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Synthesis of L-arabinitol and xylitol monomers for the preparation of polyamides. Preparation of an L-arabinitol-based polyamide

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Abstract

Dihydrochlorides of 1,5-diamino-1,5-dideoxy-2,3,4-tri-*O*-methyl-L-arabinitol (and xylitol) and pentachlorophenyl esters of 2,3,4-tri-*O*-methyl-L-arabinaric (and xylaric) acids have been prepared as suitable bifunctional monomers for linear polycondensations. A new aregic AABB-type L-arabinitol-based polyamide is also described from the corresponding monomers. It was crystalline with T_m 250 °C, optically active, and soluble in the usual organic solvents, including chloroform, and in water. Its M_w obtained by GPC was 27,500 with a polydispersity of 1.4.

Keywords: Bifunctional carbohydrate-based monomers; L-Arabinitol-based polyamide; Polycondensation reaction; Optically active polyamide

1. Introduction

For the last few years, we have been exploring the utility of some easily available monosaccharides to build high-molecular-weight materials with potential biocompatibility and biodegradability. Such carbohydrate-based polymers are considered useful materials for medical applications.[1] Several contributions to the synthesis of polymers derived from carbohydrate monomers have been made.[2–5] We have described a number of optically active carbohydrate-based polymers starting from D-glyceraldehyde, D-glucose, D-galactose, 2-amino-2-deoxy-D-glucose, L-arabinose and D-xylose, which were transformed into the appropriate active monomers for polymerization reactions.[6]

In this paper, we describe the preparation of the dihydrochlorides of 1,5-diamino-1,5-dideoxy-2,3,4-tri-*O*-methyl-L-arabinitol (**10A**) and 1,5-diamino-1,5-dideoxy-2,3,4-tri-*O*-methyl-xylitol (**10X**). We also describe the preparation of 2,3,4-tri-*O*-methyl-L-arabinaric acid (**11A**) and 2,3,4-tri-*O*-methyl-xylaric acid (**11X**) as well as their pentachlorophenyl ester derivatives **13A** and **13X**, respectively. Compounds **10A**, **10X**, **13A**, and **13X** are bifunctional monomers for linear polycondensations. We present the results of the polycondensation between **13A** and **10A** and the physico-chemical characterization of the resulting polyamide **14**.

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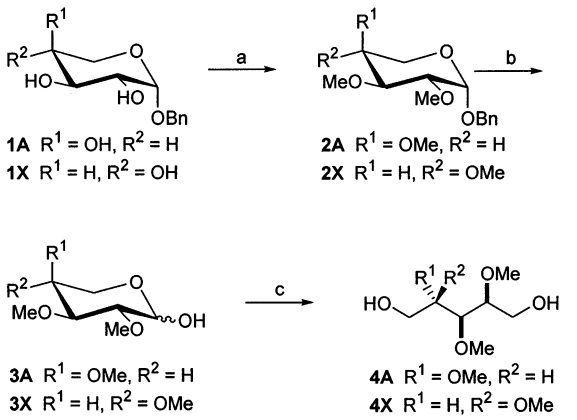
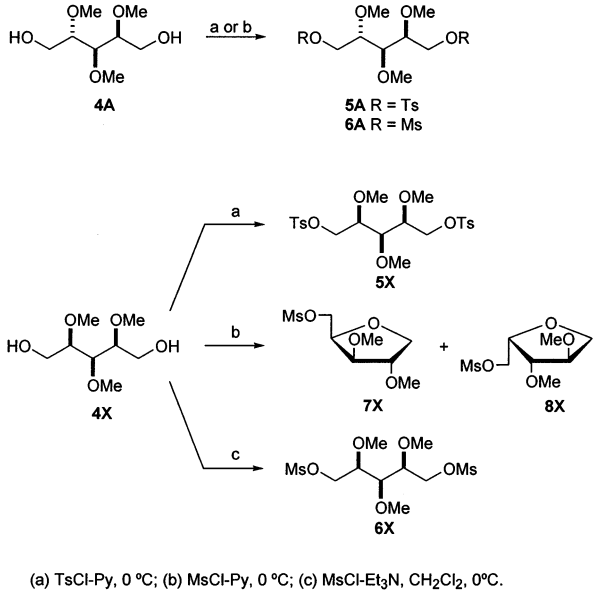
2. Results and discussion

The synthesis of diamines **10A** and **10X** was carried out from L-arabinose and D-xylose in seven steps. First, we obtained (Scheme 1) benzyl β-L-arabinopyranoside (**1A**) and benzyl α-D-xylopyranoside (**1X**) by the classical Fischer and Beensch glycoside synthesis;[7] further methylation with methyl iodide and potassium hydroxide in dimethyl sulfoxide gave **2A** and **2X**, respectively. Hydrogenolysis of the *O*-benzyl glycoside group of **2A** and **2X** gave the tri-*O*-methyl pyranosides **3A** and **3X,** in high yields. This procedure is easier than the classical method previously described.[8–10]



Scheme 1.

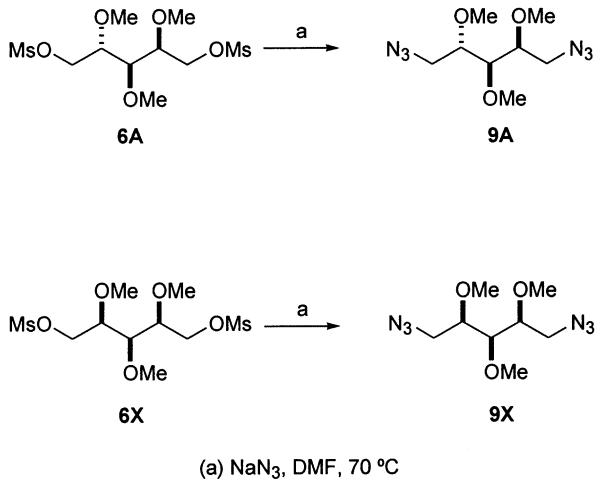


Scheme 2.

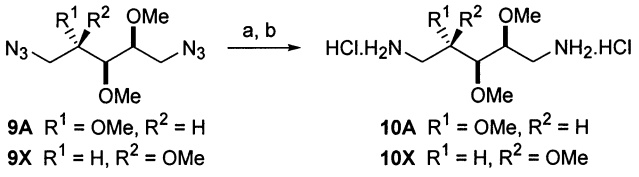
Reduction of **3A** and **3X** with sodium borohydride afforded the 1,5-diols **4A** and **4X** in excellent yields. These were transformed into the corresponding active derivatives for nucleophilic displacement with sodium azide (Scheme 2). Reaction of the primary alcohol function of **4A** and **4X** with tosyl chloride in dry pyridine at 0 °C gave the di-*O*-tosyl derivatives **5A** and **5X** in good yield. However, the two diols behaved differently with mesyl chloride in dry pyridine at 0 °C. Thus, arabinitol **4A** gave the expected di-*O*-mesyl derivative **6A** in high yield, but xylitol **4X** gave the racemic mixture of cyclic compounds **7X** and **8X** in 63% yield, after purification by column chromatography. This difference of reactivity between the two diols can be explained in terms of conformational properties of the alditol chains.[11–13] We assigned the furanoid structure to these compounds on the basis of their NMR spectra. This racemic mixture could be obtained from the meso di-*O*-mesyl derivative **6X**, previously formed, by attack either of O-4 at C-1 or of O-2 at C-5. However, when xylitol **4X** reacted with mesyl chloride in dichloromethane in the presence of triethylamine, at 0 °C, the di-*O*-mesyl xylitol derivative **6X** was obtained in 78% yield after column chromatography. This product was very unstable, and gradually became polluted by the cyclic compounds **7X** and **8X** on storing at room temperature.

The diazido derivatives **9A** and **9X** were better obtained from the corresponding mesyl derivatives **6A** and **6X** by reaction with sodium azide in dimethylformamide at 70 °C (Scheme 3). Although, formation of a small proportion of anhydroalditol derivatives was detected under these conditions, the diazido derivatives **9A** and **9X** could be isolated in good yields. The reaction of the less reactive di-*O*-tosyl derivatives **5A** and **5X** with sodium azide required higher temperature (100 °C), and higher amounts of the cyclic compounds were formed, which made the isolation of the diazido derivatives **9A** and **9X** more difficult.

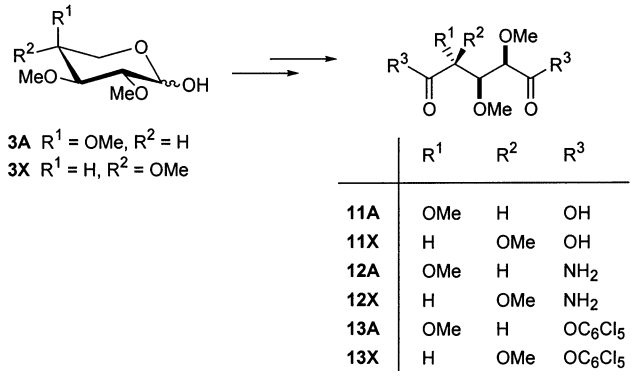
Reduction of **9A** and **9X** with lithium aluminium hydride in tetrahydrofuran followed



Scheme 3.



Scheme 4.



	R^1	R^2	R^3
11A	OMe	H	OH
11X	H	OMe	OH
12A	OMe	H	NH_2
12X	H	OMe	NH_2
13A	OMe	H	OC_6Cl_5
13X	H	OMe	OC_6Cl_5

Scheme 5.

by treatment with hydrogen chloride gave the diamine hydrochlorides **10A** and **10X** in very good yields (Scheme 4). In order to obtain **10A** and **10X**, we also tried the reduction of diamides **12A** and **12X**[14,15] with borane and with lithium aluminium hydride, but complex mixtures of products were formed in all cases.

Oxidation of **3A** and **3X** with nitric acid at 70–80 °C gave tri-*O*-methyl-L-arabinaric and tri-*O*-methyl-xylaric acids **11A** and **11X**, respectively, in very high yields (Scheme 5), both previously characterized as dimethyl esters.[14,15] The active dipentachlorophenyl esters **13A** and **13X** were easily obtained from the corresponding glycaric acid with pentachlorophenol and dicyclohexylcarbodiimide in dichloromethane.

We carried out several polycondensation reactions of the active ester **13A** with the diamine **10A** under different conditions (Table 1) to obtain the polyamide **14** (Scheme 6). The best results were obtained by using the diamine dihydrochloride and *N*-methylpyrrolidinone (NMP) as solvent and *N*-ethyl-*N*,*N*-diisopropylamine (EDPA) as a base, at 45 °C for 4 days. At room temperature, we obtained a polyamide of lower molecular weight. The synthesis of stereoregular AABB-type polyamides by condensation of a diacid with a diamine requires the existence of a twofold axis of symmetry in the monomers. Since **10A** and **13A** are asymmetric molecules, their polycondensation should lead to an aregic, non-stereoregular polyamide due to the non-regioselective additions of the monomers, which was confirmed by its ^{13}C NMR spectrum. Thus, we observed three signals (one of them double) for the carbonyl groups, corresponding to the four stereochemical possibilities for the dyads centered on the arabinaric unit (Scheme 7). The polyamide **14** was optically active, and it was soluble in the usual organic solvents, including chloroform, and very soluble in water. The thermal behavior of this polyamide was studied by differential scanning calorimetry (DSC). In all experiments, broad endotherms associated with melting appeared during the first heating cycle. Several peaks were observed in these traces, a common feature with polyamides usually interpreted as due to the fusion of several populations of different-sized crystallites.[16] When **14** was annealed at 165 °C for 3 h, it produced a trace consisting of a single peak at a higher temperature than that observed in the heating traces of the untreated samples. The melting point (T_m) of the polyamide was taken as the maximum of the peak appearing at 250 °C ($\Delta H = 39.5$ J/g). The occurrence of such a well-defined melting peak indicates the ability of **14** to produce well-formed crystallites despite the non-stere-

Table 1
Different conditions for the preparation of polyamide **14**

Diamine (**10A**)	Solvent	Temperature (°C)	Time (days)	Yield (%)	M_w [a]	M_w/M_n
Dihydrochloride	NMP (EDPA)	45	4	77	27,500	1.4
Dihydrochloride	$CHCl_3$ (EDPA)	25	2	55	11,900	1.6
Dihydrochloride	DMF (EDPA)	25	2	70	11,100	1.5
Dihydrochloride	HMPA (EDPA)	45	4	70	5100	1.4
Free base	NMP	45	5	70	1200	1.4
Free base	$CHCl_3$	25	5	30	3300	1.2

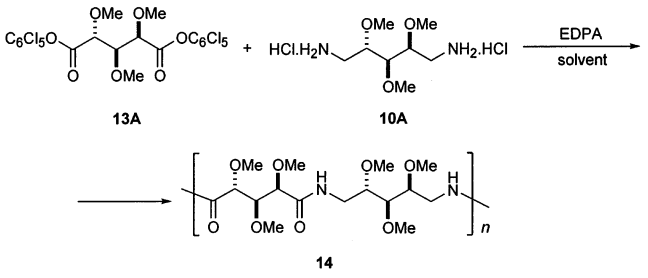
[a] Determined by GPC analysis with polystyrene standards using $CHCl_3$ as a mobile phase.

oregular microstructure anticipated for this polyamide.

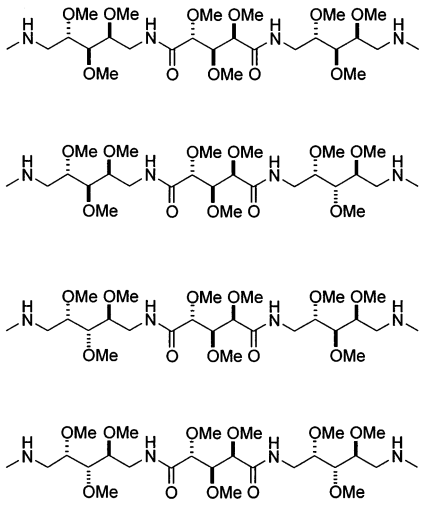
3. Experimental

General methods.—Chemicals were all used as purchased from the Aldrich Chemical Co. Solvents were dried and purified, when necessary, by appropriate standard procedures. Melting points are uncorrected. Optical rotations were measured at 20 ± 5 °C (5-cm cell). TLC was performed on Silica Gel 60 F_{254} (E. Merck) with detection by UV light or charring with H_2SO_4. Flash-column chromatography was performed using Silica Gel 60 (230–400 mesh, E. Merck). Elemental analyses were determined in the Microanalysis Laboratories at the Universidad Complutense de Madrid. FTIR spectra were obtained from films or KBr discs. For NMR spectra, chemical shifts are reported as parts per million down field from Me_4Si. Mass spectra were recorded on a Micromass AUTOSPECQ mass spectrometer equipped with a combined EI-CI source, using methane as ionizing gas. High resolution mass spectra (HRMS) (EI 70 eV) were obtained with a resolution of 10,000. Gel-permeation chromatography (GPC) analyses were carried with two styragel® HR columns placed in series, using $CHCl_3$ as solvent at a flow rate of 1 mL/min. Molecular weight studies were determined relative to polystyrene. Intrinsic viscosity measurements were determined in dichloroacetic acid (DCA) with a semi-micro-viscosimeter placed in a water bath with the temperature maintained at 25.0 ± 0.1 °C. Calorimetry measurements and thermal treatments were carried out under a nitrogen atmosphere on a DSC instrument calibrated with indium. Samples of about 2–3 mg weight were heated at a rate of 20 °C/min and cooled at different rates depending on the purpose.

*Benzyl 2,3,4-tri-*O*-methyl-β-*L*-arabinopyranoside* (**2A**).—To a solution of **1A**[7] (10.66 g, 44 mmol) in dry Me_2SO (70 mL) were added freshly powdered KOH (14.66 g, 260 mmol) and MeI (9.72 mL, 153 mmol), and the mixture was stirred at rt overnight. The solution was diluted with water (25 mL) and extracted



Scheme 6.



Scheme 7. Stereochemical possibilities for the dyads centred on the arabinaric unit.

with CH_2Cl_2 (4 × 50 mL). The combined extracts were dried (anhyd $MgSO_4$) and concentrated to give an oily residue, which was dried under diminished pressure. The residue was purified by flash-column chromatography (2:1 ether–hexane) and the title compound was isolated as a colorless oil (10.8 g, 86.3%): $[\alpha]_D$ + 208° (*c* 1, CH_2Cl_2); IR (film): *v* 3030 cm^{-1} (Ph). ^1H NMR ($CDCl_3$, 200 MHz): δ 7.19–7.03 (m, 5 H, OCH_2Ph), 4.76 (d, 1 H, $J_{1,2}$ 1.58 Hz, H-1), 4.50 (d, 1 H, *J* 12.2 Hz, OCH_2Ph), 4.35 (d, 1 H, OCH_2Ph), 3.55 (dd, 1 H, $J_{4,5}$ 2.2, $J_{5,5'}$ 12.7 Hz, H-5), 3.40 (m, 4 H, H-2, H-3, H-4, H-5′), 3.24, 3.21, 3.18 (3s, 9 H, 3 OMe); ^{13}C NMR (50 MHz): δ 136.6, 127.5, 127.1, 126.9, 126.7 (OCH_2Ph), 95.16 (C-1), 77.5, 76.8, 74.9 (C-2/C-3/C-4), 68.2 (OCH_2Ph), 58.0 (C-5), 57.8, 56.7, 56.5 (3 OMe); CIMS: *m*/*z* 283 $[M + H]^+$. Anal. Calcd for $C_{15}H_{22}O_5$: C, 63.81; H, 7.85. Found: C, 63.64; H, 7.87.

Benzyl 2,3,4-tri-O-*methyl*-α-D-*xylopyranoside* (**2X**).—A solution of **1X**[7] (10.66 g, 44.0 mmol) in dry Me_2SO was treated with MeI and KOH as described above for **2A** and the mixture was stirred at rt for 24 h. The resulting white suspension was treated with water (30 mL) and **2X** was obtained as a white solid. It was filtered, washed thoroughly with water, and finally air-dried (12.4 g, quantitative): mp 72–74 °C (from EtOH); $[\alpha]_D$ + 124.5° (*c* 0.53, $CHCl_3$); IR (KBr): *v* 3030 cm^{-1} (Ph). ^1H NMR ($CDCl_3$, 200 MHz): δ 7.30–7.20 (m, 5 H, OCH_2Ph), 4.86 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 4.70 (d, 1 H, *J* 12.2 Hz, OCH_2Ph), 4.48 (d, 1 H, OCH_2Ph), 3.65 (dd, 1 H, $J_{4,5}$ 5.6, $J_{5,5'}$ 11.0 Hz, H-5), 3.50–3.35 (m, 2 H, H-3, H-5′), 3.25–3.15 (m, 1 H, H-4), 3.10 (dd, 1 H, $J_{2,3}$ 9.4 Hz, H-2), 3.57, 3.42, 3.35 (3s, 9 H, 3 OMe); ^{13}C NMR (50 MHz): δ 136.9, 128.2, 127.9, 127.6, (OCH_2Ph), 94.5 (C-1), 82.2, 81.3, 79.6 (C-2, C-3, C-4), 68.5 (OCH_2Ph), 59.4 (C-5), 60.7, 58.7, 58.3 (3 OMe); CIMS: *m*/*z* 175 $[M - OBn]^+$. Anal. Calcd for $C_{15}H_{22}O_5$: C, 63.81; H, 7.85. Found: C, 63.75; H, 7.84.

2,3,4-Tri-O-*methyl*-L-*arabinopyranose* (**3A**).—To a solution of **2A** (8.4 g, 29 mmol) in MeOH (125 mL) was added 10% Pd–C (2.5 g) and the mixture was treated with H_2 (45 psi) for 24 h at rt. The catalyst was filtered, washed with MeOH and the filtrate concentrated to give **3A** as an oil (4.8 g, 84%). Physical constants were identical to those described.[8]

2,3,4-Tri-O-*methyl*-D-*xylopyranose* (**3X**).—A solution of **2X** (6 g, 20 mmol) in MeOH (90 mL) was hydrogenated as described for **3A** to obtain **3X** as an oil (4 g, 98%), which crystallized from ether–hexane. Physical constants were identical to those described.[9,10]

2,3,4-Tri-O-*methyl*-L-*arabinitol* (**4A**).—A solution of **3A** (7.63 g, 39.7 mmol) in 1:1 MeOH–water (75 mL) was stirred with $NaBH_4$ (751 mg, 19.8 mmol) for 4 h. The solution was treated with Dowex 50 × 8 (H^+) resin, filtered and the filtrate was repeatedly co-evaporated with MeOH and concentrated to a pure syrup, which crystallized after treatment with cold ether (5.76 g, 74.8%): mp 61–62 °C; $[\alpha]_D$ − 2° (*c* 0.56, CH_2Cl_2); IR: *v* 3400 cm^{-1} (OH); ^1H NMR ($CDCl_3$, 200 MHz): δ 3.90–3.60 (m, 4 H, H-1, H-1′, H-5, H-5′), 3.45–3.30 (m, 3 H, H-2, H-3, H-4), 3.48, 3.46, 3.40 (3s, 9 H, 3 OMe); ^{13}C NMR (50 MHz): δ 80.7, 80.5, 80.0 (C-2/C-3/C-4), 60.7, 59.4 (C-1/C-5), 60.4, 58.5, 57.4 (3 OMe); CIMS: *m*/*z* 195 $[M + H]^+$. Anal. Calcd for $C_8H_{18}O_5$: C, 49.47; H, 9.34. Found: C, 49.46; H, 9.14.

2,3,4-Tri-O-*methyl-xylitol* (**4X**).—It was prepared from **3X** (3.2 g, 16.6 mmol) as described for **4A**. The oily residue was purified by flash-column chromatography (first Et_2O, then 10:1 CH_2Cl_2–MeOH) to give **4X** as a syrup (2.94 g, 90%). IR: *v* 3400 cm^{-1} (OH); ^1H NMR ($CDCl_3$, 200 MHz): δ 3.44, (s, 3 H, OMe), 3.37 (s, 6 H, 2 OMe), 3.77–3.30 (m, rest of the protons); ^{13}C NMR (50 MHz): δ 80.6 (C-2, C-3, C-4), 62.5 (C-1, C-5), 60.0 (OMe), 57.9 (2 OMe); CIHRMS Calcd for $C_8H_{18}O_5$: 195.1232. Found: 195.1233. Anal. Calcd for $C_8H_{18}O_5 \cdot 0.3\ H_2O$: C, 48.13; H, 9.39. Found: C, 48.17; H, 9.25.

2,3,4-Tri-O-*methyl-1,5-di*-O-*tosyl*-L-*arabinitol* (**5A**).—A cold (0–5 °C) solution of **4A** (100 mg, 0.51 mmol) in dry pyridine (1 mL) was stirred with tosyl chloride (244 mg, 1.28 mmol) for 2 h. The suspension was diluted with CH_2Cl_2 and the solution washed with water, dried and concentrated to a syrup that was purified by flash-column chromatography (3:1 Et_2O–hexane). The title compound was isolated as a syrup (152 mg, 59%), $[\alpha]_D$ − 10°

(c 0.5, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.80 (dd, 4 H, C_6H_4), 7.30 (dd, 4 H, C_6H_4), 4.30 (m, 1 H, $J_{4,5}$ 2.4, $J_{5,5'}$ 10.9 Hz, H-5/H-1), 4.10 (m, 3 H, H-5′, H-1/H-5, H-1′), 3.55 (dt, 1 H, J 2.4, J 6.2 Hz, H-3/H-2), 3.40 (m, 1 H, H-4), 3.20 (m, 1 H, H-2/H-3), 3.32, 3.25, 3.20 (3s, 3 H each, OMe), 2.42 (s, 3 H, Me–C_6H_4); ^{13}C NMR (50 MHz): δ 145.0, 144.9, 132.6, 132.5, 129.9, 127.9 (C_6H_4), 78.4, 77.9, 78.8 (C-2–C-4), 67.9, 67.4 (C-1/C-5), 60.6, 59.4, 57.6 (3 OMe), 21.6 (Me–C_6H_4). Anal. Calcd for $C_{22}H_{30}O_9S_2$: C, 52.57; H, 6.01; S, 12.76. Found: C, 52.30; H, 6.03, S, 12.35.

1,5-Di-O-*mesyl*-*2,3,4-tri*-O-*methyl*-L-*arabinitol* (**6A**).—A cold (0–5 C) solution of **4A** (2.5 g, 12.9 mmol) in dry pyridine (10 mL) was stirred with mesyl chloride (3 mL, 38.6 mmol) for 1 h. The reaction mixture was diluted with water (10 mL) and extracted with CH_2Cl_2 (4×30 mL). The combined extracts were dried (anhyd $MgSO_4$) and concentrated to give **6A** as a solid (4.16 g, 92%), mp 59–61 °C (from CH_2Cl_2–hexane); $[\alpha]_D$ −8° (c 0.5, CH_2Cl_2); IR: ν 1355 and 1175 cm^{-1} (SO_2); ^{1}H NMR ($CDCl_3$, 200 MHz): δ 4.58 (dd, 1 H, $J_{4,5}$ 2.4, $J_{5,5'}$ 11.4 Hz, H-5), 4.25 (dd, 1 H, $J_{4,5'}$ 3.8 Hz, H-5′), 4.32 (ABX fragment, 2 H, H-1, H-1′), 3.68 (dt, 1 H, $J_{2,3}$ 2.6, $J_{3,4}$ 6.1 Hz, H-3), 3.53 (m, 1 H, H-4), 3.35 (m, 1 H, H-2), 3.45, 3.43, 3.40 (3s, 3 H each, 3 OMe), 3.02, 3.01 (2s, 6 H, 2 OMs); ^{13}C NMR (50 MHz), δ 78.3, 78.1 (C-2–C-4), 67.7, 67.2 (C-1/C-5), 60.7, 59.5, 57.8 (3 OMe), 37.5, 37.3 (2 OMs); CIMS: m/z 350 $[M+H]^+$. Anal. Calcd for $C_{10}H_{22}O_9S_2$: C, 34.28; H, 6.33; S, 18.30. Found: C, 33.99; H, 6.38, S, 18.01.

2,3,4-Tri-O-*methyl*-*1,5-di*-O-*tosyl*-*xylitol* (**5X**).—It was prepared from **4X** (100 mg, 0.51 mmol) as described for **5A**. The reaction mixture was concentrated to dryness and the resulting solid was treated with water (10 mL). The white solid was filtered, washed with water, Et_2O, then dried to give **5X** (242 mg, 94%), mp 121–123 °C (from EtOAc–hexane); IR: ν 1365 and 1180 cm^{-1} (SO_2); ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.75 (m, 4 H, C_6H_4), 7.32 (d, 4 H, C_6H_4), 4.15 (dd, 2 H, J 4.5, J 10.6 Hz, H-5, H-1), 4.00 (dd, 2 H, J 6.1, J 10.6 Hz H-5′, H-1′), 3.58 (dt, 2 H, J 4.4 Hz, H-2, H-4), 3.30 (m, 1 H, H-3), 3.28 (s, 6 H, 2 OMe), 3.24, (s, 3 H, OMe), 2.41 (s, 6 H, Me–C_6H_4); ^{13}C NMR (50 MHz), δ 144.9, 132.5, 129.8, 127.9 (C_6H_4), 78.3 (C-3), 77.3 (C-2, C-4), 68.9 (C-1, C-5), 59.6, 58.7 (3 OMe), 21.5 (Me–C_6H_4). Anal. Calcd for $C_{22}H_{30}O_9S_2$: C, 52.57; H, 6.01; S, 12.76. Found: C, 52.62; H, 6.12, S, 12.54.

1,5-Di-O-*mesyl*-*2,3,4-tri*-O-*methyl*-*xylitol* (**6X**).—To a cold (0–5 °C) solution of **4X** (1.06 g, 5.46 mmol) in dry CH_2Cl_2 (10 mL) was added triethylamine (1.75 mL, 12.56 mmol), then mesyl chloride (0.96 mL, 12.56 mmol) and the mixture was stirred for 1.5 h at the same temperature. The mixture was diluted with a large excess of CH_2Cl_2 (200 mL) and washed successively with a satd solution of $NaHCO_3$ and brine. The combined extracts were dried (anhyd $MgSO_4$) and concentrated to a syrup, which was purified by flash-column chromatography (Et_2O) to give **6X** as a colorless syrup that crystallized on standing in the refrigerator (1.49 g, 77.8%); ^{1}H NMR ($CDCl_3$, 200 MHz): δ 4.35 (dd, 2 H, J 4.2, J 10.9 Hz, H-1, H-5), 4.20 (dd, 2 H, J 6.1, J 10.9 Hz, H-1′, H-5′), 3.65 (m, 2 H, H-2, H-4), 3.40 (m, 1 H, H-3), 3.41 (s, 3 H, OMe), 3.39 (s, 6 H, 2 OMe), 2.97 (s, 6 H, 2 OMs); ^{13}C NMR (50 MHz): δ 78.2 (C-3), 77.6 (C-2, C-4), 68.6 (C-1, C-5), 59.7, 58.7 (3 OMe), 37.0 (2 OMs); CIHRMS Calcd for $C_{10}H_{22}O_9S_2$: 351.0783. Found: 351.0776.

Reaction of **4X** *with mesyl chloride in dry pyridine: isolation of 1,4-anhydro-5*-O-*mesyl*-*2,3-di*-O-*methyl and xylitol* (**7X** and **8X**).—A cold (0–5 °C) solution of **4X** (2.65 g, 13.65 mmol) in dry pyridine (10 mL) was stirred with mesyl chloride (3.17 mL, 40.95 mmol) for 5 h at the same temperature. The reaction was diluted with water (10 mL) and extracted with CH_2Cl_2 (4×30 mL). The combined extracts were dried (anhyd $MgSO_4$) and concentrated to a syrup which was purified by flash-column chromatography (9:1 Et_2O–hexane) to give the racemic mixture of **7X** and **8X** (1.1 g, 62.8%); $[\alpha]_D$ 0° (c 0.5, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 4.37 (dd, 1 H, $J_{4,5}$ 4.3, $J_{5,5'}$ 10.9 Hz, H-5), 4.28 (dd, 1 H, $J_{4,5'}$ 7.4 Hz, H-5′), 4.19 (m, 1 H, H-4), 4.02 (dd, 1 H, $J_{1,2}$ 4,6, $J_{1,1'}$ 10 Hz, H-1), 3.84 (dt, 1 H, J 1.5, J 1.7 Hz, H-2), 3.75 (m, 2 H, H-1′, H-3), 3.35, 3.32 (2s, 3 H each, 2 OMe), 2.99 (s, 3 H, OMs); ^{13}C

NMR (125 MHz): δ 83.8 (C-3), 83.1 (C-2), 77.9 (C-4), 71.1 (C-1), 68.4 (C-5), 57.7, 56.9 (2 OMe), 37.4 (OMs); CIMS: *m/z* 241 $[M+H]^+$. Anal. Calcd for $C_8H_{16}O_6S$: C, 39.65; H, 6.75; S, 13.00. Found: C, 39.99; H, 6.71, S, 13.34. CH_2Cl_2

1,5-Diazido-1,5-dideoxy-2,3,4-tri-O-*methyl*-L-*arabinitol* (**9A**).—To a solution of **6A** (3.95 g, 11.3 mmol) in dry DMF (25 mL) was added NaN_3 (1.88 g, 29.3 mmol) and the suspension was stirred at 70 °C for 24 h. The reaction mixture was diluted with acetone and filtered through diatomaceous earth. The solids were washed with CH_2Cl_2 and the combined extracts and the organic solution were concentrated to a residue. Flash-column chromatography (1:1 Et_2O-hexane) of the residue gave **9A** as a yellowish liquid (2.49 g, 90%); $[\alpha]_D$ −65.5° (*c* 0.6, CH_2Cl_2); IR: *ν* 2100 cm^{-1} (N_3); ^1H NMR ($CDCl_3$, 200 MHz): δ 3.70–3.24 (m, 7 H), 3.46, 3.44, 3.42 (3s, 9 H, 3 OMe); ^{13}C NMR (50 MHz), δ 75.5, 79.3 (C-2, C-3, C-4), 60.9, 59.2, 57.5 (3 OMe), 50.8, 49.4 (C-1, C-5); CIHRMS Calcd for $C_8H_{16}O_3N_6$: 245.1352. Found: 245.1369.

1,5-Diazido-1,5-dideoxy-2,3,4-tri-O-*methyl*-*xylitol* (**9X**).—It was obtained from **6X** (1.48 g, 4.2 mmol) as described for **9A**. Flash-column chromatography (1:1 Et_2O–hexane) of the residue gave **9X** as a yellowish liquid (0.6 g, 58%). IR: 2100 cm^{-1} (N_3); ^1H NMR ($CDCl_3$, 200 MHz): δ 3.48 (OMe), 3.43 (2 OMe), 3.50–3.33 (rest of the protons); ^{13}C NMR (50 MHz): δ 79.6 (C-3), 79.5 (C-2, C-4), 60.3, 58.5 (3 OMe), 50.7 (C-1, C-5); CIHRMS Calcd for $C_8H_{16}O_3N_6$: 245.1362. Found: 245.1371.

1,5-Diamino-1,5-dideoxy-2,3,4-tri-O-*methyl*-L-*arabinitol dihydrochloride* (**10A**).—To a solution of **9A** (356 mg, 1.46 mmol) in dry THF (8 mL) was added 1 M $LiAlH_4$ in THF (8.76 mL) under Ar and the mixture was stirred for 2 h. A satd sodium sulfate solution was added and the suspension was filtered through diatomaceous earth. The solid was washed with THF (60 mL) and the filtrate concentrated to a syrup, which was dried under diminished pressure. This syrup was treated with a 10% solution of HCl in EtOAc (15 mL), and the hydrochloride **10A** was obtained as a solid, which was filtered and washed with EtOAc (348 mg, 90% from the base), mp (dec.) 268–270 °C; $[\alpha]_D$ −25° (*c* 0.5, water); IR: *ν* 2936 cm^{-1} (NH_3^+); ^1H NMR (Me_2SO-d_6, 200 MHz): δ 8.27 (bs, 4 H, 2 NH_2), 3.70–3.60 (m, 3 H, H-2, H-3, H-4), 3.40, 3.39, 3.35 (3s, 9 H, 3 OMe), 3.00–2.75 (m, 4 H, H-1, H-1′, H-5, H-5′); ^{13}C NMR (50 MHz): δ 78.8, 77.9, 77.7 (C-2, C-3, C-4), 59.7, 58.8, 57.6 (3 OMe), 39.1 (C-1, C-5). CIMS: *m/z* 193 $[M+H]^+$. Anal. Calcd for $C_8H_{22}Cl_2N_2O_3$: C, 36.24; H, 8.36; N, 10.56. Found: C, 36.56; H, 8.22, N, 10.24.

1,5-Diamino-1,5-dideoxy-2,3,4-tri-O-*methyl*-*xylitol dihydrochloride* (**10X**).—It was prepared from **9X** (0.6 g, 2.47 mmol) as described for **10A**. The hydrochloride **10X** was obtained as a solid, which was filtered and washed with EtOAc (0.6 g, 92%), mp 103–106 °C; IR: *ν* 2936 cm^{-1} (NH_3^+); ^1H NMR (DMSO-d_6, 200 MHz): δ 8.2 (bs, 4 H, 2 NH_2), 3.65 (m, 3 H, H-2, H-3, H-4), 3.40 (s, 3 H, OMe), 3.37 (s, 6 H, 2 OMe), 3.00–2.80 (m, 4 H, H-1, H-1′, H-5, H-5′); ^{13}C NMR (50 MHz): δ 79.1 (C-3), 76.2 (C-2, C-4), 59.0, 58.4 (3 OMe), 39.1 (C-1, C-5). Anal. Calcd for $C_8H_{22}Cl_2N_2O_3 \cdot 0.3\ H_2O$: C, 35.50; H, 8.41; N, 10.34. Found: C, 35.60; H, 8.49, N, 10.05.

2,3,4-Tri-O-*methyl*-L-*arabinaric acid* (**11A**).—To a solution of **3A** (5.1 g, 26.6 mmol) in water (5 mL) was added nitric acid (60%, 10 mL) and the mixture was heated at 70–80 °C with stirring for 24 h. The reaction was diluted with water (200 mL) and the residue co-evaporated several times with water and finally with toluene. Flash-column chromatography (20:1 CH_2Cl_2–MeOH) of the residue afforded the title compound as a syrup that crystallized on standing (5.7 g, 97%), mp 88–89 °C; $[\alpha]_D$ +32° (*c* 1, CH_2Cl_2); IR: *ν* 1730 cm^{-1} (CO); ^1H NMR ($CDCl_3$, 200 MHz): δ 9.17 (bs, 2 H, COOH), 4.03–3.91 (m, 3 H, H-2, H-3, H-4), 3.45, 3.40, 3.36 (3s, 9 H, 3 OMe); ^{13}C NMR (50 MHz): δ 175.0, 174.9 (C-1, C-5), 81.5, 79.0, 78.9 (C-2, C-3, C-4), 60.3, 59.4, 58.6 (3 OMe). CIMS: *m/z* 223 $[M+H]^+$. Anal. Calcd for $C_8H_{14}O_7$: C, 43.24; H, 6.35. Found: C, 42.99; H, 6.53.

2,3,4-Tri-O-*methyl*-*xylaric acid* (**11X**).—It was prepared from **3X** (4.0 g, 20.8 mmol) as described for **11A**. Flash-column chromatography (20:1 CH_2Cl_2–MeOH) of the residue afforded the title compound as a syrup (4.7 g, quant.). IR: *ν* 1730 cm^{-1} (CO); ^1H NMR

($CDCl_3$, 200 MHz): δ 9.00 (bs, 2 H, COOH), 4.05–3.93 (m, 3 H, H-2, H-3, H-4), 3.49, 3.44, (2s, 9 H, 3 OMe); ^{13}C NMR (50 MHz): δ 174.5 (C-1, C-5), 81.6 (C-3), 78.5 (C-2, C-4), 60.2, 59.4 (3 OMe). CIHRMS Calcd for $C_8H_{14}O_7$: 223.0817. Found: 223.0818.

Pentachlorophenyl 2,3,4-tri-O-*methyl*-L-*arabinarate* (**13A**).—To a cold (0–5 °C) solution of **11A** (1.03 g, 4.67 mmol) in dry CH_2Cl_2 (12 mL) were added pentachlorophenol (2.48 g, 9.34 mmol), *N*,*N*-dicyclohexylcarbodiimide (2.48 g, 9.34 mmol) and *N*,*N*-dimethylaminopyridine (15 mg). The mixture was stirred at rt overnight, then diluted with CH_2Cl_2 (50 mL) and the dicyclohexylurea formed was filtered through diatomaceous earth. The filtrate was washed with 5% aq solution of AcOH, then with water, dried (anhyd $MgSO_4$) and concentrated to a residue. Flash-column chromatography (1:5 Et_2O–petroleum ether) of this residue afforded **15A** as a solid (2.37 g, 71%), mp 137–139 °C; $[\alpha]_D$ + 39° (*c* 0.5, CH_2Cl_2); IR: ν 1780 cm^{-1} (CO); ^1H NMR ($CDCl_3$, 200 MHz): δ 4.5 (d, 1 H, *J* 1.8 Hz, H-2/H-4), 4.35 (m, 2 H, H-3, and H-2/H-4), 3.68, 3.67, 3.51 (3s, 9 H, 3 OMe). ^{13}C NMR (50 MHz), δ 167.4, 167 (C-1, C-5), 143.7, 132.2, 132.0, 127.3 (C_6Cl_5), 80.6 (C-3), 79.0 (C-2, C-4), 60.7, 60.0, 59.6 (3 OMe). Anal. Calcd for $C_{20}H_{12}Cl_{10}O_7$: C, 33.42; H, 1.68. Found: C, 33.71; H, 1.84.

Pentachlorophenyl 2,3,4-tri-O-*methyl-xylarate* (**13X**).—It was prepared from **11X** (1.0 g, 4.59 mmol) as described for **13A**. Compound **13X** was obtained as a solid (2.0 g, 61%) after column chromatography, mp 156–159 °C (from CCl_4); IR: ν 1793, 1775 cm^{-1} (CO). ^1H NMR ($CDCl_3$, 200 MHz): δ 4.50 (d, 2 H, *J* 5 Hz, H-2, H-4), 4.30 (t, 1 H, *J* 5 Hz, H-3), 3.70, 3.40 (2s, 9 H, 3 OMe); ^{13}C NMR (50 MHz): δ 166.4 (C-1, C-5), 132.2, 132.0, 128.8, 127.3 (C_6Cl_5), 81.0 (C-3), 80.4 (C-2, C-4), 61.6, 59.8 (3 OMe). Anal. Calcd for $C_{20}H_{12}O_7Cl_{10}$: C, 33.42; H, 1.68. Found: C, 33.61; H, 1.91.

Poly(1,5-dideoxy-2,3,4-tri-O-*methyl*-L-*arabinitol-2′,3′,4′-tri*-O-*methyl*-L-*arabinaramide)* (**14**).—To a solid mixture of **10A** (138.2 mg, 0.52 mmol) and **13A** (375 mg, 0.52 mmol), under N_2, dry *N*-methylpyrolidinone (2 ml) and *N*-ethyl-*N*,*N*-diisopropylamine (0.36 ml, 4 mmol) were added and the mixture was stirred at 45 °C for 4 days. The reaction mixture was diluted with acetone (6 mL) and added dropwise to Et_2O (200 mL) with stirring. The precipitated white solid was filtered and washed with ether and dried under diminished pressure at 40 °C, to obtain **14** (167 mg, 77%), T_m 250 °C (ΔH = 39.5 J/g); $[\alpha]_D$ + 31° (*c* 0.52, CH_2Cl_2); $[\eta]$ 0.4 dL/g; M_w 27500, M_w/M_n 1.4; IR: ν 1677 (amide I), 1528 cm^{-1} (amide II); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 170.6, 170.4, 170.3 (CO), 82.1, 81.9, 81.7, 81.6, 81.5, 81.1, 79.3, 79.0, 77.0 (CH, main chain), 60.8, 60.7, 59.6, 59.5, 58.8, 58.7, 58.3, 58.2, 57.4 (OMe), 39.2, 37.8 (CH_2, main chain). Anal. Calcd for $C_{16}H_{30}O_8N_2 \cdot 0.5\ H_2O$: C, 49.60; H, 8.06; N, 7.23. Found: C, 49.47; H, 8.30; N, 7.31.

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