Linear Polyesters of the Poly[alkylene (and *co*-arylene) dicarboxylate] Type Derived from Carbohydrates

María de Gracia García-Martín, Rocío Ruiz Pérez, Elena Benito Hernández, and Juan Antonio Galbis*

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

Received June 14, 2006; Revised Manuscript Received September 4, 2006

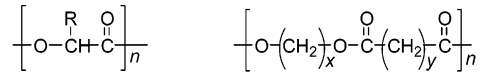
ABSTRACT: A variety of carbohydrate-based polyesters of the poly(alkylene dicarboxylate) type were obtained by polycondensation reactions of the alditols 2,3,4-tri-*O*-methyl-L-arabinitol and 2,3,4-tri-*O*-methylxylitol, and the aldaric acids 2,3,4-tri-*O*-methyl-L-arabinaric acid and 2,3,4-tri-*O*-methylxylaric acid. Butanediol and adipic acid were also used as comonomers. Co-polyesters of the poly(alkylene-*co*-arylene dicarboxylate) type were obtained using bisphenols as comonomers. Chemical polycondensation reactions were conducted in bulk or in solution. Enzymatic polycondensation reactions of adipic acid with the above-mentioned alditols were carried out successfully using Lipozyme and Novozyme 435. Depending on the chemical structure, the new polyesters were syrups, gums, or amorphous solids, and were characterized by ^{1}H and ^{13}C NMR spectroscopies, GPC, viscosimetry, and DSC measurements. The hydrolytic degradations of some of these polyesters are also described.

Introduction

Biodegradable polymers obtained from renewable natural sources are currently receiving increasing attention because they are an alternative to the traditional petroleum-based plastics.[1−3] Solid-waste management of plastics of agricultural or alimentary origin is demanding a rapid development of new biodegradable plastics.[4,5] Another important application is in biomedicine, and in this field, biocompatibility is a required feature for resorbable biomedical devices.[2,3] Biopolymers can be produced by biological systems, or chemically synthesized from biological starting materials (e.g., carbohydrates, natural fats or oils, etc.). Currently, aliphatic polyesters are considered the most economically competitive of the biodegradable polymers,[6] and synthetic polyesters are expected to be degraded nonspecifically by some enzymes, such as lipases.[2] Although such polyesters are biodegradable, they often lack good thermal and chemical properties. On the other hand, aromatic polyesters—such as PET (poly(ethylene terephthalate))—have excellent mechanical properties, but are resistant to degradation by chemical or biological agents.

Aliphatic polyesters may be classified into two groups, depending on the bond constitution of the monomers: poly(hydroxy acid)s [i.e., polyhydroxyalkanoates (PHAs)] and poly(alkylene dicarboxylate)s.[7] The former are polymers of hydroxy acids (α, *β*, ..., *ω*-hydroxy acids), obtained by ring-opening polymerization or polycondensation reactions. The latter are synthesized by the polycondensation reaction of diols with dicarboxylic acids. Depending on the mechanism of biodegradation, polyesters can also be classified broadly into two groups: those degraded by enzymatic hydrolysis, and those not degraded by enzymes, although both groups are generally susceptible, in some degree, to both kinds of hydrolysis.

It is well-known that polymers having hydrophilic moieties in their repeating units show an enhanced biodegradability. Synthetic carbohydrate-based polymers having hydrophilic groups would be excellent candidates for biomedical applications because of their inherent properties of biocompatibility and biodegradability.[3] Our earlier results on the preparation and characterization of carbohydrate-based polymers such as polyamides,[8,9] poly(vinylsaccharides),[10] and polycarbonates,[11] which showed a medium-to-high degree of hydrophilicity, let us explore an approach to the preparation of linear carbohydrate-based polyesters of the poly(alkylene dicarboxylate) and poly(alkylene-*co*-arylene dicarboxylate) type, and whose general structures are depicted in Scheme 1. The preparation of these polyesters was carried out by chemical polycondensation reactions and, in some cases, enzymatically.



Poly(α-hydroxy acid)s Poly(alkylene dicarboxylate)s

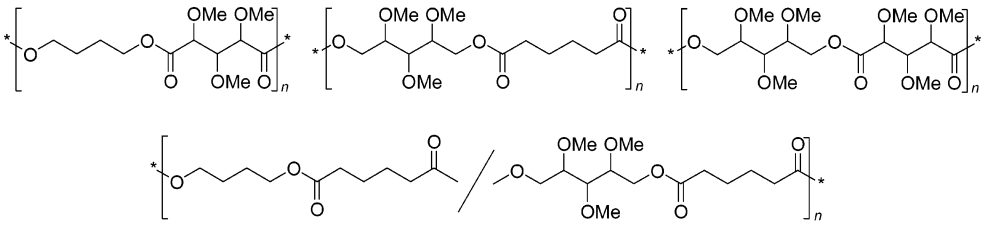
Experimental Section

General Methods. Solvents were dried and purified, when necessary, by appropriate standard procedures. Optical rotations were measured at 20 ± 5 °C (1 cm cell). Elemental analyses were determined in the Microanalysis Laboratories of the CSIC, Isla de la Cartuja, Seville, Spain. FT-IR spectra were obtained from films or KBr disks. NMR spectra were recorded with a Bruker 200 AC−P spectrometer. Ten and 30 mg of sample dissolved in 1 mL of $CDCl_3$ were used for ^{1}H and ^{13}C spectra, respectively. Chemical shifts are reported as parts per million downfield from Me_4Si. Gel permeation chromatography (GPC) analyses were carried with two Styragel HR columns (7.8 × 300 mm) placed in series, using chloroform as the mobile phase at a flow rate of 1 mL/min. Molecular weights were estimated against polystyrene standards. Intrinsic viscosity measurements were carried out in dichloroacetic acid with a Cannon-Ubbelohde 100/L30 or 150/L12 semimicroviscometer at 25.0 ± 0.1 °C. The thermal behavior of the polyesters was examined by DSC, using a Perkin-Elmer DSC-7 calibrated with indium. DSC data were obtained from samples of about 4−5 mg, at heating/cooling rates of 20 °C/min or 10 °C/min depending on the purpose, and under a nitrogen flow. Hydrolytic degradation experiments were carried out on films prepared by casting at room temperature from a 5% (w/v) solution in dichloromethane. Films (100−200 *μ*m in thickness) were separately submerged in one of the following buffers: 0.1 M Na_2HPO_4/KH_2PO_4 (pH 7.4) or 0.1 M H_3PO_4/0.1 M NaCl (pH 4.0). Hydrolysis was carried out by incubation at 37,

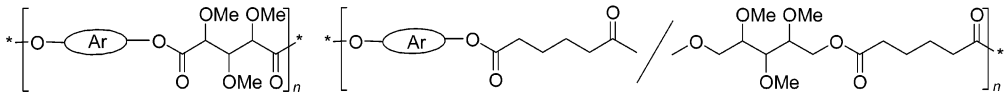
* Corresponding author. E-mail: jgalbis@us.es.

10.1021/ma061325o CCC: $33.50
Published on Web 10/17/2006

Scheme 1. Carbohydrate-Based Polyesters

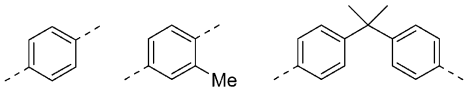


Carbohydrate-based polyesters of the poly(alkylene dicarboxylate) type

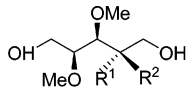


Carbohydrate-based polyesters of the poly(arylene dicarboxylate) type and poly(alkylene-co-arylene dicarboxylate) type

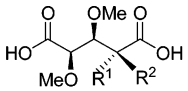
Sugar Moiety Configuration: L-*Arabino* or *Xylo*



Scheme 2. Carbohydrate Monomers for Polycondensation Reactions



Alditol	R^1	R^2
1Ar, L-Arabinitol	OMe	H
1Xy, Xylitol	H	OMe



Aldaric acid	R^1	R^2
2Ar, L-Arabinaric	OMe	H
2Xy, Xylaric	H	OMe

60, or 80 °C, and samples were taken at selected time points. The recovered samples were washed with distilled water, and dried to constant weight in a vacuum. The evolution of degradation was followed by sample weighing and GPC analysis.

Preparation of Polyesters. General Methods. Method A. Catalytic Polymerization of 2,3,4,-Tri-*O*-methyl-L-arabinitol (1Ar) and Butanediol with Adipic Acid. To a stirred mixture of **1Ar** (1.0 mmol), butanediol (1.0 mmol), and adipic acid (2.0 mmol) was added, under argon, titanium(IV) isopropoxide (4 μL). The mixture was first heated at 140 °C for 15 min, then the temperature was slowly increased to 180 °C, and the mixture was kept at this temperature for 24 h. Then a pressure of 0.5−0.1 mmHg at 160 °C was applied to the mixture for a period of 3−4 h. The residue thus obtained was cooled (−20 °C) and treated with diethyl ether and acetone/methanol to give a solid. When the mixture was left to reach room temperature, the solid became gummy. The solvents were decanted, and the syrup was dried under vacuum.

Poly(2,3,4-tri-*O*-methyl-L-arabinitol adipate-*co*-tetramethylene glycol adipate) (PE3). IR: ν_{max} 1733 cm^{-1} (CO). ^{1}H NMR ($CDCl_3$): δ 4.65−4.60 (m, H-1, H-5), 4.39−4.01 (m, 6 H, H-1′, H-5′, 2 OCH_2), 3.70−3.33 (m, 3 H, H-2, H-3, H-4), 3.49, 3.45, 3.42 (3 s, 9H, 3 OMe), 2.40−2.30 (m, 4 H, 4 CH_2CO), 1.80−1.60 (m, 8 H, 4 CH_2). ^{13}C NMR: δ 173.3, 173.0 (CO), 79.8, 78.0 (C-2, C-3, C-4), 63.8, 63.2 (C-1, C-5, OCH_2), 60.8, 59.2, 57.9 (OMe), 33.8, 33.4 (CH_2CO), 25.3, 24.3, 24.1 (4 CH_2). Anal. Calcd for $C_{24}H_{40}O_{11}$: C, 57.30; H, 7.99. Found: C, 57.04; H, 7.67.

Method B. Reaction of 2,3,4-Tri-*O*-methylxylitol (1Xy) or 2,3,4-Tri-*O*-methyl-L-arabinitol (1Ar) with Adipoyl Chloride. A solution of the corresponding alditol **1Xy** or **1Ar** (194 mg, 1.0 mmol) in freshly distilled nitrobenzene (1.5 mL) was bubbled with argon for 15 min, then heated to 100 °C, and adipoyl chloride (0.15 mL, 1.0 mmol) was added. The reaction mixture was heated at 140 °C for 4 h and at 120 °C overnight, keeping up a stream of argon in order to eliminate the hydrogen chloride formed. Then the pressure was reduced to 0.5−0.1 mmHg to remove the solvent, the residue was diluted with dichloromethane (5 mL), and the solution was added dropwise with stirring into diethyl ether (200 mL). When oily or gummy polymers were obtained, the solvents were decanted, and the residues dried under vacuum. In the case of the solids, they were filtered off, and dried under vacuum.

Copolymerizations with butanediol or bisphenols were carried out as described above in the ratio alditol/(butanediol or bisphenol)/adipoyl chloride 1:1:2.

Poly(2,3,4-tri-*O*-methyl-L-arabinitol adipate-*co*-tetramethylene glycol adipate) (PE3). IR: ν_{max} 1733 cm^{-1} (CO). ^{13}C NMR ($CDCl_3$): δ 172.8, 172.6, 172.5 (CO), 79.1, 77.4 (C-2, C-3, C-4), 63.4, 62.6, 61.2 (C-1, C-5, OCH_2), 60.4, 58.8, 57.4 (OMe), 33.4 (CH_2CO), 24.8 (CH_2), 23.9 (CH_2). Anal. Calcd for $C_{24}H_{40}O_{11}$: C, 57.30; H, 7.99. Found: C, 57.13; H, 8.02.

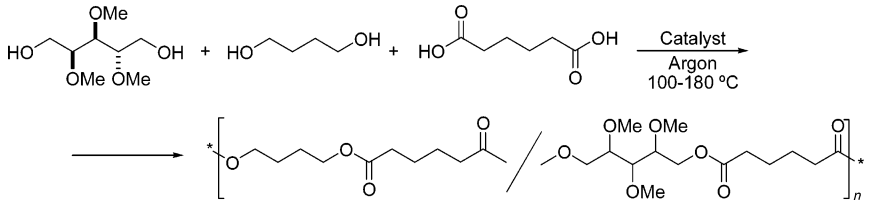
Poly(2,3,4-tri-*O*-methyl-L-arabinitol adipate) (PE4). IR: ν_{max} 1734 cm^{-1} (CO). ^{1}H NMR ($CDCl_3$): δ 4.66−4.57 (m, 2 H, H-1, H-5), 4.39−4.03 (m, 2 H, H-1′, H-5′), 3.69−3.20 (m, 3 H, H-2, H-3, H-4), 3.49, 3.45, 3.42 (3s, 9 H, 3 OMe), 2.45−2.31 (m, 4 H, 2 CH_2CO), 1.77−1.64 (m, 4 H, 2 CH_2). ^{13}C NMR: δ 173.6, 172.9 (CO), 79.8, 78.1 (C-2, C-3, C-4), 63.3, 61.9 (C-1, C-5), 60.8, 59.3, 57.9 (OMe), 33.8, 24.3 (CH_2). Anal. Calcd for $C_{14}H_{24}O_7$: C, 55.25; H, 7.95. Found: C, 54.55; H, 7.66.

Poly(2,3,4-tri-*O*-methylxylitol adipate) (PE5). IR: ν_{max} 1735 (CO) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 4.30 (dd, 2 H, $J_{1,2} = J_{4,5}$ 4.3 Hz, $J_{1,1'} = J_{5,5'}$ 11.8 Hz, H-1, H-5), 4.15 (dd, 2 H, $J_{1',2} = J_{4,5'}$ 6.0 Hz, $J_{1,1'}$ $J_{5,5'}$ 11.8 Hz, H-1′, H-5′), 3.45 (m, 3 H, H-2, H-3, H-4), 3.47 (s, 3 H, OMe), 3.42 (s, 6 H, 2 OMe), 2.35 (m, 4 H, 2 CH_2CO), 1.65 (m, 4 H, 2 CH_2). ^{13}C NMR: δ 172.9 (CO), 80.0, 78.3 (C-2, C-3, C-4), 63.5 (C-1, C-5), 60.3, 58.7 (OMe), 33.7, 24.2 (CH_2). Anal. Calcd for $C_{14}H_{24}O_7 \cdot H_2O$: C, 55.25; H, 7.95. Found: C, 54.75; H, 7.64.

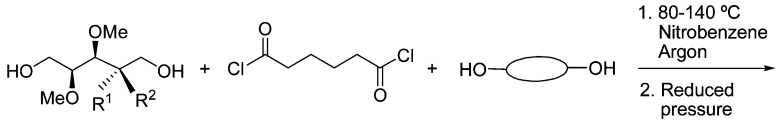
Poly(2,3,4-tri-*O*-methyl-L-arabinitol adipate-*co*-1,4-phenylene adipate) (PE6). IR: ν_{max} 1749 cm^{-1} (CO). ^{1}H NMR ($CDCl_3$): δ 7.07 (s, 4 H, aromatic), 4.70−3.95 (m, 4 H, H-1, H-1′, H-5, H-5′), 3.64−3.20 (m, 12 H, H-2, H-3, H-4, 3 OMe), 2.70−2.24 (m, 4 H, 2 CH_2CO), 1.94−1.46 (m, 4 H, 2 CH_2). ^{13}C NMR: δ 173.6, 172.8, 171.5, 168.8 (CO), 174.9 (aromatic), 122.3 (aromatic), 79.5, 77.8 (C-2, C-3, C-4), 63.6, 61.6 (C-1, C-5), 60.8, 59.2, 57.8 (OMe), 34.7, 33.8, 33.7, 24.1, 23.9, 23.4, 23.2 (CH_2). Anal. Calcd for $C_{26}H_{36}O_{11} \cdot H_2O$: C, 57.56; H, 7.06. Found: C, 57.60; H, 6.5.

Poly(2,3,4-tri-*O*-methylxylitol adipate-*co*-1,4-phenylene adipate) (PE7). IR: ν_{max} 1749 (CO) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.00 (s, 4 H, aromatic), 4.25 (m, 4 H, H-1, H-1′, H-5, H-5′), 3.50 (m, 3 H, H-2, H-3, H-4), 3.49 (s, 3 H, OMe), 3.43 (s, 6H, 2 OMe), 2.60 (m, 2 H, CH_2CO), 2.45 (m, 2H, CH_2CO), 1.75 (m, 4 H, 2 CH_2). ^{13}C NMR: δ 173.0, 171.6 (CO), 147.9, 122.4 (aromatic), 79.9, 78.3 (C-2, C-3, C-4), 63.5 (C-1, C-5), 60.5, 58.7 (OMe), 33.8, 33.7,

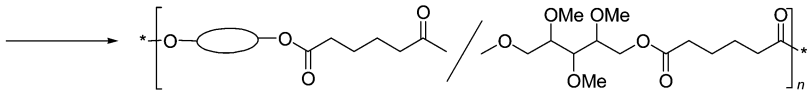
Scheme 3. Method A: Catalytic Synthesis of Co-Polyester PE3 from 1Ar and Butanediol with Adipic Acid



Scheme 4. Method B: From 1Ar and 1Xy and Diols or Bisphenols with Adipoyl Chloride in Solution



1Ar, R^1 = OMe, R^2 = H (L-*Arabino)*
1Xy, R^1 = H, R^2 = OMe (*Xylo)*



Polyester[a]	Sugar Configuration	HO—⬭—OH
PE3	L-*Arabino*	Butanediol
PE4	L-*Arabino*	———
PE5	*Xylo*	———
PE6	L-*Arabino*	Hydroquinone
PE7	*Xylo*	Hydroquinone
PE8	L-*Arabino*	Methyl-hydroquinone
PE9	*Xylo*	Methyl-hydroquinone
PE10	L-*Arabino*	Bisphenol A
PE11	*Xylo*	Bisphenol A

[a]For **PE3**, **PE6-PE11**, the monomer ratio Sugar-Diol-Adipoyl chloride was 1:1:2

24.2 (CH_2). Anal. Calcd for $C_{26}H_{36}O_{11} \cdot 0.1\ H_2O$: C, 59.34; H, 6.88. Found: C, 59.00; H, 6.69.

Poly[2,3,4-tri-*O*-methyl-L-arabinitol adipate-*co*-1,4-(methylphenylene) adipate] (PE8). IR: ν_{max} 1735 cm^{-1} (CO). ^1H NMR ($CDCl_3$): δ 7.07−6.80 (m, 3 H, aromatic), 4.73−3.98 (m, 4 H, H-1, H-1′, H-5, H-5′), 3.73−3.22 (m, 3 H, H-2, H-3, H-4), 3.50, 3.46, 3.43 (3 s, 9 H, 3 OMe), 2.73−2.29, (m, 4 H, 2 CH_2CO), 2.16 (s, 3 H, Me), 1.97−1.58 (m, 4 H, 2 CH_2). ^{13}C NMR: δ 173.0, 171.7, 171.3 (CO), 148.0, 146.7 (aromatic), 131.4 (aromatic), 123.8, 122.6, 122.5 (aromatic), 79.6, 78.0 (C-2, C-3, C-4), 63.2, 61.9 (C-1, C-5), 60.8, 59.2, 57.9 (OMe), 33.7, 33.4 (CH_2CO), 24.1, 24.0 (CH_2), 16.3 (Me). Anal. Calcd for $C_{27}H_{38}O_{11} \cdot 0.5\ H_2O$: C, 59.22; H, 7.18. Found: C, 58.73; H, 7.10.

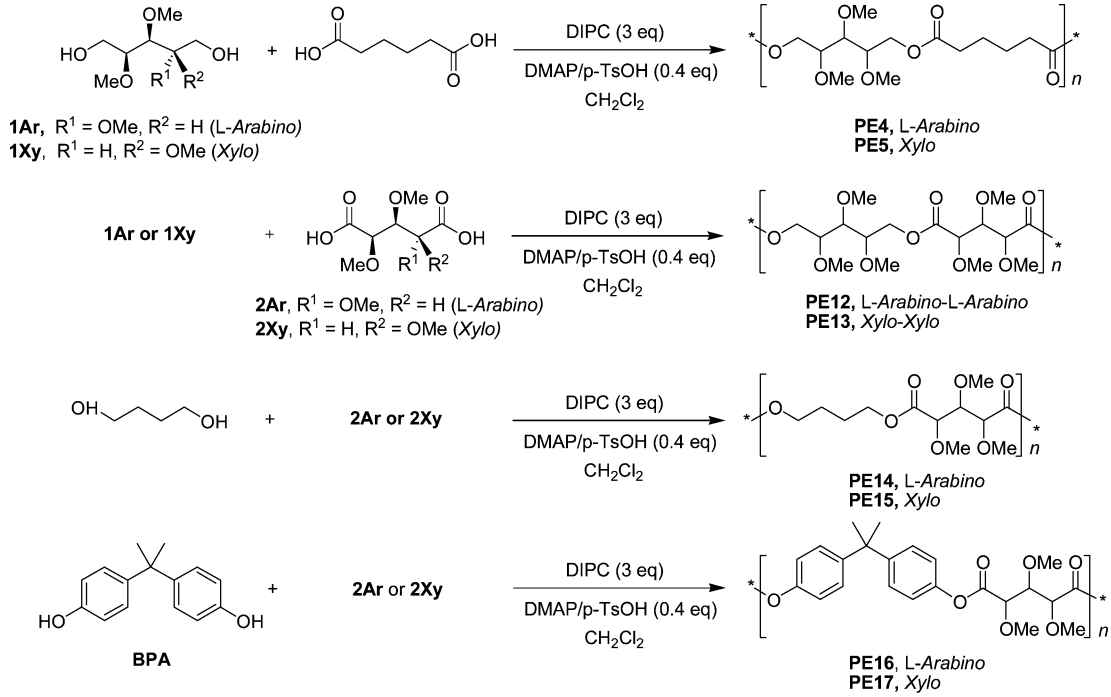
Poly[2,3,4-tri-*O*-methylxylitol adipate-*co*-1,4-(methylphenylene) adipate] (PE9). IR: ν_{max} 1735 (CO) cm^{-1}. ^1H NMR ($CDCl_3$): δ 6.95 (m, 3 H, aromatic), 4.25 (ddd, 2 H, $J_{1,2} = J_{4,5}$ 4.0 Hz, $J_{1,1'} = J_{5,5'}$ 11.8 Hz, H-1, H-5), 4.17 (ddd, 2 H, $J_{1',2} = J_{4,5'}$ 6.0 Hz, $J_{1,1'} = J_{5,5'}$ 11.8 Hz, $J_{1',3} = J_{3,5'}$ 3.1 Hz, H-1′, H-5′), 3.60 (m, 2 H, H-2, H-4), 3.49 (s, 3 H, OMe), 3.43 (s, 6 H, 3 OMe), 3.35 (m, 1 H, H-3), 2.60 (m, 2 H, CH_2CO), 2.35 (m, 2 H, CH_2CO), 2.13, 2.12 (2 s, 3 H, Me), 1.75 (m, 4 H, $2CH_2$). ^{13}C NMR: δ 172.9, 171.6, 171.3 (CO), 147.9, 146.6, 131.4, 123.8, 122.6, 119.7 (aromatic), 80.0, 78.4 (C-2, C-3, C-4), 63.5 (C-1, C-5), 60.4, 58.7 (OMe), 33.8, 33.7, 24.2 (CH_2), 16.3 (Me). Anal. Calcd for $C_{27}H_{38}O_{11}$: C, 60.00; H, 7.04. Found: C, 59.91; H, 6.83.

Poly(2,3,4-tri-*O*-methyl-L-arabinitol adipate-*co*-4,4′-isopropylidenediphenol adipate) (PE10). IR: ν_{max} 1736 cm^{-1} (CO). ^1H NMR ($CDCl_3$): δ 7.29−7.19 (m, 4 H, aromatic), 7.03−6.94 (m, 4 H, aromatic), 4.68−4.59 (m, 2 H, H-1, H-5), 4.43−4.04 (m, 2 H, H-1′, H-5′), 3.71−3.29 (m, 3 H, H-2, H-3, H-4), 5.35, 3.46, 3.43 (3 s, 9 H, 3 OMe), 2.67−2.34 (m, 4 H, 2 CH_2CO), 1.93−1.62 (m, 4 H, 2 CH_2), 1.67 (s, 6 H, CMe_2). ^{13}C NMR: δ 173.1, 172.9, 171.8 (CO), 148.6, 147.8 (aromatic), 127.8, 120.9, 114.8 (aromatic), 79.8, 78.0 (C-2, C-3, C-4), 63.2 (C-1, C-5), 60.8, 59.2, 57.8 (OMe), 42.5 (CMe_2), 34.0, 33.8 (OC−CH_2), 30.9 (CMe_2), 24.3 (CH_2). Anal. Calcd for $C_{35}H_{46}O_{11}$: C, 65.21; H, 7.14. Found: C, 64.84; H, 6.84.

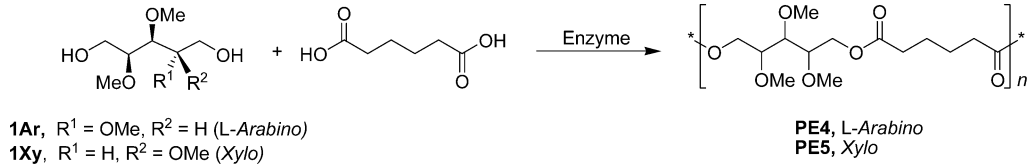
Poly(2,3,4-tri-*O*-methylxylitol adipate-*co*-4,4′-isopropylidenediphenol adipate) (PE11). IR: ν_{max} 1736 (CO) cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.20 (m, 4 H, aromatic), 6.95 (m, 4 H, aromatic), 4.30 (ddd, 2 H, $J_{1,2} = J_{4,5}$ 4.3 Hz, $J_{1,1'} = J_{5,5'}$ 11.8 Hz, $J_{1,3} = J_{3,5}$ 2.6 Hz, H-1, H-5), 4.20 (ddd, 2 H, $J_{1',2} = J_{4,5'}$ 6.0 Hz, $J_{1,1'} = J_{5,5'}$ 11.8 Hz, $J_{1',3} = J_{3,5'}$ 2.4 Hz, H-1′, H-5′), 3.60 (m, 2 H, H-2, H-4), 3.49 (s, 3 H, OMe), 3.43 (s, 6 H, 2 OMe), 3.35 (m, 1 H, H-3), 2.60 (m, 2 H, CH_2CO), 2.35 (m, 2 H, CH_2CO), 1.75 (m, 4 H, 2 CH_2), 1.63 (s, 6 H, CMe_2). ^{13}C NMR: δ 173.0, 171.8 (CO), 148.5, 147.8, 127.8, 120.8 (aromatic), 80.0, 78.4 (C-2, C-3, C-4), 63.5 (C-1, C-5), 60.4, 58.7 (OMe), 42.4 (CMe_2), 33.9, 33.7, 24.2 (CH_2), 30.9 (CMe_2). Anal. Calcd for $C_{35}H_{46}O_{11}$: C, 65.21; H, 7.14. Found: C, 65.62; H, 7.03.

Method C. Polymerization of Aliphatic Diols or Bisphenol A and Pentitols (1Xy and 1Ar) with Adipic Acid or Aldaric Acids in Solution, in the Presence of Condensing Agents. To a stirred solution of adipic acid or the aldaric acid **2Xy** or **2Ar** (1.5 mmol) and the pentitol **1Xy** or **1Ar** (1.5 mmol) or the corresponding diol or bisphenol A (1.5 mmol) in dichloromethane (5 mL) were added, under argon, *N*,*N*-(dimethylamino)pyridine-*p*-toluenesulfonic acid (374 mg, 1.12 mmol) and *N*,*N*′-diisopropylcarbodiimide (1.17 mL, 7.5 mmol), and the mixture was stirred for 3 days. Then the reaction mixture was diluted with dichloromethane, the solids were filtered off and washed with dichloromethane, and the filtrate was

Scheme 5. Method C: From Alditols 1Ar and 1Xy with Adipic Acid, Pentitols with Aldaric Acids 2Ar and 2Xy, Butanediol and Aldaric Acids, and Bisphenol-A (BPA) and Aldaric Acids in Solution, in the Presence of Condensing Agents



Scheme 6. Method D: Enzymatic Synthesis of PE4 and PE5 with Lipozyme and Novozyme 435, in Diphenyl Ether or in Bulk, Respectively



evaporated to dryness. The residue was treated with diethyl ether, filtered, and dried under vacuum.

Poly(2,3,4-tri-*O*-methyl-L-arabinitol adipate) (PE4). FT-IR and ^{1}H and ^{13}C NMR spectra were identical to those of **PE4** obtained by method B.

Poly(2,3,4-tri-*O*-methylxylitol adipate) (PE5). FT-IR and ^{1}H and ^{13}C NMR spectra were identical to those of **PE5** obtained by method B.

Poly(2,3,4-tri-*O*-methyl-L-arabinitol 2,3,4-tri-*O*-methyl-L-arabinate) (PE12). IR: ν_{max} 1749 cm^{-1} (CO). ^{1}H NMR ($CDCl_3$): ^{1}H, δ 4.89−4.03 [m, 4 H, H-1, H-1′, H-5, H-5′ (of L-arabinitol unit)], 4.00−3.25 [m, 3 H, H-2, H-3, H-4 (L-arabinitol unit), 21 H, H-2″, H-3″, H-4″ (L-arabinaric acid unit), 6 OMe]. ^{13}C NMR: δ 171.5, 170.7 (CO), 81.7, 80.6, 79.7, 79.1, 78.2 (CH), 61.0, 60.9, 59.4, 59.3, 58.4, 58.3 (OMe), 59.2, 59.1 (CH_2). Anal. Calcd for $C_{16}H_{28}O_{10}$: C, 50.52; H, 7.42. Found: C, 52.17; H, 7.57.

Poly(2,3,4-tri-*O*-methylxylitol 2,3,4-tri-*O*-methyl xylarate) (PE13). IR: ν_{max} 1741 (CO) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 4.45−3.55 (m, 10 H, rest of the protons) 3.50−3.30 (m, 18 H, 6 OMe). ^{13}C NMR: δ 170.1 (CO), 82.1, 79.4 (CH), 59.9, 59.6, 59.1, 58.7 (OMe), 64.3 (CH_2). Anal. Calcd for $C_{16}H_{28}O_{10}$: C, 50.52; H, 7.42. Found: C, 50.47; H, 7.42.

Poly(butylene glycol 2,3,4-tri-*O*-methyl-L-arabinate) (PE14). IR: ν_{max} 1741 cm^{-1} (CO). ^{1}H NMR ($CDCl_3$): δ 4.18 (m, 1 H, H-3), 4.00−3.50 (m, 6 H, H-2, H-4, 2 OCH_2), 3.42, 3.33, 3.24 (3 s, 9 H, 3 OMe), 1.07 (m, 4 H, 2 CH_2). ^{13}C NMR: δ 171.3, 170.7 (CO), 81.6, 79.2, 78.8 (C-2, C-3, C-4), 64.4 (OCH_2), 60.1, 59.2, 58.2 (OMe), 25.1, 25.0 (CH_2). Anal. Calcd for $C_{12}H_{20}O_7$: C, 52.17; H, 7.30. Found: C, 52.51; H, 7.50.

Poly(butylene glycol 2,3,4-tri-*O*-methyl xylarate) (PE15). IR: ν_{max} 1739 (CO) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 4.25−4.15 (m, 3 H, H-2, H-3, H-4), 4.00−3.75 (m, 4 H, 2 OCH_2), 3.50−3.35 (m, 9 H, 3 OMe), 1.80−1.70 (m, 4 H, 2 CH_2). ^{13}C NMR: δ 170.1 (CO), 81.9, 80.9 (CH), 60.1, 59.0 (OMe), 64.3, 25.1 (CH_2). Anal. Calcd for $C_{12}H_{20}O_7$: C, 52.17; H, 7.30. Found: C, 52.48; H, 6.96.

Poly(4,4′-isopropylidenediphenol 2,3,4-tri-*O*-methyl-L-arabinate) (PE16). IR: ν_{max} 1764 cm^{-1} (CO). ^{1}H NMR ($CDCl_3$): δ 7.15 (m, 8 H, aromatic), 4.34−4.06 (m, 3 H, H-2, H-3, H-4), 3.60, 3.52, 3.49 (3 s, 9 H, 3 OMe), 1.65 (s, 6 H, CMe_2). ^{13}C NMR: δ 169.8, 169.2 (CO), 148.2, 148.1 (aromatic), 127.9, 120.6 (aromatic), 81.8, 79.6, 79.3 (C-2, C-3, C-4), 60.6, 59.5, 58.6 (OMe), 42.4 (*C*Me_2), 30.8 (C*Me*$_2$). Anal. Calcd for $C_{23}H_{26}O_7 \cdot 1.5\ H_2O$: C, 65.40; H, 6.12. Found: C, 65.68; H, 6.16.

Poly(4,4′-isopropylidenediphenol 2,3,4-tri-*O*-methyl xylarate) (PE17). IR: ν_{max} 1759 (CO) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.20 (m, 4 H, aromatic), 7.05 (m, 4 H, aromatic), 4.30 (m, 1 H, H-3), 4.15 (m, 2 H, H-2, H-4), 3.61 (s, 3 H, OMe), 3.53 (s, 6 H, 2 OMe), 1.65 (s, 6 H, CMe_2). ^{13}C NMR: δ 168.8 (CO), 148.2, 148.1, 127.9, 120.7 (aromatic), 82.2, 79.6 (C-2, C-3, C-4), 60.6, 59.4 (OMe), 42.5 (*C*Me_2), 30.9 (C*Me*$_2$). Anal. Calcd for $C_{23}H_{26}O_7 \cdot 0.5\ H_2O$: C, 65.24; H, 6.43. Found: C, 65.57; H, 6.38.

Method D. Enzymatic Synthesis of Polyesters PE4 and PE5 with B Lipase from *Candida antarctica* in Bulk, or Lipozyme in Diphenyl Ether. D1. A mixture of the corresponding pentitol (**1Ar** or **1Xy**) (97 mg, 0.5 mmol), adipic acid (73 mg, 0.5 mmol), and B lipase from *C. antarctica* (25 mg) was stirred at approximately 220 rpm, under an inert atmosphere, at 60 °C for 7 h. Then the pressure was reduced to 80 mmHg, and stirring continued for 2 days at the same temperature. Dichloromethane was added to the reaction mixture (30 mL), the enzyme was filtered off through diatomaceous earth, and the filtrate was evaporated to dryness to get a colorless residue. The ^{1}H and ^{13}C NMR spectra were identical to those of the polymers obtained with adipoyl chloride (method B).

Table 1. Yield and Some Physical Constants of Polyesters PE3−PE11

polyester	yield (%)	$[\alpha]_D$ (deg)[a]	$[\eta]_D$ (dL/g)[b]	Mw[c]	M_w/M_n[c]	T_g (deg)[d]	T_d (°C)[e]	consistency[f]
PE3	65 (40)[g]	−4.8 (−2.4)[g]	0.24 (0.1)[g]	15240 (5470)[g]	1.7 (1.5)[g]	2	190	gum
PE4	75	−3.5	0.23	12000	1.4	−17	230	gum
PE5	56	0	0.3	22700	1.5	−20	230	gum
PE6	50	−4.8[h]	0.15	15800	1.6	63	263	amorphous solid
PE7	60	0	0.14	30800	1.6	51	250	amorphous solid
PE8	68	−3.7	0.11	33200	1.6	62	250	gum
PE9	84	0	0.23	13800	1.8	54	200	gum
PE10	76	−8.2[i]	0.3	15800	1.4	11	150	gum
PE11	70	0	0.25	15750	1.5	42	270	amorphous solid

[a] *c* 0.5, dichloromethane, at 25 °C. [b] In dichloroacetic acid at 25 ± 0.1 °C. [c] By GPC against polystyrene standards, using chloroform as a mobile phase. [d] Glass transition temperature measured by DSC. [e] Decomposition temperature measured by DSC. [f] At room temperature. [g] Prepared by Method A. [h] *c* 0.5, dichloromethane-methanol, at 25 °C. [i] *c* 1, dichloromethane, at 25 °C.

Table 2. Yield and Some Physical Constants of Polyesters PE4, PE5, PE12-PE17

polyester	yield (%)	$[\alpha]_D$ (deg)[a]	$[\eta]_D$ (dL/g)[b]	M_w[c]	M_w/M_n[c]	T_g (°C)[d]	T_d (°C)[e]	consistency[f]
PE4	55			15200	1.3			gum
PE5	60			17700	1.6			gum
PE12	40	+10.8	0.19	25300	1.4	30	232	amorphous solid
PE13	70	0	0.13	25600	1.5	12	220	amorphous solid
PE14	65	+56.3	0.13	6500	1.4	−12	250	gum
PE15	60	0	0.13	9600	1.3	−10	212	gum
PE16	70	+46.3	0.19	8700	1.1	86	250	amorphous solid
PE17	80	0	0.16	12500	1.5	70	260	amorphous solid

[a] *c* 0.5, dichloromethane, at 25 °C. [b] In dichloroacetic acid at 25 ± 0.1 °C. [c] By GPC against polystyrene standards, using chloroform as a mobile phase. [d] Glass transition temperature measured by DSC. [e] Decomposition temperature measured by DSC. [f] At room temperature.

Table 3. Compared Yields, Molecular Weights,[a] and Polydispersities[a] of Polyesters 4 and 5

	method B			method C			method D[b,c]		
polyester	yield (%)	M_w	M_w/M_n	yield (%)	M_w	M_w/M_n	yield (%)	M_w	M_w/M_n
4	75	9500	1.5	75	15200	1.3	65[b]	11400[b]	1.1[b]
							73[c]	11500[c]	1.9[c]
5	85	22700	1.5	80	17700	1.6	70[b]	13700[b]	1.2[b]
							72[c]	7250[c]	1.2[c]

[a] Determined by GPC using chloroform as a mobile phase. [b] Lipozyme immobilized from *M. miehei* (Lipozyme) in diphenyl ester, at 37 °C and 1 mmHg. [c] Lipase from *C. antarctica* (Novozyme 435) in bulk at 60 °C and 90 mmHg.

D2. To a solution of the corresponding alditol (291 mg, 1.5 mmol) and adipic acid (249.2 mg, 1.5 mmol) in diphenyl ether (2.5 mL) was added Lipozyme IM (250 mg), and the mixture was stirred, at approximately 600 rpm, for 24 h at 37 °C under an inert atmosphere. Then the pressure was reduced to 1 mmHg, and stirring continued for 3 days. Finally, the mixture was diluted with dichloromethane, the enzyme was filtered off through diatomaceous earth and washed with this same solvent, and the filtrates were evaporated to dryness to get a sticky colorless residue, which was characterized by NMR and GPC. The ^{1}H and ^{13}C NMR spectra were identical to those of the polymers obtained with adipoyl chloride (method B).

Poly(2,3,4-tri-*O*-methyl-L-arabinitol adipate) (PE4). FT-IR and ^{1}H and ^{13}C NMR spectra were identical to those of **PE4** obtained by method B.

Poly(2,3,4-tri-*O*-methylxylitol adipate) (PE5). FT-IR and ^{1}H and ^{13}C NMR spectra were identical to those of **PE5** obtained by method B.

Results and Discussion

Aromatic co-polyesters of the polyethylene- and polybutyleneterephthalate (PET and PBT) type have recently been synthesized in our group starting from the alditols 2,3,4-tri-*O*-methyl-L-arabinitol (**1Ar**) and 2,3,4-tri-*O*-methylxylitol (**1Xy**).[12,13] We now present the synthesis and characterization of different types of linear polyesters based on the alditols **1Ar** and **1Xy** and the aldaric acids 2,3,4-tri-*O*-methyl-L-arabinaric acid (**2Ar**) and 2,3,4-tri-*O*-methylxylaric acid (**2Xy**) (Scheme 2). We had previously described the preparation of these monomers.[8]

Four different methods were employed for the preparation of the new polyesters (Schemes 3−6).

Method A (Scheme 3) consisted of the catalytic polymerization of L-arabinitol (**1Ar**) and butanediol with adipic acid. The best results were obtained when titanium(IV) tetraisopropoxide was used as catalyst. To evaluate the feasibility of this method, we carried out the polymerization of adipic acid with butanediol in the presence of that catalyst, and a polyester was obtained with physical features and yield similar to those of the one described in the literature.[14] However, when L-arabinitol **1Ar** was employed as monomer or comonomer, lower yields were obtained. Thus, **PE3** was obtained in 40% yield and an average molecular weight (M_w) of 5500 g/mol and M_w/M_n 1.5. Using **1Ar** as the sole diol monomer, the polymer was obtained in very low yield—approximately 11%—and was isolated in the form of a dark gum. From monomer **1Xy**, this procedure gave unsuccessful results, probably due to this alditol's lower thermal stability. These results let us to explore milder polycondensation procedures.

In method B, the alditols **1Ar** or **1Xy** were made to react with adipoyl chloride, in nitrobenzene as solvent, under an inert atmosphere and at temperatures ranging from 80 to 140 °C; finally, a reduced pressure of approximately 0.5−0.1 mmHg was applied to the reaction mixture. Butanediol and bisphenols such as hydroquinone, methylhydroquinone, and 4-(2-(4-hydroxyphenyl)propan-2-yl)phenol (bisphenol A, BPA) were also used as comonomers. Some data corresponding to the polyesters **PE3-11** obtained by this method are collected in Table 1.

The yields of the PEs obtained by method B were in the range 50−84%. The M_w of the fully aliphatic polyesters ranged from 12000 to 15000, and M_w/M_n was 1.5−1.7. Higher M_w were

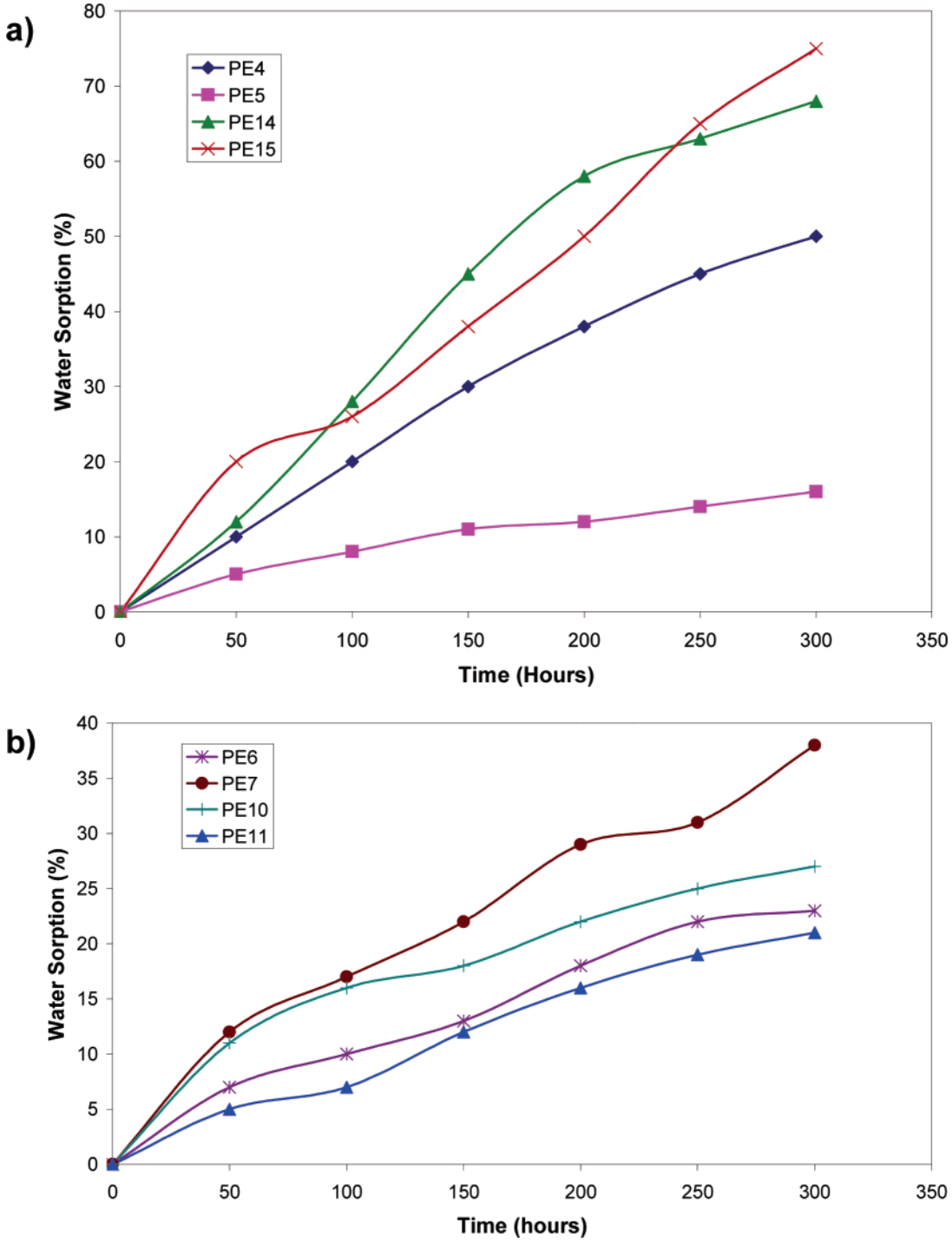


Figure 1. Moisture sorption of selected homopolyesters (a) and copolyesters (b) as a function of time at room temperature and under 100% relative humidity.

obtained for co-polyesters having bisphenol repeating units. As expected, polyesters based on L-arabinitol displayed optical activity, whereas the xylitol-based ones were optically inactive due to the symmetry of the sugar monomer.

The molar composition of co-polyesters **PE3** and **PE6**−**PE11**, having two different diol moieties, was determined from ^{1}H NMR and elemental analysis. They were found to be similar to the starting molar feed ratio for alditol/diol (or bisphenol)/adipoyl chloride 1:1:2.

Method C involved the polycondensation between alditols (**1Ar** and **1Xy**) and diols with adipic acid or aldaric acids (**2Ar** and **2Xy**), using condensing agents such as diisopropylcarbodiimide and the salt of dimethylamino pyridine/*p*-toluenesulfonic acid,[15] in dichloromethane, at room temperature (Scheme 5). The advantage of this method is the direct use of dicarboxylic acids, without previous activation, and the facile manipulation of the reaction mixture. The polyesters were obtained in yields of 55−80%, with medium M_w and narrow polydispersity values. In some cases, purification of the resulting polyesters was laborious. Some features of the polyesters **PE4**, **PE5**, and **PE12**−**PE17** thus obtained are shown in Table 2.

Following two recently published reviews on the enzymatic synthesis of polyesters via polycondensation[16] or ring-opening polymerization,[17] we also tried an approach to the enzymatic synthesis of aliphatic polyesters having carbohydrate moieties. Our best results were obtained from alditols **1Ar** and **1Xy** and

Table 4. Compared Qualitative Solubilities of Polyesters[a]

solvent	PE3	PE4	PE5	PE6	PE7	PE8	PE9	PE10	PE11	PE12	PE13	PE14	PE15	PE16	PE17
water	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
Et_2O	+	±	−	−	−	−	−	+	−	−	−	−	−	−	−
EtOH	−	−	−	−	−	−	−	±	−	±	++	+	++	−	−
$CHCl_3$	++	++	++	±	++	++	++	++	++	++	++	++	++	++	++
acetone	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
DMSO	++	++	++	+	+	+	+	+	+	++	++	+	++	++	+
DMF	++	++	++	++	++	++	++	++	++	++	++	++	++	++	+
DCA	++	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HFP	++	++	+	++	+	++	++	++	+	++	+	++	+	++	+
TFE	++	++	++	++	++	+	+	+	++	+	++	++	++	++	++

[a] Key: (−) insoluble; (±) soluble on warming at 50−60 °C; (+) soluble; (++) very soluble at room temperature. HFP: hexafluoro-2-propanol. TFE: 2,2,2-trifluoroethanol.

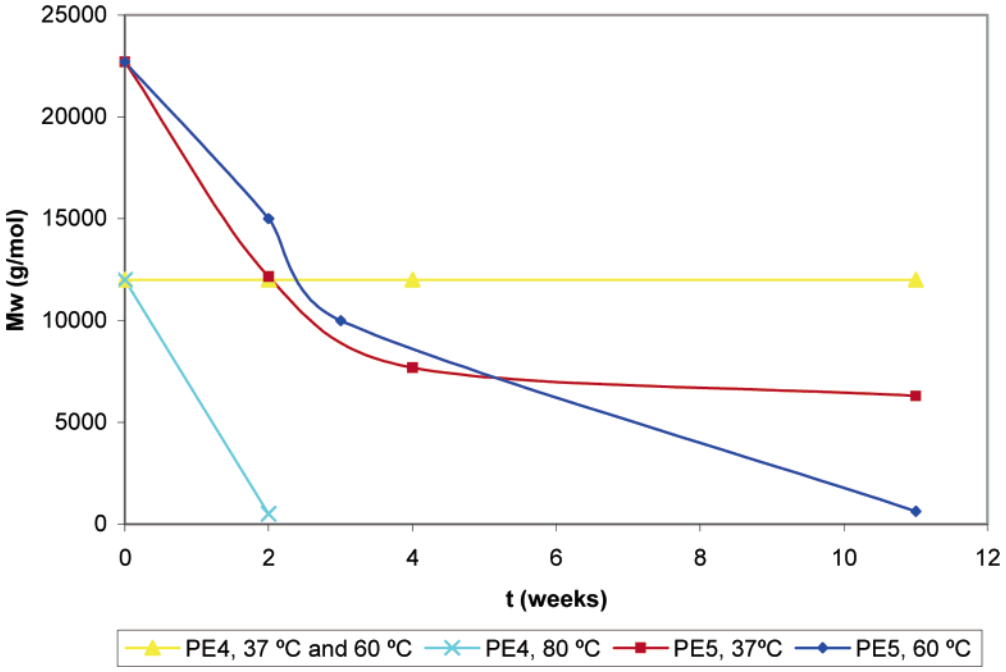


Figure 2. Hydrolytic degradation of **PE4** and **PE5** at pH 7.4 and different temperatures.

adipic acid, with Lipozyme (immobilized lipozyme from *Mucor miehei*) in diphenyl ether, and Novozyme 435 (lipase from *C. antarctica*) in bulk. Polyesters **PE4** and **PE5** thus obtained showed M_w between 7250 and 13700, and the highest polydispersity was 1.9 (Scheme 6). Compared results for the synthesis of polyesters **PE4** and **PE5** by three different methods are collected in Table 3. Attempts at enzymatic polycondensation reactions between diols or alditols with aldaric acids gave unsuccessful results.

All the polyesters here described were soluble in chloroform and polar aprotic solvents, and proved to be hygroscopic materials (Figure 1). The qualitative solubilities determined are compared in Table 4.

Thermal Analysis. The consistency at room temperature of the polyesters here described varied with chemical structure from syrups or gums to amorphous solids. The thermal properties of the polyesters have been analyzed using DSC. The characteristic parameters resulting from these measurements are given in Tables 1 and 2. In general, those polyesters having a gummy consistency or being amorphous solids did not show well-defined endotherms corresponding to melting transitions. In addition, signs of decomposition were observed. The second-order thermal transitions were observed, in general, during the second heating traces after a first cycle of heating to about 100−110 °C followed by rapid cooling to −40 °C. Many well-known aliphatic polyesters (e.g. Bionolle) present low melting temperature (T_m) and negative glass transition temperature (T_g). In our case, **PE3**, **PE4**, and **PE5** were gums with T_g in the range −20 to 2 °C, and showed signs of decomposition on heating above 200 °C. Copolyesters **PE6** and **PE7**, containing hydroquinone in their repeating units, were amorphous solids with T_g about 50−60 °C. On the other hand, **PE8** and **PE9**—based on methylhydroquinone—were gums with T_g around 60 °C. **PE7-PE9** showed melting with decomposition in the range 180−260 °C. **PE10** and **PE11**—based on BPA—presented T_g

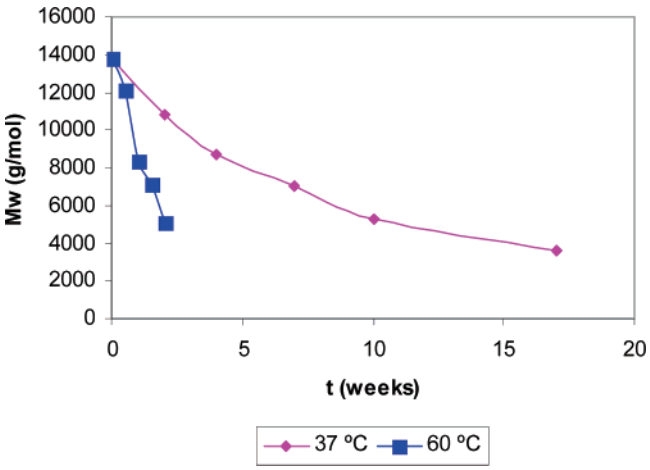


Figure 3. Hydrolytic degradation of **PE9** at pH 7.4.

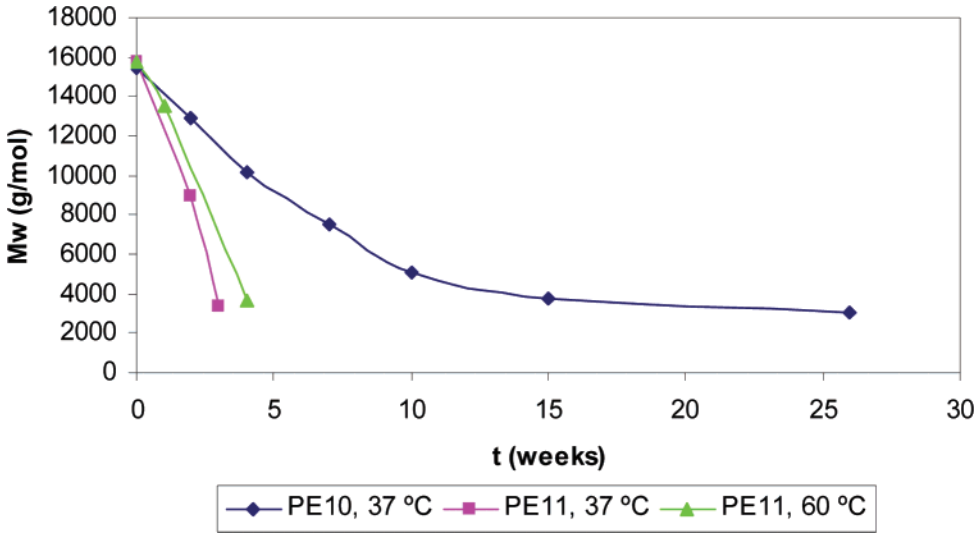


Figure 4. Hydrolytic degradation of **PE10** and **PE11** at pH 7.4 and different temperatures.

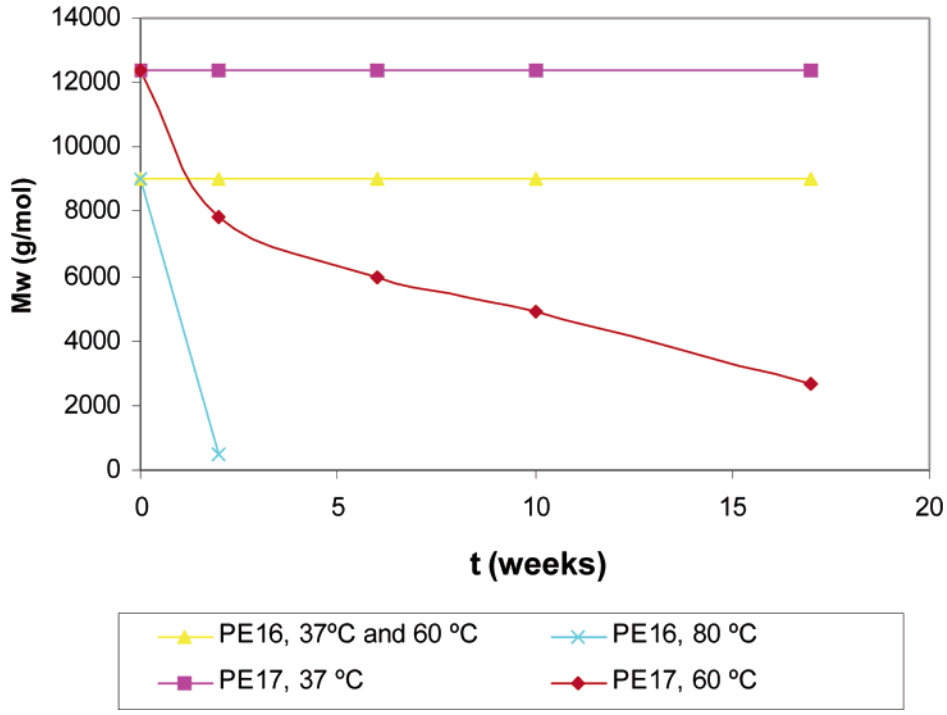


Figure 5. Hydrolytic degradation of **PE16** and **PE17** at pH 4.0 and different temperatures.

values of 11 and 42 °C, respectively, and decomposed above 150 and 270 °C.

The polyesters **PE12** and **PE13**—fully based on carbohydrates—with L-*arabino* and *xylo* configurations respectively, were amorphous solids having positive T_g values.

When butanediol was used as comonomer, the corresponding co-polyesters **PE14** and **PE15** were gums having negative T_g around −10 °C. Finally, the copolymerization with BPA gave amorphous solids with T_g in the range 70−80 °C.

Hydrolytic Degradation Studies. Studies of hydrolytic degradation of some of the polyesters here described were carried out. Thus, **PE4** and **PE5**, based on L-arabinitol and xylitol respectively, showed different behavior under the same conditions of hydrolysis. Figure 2 shows the evolution of these processes. **PE4** did not show any sign of hydrolysis at pH 7.4 and 37 or 60 °C, but a rapid hydrolysis was observed at 80 °C. On the other hand, **PE5** was degraded after incubation at neutral pH at both 37 or 60 °C: the M_w had decreased some 50% after 3 weeks.

Figure 3 displays the hydrolysis of **PE9** at pH 7.4, 37 and 60 °C. When the samples were incubated at 60 °C (6 deg higher than its T_g), the rate of hydrolysis increased, resulting in a loss of 50% of the M_w in a week, and a loss of 70% of the M_w in 2 weeks.

PE10 and **PE11**, having BPA as the repeating unit, were degraded at pH 7.4 and 37 °C (Figure 4)**. PE10** lost 85% of its M_w after 26 weeks of incubation, while the xylitol-based **PE11** showed a similar result in 3 weeks.

PE16—based on L-arabinaric acid—did not show any sign of degradation at pH 7.4 and pH 4.0, at 37 and 60 °C. However, at 80 °C (the T_g found for **PE16** was 86 °C), a rapid total hydrolysis was detected. **PE17**—based on xylaric acid—was hydrolyzed at pH 4.0 and 60 °C (T_g 70 °C), with a 50% degradation being observed after 6 weeks. These results are collected in Figure 5.

Concluding Remarks. New carbohydrate-based polyesters obtained from alditols and/or aldaric acids having L-*arabino* or *xylo* configurations have been prepared by chemical polycon-

densation reactions. The enzymatically catalyzed synthesis worked satisfactorily when we started from alditols and adipic acid, but it failed from pentaric acids. The properties of these polyesters depended on their constitution and, in general, on the configuration of the carbohydrate-based moiety. All the polyesters were soluble in the usual organic solvents, and were hygroscopic. The hydrolytic degradation studies of some of them demonstrated that they can be degraded at neutral or acid pH and at temperatures close to their respective T_g.

Acknowledgment. We thank the CICYT (Comisión Interministerial de Ciencia y Tecnología) of Spain for financial support (Grant MAT2003-06955-C02).

References and Notes

(1) Söderqvist, M.; Liu, Y.; Albertsson, A.-C.; Ranucci, E.; Karlsson, S. *Adv. Polym. Sci.* **2002**, *157*, 139−161.
(2) *Biopolymers: Biology, Chemistry, Biotechnology, Applications*; Steinbüchel, A., Series Ed.; Wiley-VCH: New York, 2002.
(3) Yokoe, M.; Aoi, K.; Okada, M. *J. Polym. Sci., Polym. Chem.* **2005**, *43*, 3909−3919.
(4) *Green Plastics*; Stevens, A. S., Ed.; Princeton University Press: Princeton, NJ, 2002.
(5) *Biodegradable Polymers and Plastics*; Vert, M., Feije, J., Albertsson, G., Scott, G., Chiellini, E., Eds.; The Royal Society of Chemistry: Cambridge, England, 1992.
(6) Mani, R.; Bhattacharya, M.; Leriche, Ch.; Nie, L.; Bassi, S. *J. Polym. Sci., Part A: Polym. Chem.* **2002**, *40*, 3232−3239 and references therein.
(7) Sudesh, K.; Doi, Y. Polydroxyalkanoates. In *Handbook of Biodegradable Polymers*; Bastoli, C., Ed.; Rapra Technology Ltd.: Shrewsbury, U.K., 2005.
(8) García-Martín, M. G.; Ruiz Pérez, R.; Benito Hernández, E.; Galbis, J. A. *Carbohydr. Res.* **2001**, *333*, 95−103.
(9) García-Martín, M. G.; Benito Hernández, E.; Ruiz Pérez, R.; Alla, A.; Muñoz-Guerra, S.; Galbis, J. A. *Macromolecules* **2004**, *37*, 5550−5556.
(10) García-Martín M. G.; Jiménez-Hidalgo, C.; Al-Kass, S. S. J.; Caraballo, I.; de Paz, M. V.; Galbis, J. A. *Polymer* **2000**, *41*, 821−826.
(11) García-Martín, M. G.; Ruiz Pérez, R.; Benito Hernández, E.; Espartero, J. L.; Muñoz-Guerra, S.; Galbis, J. A. *Macromolecules* **2005**, *38*, 8664−8670.
(12) Zamora, F.; Hakkou, K.; Alla; Espartero, J. L.; Muñoz-Guerra, S.; Galbis, J. A. *J. Polym. Sci., Part A: Polym. Chem.* **2005**, *43*, 6394−6410.
(13) Alla, A.; Hakkou, Kh.; Zamora, F.; Martínez de Ilarduya, A.; Galbis, J. A.; Muñoz-Guerra, S. *Macromolecules* **2006**, *39*, 1410−1416.
(14) Albertsson, A. C.; Ljungquist, O. *J. Macromol. Sci.—Chem.* **1986**, *A23*, 393−409.
(15) Brocchini, S.; James, K.; Tangpasuthadol, V.; Kohn, J. *J. Am. Chem. Soc.* **1997**, *119*, 4553−4554.
(16) Uyama, H.; Kobayashi, Sh. *Adv. Polym. Sci.* **2006**, *194*, 133−158.
(17) Matsumura, Sh. *Adv. Polym. Sci.* **2006**, *194*, 95−132.

MA061325O