Stereoregular Poly-*O*-Methyl [*m,n*]-Polyurethanes Derived From D-Mannitol

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ABSTRACT: Novel linear carbohydrate-derived [*m,n*]-polyurethanes are successfully prepared using D-mannitol as renewable and low cost starting material. The key comonomer, 1,6-di-*O*-phenylcarbonyl-2,3,4,5-tetra-*O*-methyl-D-mannitol is polymerized with a diamine synthesized from D-mannitol or with alkylenediamines. These polymerization reactions afford, respectively, a [*6,6*]-polyurethane entirely based on a carbohydrate derivative or [*m,n*]-polyurethanes constituted by a poly-*O*-methyl substituted unit alternating with a polymethylene chain. All these polymers are stereoregular, as result of the C_2 axis of symmetry of mannitol. The optically active polyurethanes are characterized by standard methods (FTIR, RMN, GPC, TGA, and DSC). Thus, GPC analysis reveals weight-average molecular weights between 18,000 and 25,000 Da. Thermal studies (DSC) indicate that the polymers obtained are amorphous materials with T_g values dependent on the structure and chain length of the diamine constituent. © 2012 Wiley Periodicals, Inc. J Polym Sci Part A: Polym Chem 51: 463–470, 2013

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INTRODUCTION Polyurethanes are chemically stable polymers with high resistance to hydrolysis. The hydrolytic stability, although highly desirable for most traditional applications of polyurethanes, prevents their temporal uses that are of interest in biomedicine. This is an attractive field given the extremely good biocompatibility of polyurethanes.[1] A successful approach to prepare new polymers with enhanced hydrophilicity and biodegradability consist in the incorporation into the polymer chain of hydrophilic units, such as those derived from carbohydrates.[2–5] As a renewable resource, carbohydrates are able to provide a large variety of functionalized molecules, which are suitable monomers for polycondensations.

A good number of polyurethanes based on simple sugars have been synthesized so far. Selectively protected carbohydrate-derived diols have been polymerized with diisocyanate monomers to afford [*m,n*]-polyurethanes. Muñoz-Guerra and Galbis have used this type of methodology using as diol comonomers *O*-protected or free alditols (mostly L-threitol, L-arabinitol, and xilitol),[6–14] anhydroalditols,[15,16] or tartaric acid.[17] The procedure has also been applied to diols derived from hexoses[18,19] and aldaro[20] or aldonolactones.[21] An alternative approach consists in the activation of two functional groups that are made to react with the appropriate comonomer. Thus, carbohydrate-based chloroformates[22,23] or diisocyanates[24] have been used as precursors of polyurethanes or poly(urea-urethanes). A similar strategy, described by Höcker and coworkers,[25–27] is based on the use of phenoxycarbonyl groups for the activation of the primary hydroxyl groups that are able to react with diamines to yield [*m,n*]-polyurethanes.

In recent years, we have been involved in the synthesis of carbohydrate-based [*n*]-polyurethanes under environmentally friendly conditions.[28–30] The procedures used do not use toxic phosgene, and no manipulation of isocyanates is required. Furthermore, the polymerizations are conducted under mild conditions that are convenient for carbohydrate derivatives. In connection with this previous work, we report here the environmentally benign preparation of a per-*O*-methyl-[*m,n*]-polyurethane entirely based in D-mannitol. Additionally, polyurethanes were obtained using the same diol comonomer and alkylene diamines of varied lengths. The optically active, stereoregular polymers were fully characterized, and their thermal properties are described.

EXPERIMENTAL

General Methods

D-Mannitol was purchased from Aldrich Chemical Company and used as received. Analytical thin-layer chromatography (TLC) was performed on Silica Gel 60 F254 (E. Merck)

Additional Supplementary Information may be found in the online version of this article.

aluminum-supported plates (layer thickness 0.2 mm). Visualization of the spots was effected by exposure to UV light or by charring with a solution of 5% (v/v) sulfuric acid in EtOH, containing 0.5% *p*-anisaldehyde. For unprotected amines, the plates were heated after immersion in a solution of ninhydrin in acetone. Column chromatography was performed with Silica Gel 60 (230–400 mesh, E. Merck). Optical rotations were measured with a Perkin–Elmer 343 digital polarimeter at 25 °C and are expressed in cm^3 $(g\ dm)^{-1}$, concentrations are given in g cm^{-3}. Nuclear magnetic resonance (NMR) spectra were recorded with a Bruker AMX 500 instrument (^1H: 500 MHz; ^{13}C: 125.7 MHz) or a Bruker AC 200, in $CDCl_3$ solutions (tetramethylsilane as an internal standard) unless otherwise indicated. The assignments were assisted by 2D COSY, DEPT, and HSQC techniques. IR spectra (films) were recorded with a Nicolet 510P Fourier transform infrared (FTIR) spectrometer. Gel permeation chromatography (GPC) was performed using Styragel columns (Waters), with THF as solvent at a flow rate of 1.0 mL min^{-1}. The calibration was performed using polystyrene standards. Thermogravimetric analysis (TGA) was performed in a Shimadzu TGA-51 instrument; samples of about 2 mg were heated at a rate of 10 °C min^{-1}. Differential scanning calorimetry (DSC) was conducted with a DSC Q20 TA instrument. Samples of about 2 mg were heated from 50 to 200 °C at a rate of 20 °C min^{-1}, then cooled at 5 °C min^{-1} to 50 °C (isothermic 5 min), and finally heated at 10 °C min^{-1} to 200 °C. High resolution mass spectrometry (HRMS-ESI) was performed in a Bruker microTOF-Q II instrument.

2,3,4,5-Tetra-O-acetyl-1,6-dibromo-1,6-dideoxy-D-mannitol (2)
To a suspension of D-mannitol (**1**, 1.11 g; 6.1 mmol) in dioxane (16 mL) was added acetyl bromide (1.1 mL; 13.6 mmol). The mixture was stirred in the dark at room temperature (rt) for 48 h and then concentrated *in vacuo*. The residue was dissolved in pyridine (2 mL) and acetic anhydride (2 mL) was added, after 24 h the mixture was concentrated. The crude product was purified by column chromatography (toluene-EtOAc 19:1) to give **2** (1.84 g; 64%) as a white solid; mp 122–124 °C (lit.[31] 121–123 °C, from EtOH); $[\alpha]_D^{25} = +27.6$ ($c = 1.2$ in CH_2Cl_2) (lit.[31] +29.6). HRMS (ESI, Q-Tof, *m/z*): $[M + Na]^+$, calcd for $[C_{14}H_{20}Br_2O_8Na]^+$: 496.9417, found: 496.9451.

2,3,4,5-Tetra-O-acetyl-1,6-diazido-1,6-dideoxy-D-mannitol (3)
To a stirred solution of Compound **2** (1.17 g, 2.46 mmol) in DMF (16 mL) was added NaN_3 (0.64 g, 9.85 mmol). The mixture was stirred at 80 °C for 2 h and concentrated. The residue was redissolved in EtOAc, and the mixture was filtered through a celite bed. The filtrate was concentrated to afford syrupy **3** (0.96 g, 97%). This compound was pure enough to be used for the next step without further purification. An analytical sample gave $[\alpha]_D^{25} = +39.8$ ($c = 1.0$ in CH_2Cl_2) (lit.[32] +33.0); ^1H NMR (200 MHz, $CDCl_3$, δ): 2.11, 2.12 (6H each, 2s, $COCH_3$), 3.27 (2H, dd, $J_{1a,1b}$ ($J_{6a,6b}$) 13.5, $J_{1b,2}$ ($J_{5,6b}$) 5.5 Hz, H-1b/H-6b), 3.48 (2H, dd, $J_{1a,1b}$ ($J_{6a,6b}$) 13.5, $J_{1b,2}$ ($J_{5,6b}$) 3.4 Hz, H-1a/H-6a), 5.04 (2H, m, $J_{1a,2}$ ($J_{5,6a}$) 3.4, $J_{1b,2}$ ($J_{5,6b}$) 5.5, $J_{2,3}$ ($J_{4,5}$) 8.6 Hz, H-2/H-5), 5.42 (2H, d, $J_{2,3}$ ($J_{4,5}$) 8.6 Hz, H-3/H-4); ^{13}C NMR (50.3 MHz, $CDCl_3$, δ_C): 20.6, 20.8 ($COCH_3$), 50.7 (C-1/C-6), 68.1 (C-3/C-4), 68.5 (C-2/C-5), 169.7, 169.9 (CO). Anal. calcd for $C_{14}H_{20}N_6O_8$: C 42.00, H 5.04, N 20.99. Found: C 41.75, H 5.13, N 21.11. HRMS (ESI, Q-Tof, *m/z*): $[M + Na]^+$, calcd for $[C_{14}H_{20}N_6O_8Na]^+$: 423.1235, found: 423.1285.

1,6-Diazido-1,6-dideoxy-2,3,4,5-tetra-O-methyl-D-mannitol (4)
To a stirred solution of Compound **3** (0.95 g, 2.38 mmol) in DMSO (9.6 mL) was added finely powdered NaOH (1.52 g, 38 mmol). The mixture was stirred at rt for 30 min and, on cooling in an ice bath, MeI (4.6 mL, 74 mmol) was added. After stirring for 2 h, the reaction mixture was partitioned between CH_2Cl_2-H_2O 1:1 (80 mL). The aqueous layer was extracted with CH_2Cl_2 (50 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (toluene-EtOAc 4:1), to give syrupy **4** (0.53 g, 77%). $[\alpha]_D^{25} = +43.5$ ($c = 1.7$ in CH_2Cl_2) (lit.[33] +24.1); ^1H NMR (500 MHz, $CDCl_3$, δ): 3.32 (2H, dd, $J_{1a,1b}$ ($J_{6a,6b}$) 13.4, $J_{1b,2}$ ($J_{5,6b}$) 3.6 Hz, H-1b/H-6b), 3.27, 3.28 (12H, 2s, CH_3O), 3.47 (2H, m, H-2/H-5), 3.58 (2H, d, $J_{2,3}$ ($J_{4,5}$) 7.9 Hz, H-3/H-4), 3.80 (2H, dd, $J_{1a,1b}$ ($J_{6a,6b}$) 13.4, $J_{1a,2}$ ($J_{5,6a}$) 2.6 Hz, H-1a/H-6a); ^{13}C NMR (50.3 MHz, $CDCl_3$, δ): 48.9 (C-1/C-6), 56.9, 60.8 (CH_3O), 79.0 (C-3/C-4), 79.7 (C-2/C-5). Anal. calcd for $C_{10}H_{20}N_6O_4$: C 41.66, H 6.99, N 29.15. Found: C 41.50, H 7.14, N 28.86. HRMS (ESI, Q-Tof, *m/z*): $[M + Na]^+$, calcd for $[C_{10}H_{20}N_6O_4Na]^+$: 311.1438, found: 311.1450.

1,6-Diamino-1,6-dideoxy-2,3,4,5-tetra-O-methyl-D-mannitol (5)
To a solution of Compound **4** (0.17 g, 0.6 mmol) in MeOH (6 mL) was added 10% Pd-C (0.017 g) and the mixture was treated with H_2 (45 psi) for 3 h. The catalyst was filtered off and washed with MeOH, and the filtrate was concentrated to give syrupy **5** (0.17 g, 99%); $[\alpha]_D^{25} = +29.1$ ($c = 1.0$ in $CHCl_3$); (lit.[33] + 20, for a hydrated form). HRMS (ESI, Q-Tof, *m/z*): $[M + H]^+$, calcd for $[C_{10}H_{25}N_2O_4]^+$: 237.1808, found: 237.1816; $[M + Na]^+$, calcd for $[C_{10}H_{24}N_2O_4Na]^+$: 259.1628, found: 259.1638.

2,3,4,5-Tetra-O-methyl-1,6-di-O-trityl-D-mannitol (7)
Compound **7** was synthesized according to the procedure described by Galbis and coworkers.[34]

2,3,4,5-Tetra-O-methyl-D-mannitol (8)
A solution of Compound **7** (0.54 g, 0.75 mmol) in anhydrous CH_2Cl_2 (6.8 mL) was cooled in an ice bath, and trifluoroacetic acid (0.77 mL, 10 mmol) was slowly added. After 30 min, the mixture was allowed to reach rt, and it was stirred for additional 24 h. On addition of MeOH (6 mL), the solution was concentrated. The residue was purified by column chromatography (hexane-EtOAc 2:3) to afford **8** (0.14 g, 77%); $[\alpha]_D^{25} = +7.7$ ($c = 0.9$ in $CHCl_3$) (lit.[34] +12); ^1H NMR (500 MHz, $CDCl_3$, δ): 2.10 (2H, s, OH), 3.37 (2H, ddd, $J_{1a,2}$ ($J_{5,6a}$) 2.7, $J_{1b,2}$ ($J_{5,6b}$) 3.3, $J_{2,3}$ ($J_{4,5}$) 7.9 Hz, H-2/H-5), 3.42 (6H, s, CH_3O), 3.52 (6H, s, CH_3O), 3.54 (2H, d, $J_{2,3}$ ($J_{4,5}$) 7.9 Hz, H-3/H-4), 3.72 (2H, dd, $J_{1a,1b}$ ($J_{6a,6b}$) 12.1, $J_{1b,2}$ ($J_{5,6b}$) 2.6 Hz, H-1b/H-6b), 3.98 (2H, dd, $J_{1a,1b}$ ($J_{6a,6b}$) 12.1, $J_{1a,2}$ ($J_{5,6a}$) 3.4 Hz, H-1a/H-6a); ^{13}C NMR (125.7 MHz, $CDCl_3$, δ): 56.7, 60.8 (CH_3O), 58.8 (C-1/C-6), 78.7 (C-3/C-4), 80.1 (C-2/C-5).

TABLE 1 Polymerization of Comonomers 5 and 9 and Properties of Polyurethane 10

Entry	Solvent	Monomer (M)	DIPEA (M)	Time (d)	Yield (%)	M_w[a]	M_n[a]	M_w/M_n	M_n[b]
1	DMF	0.1	0.4	2	58	4,850	4,390	1.10	4,710
2	DMF	0.5	3.0	4	57	4,160	3,750	1.11	4,100
3	THF	0.1	0.4	4	72	5,170	4,270	1.21	5,230
4	THF	0.5	3.0	7	61	14,170	12,780	1.11	10,180
5	THF	0.5	1.5	4	70	21,020	14,960	1.40	11,550

[a] Determined by SEC.

[b] Determined by end-group analysis based on ^{1}H NMR spectroscopy.

HRMS (ESI, Q-Tof, *m/z*): $[M + Na]^+$, calcd for $[C_{10}H_{22}O_6Na]^+$: 261.1309, found: 261.1318.

1,6-Di-O-phenyloxycarbonyl-2,3,4,5-tetra-O-methyl-D-mannitol (9)

To a solution of Compound **8** (0.2 g, 0.8 mmol) in dry pyridine (2.5 mL), phenylchloroformate (0.28 mL, 1.81 mmol) was added. The mixture was stirred at rt for 2 h. After subsequent addition of MeOH and toluene, the mixture was concentrated and purified by column chromatography (hexane/EtOAc 4:1) to yield **9** as a white crystalline solid (0.33 g, 85% from **5**); mp 97–99 °C; $[\alpha]_D^{25} = +42.0$ (c = 1.0 in $CHCl_3$); IR (KBr): ν = 1764 cm^{-1} (s, C=O); ^{1}H NMR (500 MHz, $CDCl_3$, δ): 3.50 (6H, s, CH_3O), 3.53 (6H, s, CH_3O), 3.59 (2H, ddd, $J_{1a,2}$ ($J_{5,6a}$) 2.3, $J_{1b,2}$ ($J_{5,6b}$) 3.4, $J_{2,3}$ ($J_{4,5}$) 8.0 Hz, H-2/H-5), 3.66 (2H, d, $J_{2,3}$ ($J_{4,5}$) 8.0 Hz, H-3/H-4), 4.33 (2H, dd, $J_{1a,1b}$ ($J_{6a,6b}$) 12.0, $J_{1b,2}$ ($J_{5,6b}$) 3.4 Hz, H-1b/H-6b), 4.92 (2H, dd, $J_{1a,1b}$ ($J_{6a,6b}$) 12.0, $J_{1a,2}$ ($J_{5,6a}$) 2.1 Hz, H-1a/H-6a), 7.43-7.22 (10H, m, H-aromatic); ^{13}C NMR (125.7 MHz, $CDCl_3$, δ): 57.2, 60.8 (CH_3O), 65.2 (C-1/C-6), 78.2 (C-3/C-4), 78.7 (C-2/C-5), 121.0, 126.0, 129.4, 151.1 (C-aromatic), 153.7 (CO). Anal. calcd for $C_{24}H_{30}O_{10}$: C 60.24, H 6.32. Found: C 60.50, H 6.68. HR-MS (ESI, Q-Tof, *m/z*): $[M + Na]^+$, calcd for $[C_{24}H_{30}O_{10}Na]^+$: 501.1731, found: 501.1732.

General Procedure for the Polymerization

To an equimolar mixture of α,ω-diamine (**5, 11–13**) and **9** (0.2–0.3 mmol) in THF or DMF, DIPEA was added. The mixture was stirred under argon atmosphere under the conditions indicated in Table 1. The reaction temperature was 85 °C, except for Entry 2 that was 100 °C. Then, the solvent was evaporated, and the residue was purified by dissolution in CH_2Cl_2 and precipitation with hexane. This procedure was repeated three times.

Preparative Scale Synthesis of Polyurethanes 10, 14–16

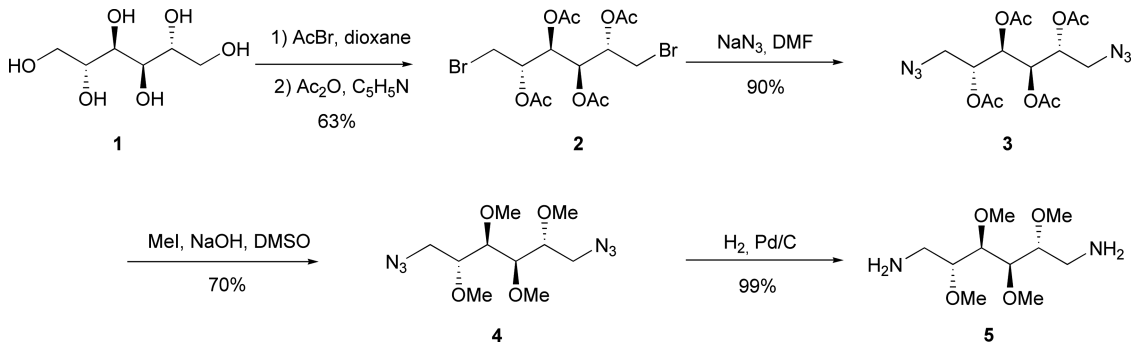
For the synthesis of **10** in preparative scale, the dicarbonate **9** (0.223 g, 0.47 mmol) and the diamine **5** (0.111 g, 0.47 mmol) were dissolved in THF, and the polymerization was conducted under the conditions of Table 1, Entry 5. Polyurethane **10** was isolated as a white foam; $[\alpha]_D^{25} = +11.4$ (c = 0.7 in MeOH); IR (KBr): ν = 3338 (w, N—H), 1718 (s, C=O), 1524 cm^{-1} (s, N—H); ^{1}H NMR (500 MHz, $CDCl_3$, δ) 3.42, 3.43, 3.48, 3.53 (6H each, 4s, CH_3O), 3.41–3.54 (12H, m, C*H*OCH_3, CH_2N), 4.14 (2H, d, $J_{1a,1b}$ ($J_{6a,6b}$) 10.9 Hz, CH_2O), 4.66 (2H, d, $J_{1a,1b}$ ($J_{6a,6b}$) 10.9 Hz, CH_2O), 5.15 (2H, br s, NH). ^{13}C NMR (125.7 MHz, $CDCl_3$, δ) 39.3 (CH_2N), 56.9, 60.7, 60.9 (4 CH_3O), 61.7 (CH_2O), 78.3, 78.7, 79.1, 79.9 (C*H*OCH_3), 156.5 (CO_2NH). Anal. calcd for $[C_{22}H_{42}N_2O_{12}.(H_2O)_{0.5}]_n$: C 49.34, H 8.09, N 5.23. Found: C 49.13, H 7.96, N 5.37.

Polyurethanes **14** and **15** were prepared as described for **10**. In the case of **16**, DIPEA was used as solvent to give a 0.5 M initial concentration of comonomers **9** and **13**. The polymerization reaction was conducted at 85 °C for 48 h.

Polyurethane **14**, $[\alpha]_D^{25} = +11.0$ (c = 0.8 in $CHCl_3$); IR (KBr): ν = 3334 (w, N—H), 2937 (s, C—H), 1704 (s, C=O), 1539 cm^{-1} (s, N—H); ^{1}H NMR (500 MHz, $CDCl_3$, δ): 1.33 (4H, s, CH_2-3′, CH_2-4′), 1.50 (4H, t, $J_{2',3'}$ ($J_{4',5'}$) 6.1 Hz, CH_2-2′, CH_2-5′), 3.17 (4H, q, $J_{1',2'} = J_{1',NH}$ ($J_{5',6'} = J_{6',NH}$) 6.1 Hz, CH_2-1′, CH_2-6′), 3.40, 3.45 (6H each, 2s, CH_3O), 3.47 (2H, d, H-2, H-5), 3.54 (2H, d, $J_{2,3}$ ($J_{4,5}$) 8.1 Hz, H-3, H-4), 4.08 (2H, d, $J_{1a,1b}$ ($J_{6a,6b}$) 11.7 Hz, H-1a, H-6a), 4.65 (2H, d, $J_{1a,1b}$ ($J_{6a,6b}$) 11.7 Hz, H-1b, H-6b), 4.90 (2H, br s, NH). ^{13}C NMR (125.7 MHz, $CDCl_3$, δ): 26.3 (CH_2-3′, CH_2-4′), 29.8 (CH_2-2′, CH_2-5′), 40.9 (CH_2-1′, CH_2-6′), 56.7, 60.6 (CH_3O), 61.0 (CH_2O), 78.2, 78.5 (C*H*OCH_3), 156.4 (CO_2NH). Anal. calcd for $[C_{20}H_{40}N_2O_8]_n$: C 53.19, H 8.43, N 6.89. Found: C 53.21, H 8.20, N 6.90.

Polyurethane **15**, $[\alpha]_D^{25} = +9.4$ (c = 0.8 in $CHCl_3$); IR (KBr): ν = 3338 (w, N—H), 2932 (s, C—H), 1704 (s, C=O), 1535 cm^{-1} (s, N—H); ^{1}H NMR (500 MHz, $CDCl_3$, δ): 1.27 (8H, s, CH_2-3′−CH_2-6′), 1.46 (4H, s, CH_2-2′, CH_2-7′), 3.14 (4H, d, $J_{1',NH}$ ($J_{8',NH}$) 5.4 Hz, CH_2-1′, CH_2-8′), 3.38, 3.43 (6H each, 2s, CH_3O), 3.38-3.52 (4H, m, H-2−H-5), 4.06 (2H, d, $J_{1a,1b}$ ($J_{6a,6b}$) 12.2 Hz, H-1a, H-6a), 4.63 (2H, d, $J_{1a,1b}$ ($J_{6a,6b}$) 12.2 Hz, H-1b, H-6b), 4.85 (2H, br s, NH). ^{13}C NMR (125.7 MHz, $CDCl_3$, δ): 26.6 (CH_2-4′, CH_2-5′), 29.1 (CH_2-3′, CH_2-6′), 29.8 (CH_2-2′, CH_2-7′), 41.0 (CH_2-1′, CH_2-8′), 56.7, 60.6 (CH_3O), 60.9 (CH_2O), 78.1, 78.4 (C*H*OCH_3), 156.3 (CO_2NH). Anal. calcd for $[C_{20}H_{38}N_2O_8.(H_2O)_{0.5}]_n$: C 54.16, H 8.86, N 6.32. Found: C 53.96, H 8.84, N 6.16.

Polyurethane **16**, $[\alpha]_D^{25} = +7.3$ (c = 1.2 in $CHCl_3$); IR (KBr): ν = 3337 (w, N—H), 2928 (s, C—H), 1704 (s, C=O), 1535 cm^{-1} (s, N—H); ^{1}H NMR (500 MHz, $CDCl_3$, δ): 1.23, 1.26 (16H, 2 s, H-3′−H-10′), 1.47 (4H, m, H-2′, H-11′), 3.16 (4H, d, $J_{1',NH}$ ($J_{12',NH}$) 6.2 Hz, H-1′, H-12′), 3.40, 3.44 (6H each, 2s, CH_3O), 3.40–3.53 (4H, m, H-2−H-5), 4.07 (2H, dd, $J_{1a,2}$ ($J_{5,6a}$) 2.8, $J_{1a,ab}$ ($J_{6a,6b}$) 12.2 Hz, H-1a, H-6a), 4.63 (2H, d, $J_{1a,ab}$ ($J_{6a,6b}$) 12.2 Hz, H-1b, H-6b), 4.81 (2H, br s, NH). ^{13}C NMR (125.7 MHz, $CDCl_3$, δ): 26.7, 29.2, 29.5 (CH_2-3′−CH_2-10′), 29.9 (CH_2-2′, CH_2-11′), 41.1 (CH_2-1′, CH_2-12′), 56.7, 60.6 (CH_3O), 61.0 (CH_2O), 78.2, 78.4 (C-2−C-5), 156.3 (CO_2NH). Anal. calcd for $C_{24}H_{46}N_2O_8$: C 58.75, H 9.45, N 5.71. Found: C 58.51, H 9.64, N 5.60.



SCHEME 1 Synthesis of 1,6-diamine **5** derived from D-mannitol.

RESULTS AND DISCUSSION

The α,ω-diazidoderivative **3** was used as precursor of the 1,6-diamino-1,6-dideoxy-D-mannitol (**5**). The most commonly used preparations of α,ω-diazidoalditols start from *bis*-epoxides,[35] *bis*-sulfonates,[36] *bis*-cyclic sulfites,[32] or *bis*-halogeno derivatives.[32,37] We have used the 1,6-dibromo derivative **2** (Scheme 1) as it is readily obtained from mannitol (**1**) through a one-pot procedure. Nucleophilic substitution of the bromine atoms in **2** by azide afforded the 1,6-diazide derivative **3**. The subsequent replacement of the acetoxy groups of **2** by methyl ethers, using methyl iodide in alkaline DMSO, led to **4**. Hydrogenolysis of the azide function of **4** under neutral conditions afforded the 1,6-diamine derivative **5** (40% overall yield from **1**). This compound has been previously synthesized by Galbis and coworkers[33] through a longer (eight steps) and lower yielding route from **1**.

The 1,6-diphenylcarbonate **9** was readily prepared from D-mannitol (**1**) via the intermediate per-*O*-methyl-1,6-di-*O*-trityl derivative **7**[34] (Scheme 2). Acid hydrolysis of the trityl ether groups of **7** with trifluoroacetic acid in CH_2Cl_2 gave 2,3,4,5-tetra-*O*-methyl-D-mannitol (**8**). The terminal free hydroxyl groups in **8** were converted into phenylcarbonates by treatment with phenylchloroformate in pyridine.

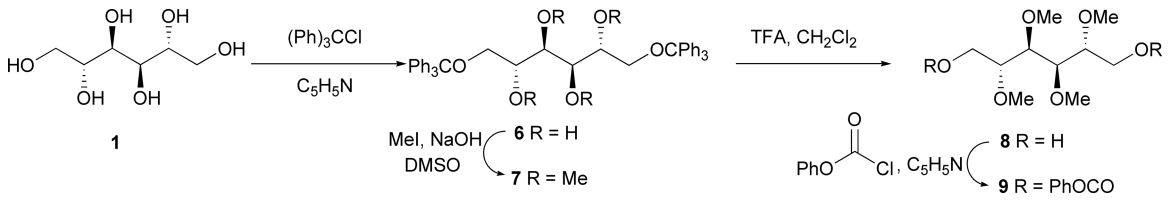
In accordance with the presence of a C_2 axis of symmetry in the structure of both comonomers **5** and **9**, their ^{13}C NMR spectra exhibited just one signal for the chemically equivalent carbon atoms (C-1/C-6, C-2/C-5, and C-3/C-4). Similarly, the ^1H NMR spectra of **5** and **9** showed a single signal for symmetric protons. The equivalent methyl and phenyloxycarbonyl groups presented an analogous behavior.

The preparation of a stereoregular polyurethane starting from the diamine **5** and dicarbonate **9** relies on the C_2 symmetry of these two chiral comonomers. As the reacting groups in each unit are equivalent, the formation of regioisomers during the polycondensations is prevented, and a stereoregular polymer is obtained.

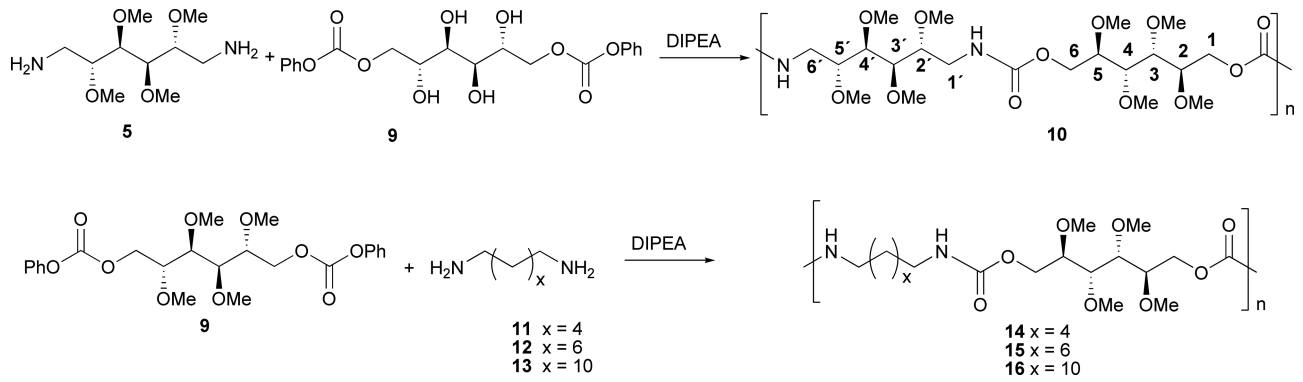
The polymerization of equimolar amounts of comonomers **5** and **9** was performed using tetrahydrofuran (THF) or *N,N*-dimethylformamide (DMF) as solvents and in the presence of an excess of *N,N*-diisopropylethylamine (DIPEA). The conditions of the polymerization reaction were optimized to obtain polyurethane **10** in good yield and with a high-molecular weight. Selected results are shown in Table 1. The use of DMF as polymerization solvent led to low-molecular weights, even when the polycondensation reaction was conducted with high concentration of comonomers (Entry 2). Polymerizations performed in THF gave more satisfactory results. An increase in the concentration of the reacting comonomers produced an increment in the molecular weight of the polymer. However, high concentration of DIPEA and long polymerization times (Entry 4) led to lower yields, probably because of the increased degradation of the amines (the reaction mixtures became dark), which hinders the isolation and purification of the polyurethane. The optimized conditions for the preparation of **10** correspond to those indicated in Entry 5. Therefore, they were applied for the preparative scale synthesis of the polymer, which was obtained with reproducible yields (>70%) and M_w values similar to those reported in Entry 5.

The same reaction conditions were also used for the synthesis of polyurethanes **14** and **15** (Scheme 3). However, the polymerization of **9** with dodecamethylenediamine (**13**) was performed using DIPEA as solvent, as **13** was not soluble in THF. The polymers were purified by dissolution in CH_2Cl_2 and precipitation with hexane. The isolated yields are reported in Table 2.

The evolution of the polymerization could be followed by ^1H NMR spectroscopy. In fact, the spectrum of the purified



SCHEME 2 Synthesis of 1,6-di-*O*-phenylcarbonate **9** derived from D-mannitol.



SCHEME 3 Synthesis of polyurethanes **10**, **14–16.**

polyurethane **10** (Entry 5) was quite simple, as shown in Figure 1(a). The resonance of the urethane proton (NH) appeared at lower field, and then signals were detected for the protons H-1a/H-6a and H-1b/H-6b of the methylene groups linked to oxygen. All the other signals due to the protons of the polymer chain appeared as a complex multiplet, overlapped with the four singlets of the methyl ethers. The ^{1}H NMR spectra of polymers having low-molecular weight showed signals due to terminal groups [Fig. 1(b)]. For example, the polyurethane prepared according to the conditions of Entry 3, exhibited additional signals corresponding to the protons of the methylene group bonded to the phenylcarbonate. The chemical shifts of these resonances were similar to those of the analog function in the comonomer **9**. In addition, the integrals of the terminal methylene group signals are coincident with those of the aromatic protons of the phenyloxy group. The end-group analysis allowed us to determine the molecular weight (M_n) of the polyurethane **10** obtained under the various conditions studied.

The ^{13}C NMR spectrum of **10** (Entry 5) (Fig. 2) showed distinctive signals for the urethane carbon (156.5 ppm), the methylene carbons bonded to oxygen (61.3 ppm) and to nitrogen (39.1 ppm) and those corresponding to the methyl ether groups (~60 ppm). Interestingly, in the ^{13}C NMR spectrum of polyurethane **10** of low-molecular weight, the phenyloxy carbons of the terminal groups exhibited much higher intensity with respect to the corresponding CHO signals and also much more intense if compared with the integrals estimated from the ^{1}H NMR spectrum. These results suggest that the carbons of the more exposed terminal aromatic groups and the carbons of the polymer chain have considerably different relaxation times.

The NMR spectra of **10** were also recorded in DMSO-d_6 solution, as the N*H* and *C*O signals of urea functionalities are well separated.[28,38] The fact that only signals due to urethane atoms appeared, excluded the formation of urea linkages ($\delta_{NH} \sim 6.1$) during the polymerization. However, the ^{1}H NMR spectrum of **10** in DMSO-d_6 revealed the presence of both the *trans* ($\delta \sim 7.17$) and *cis* ($\delta \sim 6.83$) carbamate forms (ratio *trans-cis*, 84:14), as reported for common polyurethanes.[38,39]

The FTIR spectrum of **10** showed characteristic absorptions for the urethane group at 3337 (wide, NH stretching), 1718 (strong, urethane carbonyl stretching), and 1524 cm^{-1} (strong, NH band II). In coincidence with the NMR data, the peak due to urea carbonyl (~1660 cm^{-1}) was absent for all samples. The spectrum of polyurethane **10**, Entry 3, exhibited a strong absorption at 1718 cm^{-1} and a shoulder at 1764 cm^{-1}, which was assigned to the carbonate absorption, as it was coincident with the peak observed for dicarbonate **9**. Polyurethanes **14–16** presented, similar to **10**, the bands corresponding to the urethane group (Table 2). In addition, the CH absorption at 2930 cm^{-1} became progressively more intense from **14** to **16**, due to the increasing length of the polymethylene chain.

Thermal Analysis

The thermal stability of the polyurethanes was evaluated by TGA under an inert atmosphere, in the range of 50 to 500 °C. The TG curves showed that decomposition takes place through one or two stage processes, and the decomposition temperatures (T_d), calculated from the corresponding derivative traces, were similar for the four polymers (Table 1).

TABLE 2 Properties of Polyurethanes 10, 14–16

PU	Yield (%)	M_w[a]	M_n[a]	M_n/M_w	Mn[b]	$[\alpha]_D$	FTIR ($HNCO_2$, cm^{-1})	T_g (°C)	T_d (°C)
10	70	21,020	14,960	1.35	11,550	11.4	1,718, 1,524	61.2	303.8
14	69	24,250	17,490	1.99	17,540	11.0	1,704, 1,539	53.3	311.9
15	81	17,820	13,170	2.00	n.d.[c]	9.4	1,704, 1,535	53.1	327.4
16	77	18,860	14,470	1.66	11,340	7.3	1,704, 1,535	38.5	304.3

[a] Determined by SEC.
[b] Determined by end-group analysis based on ^{1}H NMR spectroscopy.
[c] Terminal groups were not detected.

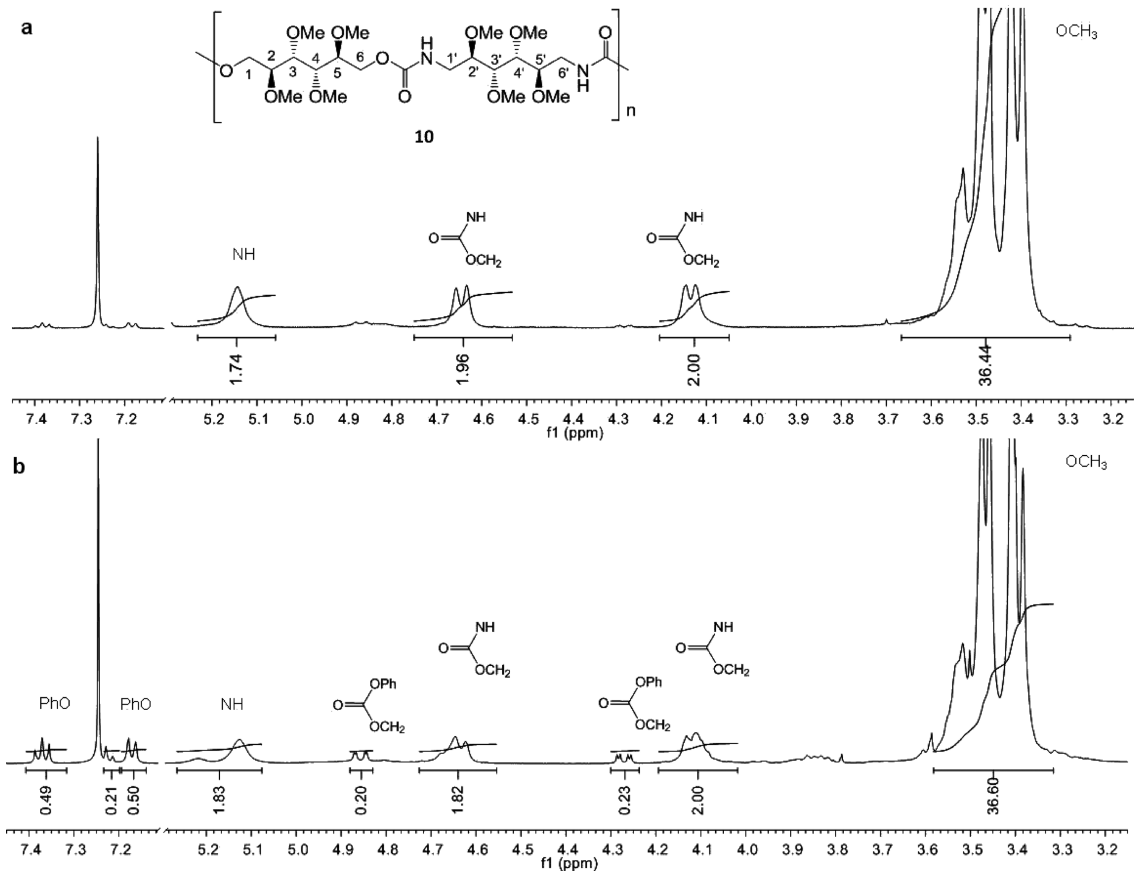


FIGURE 1 ^{1}H NMR spectra of polyurethane **10** (a) Entry 5, Table 1; (b) Entry 3, Table 1.

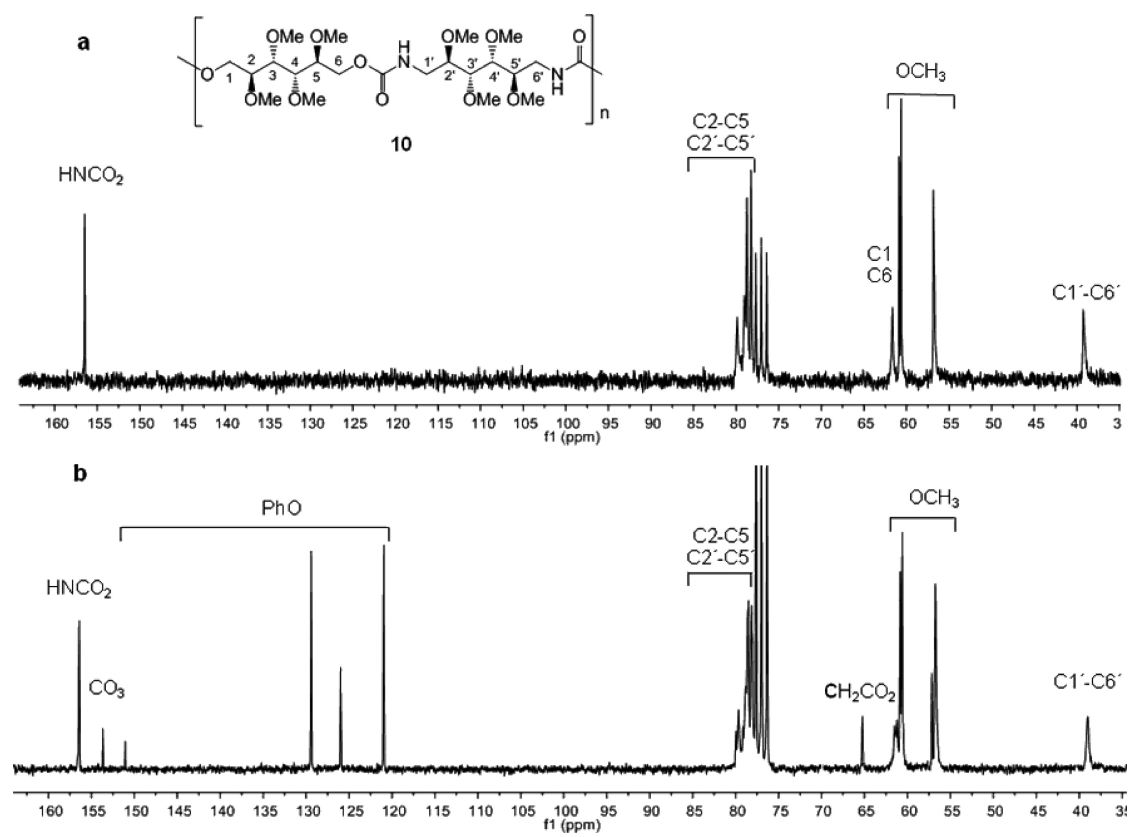


FIGURE 2 ^{13}C NMR spectra of polyurethane **10** (a) Entry 5, Table 1; (b) Entry 3, Table 1.

The DSC traces for polyurethanes **14**–**16** did not show any thermal transitions during the first heating cycle. Therefore, we are dealing with amorphous materials. Similarly, polyurethanes derived from hexamethylene diisocyanate and threitol, arabinitol and xylitol, with their secondary hydroxyl groups protected as methyl ethers, are essentially amorphous polymers displaying DSC traces absent of any heat change.[6] The lack of crystallinity may be attributed to the effect of alternating unsubstituted and *O*-methyl substituted units that could distort severely the packing of the polymer chain. However, polyurethane **10**, having both comonomers *O*-methyl substituted, showed for the first heating cycle two weak and broad endotherms with low ΔH values, which may be interpreted as arising from a small crystalline fraction present in the material. On cooling after the first heating, all the polymers studied here showed glass transitions (T_g) at well-defined temperatures. The same T_g values were measured for subsequent heating and cooling cycles. The heating DSC traces for samples quenched from the melt exhibited T_g values that were highly dependent on the constitution of the polymers. In agreement with the behavior of similar materials,[6,9] the replacement of the polymethylene chain by the diamine derived from D-mannitol led to an increment in T_g. On the other hand, the smaller T_g value corresponded to polyurethane **16**, having the longer and more flexible polymethylene chain. It has been reported that the values of T_g usually decrease with increase in the length of the oligoethylene spacers in the polyurethane backbone.[40] This is an important observation as the thermal properties, particularly the T_g, of polyurethanes can be tuned by using appropriate diamines.

CONCLUSIONS

A set of novel linear and homogeneous [*m,n*]-polyurethanes with enhanced hydrophilicity have been successfully prepared using D-mannitol as starting material. As this alditol possesses a C_2 axis of symmetry, the terminal functional groups are homotopic, and hence the resulting polymers are stereoregular. Under optimized conditions, the key comonomer 1,6-di-*O*-phenyloxycarbonyl-2,3,4,5-tetra-*O*-methyl-D-mannitol (**9**) reacted with a mannitol-derived diamine to afford a [*6,6*]-polyurethane entirely based on a sugar precursor. A similar polymerization with alkylenediamines led to polymers with a repeating unit constituted by a poly-*O*-methyl substituted residue alternating with a polymethylene chain.

The structure and homogeneity of the new polymers was confirmed by NMR and FTIR spectroscopies. The DSC analysis revealed that the polyurethanes obtained are essentially amorphous materials. Quenched from the melt they presented T_g values in the range 38–61 °C, that were dependent on the structure and length of the diamine comonomer. The maximum decomposition rate took place above 300 °C.

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REFERENCES AND NOTES

1 Jayabalan, M.; Lizymol, P. P.; Thomas, V. *Polym. Int.* **2000,** *49*, 88–92.

2 Galbis, J. A.; García-Martín, M. G. *Top. Curr. Chem.* **2010,** *295*, 147–176.

3 Van De Manakker, F.; Vermonden, T.; Van Nostrum, C. F.; Hennink, W. E. *Biomacromolecules* **2009,** *10*, 3157–3175.

4 Okada, M. *Prog. Polym. Sci.* **2002,** *27*, 87–133.

5 Varela, O.; Orgueira, H. A. *Adv. Carbohydr. Chem. Biochem.* **1999,** *55*, 137–174.

6 Paz, M. V.; Marín, R.; Zamora, F.; Hakkou, K.; Alla, A.; Galbis, J. A.; Muñoz-Guerra, S. *J. Polym. Sci. Part A: Polym. Chem.* **2007,** *45*, 4109–4117.

7 Paz, M. V.; Aznar, J. A.; Galbis, J. A. *J. Carbohydr. Chem.* **2008,** *27*, 120–140.

8 Marín, R.; Muñoz-Guerra, S. *J. Polym. Sci. Part A: Polym. Chem.* **2008,** *46*, 7996–8012.

9 Marín, R.; Paz, M. V.; Ittobane, N.; Galbis, J. A.; Muñoz-Guerra, S. *Macromol. Chem. Phys.* **2009,** *210*, 486–494.

10 De Paz, M. V.; Zamora, F.; Begines, B.; Ferris, C.; Galbis, J. A. *Biomacromolecules* **2010,** *11*, 269–276.

11 Ferris, C.; Violante de Paz, M.; Zamora, F.; Galbis, J. A. *Polym. Degrad. Stab.* **2010,** *95*, 1480–1487.

12 Ferris, C.; De Paz, M. V.; Galbis, J. A. *J. Polym. Sci. Part A: Polym. Chem.* **2011,** *49*, 1147–1154.

13 Begines, B.; Zamora, F.; Roffé, I.; Mancera, M.; Galbis, J. A. *J. Polym. Sci. Part A: Polym. Chem.* **2011,** *49*, 1953–1961.

14 Ferris, C.; De Paz, M. V.; Galbis, J. A. *Macromol. Chem. Phys.* **2012,** *213*, 480–488.

15 Marín, R.; Muñoz-Guerra, S. *J. Appl. Polym. Sci.* **2009,** *114*, 3723–3736.

16 Marín, R.; Alla, A.; Martínez De Ilarduya, A.; Muñoz-Guerra, S. *J. Appl. Polym. Sci.* **2012,** *123*, 986–994.

17 Marín, R.; De Ilarduya, A. M.; Muñoz-Guerra, S. *J. Polym. Sci. Part A: Polym. Chem.* **2012,** *123*, 986–994.

18 Garçon, R.; Clerk, C.; Gesson, J.-P.; Bordado, J.; Nunes, T.; Caroço, S.; Gomes, P. T.; Minas da Piedade, M. E.; Rauter, A. P. *Carbohydr. Polym.* **2001,** *45*, 123–127.

19 Hashimoto, K.; Yaginuma, K.; Nara, S.-I.; Okawa, H. *Polym. J.* **2005,** *37*, 384–390.

20 Hashimoto, K.; Wibullcksanakul, S.; Okada, M. *J. Polym. Sci. Part A: Polym. Chem.* **1995,** *33*, 1495–1503.

21 Yamanaka, C.; Hashimoto, K. *J. Polym. Sci. Part A: Polym. Chem.* **2002,** *40*, 4158–4166.

22 Thiem, J.; Luders, H. *Makromol. Chem.* **1986,** *187*, 2775–2785.

23 Bachmann, F.; Reimer, J.; Ruppenstein, M.; Thiem, J. *Macromol. Rapid Commun.* **1998,** *19*, 21–26.

24 Bachmann, F.; Ruppenstein, M.; Thiem, J. *J. Polym. Sci. Part A: Polym. Chem.* **2001,** *39*, 2332–2341.

25 Ubaghs, L.; Fricke, N.; Keul, H.; Höcker, H. *Macromol. Rapid Commun.* **2004,** *25*, 517–521.

26 Prömpers, G.; Keul, H.; Höcker, H. *Des. Monomers Polym.* **2005,** *8*, 547–569.

27 Prömpers, G.; Keul, H.; Höcker, H. *Green Chem.* **2006,** *8*, 467–478.

28 Gomez, R. V.; Varela, O. *Macromolecules* **2009,** *42*, 8112–8117.

29 Arce, S. M.; Kolender, A. A.; Varela, O. *Polym. Int.* **2010,** *59*, 1212–1220.

30 Kolender, A. A.; Arce, S. M.; Varela, O. *Carbohydr. Res.* **2011,** *346*, 1398–1405.

31 Crombez-Robert, C.; Benazza, M.; Fréchou, C.; Demailly, G. *Carbohydr. Res.* **1997,** *303*, 359–365.

32 Glaçon, V.; Benazza, M.; El Anzi, A.; Beaupère, D.; Demailly, G. *J. Carbohydr. Chem.* **2004,** *23*, 95–110.

33 Mancera, M.; Roffé, I.; Rivas, M.; Silva, C.; Galbis, J. A. *Carbohydr. Res.* **2002,** *337*, 607–611.

34 Mancera, M.; Roffé, I.; Rivas, M.; Silva, C.; Galbis, J. A. *Carbohydr. Res.* **2003,** *338*, 1115–1119.

35 Le Merrer, Y.; Duréault, A.; Greck, C.; Micas-Languin, D.; Gravier, C.; Depezay, J.-C. *Heterocycles* **1987,** *25*, 541–548.

36 (a) Le Merrer, Y.; Gauzy, L.; Gravier-Pelletier, C.; Depezay, J.-C. *Bioorg. Med. Chem.* **2000,** *8*, 307–320; (b) Fitremann, J.; Duréault, A.; Depezay, J.-C. *Tetrahedron Lett.* **1994,** *35*, 1201–1204.

37 Nazhaoui, M.; Joly, J. P.; Kitane, S.; Berrada, M. *J. Chem. Soc. Perkin Trans. 1* **1998,** *22*, 3845–3850.

38 Rokicki, G.; Piotrowska, A. J. *Polymer* **2002,** *43*, 2927–2935.

39 Versteegen, R. M.; Sijbesma, R. P.; Meijer, E. W. *Angew. Chem. Int. Ed. Engl.* **1999,** *38*, 2917–2919.

40 Deepa, P.; Jayakannan, M. *J. Polym. Sci. Part A: Polym. Chem.* **2008,** *46*, 2445–2458.