DOI: 10.1021/ma9014643

Macromolecules
ARTICLE

Synthesis of Polyhydroxy [*n*]-Polyurethanes Derived from a Carbohydrate Precursor

Romina V. Gómez and Oscar Varela*

CIHIDECAR−CONICET, Departamento de Química Orgánica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Pabellón 2, Ciudad Universitaria, 1428 Buenos Aires, Argentina

Received July 6, 2009; Revised Manuscript Received August 28, 2009

ABSTRACT: Polyhydroxy [*n*]-polyurethanes with chains formed by sugar-derived units have been synthesized. The enantiomerically pure monomeric precursor 1-amino-1-deoxy-2,3:4,5-di-*O*-isopropylidene-D-galactitol (**4**) was prepared from D-galactono-1,4-lactone (**1**) by a three-step route. Acetonation of **1** with 2,2-dimethoxypropane gave methyl 2,3:4,5-di-*O*-isopropyldene-D-galactonate (**2**). The ester group of **2** was converted into the amide and reduced with $LiAlH_4$ to afford **4**. This amino alditol was treated with di-*tert*-butyltricarbonate to produce the intermediate isocyanate derivative as activated monomer for the polymerization. The reaction conditions were adjusted to prevent the formation of urea linkages during the polycondensation. Thus, polymerization of the isocyanate monomer in THF and in the presence of $Zr(acac)_4$ as catalyst afforded the linear [*n*]-polyurethane **6**, which upon purification was practically free of urea linkages. Removal of the acetal protecting groups of **6** with 10:1 TFA−water, under conditions that did not produce hydrolysis of the polymer chain, led to the polyhydroxy [*n*]-polyurethane **8**, having all the hydroxyl groups free. Polyurethanes **6** and **8** are examples of polyhydroxy [*n*]-polyurethanes entirely obtained from a sugar precursor. They were isolated as crystalline materials that exhibited high melting temperatures and thermal stability up to 230 °C. Accordingly, the SEM analysis of **6** and **8** revealed surfaces with morphologies characteristic of crystalline polymers.

Introduction

Polyurethanes are widespread materials with many domestic and technical applications. They are also used in drug administration and biomedical instrumentation and devices.[1] These and other medical uses are a consequence of the extremely good biocompatibility of polyurethanes.[2] Because of the low in vitro adsorption and platelet adhesion to polyurethanes, they are particularly useful when contact with body fluids, like plasma and blood, is required.[3,4] However, aliphatic and aromatic polyurethanes have shown a strong resistance to degradation,[5] which prevents the use of these polymers in temporary applications, for instance as biomaterials for biodegradable endoprosthesis.[2] An approach to overcome this difficulty is the use of raw materials as replacements of some petroleum-based polymer precursors. The polymers obtained from natural products are expected to be biodegradable and nontoxic. Thus, biobased polyurethanes and their composites have been already prepared from many natural resources,[6] such as starch,[7] castor oil,[8] and natural rubber.[9] The inclusion of hydrophilic monomers into the polymer chain facilitates water attack increasing the hydrolytic degradation, and for this reason some polyurethanes containing carbohydrate-derived units have been prepared.[10] For the synthesis of sugar-based [*m*,*n*]-polyurethanes, selectively protected sugar derivatives have been employed as diol monomers. For instance, partially protected methyl α-D-glucopyranosides, having two free hydroxyl groups, reacted with hexamethylene diisocyanate to give the corresponding polyurethanes.[11] Similarly, anhydrohexitols[12,13] and acetonides of gulonolactones[14] have been employed as diol monomers that polymerized with diisocyanates. Polyurethanes have been obtained starting from polymethylenediamines and carbonate derivatives of D-mannitol[15] or galactitol[16] with the primary hydroxyl groups activated for the polycondensation. Also, conveniently protected alditols L-threitol, L-arabinitol, and xylitol have been synthesized as diol monomers and polymerized with common diisocyanate derivatives.[17−19] All these examples are referred to the synthesis of [*m*,*n*]-polyurethanes in which the diol or diamine comonomer derives from a carbohydrate. In contrast, the preparation of [*n*]-polyurethanes entirely based on an amino sugar precursor has been much less explored. In fact, just one example has been found in the literature on the synthesis of a [*n*]-polyurethane, which was prepared from 1:4,3:6-dianhydrosorbitol and using the toxic phosgene for the activation of the monomer.[20] The synthesis of even common aliphatic [*n*]-polyurethanes via isocyanate intermediates was rather difficult to accomplish due to the unavailability of a suitable procedure to prepare α,ω-isocyanate alcohol monomers. However, Meijer et al.[21] have described the use of di-*tert*-butyltricarbonate ($(Boc)_2CO_3$) for the mild conversion of the amino group of aliphatic α,ω-amino alcohols into α,ω-isocyanato alcohols, followed by polymerization. This procedure has been employed for the synthesis of a tyrosine-based polyurethane.[22] Therefore, as continuation of our work on the synthesis of polymers derived from renewable resources,[23] we describe herein the synthesis of a conveniently protected di-*O*-isopropylidene 1-amino-1-deoxyalditol and the polymerization of this monomer to give a stereoregular [*n*]-polyurethane. This material was subjected to acid removal of the acetonide protecting groups to yield a polyhydroxy [*n*]-polyurethane. These two polymers are examples of optically active, stereoregular polyhydroxy [*n*]-polyurethanes obtained from a carbohydrate precursor.

Experimental Section

General Methods. D-Galactono-1,4-lactone was used as purchased from Pfanstiehl. Solvents were dried and purified by

*Corresponding author. E-mail: varela@qo.fcen.uba.ar.

 Published on Web 09/08/2009

Table 1. Polymerization Conditions Employed for the Synthesis of 6

entry	solvent	catalyst (mol %)	monomer **4** [mol/L]	temp (°C)	time (h)	yield (%)	ratio (%) **6**:**7**
1	$CHCl_3$	NEt_3 (3.0)	0.30	25	96	63	30:70
2	$CHCl_3$	$Zr(acac)_4$ (0.1)	0.20	50	96	62	50:50
3	THF	NEt_3 (0.2)	0.30	65	96	32	20:80
4	THF	NEt_3 (3.0)	0.30	65	96	65	30:70
5	THF	$Zr(acac)_4$ (0.1)	0.90	65	48	82	80:20
6	THF	$Zr(acac)_4$ (0.1)	0.30−0.35	65	48	81	92:8

standard methods. Analytical thin-layer chromatography (TLC) was performed on Silica Gel 60 F_{254} (E. Merck) 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. Column chromatography was carried out with silica gel 60 (230−400 mesh, E. Merck). Optical rotations were measured with a Perkin-Elmer 343 digital polarimeter at 25 °C. Nuclear magnetic resonance (NMR) spectra were recorded on Bruker AC-200 or Bruker AMX-500 spectrometers. Gel permeation chromatography (GPC) was performed at room temperature with a Waters apparatus equipped with a Waters 2414 refractive index detector and Styragel HR (7.8 × 300 mm) Waters columns, using THF as mobile phase. The flow rate was 1 mL/min. Calibration was based on polystyrene standards. IR spectra were recorded with a Nicolet 510P FTIR spectrometer. MALDI-MS measurements were performed using a laser desorption time-of-flight mass spectrometer (Bruker Daltonics OminFlex instrument). Differential scanning calorimetry (DSC) was conducted with a DSC Q20 (TA Instruments). Samples of about 2 mg were heated at a rate of 10 °C/min and then cooled to room temperature, at the same rate. Thermogravimetric analysis (TG) was performed on a Shimadzu TGA-51 instrument. The surface morphology of the polyurethanes was analyzed by scanning electron microscopy (SEM) on a Zeiss Supra 40 instrument with an in-lens secondary detector.

2,3:4,5-Di-*O*-isopropylidene-D-galactonamide (3). To a saturated solution of ammonia in dry MeOH (50 mL), externally cooled at 0 °C, was added methyl 2,3:4,5-di-*O*-isopropylidene-D-galactonate[24] (**2**, 1.00 g, 3.45 mmol). The mixture was stirred at 0 °C for 1 h and then at room temperature for an additional 16 h. The solution was concentrated to afford a slightly brownish syrup, which crystallized on standing. Recrystallization from hexane−EtOAc 5:1 gave **3** (0.85 g, 89%) as white crystals; mp 101 °C, $[\alpha]_D$ −0.20 (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 6.60, 5.75 (br s, each 1H, N*H*), 4.48 (d, 1H, $J_{2,3}$ = 6.3 Hz, H-2), 4.33 (dd, 1H, $J_{2,3}$ = 6.3, $J_{3,4}$ = 5.1 Hz, H-3), 4.20 (dt, 1H, $J_{4,5}$ = 8.1, $J_{5,6}$ = 4.5, $J_{5,6'}$ = 4.1, H-5), 4.10 (dd, 1H, $J_{3,4}$ = 5.1, $J_{4,5}$ = 8.1 Hz, H-4), 3.81 (dd, 1H, $J_{5,6}$ = 4.5, $J_{6,6'}$ = 11.9, H-6), 3.73 (dd, 1H, $J_{5,6'}$ = 4.1, $J_{6,6'}$ = 11.9 Hz, H-6′), 1.98 (br s, 1H, O*H*), 1.47, 1.42 (2 s, each 3H and 9H, respectively (CH_3)$_2$C). ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 173.5 (*C*O), 111.4, 109.7 (Me_2C), 78.9, 78.5, 77.7, 76.6 (C-2-C-5), 62.4 (C-6), 27.2, 27.0, 26.9, 26.0 [(CH_3)$_2$C]. Anal. Calcd for $C_{12}H_{21}NO_6$: C, 52.35; H, 7.69; N, 5.09. Found: C, 52.60; H, 7.80; N, 5.07.

1-Amino-1-deoxy-2,3:4,5-di-*O*-isopropylidene-D-galactitol (4). To an externally cooled (0 °C) suspension of $LiAlH_4$ (0.63 g, 16.50 mmol) in anhydrous THF (40 mL) was added, under Ar, a solution of the amide **3** (0.92 g, 3.34 mmol). The mixture was heated at the reflux temperature for 8 h, under a smooth steam of Ar. The reaction mixture was allowed to reach room temperature, and EtOAc (5 mL) was slowly added with stirring, for 30 min, followed by dropwise addition of 15% aqueous NaOH (5 mL). The solid formed was collected by centrifugation and washed with hot portions of THF (3 × 15 mL). The liquids were pooled and concentrated to a syrup which was dissolved in MeOH and purified through a column filled with an ion-exchange resin (Biorex 70, carboxylate form). The column was eluted with MeOH and then with mixtures of increasing concentration of pyridine in MeOH (from 5% to 30%). The fractions that gave positive the ninhydrin test were collected and concentrated. The solid obtained was recrystallized from EtOAc−hexane 5:1 to afford the amino alditol **4** (0.61 g, 71%); mp 99−100 °C, $[\alpha]_D$ −8.8 (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 4.04 (dt, 1H, $J_{4,5}$ = 8.5, $J_{5,6}$ = 4.7, $J_{5,6'}$ = 4.3 Hz, H-5), 3.99 (ddd, 1H, $J_{1,2}$ = 3.6, $J_{1',2'}$ = 6.4, $J_{2,3}$ = 7.6 Hz, H-2), 3.81 (dd, 1H, $J_{5,6}$ = 4.7, $J_{6,6'}$ = 11.7, H-6), 3.77 (dd, 1H, $J_{2,3}$ = 7.6, $J_{3,4}$ = 8.5 Hz, H-3), 3.74 (dd, 1H, $J_{5,6'}$ = 4.3, $J_{6,6'}$ = 11.7 Hz, H-6′), 3.69 (dd, 1H, $J_{2,3}$ = 7.6, $J_{3,4}$ = 8.5 Hz, H-3), 3.05 (dd, 1H, $J_{1,2}$ = 3.6, $J_{1,1'}$ = 13,5 Hz, H-1), 2.86 (dd, 1H, $J_{1',2}$ = 6.4, $J_{1,1'}$ = 13.5 Hz, H-1′), 1.78 (br s, 3H, N*H* + O*H*), 1.40, 1.39, 1.37, 1.36 (4 s, each 3H, (CH_3)$_2$C). ^{13}C NMR ($CDCl_3$, 125.7 MHz): δ 109.7, 109.6 (Me_2C), 82.5, 81.1, 79.2, 79.1 (C-2-C-5), 62.6 (C-6), 44.1 (C-1), 27.2, 27.0, 26.9 [(CH_3)$_2$C]. Anal. Calcd for $C_{12}H_{23}NO_5$: C,55.16; H, 8.87; N, 5.36. Found: C, 55.23; H, 8.91; N, 5.27.

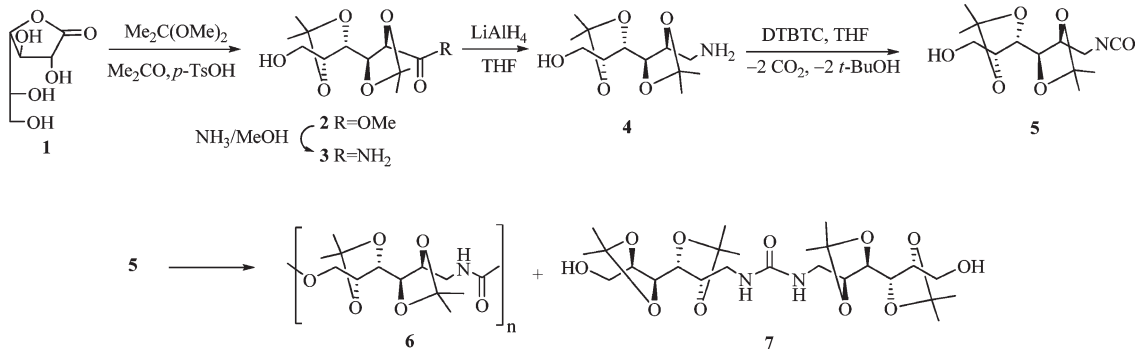
General Procedure for the Conversion of 4 into 1-Deoxy-1-isocyanate-2,3:4,5-di-*O*-isopropylidene-D-galactitol (5). To a solution of **4** (0.130 g, 0.52 mmol) in the solvent ($CHCl_3$ or THF, 0.5 mL) was added a solution of di-*tert*-butyltricarbonate (0.143 g, 0.55 mmol) in the same solvent (1.0 mL). The mixture was stirred at room temperature, under an argon atmosphere, for 30 min. A portion of the solution was concentrated in vacuum at room temperature to verify the complete conversion of **4** into the isocyanate **5**. Compound **5**: FTIR (KBr) 3407 (br, OH), 2260 cm^{-1} (s, NCO). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 4.58 (dd, 1H, $J_{5,6'}$ = 2.4, $J_{6,6'}$ = 11.2 Hz, H-6), 4.31 (dd, 1H, $J_{5,6}$ = 5.5, $J_{6,6'}$ = 11.2 Hz, H-6′), 4.27−4.05 (m, 2H), 3.80−3.77 (m, 2H), 3.73 (d, 1H, $J_{1,1'}$ = 13.9, $J_{1,2}$ = 3.3 Hz, H-1), 3.39 (dd, 1H, $J_{1,1'}$ = 13.9, $J_{1',2}$ = 4.2 Hz, H-1′), 1.46, 1.41, 1.40, 1.38 (4 s, 12H, (CH_3)$_2$C). ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 124.8 (N*C*O), 110.6, 109.8 (Me_2C), 79.6, 78.5, 78.2, 69.2 (C-2−C-5), 62.3 (C-6), 44.1 (C-1).

General Procedure for the Polymeryzation of Isocyanate 5. To a solution of **5**, obtained as described in the general procedure, was added the catalyst (TEA or 0.1% mol $Zr(acac)_4$), and the mixture was heated at the temperature and time indicated in Table 1. The gelly mass obtained was suspended in hexane, and the polymer was isolated by centrifugation. The solid was dissolved in CH_2Cl_2 and precipitated upon addition of hexane to afford the polymeric material. The yield and composition of each particular preparation are reported in Table 1.

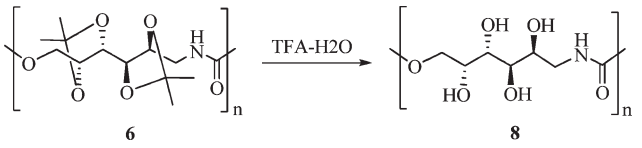
The washing liquors contained the urea **7** as a major component. Compound **7** exhibited the following spectral properties: ^{1}H NMR (DMSO-d_6, 200 MHz): δ 6.11 (br s, 1H, NH), 4.84 (br s, 1H, OH), 3.96−320 (m, 7H), 3.05 (m, 1H), 1.35, 1.34, 1.31 (3 s, 12H, (CH_3)$_2$C). ^{13}C NMR (DMSO-d_6, 50.3 MHz): δ 157.7 (N_2CO), 108.8, 108.7 (Me_2C), 80.4, 78.6, 78.5, 71.2 (C-2−C-5), 61.7 (C-6), 27.2, 27.1, 26.8 [(CH_3)$_2$C]. MALDI-TOF MS: *m*/*z* 543 ($M + Na^+$).

Synthesis of [*n*]-Polyurethane 6 in Preparative Scale. To a solution of **4** (0.19 g, 0.73 mmol) in anhydrous THF (0.6 mL) was added, under a steam of argon, a solution of $(Boc)_2CO_3$ (0.21 g, 0.80 mmol) in THF (1.5 mL). After 30 min of stirring at room temperature, 0.01 M $Zr(acac)_4$ in THF (73 μL) was added. The solution was heated to 60 °C in a screw-cup vial, under a static atmosphere of argon. After 4 h a gelly mass was formed, and to facilitate the magnetic stirring, anhydrous THF (1 mL) was incorporated with a syringe. After 48 h of stirring at 60 °C, the solid was separated by centrifugation and then dissolved in CH_2Cl_2 (1 mL). Ethyl ether (1 mL) was added, and the polymer was precipitated by dropwise addition of MeOH. Upon

Scheme 1. Synthesis of the *O*-Protected Polyhydroxy [*n*]-Polyurethane 6 via the 1-Amino-1-deoxyalditol 4



Scheme 2. *O*-Deprotection of the Acetonide Groups of 6 To Give the Polyhydroxy [*n*]-Polyurethane 8



centrifugation the solid was washed with hot MeOH (3 × 1.5 mL). Polyurethane **6** (0.17 g, 81%) was obtained as a white powder; $[\alpha]_D$ −14.7 (*c* 1.0, $CHCl_3$). FTIR (KBr): 3362 (br, NH), 1740, 1551 cm^{-1} (s, NCO_2). ^1H NMR ($CDCl_3$, 500 MHz): δ 5.31 (br s, 1H, OCON*H*), 4.48 (d, 1H, $J_{6,6'}$ = 11.2, H-6), 4.21 (m, 1H, H-5), 4.07 (m, 2H, H-2, 6′), 3.72 (t, 1H, $J_{3,4} \approx J_{4,5}$ = 8.0 Hz, H-4), 3.68 (dd, 1H, $J_{2,3} \approx J_{3,4}$ = 8.0 Hz, H-3), 3.58 (br d, 1H, $J_{1,1'}$ = 13.5 Hz, H-1), 3.44 (dd, 1H, $J_{1,1'}$ = 13.5 Hz, $J_{1',2}$ = 5.8 Hz, H-1′), 1.32 (×2), 1.31, 1.30 (3 s, 12H, $(CH_3)_2C$). ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 156.1 (NCO_2), 110.6, 110.0 (Me_2C), 79.7, 79.3, 79.1, 78.1 (C-2−C-5), 65.2 (C-6), 43.0 (C-1), 27.1, 27.0, 26.9, 26.8 [$(CH_3)_2C$]. Anal. Calcd for $(C_{13}H_{21}NO_6)_n$: C, 54.35; H, 7.37; N, 4.88. Found: C, 54.33; H 7.45; N, 4.60.

Synthesis of Polyhydroxy [*n*]-Polyurethane 8 Starting from 6. Polymer **6** (0.10 g) was stirred with a solution of TFA−H_2O 10:1 (1.0 mL). The solid immediately dissolved, and the stirring was continued at room temperature for 15 min. At this time, a gelly mass was formed and MeOH (5 mL) was added. The resulting solid was isolated by centrifugation and purified by washings with hot MeOH (3 × 2 mL) and boiling water (2 × 2 mL) to afford **8** (60 mg, 83%); $[\alpha]_D$ −103 (*c* 0,1, DMSO). FTIR (KBr): 3406 (br, OH + NH), 1712, 1544 cm^{-1} (s, NCO_2). ^{13}C NMR (DMSO-d_6, 50.3 MHz): δ 156.5 (N*C*O), 69.2, 67.8, 67.4, 65.9 (C-2−C-5), 63.0 (C-6), 43.9 (C-1). Anal. Calcd for $(C_7H_{13}NO_6)_n$: C, 40.58; H, 6.32; N, 6.76. Found: C, 40.33; H, 6.52; N, 6.61.

For the GPC analysis, compound **8** (10 mg) was acetylated with acetic anhydride (1 mL) and pyridine (1 mL). The mixture was vigorously stirred at room temperature for 20 h. The resulting solution was concentrated under vacuum, and the residue was dissolved in THF and filtered. Aliquots of this solution were analyzed using GPC.

Results and Discussion

Enantiomerically pure and crystalline 1-amino-1-deoxy-2,3:4,5-di-*O*-isopropylidene-D-galactitol (**4**), the monomer precursor of polyurethane **6**, was readily prepared from D-galactono-1,4-lactone (**1**) as depicted in Scheme 1. Acid-catalyzed acetonation of **1** with 2,2-dimethoxypropane afforded the methyl ester **2**.[24] Ammonolysis of the ester function of **2** with a solution of dry MeOH saturated with ammonia led to the crystalline amide **3**, which was subjected to reduction with lithium aluminum hydride to afford the amino alditol **4** as a crystalline product. The ^1H NMR spectrum of **4** showed coupling constant (*J*) values that were in agreement with the planar zigzag conformation of the chain, somewhat distorted by the presence of the two fused dioxolane rings. In particular, the large $J_{3,4}$ value (8.5 Hz) indicated that diacetonide rings of **4** adopted the *s-trans* conformation for the C-3−C-4 linkage. This is an important fact, as the planar zigzag conformation would facilitate the formation of the linear urethane, and preclude the formation of cyclic oligomers, during the polymerization. The conformation of **4** was confirmed on the basis of the ROESY spectrum, which showed the expected NOE contacts between H-2, H-4 and H-3, H-5.

For the polymerization, the amino group of **4** was converted into the isocyanate intermediate **5**. This was accomplished by reaction of **4** with di-*tert*-butyltricarbonate [$(Boc)_2CO_3$] in $CHCl_3$ or THF, at room temperature for 30 min. The $(Boc)_2CO_3$ was synthesized according to the reported method.[25] The structure of **5** was confirmed spectroscopically; the FTIR spectrum showed the absorptions of the isocyanate and the hydroxyl groups at 2260 and 3407 cm^{-1}, respectively. The ^1H NMR spectrum of **5** showed the absence of the resonances of the amine protons and downfield shifting of the methylene protons (H-1, H-1′) vicinal to nitrogen (>0.5 ppm), indicating the conversion of the amino into isocyanate. Additionally, in the ^{13}C NMR spectrum of **5** was observed the signal of the isocyanate carbon at 124.8 ppm.

The polymerization of the active monomer **5** was carried out in situ, in $CHCl_3$ or THF, and in the presence of zirconium(IV) acetylacetonate [Zr(acac)$_4$] or triethylamine (TEA) as catalysts. The polymeric material formed in each case was isolated by addition of ethyl ether and centrifugation. The solid was dissolved in CH_2Cl_2 and precipitated with hexane; it was dried and analyzed using FTIR and NMR spectroscopies. Selected results are shown in Table 1. In all the cases, the spectra obtained revealed the presence of urethane as well as urea linkages. Particularly, the ^1H NMR spectrum of the polymer recorded in DMSO-d_6 showed clearly the signals of the N*H* of urethane (7.37 ppm) and urea groups (6.11 ppm). In the ^{13}C NMR spectrum, resonances of the carbon atom of the carbonyl of urethane (156.1 ppm) and urea (157.7 ppm) were observed. Similar signals were reported for linear alkyl [*n*]-polyurethanes containing additional urea units in the molecule.[26] The FTIR spectrum showed characteristic absorptions for the urethane (1740 and 1551 cm^{-1}) and urea (1660 cm^{-1}) carbonyl groups. The ratio between urethane and urea, in each individual preparation shown in Table 1, was determined by integration of the N*H* signal from the ^1H NMR spectrum of the material precipitated from CH_2Cl_2−hexane. The ^1H NMR spectrum of the mother liquors revealed that, in most cases, the urea **7** was the major component. The use of $CHCl_3$ as polymerization solvent was not suitable for quantitative urethane formation (Table 1, entries 1 and 2) as the urea compound **7** was a major component of the product, regardless of the catalyst employed. Similarly, the use of NEt_3 as catalyst produced considerable amounts of urea in $CHCl_3$ (entry 1) as well as in THF (entries 3 and 4). In fact, NEt_3 is not an efficient catalyst for the polycondensation, even at relatively high concentration (3 mol %), as evidenced by the

Table 2. Properties of [*n*]-Polyurethanes 6 and 8

polyurethane	M_w[a]	M_n[a]	M_w/M_n[a]	$[\alpha]_D$	T_m[b] (ΔH)	T_d[c]
6	20 170	11 230	1.8	−14.7	212 (63.6)	315
8	16 600	12 860	1.3	−103.2	225 (139.3)	247

[a] Measured by GPC, with THF as solvent, relative to polystyrene standards. [b] Determined by DSC. Temperature in °C, ΔH in J g^{-1}. [c] Determined by TG. Temperature in °C.

considerable amount of isocyanate **5** present after 10 h of reaction.

Interestingly, the solid material obtained by polymerization of **5** in the presence of 0.2 mol % NEt_3 in THF (entry 3) consisted mostly in the *N*,*N*′-disubstituted urea **7**, as confirmed spectroscopically. The ^{1}H NMR spectrum of **7** showed a broad singlet corresponding to the terminal hydroxyl group (4.85 ppm) with the same integral as the N*H* signal, which was in agreement with the proposed structure. Furthermore, the MALDI- MS of **7** showed, as expected, the molecular ion ($M + Na^+$) at *m*/*z* 543.

Polycondensation of **5** in THF with $Zr[acac]_4$ as catalyst afforded the linear polyurethane **6** as the major product (entries 5 and 6). Under optimized conditions (entry 6) the monomer **5** was rapidly consumed, and an increasingly viscous, gelly mass was formed. In preparative scale, polymerization of **5** gave the polyurethane **6** in 81% yield, after the general work-up described above. The polymer was further purified by dissolution in CH_2Cl_2−ether 1:1 and precipitation by dropwise addition of MeOH. We verified that the urea derivative **7** remains in solution in this mixture of solvents. The FTIR spectrum (KBr) of the purified polymer **6** showed characteristic absorptions for the urethane group at 3362 (br, NH), 1740, and 1551 cm^{-1} (s, NCO_2); the peak due to the urea group (1660 cm^{-1}) was practically absent. Detailed analysis by ^{1}H NMR spectroscopy (in DMSO-d_6) showed that **6** contained a small amount (∼2%) of urea linkages, and both the *trans* (δ 7.37) and *cis* (δ 6.87) carbamate forms were observed, as reported for common polyurethanes.[21,26] Since the proportion of urea linkages is maintained even when the polyurethane was subjected to further purifications, it can be assumed that a few urea units are incorporated into the polyurethane chain, as observed for analogous preparations of alkyl [*n*]-polyurethanes.[21]

The formation of urea linkages suggests the nucleophilic attack of the amine of **4** to the isocyanate group of **5**. The amine endgroup may be regenerated from **5** by hydrolysis of the isocyanate group.[27] When catalysis is not efficient, as happens with Et_3N, the isocyanate remains in the polymerization medium for long times, increasing the possibility for hydrolysis and concomitant urea formation. In contrast, rapid consumption of **5** by polycondensation lowers the urea formation.

Polyurethane **6** was characterized by gel permeation chromatography (GPC), differential scanning calorimetry (DSC), and thermogravimetric analysis (TGA). Data are shown in Table 2. The molecular weight of polymer **6** was determined by GPC using THF as mobile phase. To increase solubility in THF, compound **6** was treated with trifluoroacetic anhydride, as previously described for polyamides.[28] The polymer obtained from the preparative scale showed a weight-average molecular weight (M_w) of 20 170, with a polydispersity of 1.8.

The thermal behavior of polyurethane **6** was studied by DSC; the thermogram corresponding to the first heating cycle showed a broad endotherm of melting (T_m = 212 °C, ΔH = 63.6 J/g). The width of this transition suggested a disperse population of crystallites sizes, as observed for polymers that precipitate from a solution.[29] When the endset of the melting was reached (220 °C), the sample was cooled to room temperature and then subjected to a second heating cycle. The thermogram recorded for the cooling process showed a glass transition (T_g = 64 °C), but no other thermal transitions took place. During the second heating cycle only the glass transition was observed. Therefore, polyurethane **6** does not crystallize from the melting, upon rapid cooling. The TGA trace for the polyurethane **6** indicated that decomposition started at 240 °C. From the TGA curve, plotted in the differential form, the temperature of decomposition (T_d = 315 °C) was determined as the maximum of the peak.

As the hydroxyl groups of polymer **6** are protected as acetal derivatives that are labile to acids, the hydrolysis of such protecting groups was attempted in order to obtain a polyhydroxylated [*n*]-polyurethane. The removal of the acetal groups of **6** was conducted with trifluoroacetic acid (TFA)−water (10:1), under conditions that have been successfully applied for hydrolysis of acetonides of [*m*,*n*]-polyurethanes.[16,19b] After 15 min of stirring at room temperature, a gelly mass was formed and upon addition of MeOH a white solid precipitated out. The solid was collected by centrifugation and purified by washings with hot MeOH and then with water. The resulting material was studied by GPC (Table 2), after treatment with acetic anhydride in THF in order to dissolve the sample in the solvent employed for the chromatography (THF). The GPC trace revealed a single peak corresponding to a M_w of 16 600, suggesting that no appreciable degradation of the polymer chain had taken place. However, at longer reaction times some hydrolytic degradation occurred as the GPC chromatograms revealed at high retention times, peaks due to oligomers with a rather wide range of molecular weights. The narrower polydispersity of polymer **8** (1.3), compared with that of **6** (1.8), could be attributed to the removal of oligomers of **8**, which remain soluble in water after the acid treatment of **6**.

The FTIR spectrum of the polyhydroxy polyurethane **8** showed a broad band centered at 3406 cm^{-1} (HO and HN) and strong absorptions characteristic of the carbamate group at 1712 and 1544 cm^{-1}. The ^{1}H NMR spectrum of **8** was rather complex, but the ^{13}C NMR spectrum recorded in DMSO-d_6 showed the absence of the signals of the isopropylidene groups and the signals of the carbons of carbamate (156.5 ppm) and those of the carbons bonded to the urethane oxygen (63.0 ppm) and urethane nitrogen (43.9 ppm) at values similar to the analogous resonances in **6**. However, the C-2−C-5 resonances in **8** were shifted upfield (∼10 ppm) with respect to those corresponding to **6**, in agreement with the removal of the isopropylidene groups.[30]

The thermal behavior of polyurethane **8** was studied by DSC and TG. The DSC thermogram revealed, during the first heating cycle, a broad endotherm (50−110 °C) that may be attributed to the loss of water, as the material is highly hygroscopic. Then, a sharp endotherm was observed, centered at 225 °C, which corresponds to the melting (ΔH = 139.3 J g^{-1}). During the cooling and a second heating cycle no thermal transitions were detected. The narrower melting range of **8** compared to that of **6** suggested a higher degree of crystallinity for **8**, which could be the result of intermolecular hydrogen bonds between the polymer chains in **8**. Probably for this reason, this polymer was slightly soluble in water and in polar organic solvents, such as DMF and DMSO. Gelation took place upon cooling warmed solutions of **8** in these solvents.

Polymer **8** was thermally less stable than **6**, according with the TG analysis, with the decomposition starting at 230 °C, immediately after the melting (T_d = 247 °C). The mass loss between 50 and 110 °C could be due to elimination of water, in agreement with the DSC thermogram.

Polymers **6** and **8** were analyzed using SEM in order to determine their surface features. The materials were isolated and purified as already described. The SEM pictures show, in agreement with the DSC data, that both polyurethanes are crystalline, although they exhibited a different morphology. Thus, the SEM images of polymer **6** revealed the formation of disordered aggregates of large platelets (up to 40 μm in width)

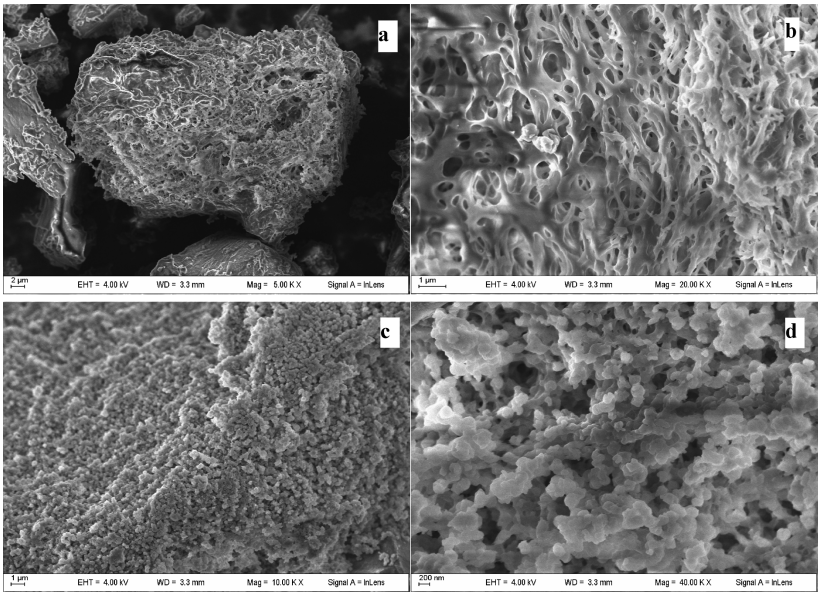


Figure 1. SEM Images for polyurethanes **6** (a, b) and **8** (c, d).

having a nonregular shape (Figure 1a). At higher magnification a complex fiberlike network morphology was observed (Figure 1b). In contrast, polyurethane **8** exhibited by SEM a surface formed by aggregates of nano/micro particles generated by precipitation (Figure 1c). The magnified image shows that the average size of particles is in the range of 20−100 nm (Figure 1d).

Conclusions

A polyhydroxy [*n*]-polyurethane with the hydroxyl groups protected as isopropylidene acetals has been synthesized by polymerization of a conveniently substituted 1-amino-1-deoxyalditol prepared from D-galactono-1,4-lactone. The amino function of the monomer was activated with di-*tert*-butyltricarbonate to the corresponding isocyanate intermediate, which was polymerized using $Zr(acac)_4$ as catalyst. The removal of the acetal groups of the resulting polymer was selectively accomplished, without hydrolysis of the carbamate linkages, to afford the corresponding polyhydroxy [*n*]-polyurethane. This polymer is particularly interesting, as it possesses all the hydroxyl groups of the chain unprotected. In contrast, the dianhydrosorbitol-based [*n*]-polyurethane previously prepared[20] has no hydroxyl groups remaining, as sorbitol has been subjected to dehydration, with formation of intramolecular ether linkages, prior to polymerization. The polyurethanes described here are linear, stereoregular, and optically active materials, with relatively high molecular weights. Furthermore, according with the DSC and SEM studies, they are crystalline and exhibited high melting temperatures and thermal stability up to 230 °C. Both polyurethanes displayed, as expected, a different solubility. The one substituted by acetonide groups was highly soluble in organic solvents such as $CHCl_3$ and CH_2Cl_2, whereas the unprotected polyhydroxy [*n*]-polyurethane was slightly soluble even in polar solvents such as water, DMF, and DMSO.

Acknowledgment. This work was supported by grants from the University of Buenos Aires (project X227), the National Research Council of Argentina (CONICET, projects PIP 5011 and 00064), and the National Agency for Promotion of Science and Technology (ANPCyT-FONCyT, project PICT-00291). O.V. is a Research Member of CONICET.

Supporting Information Available: ^1H and ^{13}C NMR spectra for polymers and precursors; FTIR spectra and DSC and TG traces for the polymers. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Nair, L. S.; Laurencin, C. T. *Prog. Polym. Sci.* **2007**, *32*, 762–798.
(2) Król, P. *Prog. Mater. Sci.* **2007**, *52*, 915–1015.
(3) Poussard, L.; Burel, F.; Couvercelle, J. P.; Merhi, Y.; Tabrizian, M.; Bunel, C. *Biomaterials* **2004**, *25*, 3473–3483.
(4) Jyh-Horng, W.; Chun-Hsu, Y. *J. Biomed. Mater. Res.* **2000**, *51*, 761–770.
(5) Chapman, T. M. *J. Polym. Sci., Part A: Polym. Chem.* **1989**, *27*, 1993–2005.
(6) Dwan'Isa, J. P.; Mohanty, A. K.; Misra, M.; Drzal, L. T. Biobased Polyurethanes and Their Composites: Present Status and Future Perspective. In *Natural Fibers, Biopolymers and Biocomposites*; Mohanty, A. K., Misra, M., Drzal, L. T., Eds.; CRC Press: Boca Raton, FL, 2005; pp 775−805.
(7) Desai, S.; Thakore, I. M.; Sarawade, B. D.; Devi, S. *Polym. Eng. Sci.* **2000**, *40*, 1200–1210.
(8) Kendagannaswamy, B. K.; Annadurai, V.; Siddaramaiah, V.; Somashekar, R. *J. Macromol. Sci., Part A: Pure Appl. Chem.* **2000**, *37*, 1617–1625.
(9) Paul, C. J.; Nair, M. R. G.; Neelakantan, N. R.; Koshy, P. *Polymer* **1998**, *39*, 6861–6874.
(10) Donnelly, M. J.; Stanford, J. L.; Still, R. H. *Carbohydr. Polym.* **1990**, *14*, 221–240.
(11) Garçcon, 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.
(12) Braun, D.; Bergmann, M. *Angew. Makromol. Chem.* **1992**, *199*, 191–205.
(13) (a) Thiem, J.; Luders, H. *Makromol. Chem.* **1986**, *187*, 2775–2785. (b) Bachmann, F.; Reimer, J.; Ruppenstein, M.; Thiem, J. *Macromol. Chem. Phys.* **2001**, *202*, 3410–3419. (c) Bachmann, F.; Ruppenstein, M.; Thiem, J. *J. Polym. Sci., Part A: Polym. Chem.* **2001**, *39*, 2332–2341.
(14) Yamanaka, C.; Hashimoto, K. *J. Polym. Sci., Part. A: Polym. Chem.* **2002**, *40*, 4158–4166.
(15) Prömpers, G.; Keul, H.; Höcker, H. *Des. Monomers Polym.* **2005**, *8*, 547–569.
(16) Prömpers, G.; Keul, H.; Höcker, H. *Green Chem.* **2006**, *8*, 467–478.
(17) 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.
(18) Paz, M. V.; Aznar, J. A.; Galbis, J. A. *J. Carbohydr. Chem.* **2008**, *27*, 120–140.
(19) (a) Marín, R.; Paz, M. V.; Ittobane, N.; Galbis, J. A.; Muñoz-Guerra, S. *Macromol. Chem. Phys.* **2009**, *210*, 486–494. (b) Marín,

R.; Muñoz-Guerra, S. *J. Polym. Sci., Part A: Polym. Chem.* **2008**, *46*, 7996–8012.
(20) Bachmann, F.; Reimer, J.; Ruppenstein, M.; Thiem, J. *Macromol. Rapid Commun.* **1998**, *19*, 21–26.
(21) Versteegen, R. M.; Sijbesma, R. P.; Meijer, E. W. *Angew. Chem., Int. Ed.* **1999**, *38*, 2917–2919.
(22) Kudo, H.; Nagai, A.; Ishikawa, J.; Endo, T. *Macromolecules* **2001**, *34*, 5355–5357.
(23) (a) Orgueira, H. A.; Varela, O. *Adv. Carbohydr. Chem. Biochem.* **2000**, *55*, 135–137. (b) Orgueira, H. A.; Erra-Balsells, R.; Nonami, H.; Varela, O. *Macromolecules* **2001**, *34*, 687–695. (c) Orgueira, H. A.; Varela, O. *J. Polym. Sci., Part A: Polym. Chem.* **2001**, *39*, 1024–1030. (d) Romero Zaliz, C. L.; Varela, O. *Tetrahedron: Asymmetry* **2003**, *14*, 2579–2586. (e) Romero Zaliz, C. L.; Varela, O. *Tetrahedron: Asymmetry* **2005**, *16*, 97–103. (f) Romero Zaliz, C. L.; Varela, O. *Carbohydr. Res.* **2006**, *341*, 2973–2977. (g) Gómez, R. V.; Varela, O. *Tetrahedron: Asymmetry* **2007**, *18*, 2190–2196.
(24) Long, D. D.; Stetz, R. J. E.; Nash, R. J.; Marquess, D. G.; Lioyd, J. D.; Winters, A. L.; Asano, N.; Fleet, G. W. J. *J. Chem. Soc., Perkin Trans. 1* **1999**, *8*, 901–908.
(25) Pope, B. M.; Yamamoto, Y.; Tarbell, D. S. *Org. Synth.* **1978**, *57*, 45–50.
(26) Rokicki, G.; Piotrowska, A. J. *Polymer* **2002**, *43*, 2927–2935.
(27) Chattopadhyay, D. K.; Raju, K. V. S. N. *Prog. Polym. Sci.* **2007**, *32*, 352–418.
(28) Jacobi, E.; Schuttenberg, H.; Schulz, R. C. *Makromol. Chem., Rapid Commun.* **1980**, *1*, 397–402.
(29) Bell, J. P.; Slade, D. E.; Dumblenton, J. H. *J. Polym. Sci., Polym. Phys. Ed.* **1968**, *6*, 1773–1781.
(30) Bock, K.; Pedersen, C. *Adv. Carbohydr. Chem. Biochem.* **1983**, *41*, 27–66.