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Synthesis and characterization of poly-*O*-methyl-[*n*]-polyurethane from a D-glucamine-based monomer

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Dedicated to Professor Dr. András Lipták on the occasion of his 75th birthday

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ABSTRACT

Aminoalditol 1-amino-1-deoxy-D-sorbitol (**1**) was readily converted into 2,3,4,5-tetra-*O*-methyl derivative **5**, a key precursor of a sugar-based [*n*]-polyurethane. For the polymerization, the free amino or primary hydroxyl groups of **5** were selectively activated and employed as starting monomers in two alternative procedures. Thus, the amino function of **5** was converted into the isocyanate derivative by treatment with di-*tert*-butyltricarbonate, and polymerized in situ in the presence of Zr(IV) acetylacetonate. The resulting poly(1-amino-1-deoxy-2,3,4,5-tetra-*O*-methyl-D-sorbitol)urethane (**8**) had a moderate molecular weight and showed the presence of urea units. The alternative synthesis of **8** involved the activation of the free hydroxyl group of **5** as the corresponding phenylcarbonate. The polymerization of this α-amino-ω-phenylcarbonate alditol monomer does not require a metal catalyst. The resulting material exhibited an improved molecular weight and higher purity than that obtained via the isocyanate. [*n*]-polyurethane **8** was highly soluble in water as well as in common organic solvents (chloroform, acetone, ethyl acetate, etc) and was obtained as an amorphous material which was characterized thermally and spectroscopically.

1. Introduction

The design of new polymers with enhanced hydrophilicity and biodegradability starting from carbohydrate-derived monomers has attracted considerable attention.[1–5] Carbohydrates are massive renewable resources able to provide monomers suitable for the synthesis of polycondensates. The inclusion of hydrophilic monomers into the polymer chain facilitates water attack, increasing the hydrolytic degradation of the material. Among the condensation polymers, a fair number of biobased polyurethanes and their composites have been prepared from many natural resources.[6] Sugar-based [*m*,*n*]-polyurethanes have been synthesized using selectively protected derivatives of hexoses,[7,8] aldaro[9] and aldonolactones,[10] alditols, [11–14] or anhydroalditols,[15,16] as diol monomers. Such diols have been polymerized with diisocyanate monomers to afford the corresponding [*m*,*n*]-polyurethanes. These polymers have also been prepared by alternative procedures from D-glycosylamines and D-glucosamine,[17] from dichloroformates of anhydrohexitols[18] or from carbonate derivatives of D-mannitol[19] and galactitol.[20]

In contrast to the rather numerous reports on sugar-based [*m*,*n*]-polyurethanes, there are just a few examples on the synthesis of their AB-type analogues ([*n*]-polyurethanes). Thus, Thiem[21] described the synthesis of a carbohydrate-derived [*n*]-polyurethane by polycondensation of 2-deoxy-1,4:3,6-dianhydro-2-isocyanato-L-iditol obtained from 1,4:3,6-dianhydrosorbitol using the toxic phosgene for conversion of the amino group into isocyanate. Recently, we have reported the synthesis of an unprotected polyhydroxy [*n*]-polyurethane from a 1-amino-1-deoxyalditol precursor(1-amino-1-deoxy-2,3:4,5-di-*O*-isopropylidene-D-galactitol) prepared from D-galactono-1,4-lactone.[22] In this case, the amino group was converted into the isocyanate under the mild conditions reported by Meijer and co-workers.[23] for aliphatic α,ω-aminoalkanols.

Here we describe, as an additional example, the synthesis of a polyhydroxy [*n*]-polyurethane having the hydroxyl groups substituted as methyl ethers. The 1-amino-1-deoxy alditol monomer **5**, precursor of the polymer, was prepared through a short route from commercially available D-glucamine.

2. Results and discussion

For the synthesis of the aminoalditol monomer, the amino and primary hydroxyl groups of D-glucamine (1-amino-1-deoxy-D-sorbitol, **1**) were protected by selective substitution with trityl chloride (Scheme 1). The resulting *N*,*O*-dityrityl derivative **2** was treated with powdered NaOH in Me_2SO and MeI for the

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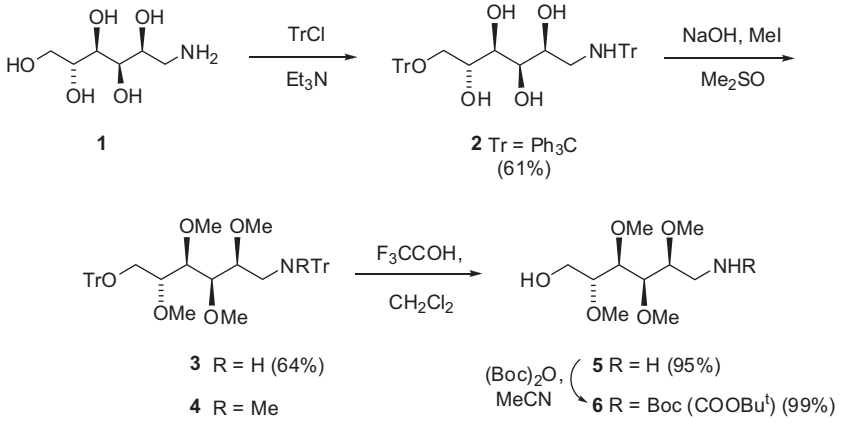


Scheme 1. Synthesis of monomer **5** and its *N*-Boc derivative **6**.

derivatization of the secondary alcohol functions as methyl ethers. This reaction afforded, together with the expected tetra-*O*-methyl derivative **3**, the *N*-methyl compound **4**, formed by additional methylation of the amine. The structure of **4** was readily established as the ^{1}H NMR spectrum showed the resonance of the *N*-methyl protons at 2.52 ppm. The signal of the *N*-methyl group was also detected at 44.1 ppm in the ^{13}C NMR spectrum of **4**, and the resonance of the methylene carbon of glucamine bonded to nitrogen underwent a strong deshielding compared with the same signal in **3**, due to N-methylation.[24]

Removal of the *N*- and *O*-trityl groups of **3** by acid hydrolysis with trifluoroacetic acid (TFA) afforded the aminoalditol **5**. To release the amine from the trifluoroacetic salt, the product was passed through a column filled with Amberlist A-26 (OH^-) ion-exchange resin. The signals of H-2–H-4 in the ^{1}H NMR spectrum of **5** collapsed into a complex multiplet between 3.30 and 3.65 ppm. However, the spectrum recorded in pyridine-d_5 admitted a first order analysis (Fig. 1). The coupling constant value between H-2 and H-3 was higher than that expected for $J_{2,3}$ in the planar zig-zag conformation of the backbone chain of **5**, and was indicative of the contribution of a sickle form ($_2G^-$) to the conformational equilibrium.[25] It is known that open-chain derivatives of glucose or sorbitol usually adopt sickle forms by rotation of the C-2–C-3 and/or C-3–C-4 bonds, in order to escape from the 1,3-parallel interaction between O-2–O-4 that occurs in the planar conformation.[26] Also, the small values for $J_{5,6a}$ and $J_{5,6b}$ (3.0 and 4.4 Hz, respectively) suggest that there is a substantial population of a rotamer through the C-5–C-6 bond ($_5G^+$) instead of the fully extended form.[25] These results are relevant to explain the behavior of **5** during the polymerization, as discussed later.

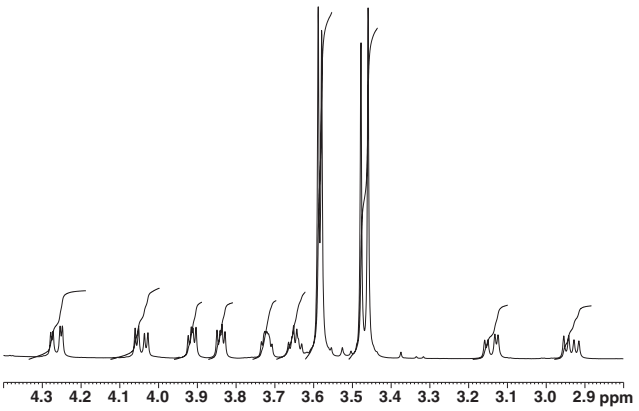
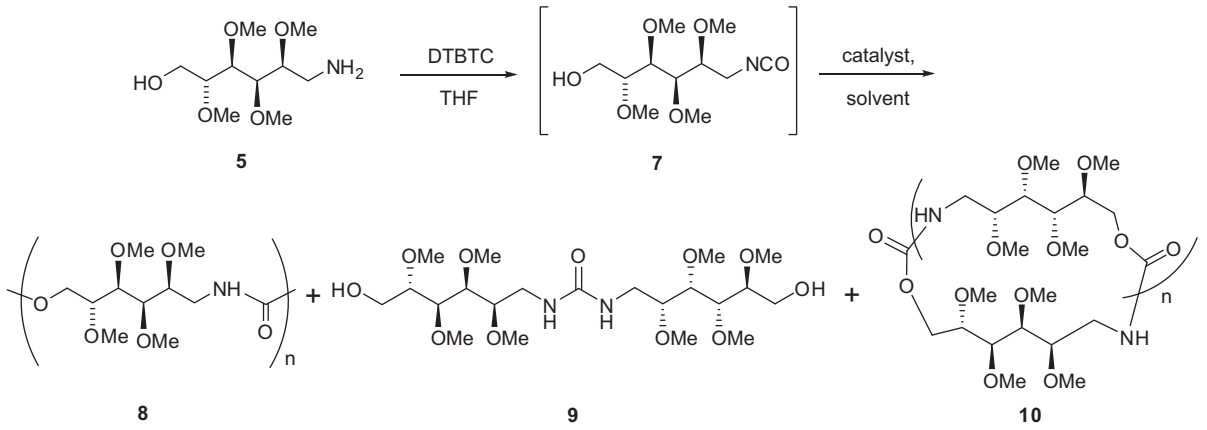


Figure 1. ^{1}H NMR spectrum of monomer **5** (C_5D_5N).

Aminoalditol **5** was treated with di-*tert*-butyltricarbonate (DTBTC) for the conversion of the amino group into isocyanate **7** (Scheme 2). The DTBTC reagent was prepared as previously reported.[27] The crude isocyanate was employed for the polymerization without isolation or purification.[22,23] However, to confirm the formation of **7**, the FTIR spectrum of the mixture was recorded. As expected, a strong band of the isocyanate group was observed at 2263 cm^{-1}. For the polymerization of **7**, $CHCl_3$ or THF was employed as solvent and the reaction was conducted in the presence of one of the catalysts listed in Table 1.

The reaction mixture of polymerization was concentrated and the polymeric material was isolated by dissolution in 2-propanol and precipitation with hexane. This operation was repeated twice, and the resulting product was dried and analyzed using FTIR, NMR and, in some selected cases, MALDI-MS and gel permeation chromatography (GPC). In general, polymer **8** was accompanied by one or two by-products. For example, the ^{1}H NMR spectrum (recorded in $CDCl_3$) of the polymeric material obtained in the Sn(ii) 2-ethylhexanoate ($Sn(oct)_2$)-polycondensation of **5** in THF (entry 3 of Table 1) showed clearly the signals of the methylene group bonded to oxygen in polyurethane **8** (4.08 and 4.51 ppm), together with a pair of down-field signals (4.68 and 4.23 ppm), which were attributed to cyclic oligomers (**10**). The spectrum exhibited also signals at higher field (3.85 and 3.66 ppm) due to the hydroxymethyl groups of the urea derivative **9**. The ^{13}C NMR spectrum confirmed these assignments, as it showed in the region of the carbonyl group only two signals, a broad one (major) at 156.5 ppm (urethane) and the other at 158.9 ppm (urea). These values are in agreement with those reported for analogous polymers.[22,28] In addition, the FTIR spectrum showed characteristic absorptions for the urethane (1733 and 1554 cm^{-1}) and urea (1660 cm^{-1}) carbonyl groups. The GPC analysis of the product indicated that we were dealing with a polydisperse material. Three main peaks were detected corresponding to M_w = 2280, 740, and 540, values consistent with the presence of polymer **8**, cyclic trimer **10** (n = 2), and urea **9**, respectively.

To confirm these results, the material was applied to a silica gel column which was eluted with 4:1 EtOAc–MeOH. Two fractions were isolated and analyzed by MALDI-MS. In these spectra the difference of *m/z* values between peaks was 263, in accordance with the repeating unit of the polymers. The fraction that eluted first from the column showed at lower *m/z* values (400–1400) two sets of signals, corresponding to $[M+H]^+$ ions of linear and cyclic oligomers. The most intense signal corresponded to the cyclic trimer. At higher *m/z* values (above 1500) the spectrum was rather complex



Scheme 2. Polymerization of **5** via isocyanate derivative **7**.

Table 1
Conditions employed for the polymerization of **5** via **7**

No.	Catalyst (mol %)	Solvent	Concentration of **7** (M)	Initiator	Product distribution **8**:**9**:**10**
1	$Zr(acac)_4$ (0.5)	$CHCl_3$	1.0	No	10:90:0
2	Et_3N (3.0)	THF	0.8	No	23:77:0
3	$Sn(oct)_2$ (1.5)	THF	1.0	No	55:18:27
4	$Zr(acac)_4$ (0.1)	THF	0.4	No	50:40:10
5	$Zr(acac)_4$ (1.0)	THF	0.4	No	66:21:13
6	$Zr(acac)_4$ (1.0)	THF	0.4	Yes	64:36:0
7	$Zr(acac)_4$ (1.0)	THF	0.7	Yes	83:17:0

due to the contribution of ions of the oligomeric species with different terminal groups. The spectrum showed series of ions with *m/z* values consistent with $[M+H]^+$ (1554, 1817, 2080, 2343) and $[M+Na]^+$ (1576, 1839, 2103, 2365) corresponding to linear oligomers, and $[M+Na]^+$ ions due to cyclic oligomers (1602, 1865, 2128). Overlapped with these series, other ions were also observed having *m/z* values separated by 263 mass units (1676, 1939, 2203, 2465). They were assigned to $[M+Na]^+$ open-chain oligomers with the terminal amino group substituted as *tert*-butyl carbamate. These urethanes could be formed by reaction of the free amino group of oligomers with the remaining DTBTC, which had been employed for the in situ preparation of isocyanate **7**. The heterogeneity of this fraction was reflected in the complexity observed in the corresponding ^1H and ^{13}C NMR spectra. In these spectra, signals were detected at 1.45 and 28.4 ppm, respectively, in agreement with the presence of the methyl groups of *tert*-butoxycarbonyl. This fact supports its inclusion as a substituent of some oligomers, as proposed in the terminal group analysis by MALDI-MS.

The MALDI-MS of the fraction that eluted later from the column showed signals due to $[M+H]^+$ and $[M+Na]^+$ ions. The most intense peaks indicated that the polyurethane contained from 5 to 20 repeating units (Fig. 2). With the data obtained from the spectrum, the M_w (2450) and M_n (2280) values were determined. The M_w value was coincident with the one estimated by GPC.

The ratio between linear and cyclic urethanes (**8** and **10**, respectively) and urea (**9**) in each individual preparation, shown in Table 1, was determined by integration of the CH_2O signals from the ^1H NMR spectrum of the material precipitated from 2-propanol–hexane, as explained above. The polymerization of **7** in $CHCl_3$ (even under optimized conditions) led to urea **9** as the major component (entry 1). Similarly, the use of Et_3N as catalyst (entry 2) was not suitable, since the urea derivative **9** was mostly produced. Urea linkages are expected to be formed by nucleophilic attack of the amine of **5** to the isocyanate function of **7**. The amine end-group

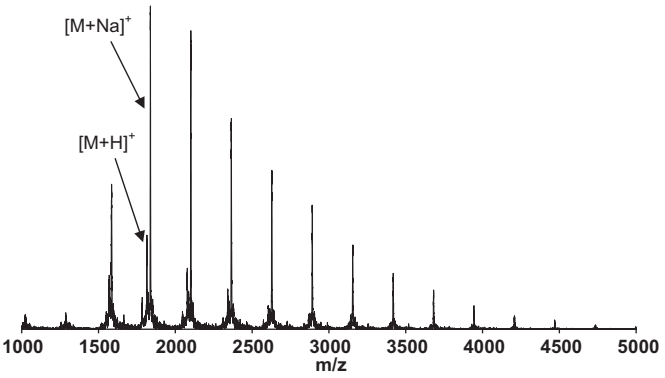


Figure 2. MALDI-MS of polyurethane **8**, obtained from **7**.

of **5** may be regenerated from **7** by hydrolysis of the isocyanato group. As Et_3N is not an efficient catalyst for the polycondensation, compound **7** remains in the polymerization medium for a long time (it was even detected after 10 h), increasing the possibility of hydrolysis and concomitant urea formation. The ^1H NMR spectrum of **9** recorded in pyridine-d_5 allowed the assignment of the signals, and particularly those of H-6a, H-6b, H-1a, H-1b and that of NH. The integral of all of them were of equal magnitude (ratio 1:1:1:1:1) confirming the proposed structure for **9**. Furthermore, the MALDI-MS of **9** showed, as expected, the pseudomolecular ions $[M+H]^+$ and $[M+Na]^+$ at *m/z* 501.3 and 523.3, respectively.

The polycondensation of **7** in THF, and in the presence of Zr(IV) acetylacetonate ($Zr(acac)_4$; 2,4-pentanedione Zr(IV) complex) as catalyst, afforded the linear polymer **8** as the major product (entries 4–7). The proportion of **8** increased with the increment in the concentration of the catalyst (entries 4 and 5) although, in turn, this might result in a lowering of the molecular weight of the polymer.[23] The formation of cyclic oligomers of low molecular weight (monomer to tetramer) could be explained taking into account the high flexibility of the monomer backbone chain, mentioned above. In contrast, no cyclic oligomers were observed in the analogous polymerization of 2,3:4,5-di-*O*-isopropylidene-D-galactitol,[22] which adopts in solution the planar zig-zag conformation with the diacetonide rings *S-trans* disposed. This arrangement would facilitate the linear elongation of the polymer chain. The formation of cyclic oligomers (**10**) could be prevented employing the *N*-Boc derivative **6** as the initiator of the polymerization. However, in all cases, and even under optimized conditions (entry 7), urea **9** was always the accompanying by-product of polyurethane **8**. This contaminant could not be eliminated even though many

procedures for the purification were attempted. The remaining urea **9** (~10%) may be associated to the polymer by intermolecular interactions. However, some urea units could be incorporated into the polymer chain, as reported for analogous preparations of [*n*]-polyurethanes from isocyanate alcohols.[22,23] In view of these results, we decided to conduct the synthesis of polyurethane **8** by an alternative route.

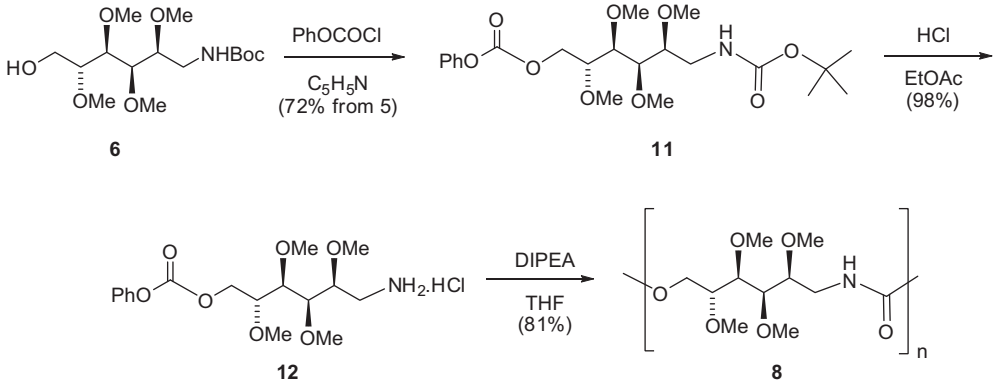
We have recently described a procedure for the synthesis of common [*n*]-polyurethanes which takes place under smooth conditions and does not require the use of metal catalysts.[29] This procedure, applied to amino alditol **5**, is illustrated in Scheme 3. The amino function of monomer **5** was selectively protected as the *N*-Boc derivative **6**, which had been used in the previous methodology as the initiator of the polymerization. The free hydroxyl group of **6** was activated for the polycondensation as the phenylcarbonate derivative **11**, which was prepared by the treatment of **6** with phenyl chloroformate.

The ^{1}H NMR spectrum of **11** showed the expected deshielding of the signals of the methylene protons vicinal to the carbonate group (>0.6 ppm) compared to those of the hydroxymethyl group in **6**. Removal of the N-protecting *tert*-butoxycarbonyl group in **11** with a saturated solution of HCl in EtOAc afforded the hydrochloride derivative **12**, as the conveniently activated monomer precursor of **8**.

The amine function of **12** may be readily released from the hydrochloride with an organic base. Therefore, the polymerization of **12** was conducted in DMF or THF, and in the presence of *N,N*-diisopropylethylamine (DIPEA). The polymerization is expected to proceed by a nucleophilic attack of the amine to the terminal phenylcarbonate with elimination of the phenyloxy as a good leaving group.[20,30] For the polycondensation, the volume of the solution was adjusted to give a 1 M final concentration of **12**, and the mixture was stirred, under argon atmosphere, at 40 °C for 3 days (Table 2). Polymer **8** was recovered and purified as for the polymerization of **7**, described above. The polyurethane was released from the accompanying rests of DIPEA hydrochloride by deionization with resin.

A higher molecular weight of **8** was obtained when THF, instead of DMF, was employed as a solvent for the polymerization. This material showed smaller polydispersity (1.37) and higher degree of polymerization (14) compared with those obtained in DMF (1.85 and 7, respectively). The FTIR spectrum of **8** showed the characteristic absorptions of the urethane NH (3366 cm^{-1}) and carbonyl groups (1733 and 1546 cm^{-1}), whereas the peak of the urea carbonyl (1660 cm^{-1}) was absent. In agreement with this result, no urea signals were detected in the NMR spectra of **8** (Fig. 3). However, low intensity signals corresponding to the terminal phenylcarbonate group of polyurethane **8** were observed. From the integral of the signals of the aromatic and CH_2OCO_2 protons, the M_n value (4210) was determined, which was consistent with the molecular weight measured using GPC (Fig. 4). Polyurethane **8** behaves as an amorphous material as analyzed by differential scanning calorimetry (DSC) that showed no thermal transitions during the first heating cycle, followed by cooling and a second heating process. The thermogravimetric analysis (TGA) for **8** indicated that the decomposition starts at 110 °C (Fig. 5). The differential curves showed two main peaks at 165.1 and 281.2 °C indicative of the decomposition in two steps.

In summary, the synthesis of chiral, enantiomerically pure [*n*]-polyurethane having four stereocenters in the repeating unit has been accomplished by two alternative procedures. The starting monomer, 1-amino-1-deoxy-2,3,4,5-tetra-*O*-methyl-D-sorbitol was readily prepared form D-glucamine. In the first instance, the amino function of the monomer was converted into the reactive isocyanate group with di-*tert*-butyltricarbonate and polymerized in situ. The resulting polymeric material contained the desired linear [*n*]-polyurethane accompanied by cyclic oligomers and a N,N′-disubstituted urea derivative as by-products. Under optimized conditions, and after laborious purification, the [*n*]-polyurethane was obtained as a material of moderate molecular weight, which showed contamination and possible incorporation of urea units into the polymer chain. In the alternative synthesis of the [*n*]-polyurethane, the free hydroxyl group of the starting monomer was activated for the polycondensation as the α-amino-ω-phenylcarbonate derivative. In this case, the polymerization took place by a nucleophilic attack of the amine (released from its hydrochloride) to the carbonate with the elimination of phenol, and no metal catalyst was required. The polycondensation conducted in THF as solvent and in the presence of DIPEA afforded, after purification, a polymer that exhibited higher molecular



Scheme 3. Polymerization of **5** via the active carbonate **12**.

Table 2
Conditions employed for the polymerization of **5** via **12**

No.	Mmol of **12**	Solvent (mL)	DIPEA (mL)	Yield of **8** (%)	M_w	M_n	M_w/M_n
1	0.262	DMF (0.20)	0.10	64	3620	1960	1.85
2	0.472	THF (0.23)	0.24	81	5210	3800	1.37

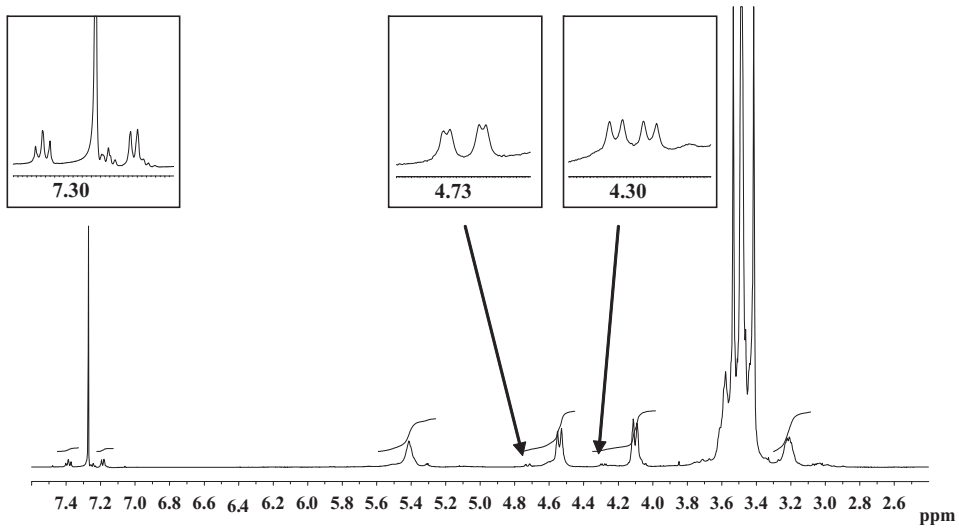


Figure 3. ^{1}H NMR spectrum of polyurethane **8** ($CDCl_3$). Superimposed are the signals of the carbonate (RCH_2OCO_2Ph) terminal group.

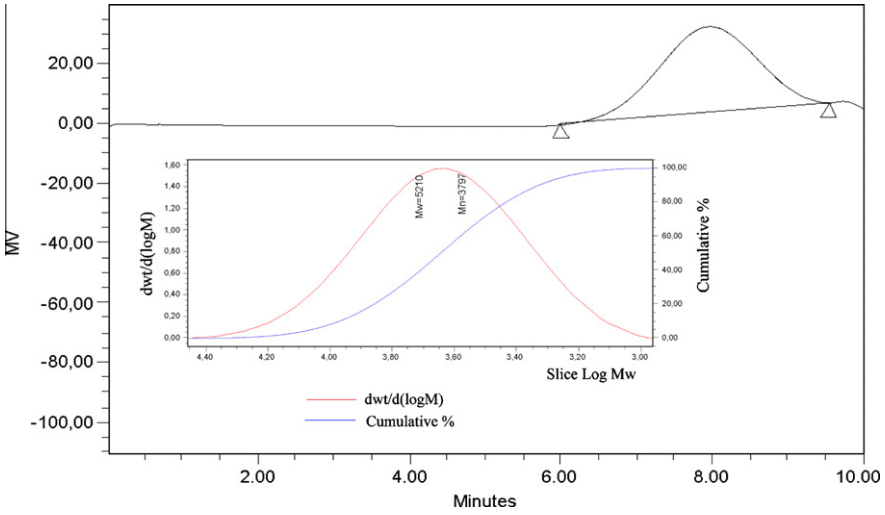


Figure 4. Gel permeation chromatography (GPC) analysis for polyurethane **8**.

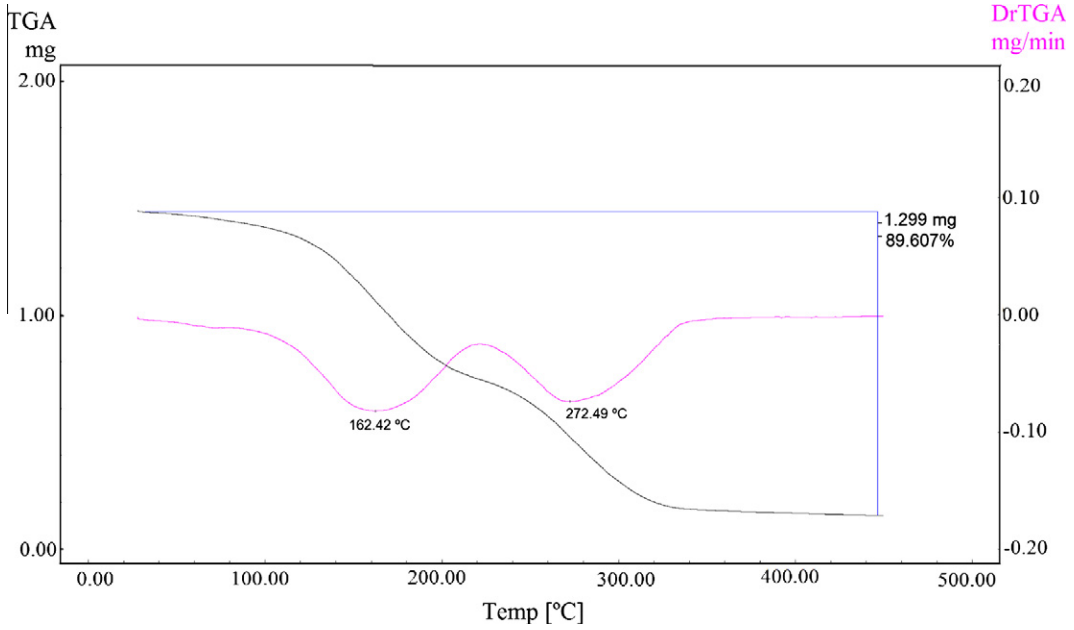


Figure 5. Thermogravimetric analysis for polyurethane **8**.

weight and higher purity than those of the polyurethane obtained in the previous preparation. Thus, the polymerization using the *O*-phenylcarbonate as active monomer seems to be more convenient for this particular aminoalditol which possesses the D-*gluco* configuration.

3. Experimental

3.1. General methods

1-Amino-1-deoxy-D-sorbitol was purchased from Aldrich Chemical Company, Inc., and used as received. Analytical thin-layer chromatography (TLC) was performed on Silica Gel 60 F254 (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. For unprotected amines, the plates were heated after immersion in a solution of ninhydrin in acetone. 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 with a Bruker AMX 500 or a Bruker AC 200 instrument, 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 FT-IR spectrometer. Gel permeation chromatography (GPC) was carried out using Styragel columns (Waters), with THF as solvent at a flow rate of 1.0 mL/min. The calibration was performed using polystyrene standards. Electron impact-mass spectra (EI-MS) were recorded with a Shimadzu QP5050A mass spectrometer, operating at 70 eV. MALDI-MS measurements were performed using a laser desorption time-of-flight mass spectrometer Bruker Daltonics OmniFlex. Dithranol (1,8,9-anthracenetriol) was used as the matrix. High resolution mass spectrometry (HRMS-ESI) was performed in a Bruker microTOF-Q II instrument. Thermogravimetric analysis (TG) was performed in a Shimadzu TGA-51 apparatus; samples of about 2 mg were heated at a rate of 10 °C/min. 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, then cooled at 5 °C/min to 50 °C (isothermic 5 min), and finally heated at 10 °C/min to 200 °C.

3.2. 1-Deoxy-6-*O*-trityl-1-*N*-tritylamino-D-sorbitol (2)

To a suspension of 1-amino-1-deoxy-D-sorbitol (**1**, 1.0 g; 5.5 mmol) in CH_2Cl_2 (20 mL) were added trityl chloride (4.0 g; 14.35 mmol) and Et_3N (2.0 mL, 14.34 mmol). The mixture was stirred at room temperature (rt) for 3 days and then concentrated in vacuo. The residue was purified by column chromatography (4:1 toluene–EtOAc) to give **2** (2.2 g; 61%) as a foam; $[\alpha]_D^{25} = -3$ (*c* 4.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3 + D_2O$) δ 2.44 (d, 2H, *J* 3.7 Hz, CH_2N), 3.30 (dd, 1H, $J_{5,6b}$ 6.0, $J_{6a,6b}$ 9.5 Hz, H-6b), 3.40 (dd, 1H, $J_{5,6a}$ 6.0 Hz, H-6a), 3.76 (m, 3H, H-2–H-4), 3.93 (q, 1H, H-5), 7.15–7.50 (m, 30H, H-aromatic); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 47.0 (C-1), 64.8 (C-6), 70.6 (Ph_3CN), 71.4 (C-5), 71.8, 72.4, 74.0 (C-2–C-4), 87.0 (Ph_3CO), 126.6, 127.2, 127.9, 128.0, 128.5, 143.6, 145.1 ($C_6H_5)_3C$. Anal. Calcd for $C_{44}H_{43}NO_5$: C, 79.37; H, 6.51; N, 2.10. Found: C, 79.59; H, 6.76; N, 2.15.

3.3. 1-Deoxy-2,3,4,5-tetra-*O*-methyl-6-*O*-trityl-1-*N*-tritylamino-D-sorbitol (3) and 1-deoxy-1-(*N*-methyl, *N*-tritylamino)-2,3,4,5-tetra-*O*-methyl-6-*O*-trityl-D-sorbitol (4)

To a stirred solution of compound **2** (2.80 g, 4.2 mmol) in Me_2SO (8 mL) was added finely powdered NaOH (3.2 g, 80 mmol). The mixture was stirred at rt for 30 min and, upon cooling in an ice bath, MeI (3.10 mL, 49.8 mmol) was added. After stirring for 1 h, an additional amount of MeI (3.10 mL, 49.8 mmol) was added and the stirring was continued for 1 h more. Water (50 mL) was slowly incorporated into the mixture, which was then partitioned between 1:1 CH_2Cl_2–H_2O (200 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 (97:3 toluene–EtOAc). The first eluting fractions from the column contained the desired compound **3**, impurified with *N*-methyl derivative **4** (0.97 g). Pure tetra-*O*-methyl derivative **3** was isolated from the following fractions (1.93 g; 64%). Compound **3** gave $[\alpha]_D^{25} = -12$ (*c* 1.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.59 (br s, 1H, NH), 2.18 (dd, 1H, $J_{1b,2}$ 7.5, $J_{1a,1b}$ 12.3 Hz, H-1b), 2.49 (dd, 1H, $J_{1a,2}$ 2.9 Hz, H-1a), 2.99 (s, 3H, CH_3O), 3.10 (dd, 1H, $J_{5,6b}$ 4.9, $J_{6a,6b}$ 10.3 Hz, H-6b), 3.30 (dd, 1H, *J* 2.0, 7.6 Hz, H-4), 3.46 (dd, 1H, dd, $J_{5,6a}$ 2.2 Hz, H-6a), 3.48, 3.50, 3.51 (3s, 3H each, CH_3O), 3.46–3.50 (m, 2H, H-3, H-5), 3.67 (dt, 1H, $J_{1b,2}$–$J_{2,3}$ 7.5 Hz, H-2), 7.18–7.54 (m, 30H, H-aromatic); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 43.9 (C-1), 58.4, 59.2, 60.1, 60.4 (CH_3O), 62.4 (C-6), 70.6 (Ph_3CN), 79.6 (C-4), 80.6, 81.0 (C-3, C-5), 82.3 (C-2), 86.6 (Ph_3CO), 126.2, 126.9, 127.7, 127.8, 128.7, 128.8, 144.1, 146.1 [($C_6H_5)_3C$]. Anal. Calcd for $C_{44}H_{43}NO_5$: C, 79.86; H, 7.12; N, 1.94. Found: C, 79.64; H, 7.22; N, 2.06.

Compound **4**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.42 (dd, 1H, $J_{1b,2}$ 7.6, $J_{1a,1b}$ 12.4 Hz, H-1b), 2.52 (s, 3H, CH_3N), 2.73 (dd, 1H,, $J_{1a,2}$ 3.0 Hz, H-1a), 3.21 (s, 3H, CH_3O), 3.31 (dd, 1H, $J_{5,6b}$ 5.1, $J_{6a,6b}$ 10.8 Hz, H-6b), 3.66, 3.69, 3.70 (3s, 3H each, CH_3O), 3.50–3.81 (m, 4H, H-3–H-5, H-6a), 3.91 (ddd, 1H, $J_{1b,2}$–$J_{2,3}$ 7.6 Hz, H-2), 7.22–7.81 (m, 30H, H-aromatic). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 44.1 (CH_3N), 58.2 (C-1), 58.6, 59.4, 60.4, 60.7 (CH_3O), 62.5 (C-6), 70.8 (Ph_3CN), 79.7 (C-4), 80.7, 81.2 (C-3, C-5), 82.5 (C-2), 86.8 (Ph_3CO), 126.5, 127.2, 128.0, 128.1, 128.2, 128.9, 144.3, 146.3 [($C_6H_5)_3C$].

3.4. 1-Amino-1-deoxy-2,3,4,5-tetra-*O*-methyl-D-sorbitol (5)

A solution of compound **3** (0.58 g, 0.80 mmol) in anhydrous CH_2Cl_2 (6.8 mL) was cooled in an ice bath and trifluoroacetic acid (0.76 mL, 10.2 mmol) was slowly added. After 30 min, the mixture was allowed to reach rt and it was stirred for additional 5 h. Upon addition of MeOH (6 mL), the solution was concentrated. The residue was partitioned between 1:1 H_2O–toluene (50 mL). The organic layer was washed with water and the combined aqueous phases were concentrated to ~2 mL. The solution was passed through a column filled with Amberlist A-26 (HO^-) ion-exchange resin to give the aminoalditol **5** (0.176 g, 93%); $[\alpha]_D^{25} = -30$ (*c* 0.6, H_2O); ^{1}H NMR (500 MHz, C_5D_5N) δ 2.97 (dd, 1H, $J_{1a,1b}$ 13.2, $J_{1b,2}$ 6.5 Hz, H-1b), 3.18 (dd, 1H, $J_{1a,2}$ 4.2 Hz, H-1a), 3.46, 3.48, 3.57, 3.58 (4s, 3H each, CH_3O), 3.69 (ddd, 1H, $J_{2,3}$ 6.3 Hz, H-2), 3.72 (ddd, 1H, $J_{4,5}$ 6.4, $J_{5,6a}$ 3.0, $J_{5,6b}$ 4.4 Hz, H-5), 3.84 (dd, 1H, $J_{3,4}$ 3.8 Hz, H-3), 3.91 (dd, 1H, H-4), 4.04 (dd, 1H, $J_{6a,6b}$ 12.1 Hz, H-6b), 4.26 (1H, dd, H-6a); ^{13}C NMR (125.7 MHz, C_5D_5N) δ 42.3 (C-1), 57.0, 58.4, 59.6 (CH_3O), 59.8 (C-6), 60.3 (CH_3O), 79.9 (C-4), 81.7 (C-3), 82.3 (C-5), 84.0 (C-2). ESI-HRMS: calcd for $[C_{10}H_{24}NO_5+H]^+$: 238.1649, $[C_{10}H_{23}NO_5+Na]^+$: 260.1468. Found *m/z*: 238.1645 and 260.1461, respectively.

3.5. 1-(*N*-*tert*-Butoxycarbonylamino)-1-deoxy-2,3,4,5-tetra-*O*-methyl-D-sorbitol (6)

To a solution of compound **5** (0.132 g, 0.557 mmol) in CH_3CN (2 mL) were added Boc_2O (0.260 mL, 1.11 mmol) and Et_3N (0.16 mL, 1.11 mmol). The mixture was stirred at rt for 16 h, and then was concentrated to yield a syrup. Purification by column chromatography (3:2 toluene–EtOAc) afforded pure **6** (0.186 g, 99%); $[\alpha]_D^{25} = +1$ (*c* 1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3 + D_2O$) δ

1.41 (s, 9H, C(CH_3)$_3$), 3.17 (dd, 1H, $J_{1b,2}$ 6.0, $J_{1a,1b}$ 14.0 Hz, H-1b), 3.31 (dt, 1H, $J_{5,6a}$–$J_{5,6b}$ 3.7, $J_{4,5}$ 6.2 Hz, H-5), 3.26–3.56 (m, 5H, H-1a, H-2–H-5), 3.39, 3.45, 3.48, 3.51 (4s, 3H each, CH_3O), 3.67 (dd, 1H, $J_{5,6b}$ 3.7, $J_{6a,6b}$ 12.1 Hz, H-6b), 3.85 (dd, 1H, $J_{5,6a}$ 3.6 Hz, H-6a), 5.01 (br s, 1H, NH); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 28.3 (C(CH_3)$_3$), 40.5 (C-1), 57.1, 58.7 (CH_3O), 59.5 (C-6), 60.3, 60.5 (CH_3O), 79.0 (C-4), 79.2 (C(CH_3)$_3$), 79.7 (C-3), 81.0 (C-5), 81.5 (C-2), 156.0 (NCO_2). ESI-HRMS: calcd for [$C_{15}H_{31}NO_7$+Na]$^+$: 360.1993. Found *m/z*: 360.2000.

3.6. General procedure for the polymerization of 5 via isocyanate 7

To a solution of **5** (0.066 g, 0.28 mmol) in THF (0.4 mL) was added DTBTC[27] (0.090 g, 0.34 mmol). The mixture was stirred at rt, under a static argon atmosphere, for 2 h. In the first occasion, a small portion was concentrated at rt in order to verify the conversion of **5** into 1-deoxy-1-isocyanate-2,3,4,5-tetra-*O*-methyl-D-sorbitol (**7**): IR (KBr, film): 3407 (br, OH) and 2263 cm^{-1} (s, NCO).

To a solution of crude **7** in $CHCl_3$ or THF was added a solution of the corresponding catalyst [Zr(acac)$_4$, Sn(oct)$_2$ or Et_3N] in the same solvent. When the polymerization was conducted in the presence of the initiator **6**, a solution of the catalyst and the initiator was prepared and, after 1 h of stirring at rt, the monomer was added. The final concentrations of monomer and reagents are shown in Table 1. The polymerization was conducted under Ar atmosphere at 40 °C for 16 h, with vigorous stirring. Then, it was concentrated and the residue was redissolved in 2-propanol (0.3 mL). The polymer was isolated by precipitation with hexane (3 mL). This procedure was repeated twice. The results of the polymerization are summarized in Table 1.

Polyurethane **8**: $[\alpha]_D^{25}$ = −2 (*c* 1.2, H_2O); IR (film): 3366 (br, NH), 1733, 1546 cm^{-1} (s, NCOO); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.20 (m, 1H, H-1b), 3.41–3.60 (m, 5H, H-1a, H-2–H-5), 3.41, 3.48, 3.49, 3.53 (4s, 3H each, CH_3O), 4.10 (d, 1H, $J_{6a,6b}$ 11.4 Hz, H-6b), 4.54 (d, 1H, H-6a), 5.41 (br s, 1H, NH). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 41.6 (C-1), 57.4, 59.1, 60.3, 60.6 (CH_3O), 61.9 (C-6), 78.8, 78.9, 79.9, 81.0 (C-2–C-5), 156.5 (CO).

N,N′-Disubstituted urea **9**: $[\alpha]_D^{25}$ = +2 (*c* 1.7, $CHCl_3$); ^{1}H NMR (500 MHz, C_5D_5N) δ 3.49, 3.51, 3.59 (3s, 3H each, CH_3O), 3.65 (m, 1H, H-1b), 3.67 (s, 3H, CH_3O), 3.75 (ddd, 1H, $J_{4,5}$ 6.1, $J_{5,6a}$ 3.2, $J_{5,6b}$ 4.6 Hz, H-5), 3.84 (dd, 1H, $J_{2,3}$ 6.3, $J_{3,4}$ 3.9 Hz, H-3), 3.94 (td, $J_{1a,2}$–$J_{2,3}$ 6.3, $J_{1b,2}$ 4.2 Hz, H-2), 4.04 (dd, 1H, H-4), 4.07 (dd, 1H, $J_{6a,6b}$ 12.0 Hz, H-6b), 4.08 (m, 1H, H-1a), 4.29 (dd, 1H, H-6a), 6.82 (t, 1H, *J* 5.8 Hz, NH); ^{13}C NMR (125.7 MHz, C_5D_5N) δ 46.6 (C-1), 57.9, 59.2, 60.5 (CH_3O), 60.7 (C-6), 60.9 (CH_3O), 80.7 (C-4), 82.2 (C-2), 82.7 (C-3), 83.2 (C-5), 160.2 (CO). ESI-HRMS: calcd for [$C_{21}H_{44}N_2O_{11}$+H]$^+$: 501.3018; [$C_{21}H_{44}N_2O_{11}$+Na]$^+$: 523.2837. Found m/*z*: 501.3030 and 523.2856, respectively.

3.7. 1-(*N-tert*-Butoxycarbonylamino)-1-deoxy-2,3,4,5-tetra-*O*-methyl-6-*O*-phenyloxycarbonyl-D-sorbitol (11)

Crude compound **6**, obtained from **5** as described above, was employed for the next reaction without further purification. After concentration of the reaction mixture of preparation of **6**, the residue was dissolved in dry pyridine (1.2 mL), and phenylchloroformate (0.070 mL, 0.56 mmol) was added. The mixture was stirred at rt for 24 h. After subsequent addition of MeOH and toluene, the mixture was concentrated and purified by column chromatography (4:1 toluene–EtOAc) to yield **12** (0.181 g, 72% from **5**); $[\alpha]_D^{25}$ = +3 (*c* 5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.45 (s, 9H, C(CH_3)$_3$), 3.21 (m, 1H, H-1b), 3.42 (m, 1H, H-2), 3.47, 3.49, 3.52, 3.55 (4s, 3H each, CH_3O), 3.54–3.57 (m, 4H, H-1a, H-3–H-5), 4.30 (dd, 1H, $J_{5,6a}$ 4.5, $J_{6a,6b}$ 11.7 Hz, H-6b), 4.72 (d, 1H, H-6a), 4.97 (br s, 1H, NH), 7.18–7.41 (m, 5H, H-aromatic); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 28.4 ((CH_3)$_3$C), 40.7 (C-1), 57.8, 58.9, 60.4, 60.7 (CH_3O), 66.4 (C-6), 71.9, 73.3, 79.8 (C-3–C-5), 79.3 ((CH_3)$_3$*C*), 81.5 (C-2), 121.0, 126.0, 129.5, 151.1 (C-aromatic), 153.7 (OCO_2), 156.0 (NCO_2). Anal. Calcd for $C_{22}H_{35}NO_9$: C, 57.75; H, 7.71; N, 3.06. Found: C, 57.49; H, 7.98; N, 3.50.

3.8. 1-Amino-1-deoxy-2,3,4,5-tetra-*O*-methyl-6-*O*-phenyloxycarbonyl-D-sorbitol hydrochloride (12)

Compound **11** (0.264 g, 0.58 mmol) was dissolved in EtOAc saturated with HCl (15 mL). The solution was stirred at rt for 20 h. After concentration, the residue was washed with EtOAc (3 × 4 mL) to give compound **12** (0.223 g, 98%); ^{1}H NMR (500 MHz, DMSO-d_6) δ 2.81 (m, 1H, H-1a), 3.04 (m, 1H, H-1b), 3.34, 3.38, 3.41, 3.43 (4s, 3H each, CH_3O), 3.43 (m, 1H, H-4), 3.56 (dd, 1H, $J_{3,4}$ 3.1, $J_{2,3}$ 6.1 Hz, H-3), 3.59 (td, 1H, $J_{5,6a}$ 2.3, $J_{4,5}$–$J_{5,6b}$ 5.7 Hz, H-5), 3.76 (ddd, 1H, *J* 2.9, $J_{2,3}$ 6.1, *J* 9.0 Hz, H-2), 4.19 (dd, 1H, $J_{6a,6b}$ 12.0 Hz, H-6b), 4.62 (dd, 1H, H-6a), 7.23–7.46 (m, 5H, H-aromatic), 8.03 (br s, 3H, NH); ^{13}C NMR (125.7 MHz, DMSO-d_6) δ 39.2 (C-1), 57.4, 58.6, 59.3, 59.4 (CH_3O), 66.9 (C-6), 76.9 (C-2), 78.0 (C-4), 78.6 (C-5), 79.2 (C-3), 121.3, 126.3, 129.7, 150.8 (C-aromatic), 153.1 (OCO_2). Anal. Calcd for $C_{17}H_{27}NO_7$·1.5HCl: C, 49.55; H, 6.97; N, 3.40. Found: C, 49.44; H, 7.34; N, 3.39.

3.9. General procedure for the polymerization of 12

To a solution of **12** (0.2 g, 0.5 mmol) in DMF or THF (0.25 mL) was added DIPEA (1.5 mmol). The volume of the solution was adjusted with the solvent to give 1 M solution of **12**. The mixture was stirred at 40 °C under Ar atmosphere for 3 days. Then, the upper phase was removed and the lower one was concentrated. The residue was dissolved in 2-propanol (0.2 mL) and precipitated with hexane (4 mL). Polyurethane **8** (0.123 g, 99%) isolated by this procedure was contaminated with DIPEA hydrochloride (according to the ^{1}H NMR spectrum). Therefore, this material was dissolved in H_2O and passed through a column containing Dowex MR-3C mixed bed resin. The polymer recovered after this procedure was free of the ammonium salt (0.107 g, 81%). The results of the polymerization are summarized in Table 2. DSC: No thermal transitions were observed after heating, cooling, and second heating cycles. TG: From rt to 450 °C, 90% mass loss; the differential curve showed two minimum peaks at 165.1 and 281.2 °C.

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