internally referenced to tetramethylsilane (TMS). IR spectra were recorded on a Thermo Nicolet IR 200 spectrometer using KBr disks. Gel permeation chromatography (GPC) was carried out using tetrahydrofuran (THF) as the mobile phase at 30 °C. GPC analysis was performed on a Perkin Elmer, Series 200, USA GPC system equipped with a refractive index detector. Molecular weights were calculated against monodisperse polystyrene standards using the Totalchrom software. Solution viscosities of copolyesters were carried out with an Ubbelohde viscometer at 30 °C. Optical rotations were measured at 25 ± 0.5 °C (1 cm cell). The thermal behavior of the copolyesters was examined by differential scanning calorimetry (DSC) using a DSC Q 200 calibrated with indium. DSC data were obtained from samples of 4–6 mg at heating/cooling rates of 10 or 20 °C min^{-1} under nitrogen. Thermogravimetric analysis (TGA) was carried out on a Perkin-Elmer Pyris-6 TGA thermobalance at a heating rate of 10 °C min^{-1} under a nitrogen atmosphere. Hydrolytic degradation experiments were carried out on films; these were separately submerged in phosphate buffer solutions (pH 7.4) at 37 °C. The samples were taken at selected time points and the evolution of degradation was followed by GPC analysis.

Hydroxyl titration

To determine the hydroxyl content in the synthesized copolyesters, a nonaqueous titration method was employed [15, 27, 28]. In general, 100 mg of copolyester was added to 4.0 mL of pyridine/acetic anhydride (3:1 v/v) solution, and then heated in an oil bath at 100 °C for 1 h. Subsequently, 2.0 mL of distilled water was added into the reaction mixture. After 0.5 h, a methanolic KOH solution (108 mM) was used to titrate the copolyester solution in triplicate with thymol blue as the indicator. Similarly, a blank titration was also conducted.

Synthesis

The copolyesters were synthesized by bulk polycondensation.

General procedure for bulk polycondensation method

Dimethyl 2,3-*O*-isopropylidene-*L*-tartarate, dimethyl succinate or dimethyl adipate, and 10% molar excess of alkanediol were taken in a Schlenk tube under nitrogen atmosphere, equipped with a Dean Stark apparatus and condenser. The reactants were stirred to a homogeneous mixture and 0.5 mol% of titanium tetraisopropoxide was added as catalyst. In the first step (esterification), the reaction mixture was heated at 110–120 °C for 6–8 h, till almost the theoretical amount of methanol was collected in the side arm of Dean Stark apparatus. In the second step (polycondensation), the Dean Stark apparatus was removed and a vacuum (0.5–1 mm Hg) was applied and the reaction mixture heated at 140–160 °C for 10–12 h till the stirring ceased. The cooled reaction mixture was then dissolved in a minimum amount of chloroform and poured into ten fold amount of methanol to precipitate the copolymer.

Poly(hexamethylene succinate) (PHS)

Dimethyl succinate (2.92 g, 20 mmol), 1,6-hexanediol (2.60 g, 22 mmol), and titanium tetraisopropoxide (37 μ L) were mixed and the reaction mixture was heated at 120 °C for 8 h in the esterification step and was heated at 160 °C for 12 h in the polycondensation step (Yield: 90%). ^1H NMR (300 MHz, CDCl_3) δ 4.19 (t, $J = 6.3$ Hz, 4H), 2.72 (s, 4H), 1.74 (s, 4H), 1.48 (s, 4H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 172.3, 64.6, 29.0, 28.4, 25.5; FT-IR (KBr disk, cm^{-1}) 2989 ($\nu_{\text{C-H}}$), 1745 ($\nu_{\text{C=O}}$), 1161 and 1104 ($\nu_{\text{C-O-C}}$).

Poly(hexamethylene 2,3-O-isopropylidene tartarate) (PHIT)

Dimethyl 2,3-*O*-isopropylidene-*L*-tartarate (3 g, 13.76 mmol), 1,6-hexanediol (1.79 g 15.14 mmol), and titanium tetraisopropoxide (21 μ L) were mixed and the reaction mixture was heated at 110 °C for 8 h in the esterification step and was heated at 160 °C for 10 h in the polycondensation step. (Yield: 87%). ^1H NMR (300 MHz, CDCl_3) δ 4.78 (s, 2H), 4.21 (m, 4H), 1.69 (m, 4H), 1.46 (s, 6H), 1.40 (s, 4H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 169.8, 113.8, 77.2, 65.7, 28.3, 26.4, 25.3; FT-IR (KBr disk, cm^{-1}) 2939 ($\nu_{\text{C-H}}$), 1736 ($\nu_{\text{C=O}}$), 1208 and 1163 ($\nu_{\text{C-O-C}}$).

Poly(hexamethylene succinate-co-hexamethylene 2,3-O-isopropylidene tartarate) (P[HS-co-HIT] 75/25)

Dimethyl 2,3-*O*-isopropylidene-*L*-tartarate (1 g, 4.58 mmol), dimethyl succinate (2 g, 13.76 mmol), 1,6-hexanediol (2.38 g, 20.17 mmol), and titanium tetraisopropoxide (28 μ L) were mixed and the reaction mixture was heated at 110 °C for 6 h in the esterification step and was heated at 160 °C for 12 h in the polycondensation step (Yield: 86%). ^1H NMR (300 MHz, CDCl_3) δ 4.75 (s, 2H), 4.19 (t, $J = 6.3$ Hz, 4H), 4.06 (t, $J = 6.3$ Hz, 12H), 2.60 (s, 12H), 1.62 (s, 16H), 1.47 (s, 6H), 1.37 (s, 16H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 172.3, 169.7, 113.7, 77.0, 65.7, 64.5, 29.0, 28.4, 26.3, 25.4; FT-IR (KBr disk, cm^{-1}) 2929 ($\nu_{\text{C-H}}$), 1741 ($\nu_{\text{C=O}}$), 1228 and 1108 ($\nu_{\text{C-O-C}}$).

Poly(hexamethylene succinate-co-hexamethylene 2,3-O-isopropylidene tartarate)
(*P[HS-co-HIT] 25/75*)

Dimethyl 2,3-*O*-isopropylidene-*L*-tartarate (3.33 g, 15.34 mmol), dimethyl succinate (0.75 g, 5.13 mmol), 1,6-hexanediol (2.66 g, 22.49 mmol), and titanium tetraisopropoxide (31 μ L) were mixed and the reaction mixture was heated at 110 °C for 7 h in the esterification step and was heated at 160 °C for 12 h in the polycondensation step (Yield: 85%). ^1H NMR (300 MHz, CDCl_3) δ 4.78 (s, 6H), 4.19 (t, $J = 6.0$ Hz, 12H), 4.08 (t, $J = 6.3$ Hz, 4H), 2.62 (s, 4H), 1.69 (m, 16H), 1.49 (s, 18H), 1.40 (s, 16H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 172.3, 169.6, 113.6, 76.9, 65.6, 64.4, 28.9, 28.2, 26.2, 25.2; FT-IR (KBr disk, cm^{-1}) 2983 ($\nu_{\text{C-H}}$), 1744 ($\nu_{\text{C=O}}$), 1213 and 1171 ($\nu_{\text{C-O-C}}$).

Poly(hexamethylene succinate-co-hexamethylene 2,3-O-isopropylidene tartarate)
(*P[HS-co-HIT] 50/50*)

Dimethyl 2,3-*O*-isopropylidene-*L*-tartarate (3.27 g, 15 mmol), dimethyl succinate (2.19 g, 15 mmol), 1,6-hexanediol (3.9 g, 33 mmol), and titanium tetraisopropoxide (47 μ L) were mixed and the reaction mixture was heated at 120 °C for 8 h in the esterification step and was heated at 160 °C for 10 h in the polycondensation step (Yield: 88%). ^1H NMR (300 MHz, CDCl_3) δ 4.77 (s, 2H), 4.21 (t, $J = 6$ Hz, 4H), 4.08 (t, $J = 6.3$ Hz, 4H), 2.62 (s, 4H), 1.66 (m, 8H), 1.49 (s, 6H), 1.39 (s, 8H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 172.2, 169.6, 113.6, 77.0, 65.5, 64.5, 28.9, 28.3, 26.2, 25.4; FT-IR (KBr disk, cm^{-1}) 2935 ($\nu_{\text{C-H}}$), 1738 ($\nu_{\text{C=O}}$), 1209 and 1163 ($\nu_{\text{C-O-C}}$).

Poly(hexamethylene adipate-co-hexamethylene 2,3-O-isopropylidene tartarate)
(*P[HA-co-HIT] 50/50*)

Dimethyl 2,3-*O*-isopropylidene-*L*-tartarate (3.27 g, 15 mmol), dimethyl adipate (2.61 g, 15 mmol), 1,6-hexanediol (3.9 g, 33 mmol), and titanium tetraisopropoxide (45 μ L) were mixed and the reaction mixture was heated at 120 °C for 8 h in the esterification step and was heated at 160 °C for 12 h in the polycondensation step (Yield: 90%). ^1H NMR (300 MHz, CDCl_3) δ 4.77 (s, 2H), 4.47 (m, 4H), 4.21 (m, 4H), 2.32 (s, 4H), 1.65 (s, 12H), 1.49 (s, 6H), 1.39 (s, 8H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 173.3, 169.7, 113.7, 77.1, 65.7, 64.3, 33.8, 28.4, 26.3, 25.5, 24.3; FT-IR (KBr disk, cm^{-1}) 2930 ($\nu_{\text{C-H}}$), 1751 ($\nu_{\text{C=O}}$), 1208 and 1106 ($\nu_{\text{C-O-C}}$).

Poly(octamethylene succinate-co-octamethylene 2,3-O-isopropylidene tartarate)
(*P[OS-co-OIT] 50/50*)

Dimethyl 2,3-*O*-isopropylidene-*L*-tartarate (2.18 g, 10 mmol), dimethyl succinate (1.46 g, 10 mmol), 1,8-octanediol (3.21 g, 22 mmol), and titanium tetraisopropoxide (30 μ L) were mixed and the reaction mixture was heated at 120 °C for 8 h in the esterification step and was heated at 160 °C for 10 h in the polycondensation step (Yield: 87%). ^1H NMR (300 MHz, CDCl_3) δ 4.77 (s, 2H), 4.20 (t, $J = 6.6$ Hz, 4H),

4.05 (t, $J = 6.9$ Hz, 4H), 2.62 (s, 4H), 1.65 (m, 8H), 1.49 (s, 6H), 1.33 (s, 16H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 172.4, 169.8, 113.8, 77.2, 65.9, 64.8, 29.1 (2 peaks overlapped), 28.5, 26.4, 25.8; FT-IR (KBr disk, cm^{-1}) 2988 ($\nu_{\text{C-H}}$), 1740 ($\nu_{\text{C=O}}$), 1214 and 1160 ($\nu_{\text{C-O-C}}$).

Poly(octamethylene adipate-co-octamethylene 2,3-O-isopropylidene tartarate)
(*P[OA-co-OIT] 50/50*)

Dimethyl 2,3-*O*-isopropylidene-*L*-tartarate (4.36 g, 20 mmol), dimethyl adipate (3.48 g, 20 mmol), 1,8-octanediol (6.42 g, 44 mmol), and titanium tetraisopropoxide (60 μL) were mixed and the reaction mixture was heated at 110 °C for 7 h in the esterification step and was heated at 160 °C for 12 h in the polycondensation step (Yield: 89%). ^1H NMR (300 MHz, CDCl_3) δ 4.77 (s, 2H), 4.20 (t, $J = 6.3$ Hz, 4H), 4.05 (t, $J = 6.6$ Hz, 4H), 2.32 (s, 4H), 1.66 (m, 12H), 1.49 (s, 6H), 1.32 (s, 16H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 172.4, 169.7, 113.7, 77.1, 65.9, 64.8, 29.4, 29.1 (2 peaks overlapped), 28.5, 26.3, 25.6; FT-IR (KBr disk, cm^{-1}) 2924 ($\nu_{\text{C-H}}$), 1739 ($\nu_{\text{C=O}}$), 1217 and 1168 ($\nu_{\text{C-O-C}}$).

General procedure for the removal of isopropylidene groups

The copolymer was first dissolved in dichloromethane and then ten molar equivalents of both trifluoroacetic acid and water were added and the reaction mixture stirred at room temperature for 30 min. After 30 min, the solvents were removed under reduced pressure and the residue was dissolved in a minimum amount of chloroform and poured into ten fold excess of diethyl ether to precipitate the copolymer.

Poly(hexamethylene tartarate) (*PHT*)

Copolyester (300 mg, 1.10 mmol), trifluoroacetic acid (0.82 mL, 11 mmol), and water (0.20 mL, 11 mmol) were taken in dichloromethane (2.5 mL). (Yield: 83%) ^1H NMR (300 MHz, CDCl_3) δ 4.55 (s, 2H), 4.31 (m, 4H), 3.33 (br, -OH), 1.70 (s, 4H) 1.41 (s, 4H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 171.6, 72.2, 66.0, 28.2, 24.9; FT-IR (KBr disk, cm^{-1}) 3449 ($\nu_{\text{O-H}}$), 2936 ($\nu_{\text{C-H}}$), 1736 ($\nu_{\text{C=O}}$), 1207 and 1162 ($\nu_{\text{C-O-C}}$).

Poly(hexamethylene succinate-co-hexamethylene tartarate) (*P[HS-co-HT] 75/25*)

Copolyester (300 mg, 0.63 mmol), trifluoroacetic acid (0.47 mL, 6.3 mmol), and water (0.11 mL, 6.3 mmol) were taken in dichloromethane (2.5 mL). (Yield: 82%) ^1H NMR (300 MHz, CDCl_3) δ 4.60 (s, 2H), 4.35 (t, $J = 6.6$ Hz, 4H), 4.10 (t, $J = 6.3$ Hz, 12H), 2.65 (s, 12H), 1.64 (s, 16H), 1.38 (s, 16H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 173.1, 171.7, 72.2, 66.6, 64.9, 29.1, 28.2, 25.1; FT-IR (KBr disk, cm^{-1}), 3454 ($\nu_{\text{O-H}}$), 2938 ($\nu_{\text{C-H}}$), 1736 ($\nu_{\text{C=O}}$), 1207 and 1163 ($\nu_{\text{C-O-C}}$).

Poly(hexamethylene succinate-co-hexamethylene tartarate) (P[HS-co-HT] 25/75)

Copolyester (400 mg, 0.84 mmol), trifluoroacetic acid (0.63 mL, 8.4 mmol), and water (0.15 mL, 8.4 mmol) were taken in dichloromethane (3 mL). (Yield: 86%) ^1H NMR (300 MHz, CDCl_3) δ 4.55 (s, 6H), 4.33 (m, 12H), 4.09 (m, 4H), 2.62 (s, 4H), 1.70 (m, 16H), 1.41 (s, 16H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 172.7, 171.7, 72.2, 66.2, 64.8, 29.1, 28.3, 25.2; FT-IR (KBr disk, cm^{-1}) 3465 ($\nu_{\text{O-H}}$), 2941 ($\nu_{\text{C-H}}$), 1751 ($\nu_{\text{C=O}}$), 1209 and 1108 ($\nu_{\text{C-O-C}}$).

Poly(hexamethylene succinate-co-hexamethylene tartarate) (P[HS-co-HT] 50/50)

Copolyester (375 mg, 0.79 mmol), trifluoroacetic acid (0.59 mL, 7.9 mmol), and water (0.14 mL, 7.9 mmol) were dissolved in dichloromethane (2.5 mL). (Yield: 85%) ^1H NMR (300 MHz, CDCl_3) δ 4.62 (s, 2H), 4.19 (m, 4H), 4.01 (t, $J = 6.3$ Hz, 4H), 3.06 (br, -OH), 2.54 (s, 4H), 1.58 (m, 8H), 1.31 (s, 8H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 172.4, 171.5, 72.1, 65.8, 64.5, 29.0, 28.3, 25.3; FT-IR (KBr disk, cm^{-1}) 3416 ($\nu_{\text{O-H}}$), 2928 ($\nu_{\text{C-H}}$), 1742 ($\nu_{\text{C=O}}$), 1212 and 1088 ($\nu_{\text{C-O-C}}$).

Poly(hexamethylene adipate-co-hexamethylene tartarate) (P[HA-co-HT] 50/50)

Copolyester (355 mg, 0.71 mmol), trifluoroacetic acid (0.53 mL, 7.1 mmol), and water (0.13 mL, 7.1 mmol) were added to dichloromethane (2.5 mL). (Yield: 83%) ^1H NMR (300 MHz, CDCl_3) δ 4.54 (s, 2H), 4.27 (m, 4H), 4.08 (t, $J = 6.0$ Hz, 4H), 2.62 (s, 4H), 2.42 (br, -OH), 1.66 (m, 12H), 1.39 (s, 8H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 174.3, 172.0, 72.5, 66.8, 65.0, 33.8, 28.4, 25.5, 24.3; FT-IR (KBr disk, cm^{-1}) 3457 ($\nu_{\text{O-H}}$), 2938 ($\nu_{\text{C-H}}$), 1736 ($\nu_{\text{C=O}}$), 1209 and 1108 ($\nu_{\text{C-O-C}}$).

Poly(octamethylene succinate-co-octamethylene tartarate) (P[OS-co-OT] 50/50)

Copolyester (406 mg, 0.768 mmol), trifluoroacetic acid (0.57 mL, 7.68 mmol), and water (0.14 mL, 7.68 mmol) were added to dichloromethane (2.5 mL). (Yield: 87%) ^1H NMR (300 MHz, CDCl_3) δ 4.54 (s, 2H), 4.24 (m, 4H), 4.09 (m, 4H), 2.61 (s, 4H), 2.03 (br, -OH), 1.66 (m, 8H), 1.40 (s, 16H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 172.5, 171.7, 72.1, 66.4, 64.9, 29.0 (2 peaks overlapped), 28.0, 25.7; FT-IR (KBr disk, cm^{-1}) 3455 ($\nu_{\text{O-H}}$), 2929 ($\nu_{\text{C-H}}$), 1739 ($\nu_{\text{C=O}}$), 1208 and 1163 ($\nu_{\text{C-O-C}}$).

Poly(octamethylene adipate-co-octamethylene tartarate) (P[OA-co-OT] 50/50)

Copolyester (364 mg, 0.65 mmol), trifluoroacetic acid (0.48 mL, 6.5 mmol), and water (0.11 mL, 6.5 mmol) were taken in dichloromethane (2.5 mL). (Yield: 88%) ^1H NMR (300 MHz, CDCl_3) δ 4.53 (s, 2H), 4.32 (m, 4H), 4.10 (m, 4H), 2.62 (s, 4H), 1.69 (m, 12H), 1.30 (s, 16H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 174.2, 171.6, 72.1, 66.3, 64.6, 29.6, 29.2 (2 peaks overlapped), 28.4, 25.4; FT-IR (KBr disk, cm^{-1}) 3449 ($\nu_{\text{O-H}}$), 2936 ($\nu_{\text{C-H}}$), 1735 ($\nu_{\text{C=O}}$), 1210 and 1168 ($\nu_{\text{C-O-C}}$).

Table 1 Characterization data for copolyesters P[HS-*co*-HIT] for different feed ratios

Copolyester	Composition (¹ H NMR)	Yield (%)	$[\alpha]_D$ (deg) ^a	$[\eta]_D$ (dL/g) ^b	M_n^c ($\times 10^3$)	M_w/M_n^c
PHS	100/0	90	0	0.28	9.7	1.6
P[HS- <i>co</i> -HIT] 75/25	77/23	86	-10.8	0.22	7.2	2.1
P[HS- <i>co</i> -HIT] 50/50	51/49	88	-39.4	0.29	8.4	2.0
P[HS- <i>co</i> -HIT] 25/75	26/74	85	-54.5	0.19	6.3	2.3
PHIT	0/100	87	-82.4	0.23	9.2	1.9

^a c 1.0, Dichloromethane, at 25 °C, ^b in chloroform at 30 ± 0.5 °C, ^c by GPC against polystyrene standards, using THF as a mobile phase

Table 2 Characterization data for copolyesters with lateral isopropylidene groups having equal feed ratio of diesters

Copolyester	Composition (¹ H NMR)	Yield (%)	$[\alpha]_D$ (deg) ^a	$[\eta]_D$ (dL/g) ^b	M_n^c ($\times 10^3$)	M_w/M_n^c
P[HS- <i>co</i> -HIT] 50/50	51/49	88	-39.4	0.29	8.4	2.0
P[HA- <i>co</i> -HIT] 50/50	51/49	90	-37.4	0.27	7.9	1.9
P[OS- <i>co</i> -OIT] 50/50	52/48	87	-37.9	0.21	6.7	2.2
P[OA- <i>co</i> -OIT] 50/50	53/47	89	-36.6	0.24	7.4	1.8

^a c 1.0, Dichloromethane, at 25 °C, ^b in chloroform at 30 ± 0.5 °C, ^c by GPC against polystyrene standards, using THF as a mobile phase

1,738 cm^{-1} (C=O stretching) in the infrared spectrum of P[HS-*co*-HIT] 50/50 (Fig. 2). The molecular weights of the copolyesters were determined by gel permeation chromatography (GPC) using THF as a mobile phase and the number average molecular weights (M_n) of the copolyesters were obtained in the range of $6.3\text{--}8.4 \times 10^3$ g mol^{-1} with a polydispersity index in the range of 1.8–2.3. In addition, the results of optical rotation measurements show that the copolyesters are optically active with specific rotation $[\alpha]_D$ values ranging from -10.8° to -82.4° . The viscosities of the copolyesters were measured in chloroform at 30 °C and are listed in Tables 1 and 2. The intrinsic viscosity $[\eta]_D$ values vary from 0.19 to 0.29 which fall in comparable range for aliphatic copolyesters with similar molecular weights reported in literature [15, 30].

Synthesis and characterization of hydroxyl-functionalized copolyesters by selective deprotection

A new series of copolyesters with lateral hydroxyl groups was synthesized by selective deprotection of the isopropylidene groups in the above polymers using trifluoroacetic acid (Scheme 2) [15, 24, 31].

Trifluoroacetic acid and water, both in ten molar equivalents were used and stirred with the copolymer having lateral isopropylidene groups for 30 min at room temperature to completely remove the protecting groups. The resulting copolymers

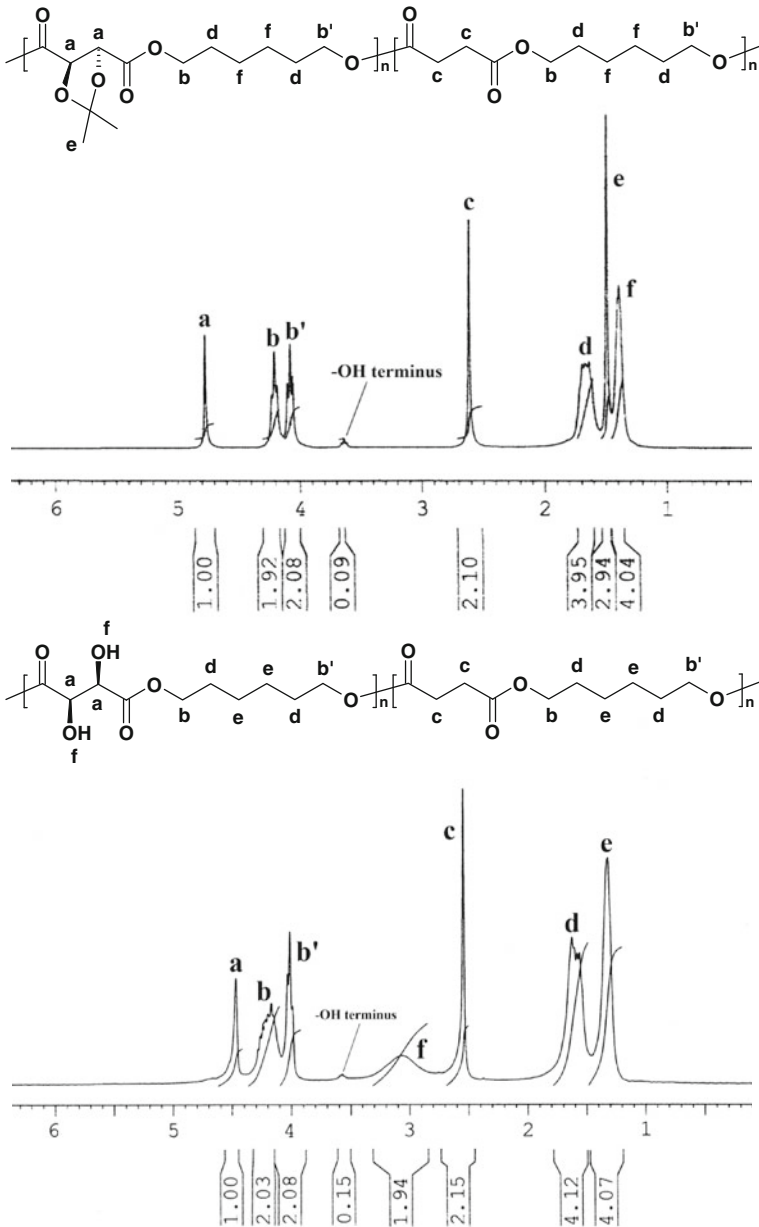


Fig. 1 ¹H NMR spectra of copolyesters P[HS-co-HIT] 50/50 and P[HS-co-HT] 50/50

were dissolved in chloroform and precipitated from diethyl ether. Table 3 summarizes the results obtained for copolyesters with lateral hydroxyl groups having different feed molar ratios.

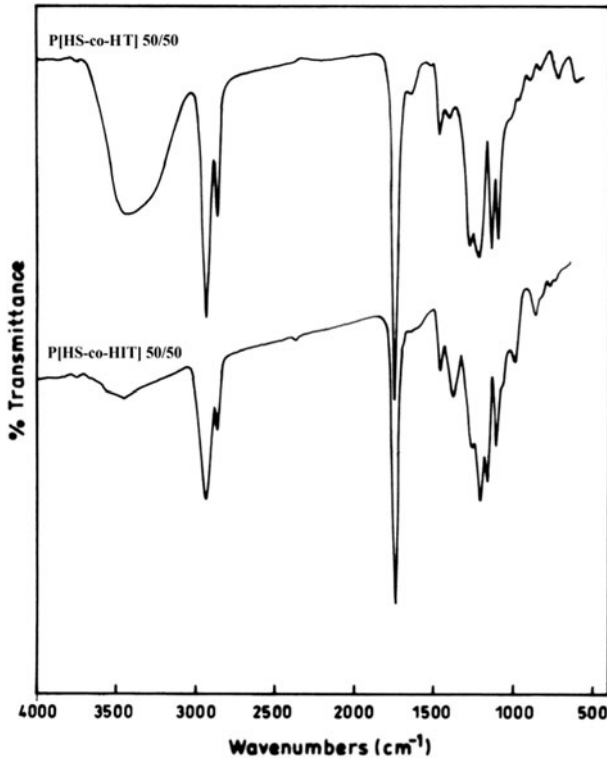
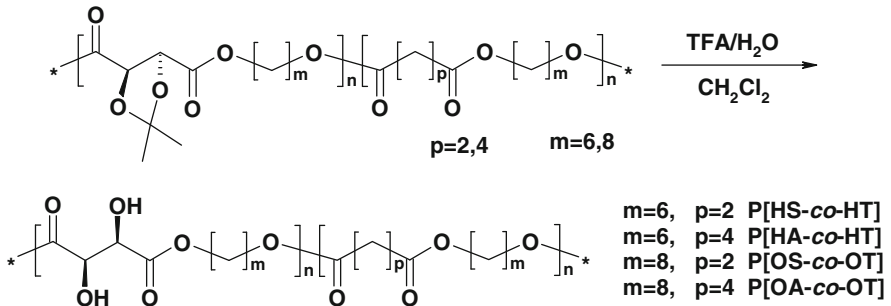


Fig. 2 FT-IR spectra of copolyesters P[HS-co-HT] 50/50 and P[HS-co-HT] 50/50



Scheme 2 Synthesis of copolyesters with lateral hydroxyl groups

The results obtained for copolyesters with lateral hydroxyl groups having equal feed ratio of diesters are summarized in Table 4.

¹H NMR spectrum of the copolyester P[HS-co-HT] 50/50 is depicted in Fig. 1 and is in good agreement with the chemical structure of the copolyester. A comparison of the ¹H NMR spectrum of P[HS-co-HT] 50/50 and P[HS-co-HT] 50/50 shows that the resonance signal at 1.49 ppm corresponding to the

Table 3 Characterization data for copolyesters P[HS-co-HT] for different feed ratios

Copolyester	Composition (¹ H NMR)	Yield (%)	[α] _D (deg) ^a	[η] _D (dL/g) ^b	M_n^c ($\times 10^3$)	M_w/M_n^c
PHS	100/0	90	0	0.28	9.7	1.6
P[HS-co-HT] 75/25	76/24	82	-9.9	0.13	4.2	2.0
P[HS-co-HT] 50/50	52/48	85	-31.2	0.17	4.8	1.9
P[HS-co-HT] 25/75	25/75	86	-47.3	0.11	3.7	2.1
PHT	0/100	84	-78.8	0.14	4.1	1.6

^a c 1.0, Dichloromethane, at 25 °C, ^b in chloroform at 30 ± 0.5 °C, ^c by GPC against polystyrene standards, using THF as a mobile phase

Table 4 Characterization data for copolyesters with lateral hydroxyl groups having equal feed ratio of diesters

Copolyester	Composition ¹ H NMR	Yield (%)	[α] _D (deg) ^a	[η] _D (dL/g) ^b	M_n^c ($\times 10^3$)	M_w/M_n^c
P[HS-co-HT] 50/50	52/48	85	-31.2	0.17	4.8	1.9
P[HA-co-HT] 50/50	51/49	83	-28.8	0.16	4.7	1.9
P[OS-co-OT] 50/50	51/49	87	-28.0	0.13	4.2	2.1
P[OA-co-OT] 50/50	51/49	88	-27.6	0.13	3.9	1.8

^a c 1.0, Dichloromethane, at 25 °C, ^b in chloroform at 30 ± 0.5 °C, ^c by GPC against polystyrene standards, using THF as a mobile phase

isopropylidene groups, completely disappears in the ¹H NMR spectrum of P[HS-co-HT] 50/50, and a new resonance signal at 3.06 ppm appears, corresponding to the hydroxyl groups. Similarly, a comparison of ¹³C NMR spectra (see supporting information Fig. S1) of P[HS-co-HIT] 50/50 and P[HS-co-HT] 50/50 shows that the resonance signals at 113.6 and 26.2 ppm, attributed to the isopropylidene groups, completely disappear upon deprotection. Furthermore, FT-IR spectra of the copolyesters before and after deprotection are depicted in Fig. 2 and the appearance of a broad band in the 3,700–3,200 cm⁻¹ can be attributed to the newly formed, H-bonded hydroxyl groups along the copolymer chain.

These data suggest complete removal of the isopropylidene protecting groups to generate pendant hydroxyl groups along the copolymer backbone. The molecular weights of the copolyesters were determined by GPC using THF as a mobile phase and the M_n of the copolyesters were obtained in the range of $3.7\text{--}4.8 \times 10^3$ g mol⁻¹ with a polydispersity index of 1.8–2.1. The optical rotation measurements show that the copolyesters are optically active with specific rotation [α]_D values from -9.9° to -78.8°. The viscosity of copolyesters was measured in chloroform at 30 °C and the intrinsic viscosity [η]_D values varied from 0.11 to 0.17 dL/g for the hydroxyl copolyesters, showing that the intrinsic viscosity [η]_D decreased on deprotection, in part due to the decrease in molecular weight after deprotection. Furthermore, a quantitative titration was conducted to determine the hydroxyl contents in the hydroxyl copolyesters by a nonaqueous hydroxyl titration method. The

experimental values of hydroxyl contents are found to be in the range of 3.24–4.43 mmol/g and this is in good agreement with the theoretical values, which lie between 3.50 and 4.63 mmol/g.

Thermal analysis

The thermal properties of the copolymers were characterized by DSC and TGA under a nitrogen atmosphere. The results from these analyses are summarized in Tables 5 and 6. The glass transition temperatures (T_g) for various feed ratios of copolyester P[HS-*co*-HIT] (Table 5; Fig. 3) having lateral isopropylidene groups are found to be in the range of -22.4 to -50.3 °C. The T_g of amorphous random copolymer is usually a function of copolymer composition and commonly it is predicted by Fox equation. The experimental T_g data of tartaric acid-based copolymers are strictly not corresponding to the Fox equation; even though follow

Table 5 Thermal characterization data for copolyesters having lateral isopropylidene groups

Copolyester	T_g (°C) ^a	T_m (°C) ^a	T_d (°C) ^b
PHS	-50.3	52.8	410.0
P[HS- <i>co</i> -HIT] 75/25	-45.0	30.8	379.4
P[HS- <i>co</i> -HIT] 50/50	-39.3	n.d.	398.8
P[HS- <i>co</i> -HIT] 25/75	-29.7	n.d.	408.7
PHIT	-22.4	n.d.	349.9
P[HA- <i>co</i> -HIT] 50/50	-44.3	n.d.	370.0
P[OS- <i>co</i> -OIT] 50/50	-47.3	n.d.	375.7
P[OA- <i>co</i> -OIT] 50/50	-48.2	19.6	345.5

^a Glass transition (T_g) and melt transition (T_m) temperatures were measured by DSC, ^b the thermal degradation temperature for maximum derivative weight loss, measured by TGA

n.d. Not detected

Table 6 Thermal characterization data for copolyesters having lateral hydroxyl groups

Copolyester	T_g (°C) ^a	T_m (°C) ^a	T_d (°C) ^b
PHS	-50.3	52.8	410.0
P[HS- <i>co</i> -HT] 75/25	-43.6	31.7	323.3
P[HS- <i>co</i> -HT] 50/50	-38.3	n.d.	355.0
P[HS- <i>co</i> -HT] 25/75	-24.0	n.d.	353.8
PHT	-8.0	n.d.	305.6
P[HA- <i>co</i> -HT] 50/50	-39.6	n.d.	305.2
P[OS- <i>co</i> -OT] 50/50	-45.9	n.d.	332.6
P[OA- <i>co</i> -OT] 50/50	n.d.	21.1	296.8

^a Glass transition (T_g) and melt transition (T_m) temperatures were measured by DSC, ^b the thermal degradation temperature for maximum derivative weight loss, measured by TGA

n.d. Not detected

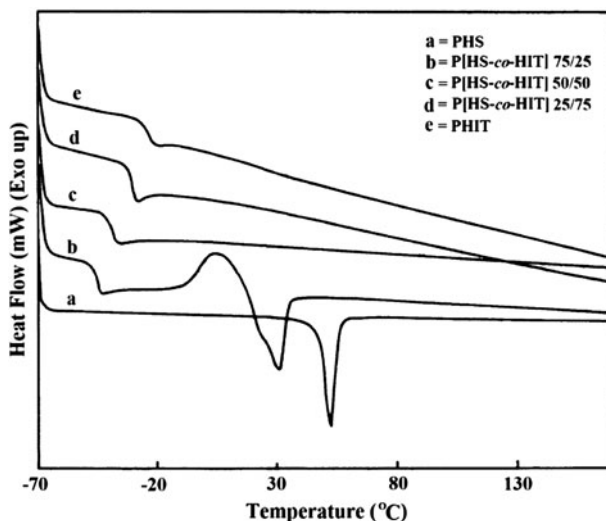


Fig. 3 DSC traces of copolyesters P[HS-co-HIT] for different feed ratios

the same trend [32]. For example, it is found that T_g increases with increasing the feed ratio of tartarate comonomer in the copolymer. The endotherms corresponding to melting transition (T_m) were observed in case of PHS and P[HS-co-HIT] 75/25 and it was found that T_m decreased as the tartarate comonomer was introduced, whereas for the other feed ratios in the copolyester P[HS-co-HIT], T_m was not observed.

The T_g for copolyesters having lateral isopropylidene groups with equal feed ratio of diesters (Table 5, see supporting information Fig. S5) were found to be in the range of -39.3 to -48.2 °C. The T_g of the copolymers decrease as the length of polymethylene chain increases suggesting increased segmental mobility in copolymer chains with increasing polymethylene chain length in the copolymer.

The T_g for the different feed ratios of copolyester P[HS-co-HT] (Table 6; Fig. 4) having lateral hydroxyl groups were found to be in the range of -8.0 to -50.3 °C and comparing the T_g of copolyesters before and after deprotection of isopropylidene groups it is found that copolyesters with lateral hydroxyl groups show slightly higher T_g , attributable to the formation of extended hydrogen bonding network from the lateral hydroxyl groups [15, 24, 33]. A T_m was observed only in the case of copolyester P[HS-co-HT] 75/25 and was found to be lower as compared to PHS but slightly higher than P[HS-co-HIT] 75/25.

The T_g for copolyesters having lateral hydroxyl groups with equal feed ratio of diesters (Table 6, see supporting information Fig. S6) are found to be in the range of -38.3 to -45.9 °C and from a comparison of the T_g of copolyesters before and after deprotection, it can be seen that copolyesters with lateral hydroxyl groups show higher T_g because of hydrogen bonding network.

The thermal stability of copolyesters was determined by TGA and the results obtained are summarized in Tables 5 and 6. The derivative weight loss traces

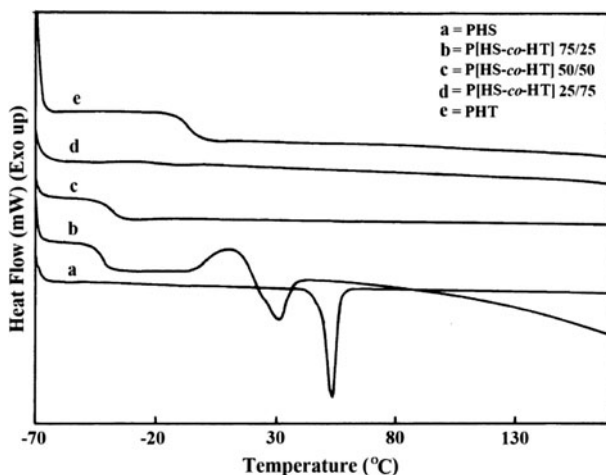


Fig. 4 DSC traces of copolyesters P[HS-*co*-HT] for different feed ratios

(dTGA) of copolyesters P[HS-*co*-HIT] and P[HS-*co*-HT] for different feed ratios are depicted in Fig. 5. It was observed that the copolyesters with lateral isopropylidene groups show higher thermal stability as compared to the copolyesters with lateral hydroxyl groups.

Hydrolytic degradation studies

The studies of hydrolytic degradation of copolyesters with different feed ratios were carried out in phosphate buffer solution (pH 7.4) at 37 °C and the degradation was followed by monitoring the molecular weight at different time intervals by GPC (Fig. 6). It was found that the hydroxyl copolyesters degrade faster as compared to isopropylidene protected copolyesters suggesting that the presence of hydroxyl groups enhance the degradability of polymer. This increase in degradation rate can be attributed to the presence of hydroxyl groups in functionalized copolyesters which improve hydrophilicity and enhance ester hydrolysis.

Conclusions

Aliphatic copolyesters were synthesized from diester derivatives of L-tartaric acid, succinic acid, adipic acid, and various alkane diols using bulk polycondensation method. The hydroxyl groups of the tartaric acid were protected and dimethyl 2,3-*O*-isopropylidene tartrate was copolymerized with dimethyl succinate and 1,6-hexane diol in different feed molar ratios. Then, a series of copolyesters were synthesized by taking equal feed molar ratio of dimethyl 2,3-*O*-isopropylidene tartrate and dimethyl succinate or dimethyl adipate with 1,6-hexane diol or 1,8-octane diol. The selective hydrolysis of isopropylidene protecting groups gave a new series of aliphatic copolyesters with pendant hydroxyl groups. The thermal

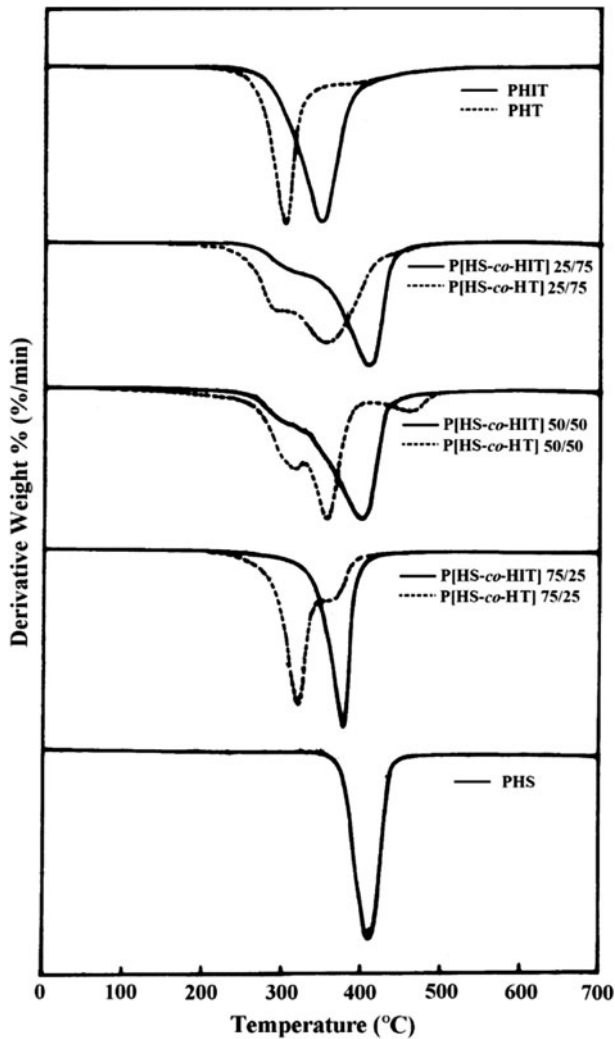


Fig. 5 dTGA traces of copolyesters P[HS-*co*-HIT] and P[HS-*co*-HT] for different feed ratios

studies of the copolymers show that the copolyesters with lateral hydroxyl groups have less thermal stability as compared to copolyesters with lateral isopropylidene groups. From the DSC measurements, it is found that T_g of the copolymers increase with increasing the amount of tartarate comonomer and T_g of copolymers decrease with increasing the length of polymethylene chain in the copolymer due to the increased segmental mobility with increasing chain length. Furthermore, it was observed that copolyesters with lateral hydroxyl groups have higher T_g as compared to copolyesters with lateral isopropylidene groups. The hydrolytic degradation studies suggest that hydroxyl-functionalized copolyesters degrade faster as compared to isopropylidene copolyesters.

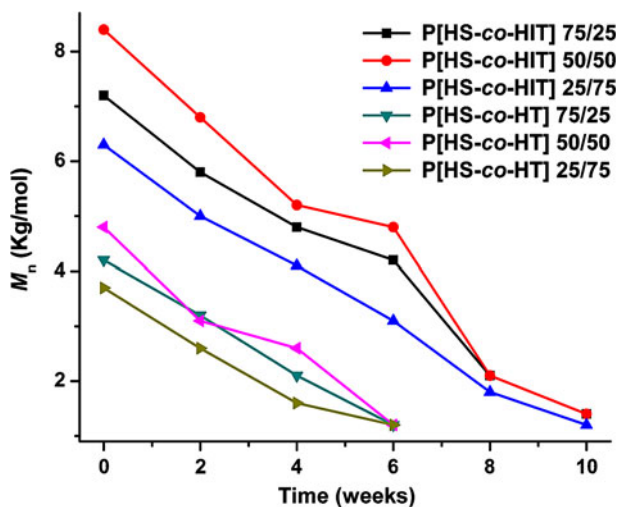


Fig. 6 Hydrolytic degradation of copolyesters at pH 7.4 at 37 °C

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