Condensation reactions of a first generation of dendritic monomer

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Dedicated to Professor Roberto Rossi and Edmundo Rúveda on their birthdays

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Abstract

In this paper we report the condensation reaction of the first generation of a dendritic monomer bearing hydroxyl or amine functional groups, with dialdehydes and diisocyanate co-monomers. Dimers and crosslinked polymers were obtained by reaction with glyoxal (Gly) and glutaraldehyde (Glu), respectively. Only crosslinked polymers were found when toluene diisocyanate (TDI) was used as co-monomers. The products were characterized by FT-IR and ^{1}H NMR spectroscopy, DSC, TGA and GPC. Two principal factors exerted influence on the condensation reactions: the availability of the functional groups of the dendritic molecule and the reactivity and size of the co-monomers.

Keywords: Dendritic monomer, condensation reaction, polyurethane

Introduction

In the last few years, the development of new synthetic materials with specific functional groups has been increasingly focused to obtain materials with controlled nanostructures.

Dendrimers are monodisperse, highly branched, multifunctional and regular structures, fairly attractive for use as nanoscopic building blocks. These structural features have aroused the interest of synthetic organic chemists, and several valuable contributions to their synthesis and characterization, have been reported over the past few years.[1-7] Current studies are mainly oriented to their potential properties and applications in such diverse areas as organic chemistry, analytical chemistry, biology, medicine, materials science, pharmacology, agrochemistry, environmental chemistry and chemical engineering.[8-11]

Owing to their synthetic properties, however, the maximum size of dendrimers is limited and their shapes are, in general, restricted to globular structures. Connecting dendritic macromolecules offer the possibility to create even larger macromolecules.

We have already reported the synthesis of multiacrylic dendrimers[12] and the thermal polymerization experiments using radical initiator.[13,14] Homopolymerization of the first generation monomers yielded up to 50% of gel fraction, while the polymerization of the second generation yielded 90 % of insoluble product. However, it has been known that these kinds of macromonomers, although very reactive and attractive building blocks which undergo fast photopolymerization by a radical mechanism,[15-17] contain about 30% unreacted C=C double bonds in acrylate polymer films after UV curing. Complete conversion was never obtained, especially when multifunctional monomers were used.

In this opportunity, we studied the use of dendritic monomer with hydroxyl and amine groups in the periphery capable to polymerize through condensation reactions.

Therefore, in this paper we report the synthesis and characterization of the first generation of a dendritic monomer (**1**) and their copolymerization with dialdehydes and diisocyanate co-monomers. New materials with potentially significant and scarcely explored properties may be attained from these novel monomers. [18-21]

Results and Discussion

I) Synthesis of monomers

The core of the monomers was synthesized following the strategy proposed by Newkome *et al*.[22] which is based on the pentaerythritol **2** and acrylonitrile reaction. (see Figure 1). After methanolysis of cyano groups of **3** and hydrolysis of methyl ester **4** to generate a tetraacid molecule **5**, a convergent synthesis was carried out activating the acid groups with 1,1'-carbonyldiimidazole (CDI) prior to their use, allowing them to react with the protected hydroxylamine **8** in THF. A complex mixture of amide and ester products in **1** could be obtained and the ratio depended on the reaction conditions. An increase in reaction time, temperature and concentration of the initial reagents led to a rise in the amide percentage. These variations may be explained by the attack of a hydroxyl group which is favored because it is less hindered, followed by an intramolecular rearrangement by attack of the amine at the ester carbonyl to yield amide. Optimal conditions for the synthesis of product **1** were studied as previously reported [7].

Therefore, dendritic monomer **1** with yields ranging from 60 to 70% was obtained and characterized by spectroscopic studies, and elemental analysis.

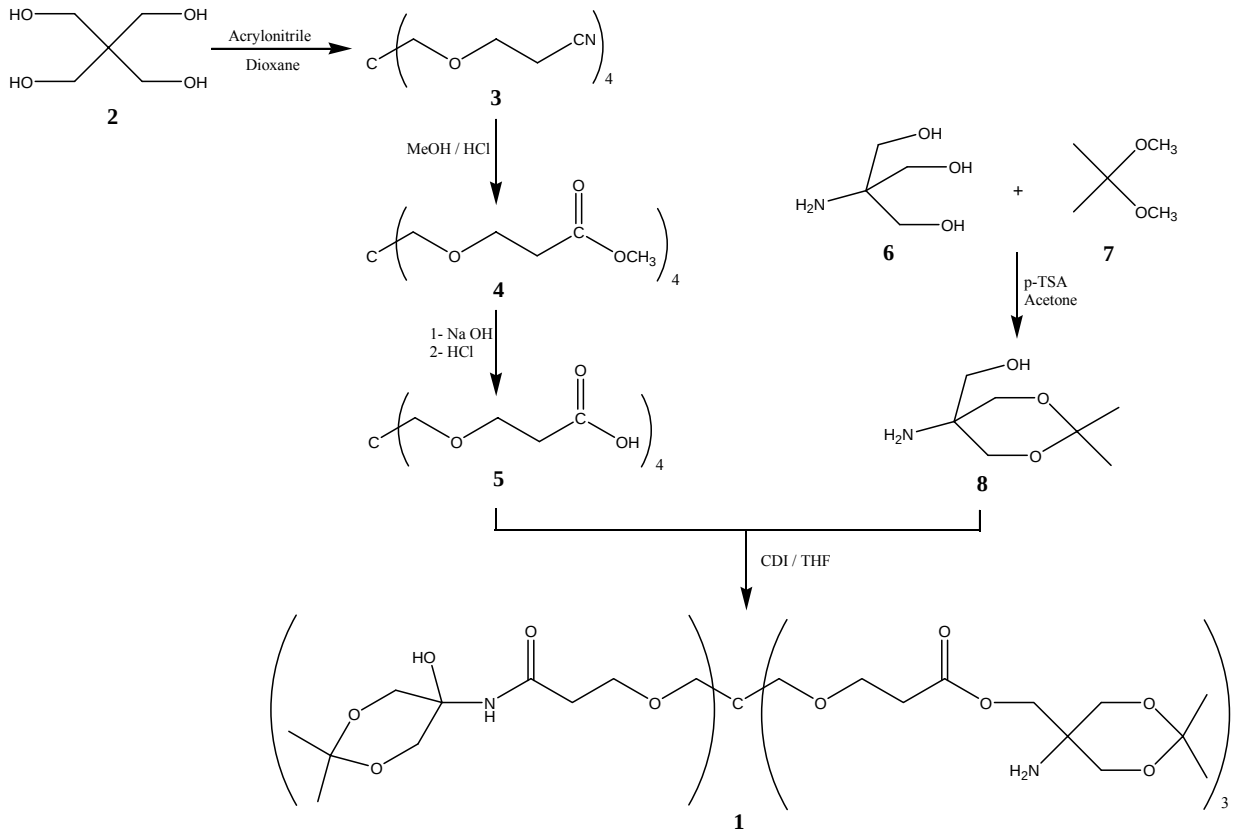

Figure 1. Synthetic pathway to dendritic monomer **1**.

Condensation reactions

General scheme of the condensation reactions are shown in Figure 2.

First, the reaction of the dendritic monomers was studied using dialdehydes as co-monomers.

The experiments were carried out at room temperature, in acid catalyzed aqueous solution, in a 1:1 equivalent ratio.

When glyoxal was used as reagent, only soluble products were found, whereas when glutaraldehyde was used, soluble products and 13% of insoluble product, **1-GLU-P,** were found after 2 h of reaction. Increasing the reaction time to 15 h did not increase the amount of insoluble product. This could be attributed to the decomposition of the acetonide and a partial hydrolysis of the ester. Since the ketonic protection would be lost, the aldehydes could generate acetals, thus it could complicate the course of the condensation reaction.

The soluble fractions were analyzed by GPC in THF, revealing dimers **1-GLY-D** (68%), and monomer plus glyoxal (no dimers), **1-GLY** (32%) for the products of reaction with glyoxal, while the soluble products by glutaraldehyde reactions were monomer plus GLU, **1-GLU** (82%) when the reaction time was 2 h and dimers, **1-GLU-D** (39%) and monomer plus GLU, **1-GLU** (58%) with 15 h of reaction time. The results are shown in Table 1.

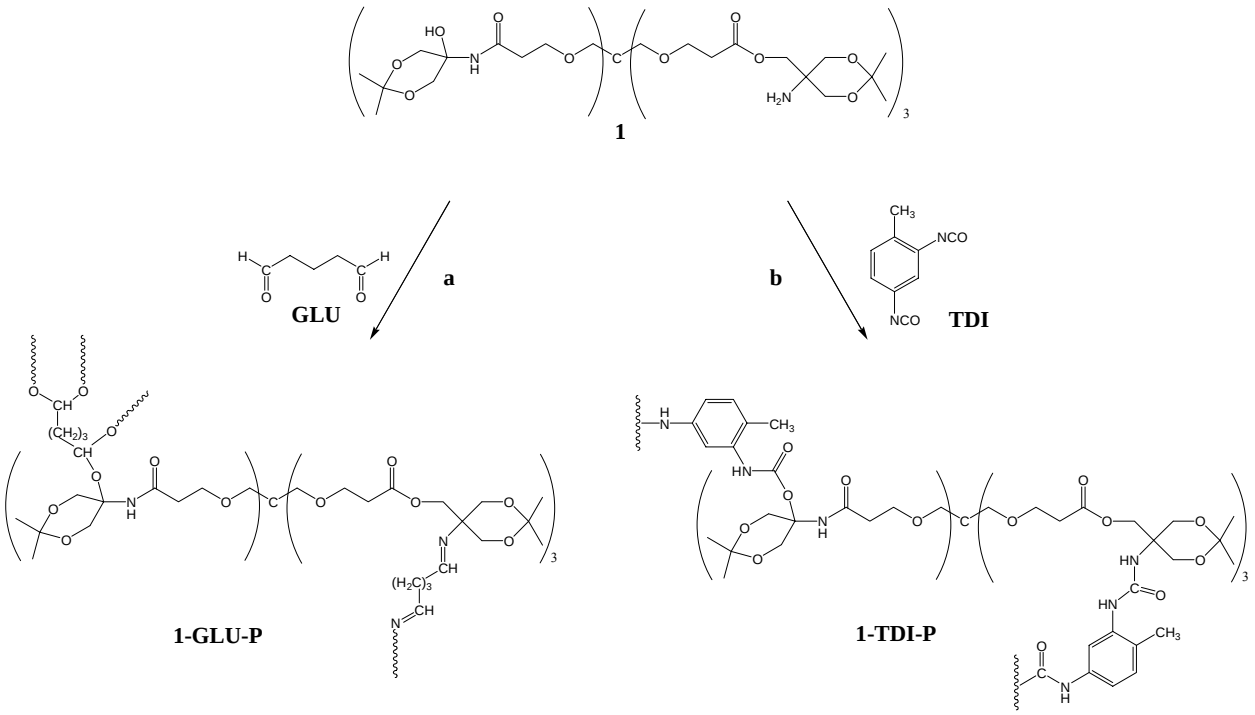

Figure 2. Condensation reactions of dendritic monomer **1** and co-monomers.

Table 1. GPC of soluble products from glyoxal and glutaraldehyde reactions

	Wt. (theor.)	Wt. (exp.)	(%)
Dendrimer **1**	996	930	100
Co-monomer			
Glutaraldehyde	1096 (1-GLU)[a]	1026	82
	1096 (1-GLU)[b]	1021	58
	2092 (1-GLU-D)[b]	1886	39
Glyoxal	1054 (1-GLY)[a]	1077	32
	2050 (1-GLY-D)[a]	2047	68

[a] Reaction time of 2 h, [b] Reaction time of 15 h.

These results demonstrated that the reactivity of the dendritic monomers with dialdehydes in those conditions was not enough to render polymer with high molecular weight in good yields, but might be improved with the incorporation of more reactive co-monomers. Meanwhile, when using a diisocyanate co-monomer, the high reactivity of these groups was capable to overcome the problem of the steric hindrance of the superficial functional groups. Therefore, a new set of experiments with toluene diisocyanate (TDI) was designed.

These reactions were performed at room temperature without catalyst, in a 1:1 equivalent ratio, either in THF solution or in bulk.

Reactions in bulk were completed after 15 h, while in solution it took 24 h for completion. Products obtained by bulk and solution experiments yielded higher than 90% of insoluble products, **1-TDI-P** for both cases. The soluble products found were monomers and TDI (10%).

The products of bulk reaction were glassy and transparent (non-swellable), while those obtained from solution reaction incorporated the solvent into the network, acquiring thus a gel appearance.

Characterization of insoluble products

The insoluble product **1-GLU-P** was only studied by TGA and **1-TDI-P** was characterized by TGA, DSC, FT-IR and their swelling behaviour in different solvents was tested.
Thermal stability studies (TGA) under nitrogen showed similar degradation profiles (see Table 2) and products slightly more stable up to 250ºC when using GLU co-monomer instead of TDI.

Table 2. Thermogravimetric Studies (TGA) of insoluble condensation products

	Residue (%W)				
	100ºC	200ºC	300ºC	400ºC	500ºC
1- GLU-P[a)]	93	75	46	34	18
1-TDI-P[a)]	98	84	36	25	15
1- TDI-P[b)]	97	85	23	24	15

[a]solution polymerization; [b]bulk polymerization.

Differential Scanning Calorimetric experiments (DSC) performed on **1-TDI-P** products, showed two endothermic transitions beginning at 170 and 250 ºC, which match a mass loss of the fastest rate of weight loss in TGA curve. Both transitions could be explained by the presence of two degradation processes; the first could be ascribed to a network degradation and the second to degradation of inner bonds of the dendritic monomers.

Swelling results are shown in Table 3, where it can be observed that the solution-polymerization products swell better in less polar solvents, while the bulk-polymerization products incorporate very little solvent into the crosslinked matrix.

Table 3. Swelling behaviour for [dendrimer-TDI] products

	Solution reaction products	Bulk reaction products
	%S = Ws – Wd / Wd [a)]	
$CHCl_3$	109	63
THF	56	29
CH_3OH	26	21

[a] Wd = dry weight; Ws = swollen weight.

Both products showed a swellably behavior more hydrophobic than hydrophilic. The soluble products were slowly studied by GPC.

Products **1-TDI-P** were characterized by FT-IR spectroscopy, and a complete disappearance of isocyanate group (ν NCO, 2275-2240 cm^{-1}) together with an increment in the number and intensity of the peaks between 1800-1500 cm^{-1}, due to the formation of ureas (RNHCONHR, ν 1660 cm^{-1}), urethane (NHCOOR, 1735-1700 cm^{-1}), and allophanates (RNHCONR'COOR', 1690-1732 cm^{-1}) [16] , could be noticed.

Comparative spectra of **1** and 1-TDI-P are shown in Figure 3.

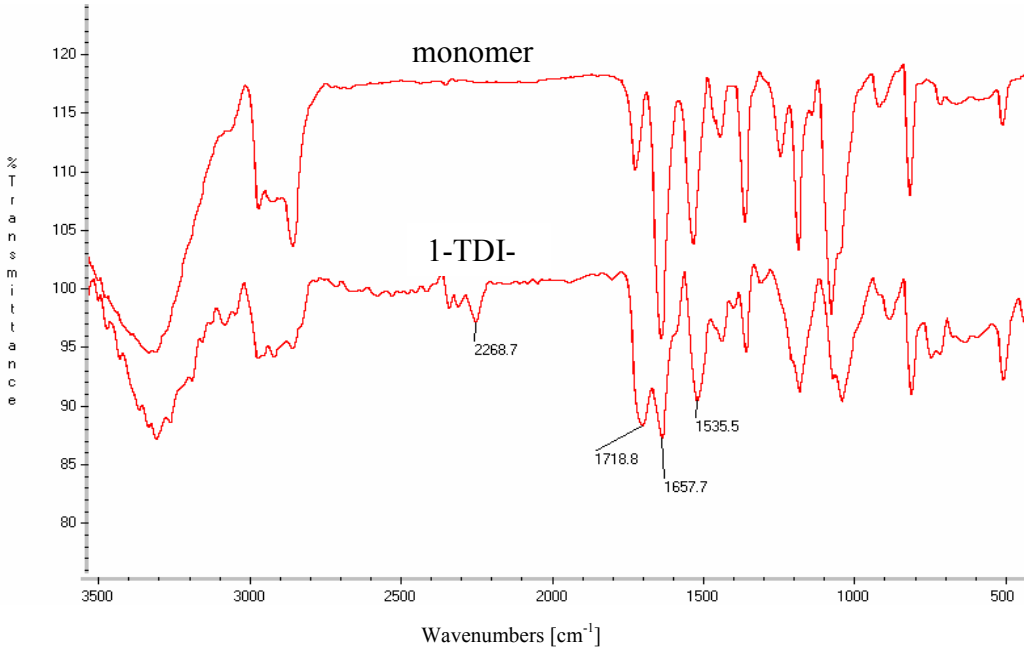

Figure 3. Comparative FT-IR spectra of dendritic monomer **1** and **1-TDI-P**.

Conclusions

There are two principal factors that exert influence on the condensation reaction of the system studied in this paper: the availability of the functional groups of the dendritic molecule and the reactivity and size of the co-monomers used.

Dendritic molecule **1** possesses four functional groups, one for each arm, which are potentially available for condensation reaction with adequate co-monomers. Nevertheless, they did not show similar reactivity front diisocyanates and dialdehydes. When the latter were used, no products with high molecular weight were found in good yields, probably due to steric hindrance.

Besides, when the more reactive co-monomer is used (TDI) and major is the length between the functional groups in the co-monomer (GLU vs. GLY), the yield of polycondensation products increased.

Experimental Section

General Procedures. Pentaerythritol was obtained from Riedel de Häen, acrylonitrile from Carlo Erba, tris (hydroxymethyl)-aminomethane (TRIS) from Anedra, 2,2-dimethoxypropane (DMP) from Aldrich, silica gel 60 from Merck, anhydrous K_2CO_3 and NaOH from Cicarelli, $CDCl_3$ and D_2O from Aldrich. All chemicals were used without purification. Solvents were obtained from Sintorgan purified by distillation and when necessary anhydrated and kept in 4Å molecular sieves. All dialdehydes and diisocianate were purchased and used as received.

Calorimetric experiments were conducted on a Hi-Res Modulated TGA 2950, Thermogravimetric Analyser and TA Instruments 2920, Modulated Differential Scanning Calorimeter, at a rate of 10 ºC/min under nitrogen atmosphere.

The Size Exclusion Chromatography (SEC) experiments were performed on a Perkin Elmer HPLC, poly(styrene-divinylbenzene) column, and refraction index detector, using THF as solvent (0.5 mL/min) at 20 ºC and polystyrene as standard.

Fourier Transform Infrared Spectra (FT-IR) were performed in a Nicolet 5SXC FTIR spectrometer on KBr discs.

NMR spectra were obtained in $CDCl_3$, on a Bruker 200 MHz NMR spectrometer. Chemical shift are given in ppm using TMS as internal standard. Elemental analyses were made by Atlantic Microlab, Inc. (Norcross, Georgia, USA).

Swelling index (S%) was measured as: %S = Ws - Wd / Wd , where

Wd = dry weight; Ws = swollen weight.

I) Monomer Synthesis

Tetranitrile 3. *(Cyanoethylation)*. Polyol **2** (33.50 g, 0.25 mol) was reacted with acrylonitrile (194 mL, 2.95 mol) in basic medium in 1.06 L of a dioxane / water mixture to favor substrate dilution. The reaction mixture was stirred for 24 h at room temperature. When the reaction was complete, the solvent was evaporated under vacuum, and the residue dissolved in chloroform and washed with water. The crude product was purified by liquid chromatography on silica gel using a sample/silica ratio of 1/20 in a column 100 cm tall and 5 cm wide and eluted with methylene chloride/ acetone (90/10 v/v). Yield was 85%, 73.9 g (0.21mol) of a white solid. Melting point ≈ room temperature.

^{13}C NMR ($CDCI_3$) δ (ppm)= 118.1(***C***N); 68.6 ($C_{4\circ}$ ***C***H_2O); 65.7 (O***C***H_2CH_2); 45.4 (***C***$_{4\circ}$); 18.6 (***C***H_2CN). ^{1}H NMR ($CDCI_3$): δ (ppm)= 3.59 (t, 8H, OC***H***$_2CH_2$); 3.40 (s, 8H, $C_{4\circ}$C***H***$_2O$); 2.69 (t, 8H, C***H***$_2CN$).

Tetramethylester 4 (Esterification). Tetranitrile **3** (34.50 g, 0.072 mol) was dissolved in 400 mL of dry methanol acidified with HCl (g), and the reaction mixture was refluxed for 3 h. After the solvent was removed under vacuum, the crude product was purified by liquid chromatography on silica gel, using a sample/silica ratio of 1/20 in a column 60 cm tall and 3.5 cm wide and eluted with methylene chloride/ acetone (90/10 v/v). Yield was 50%, 17.28 g (0.036 mol) of colorless oil.

^{13}C NMR ($CDCI_3$) δ (ppm)= 172.0 (***C***OOMe); 69.4 ($C_{4\circ}$***C***H_2O); 66.7 (O***C***H_2CH_2); 51.5 (***C***H_3); 45.3 ($C_{4\circ}$); 34.8 (***C***H_2COOR). ^{1}H NMR ($CDCl_3$) δ (ppm): 3.68 (s, 12H, OC***H***$_3$); 3.64 (t, 8H, OC***H***$_2CH_2$); 3.32 (s, 8H, $C_{4\circ}$C***H***$_2$O); 2.54 (t, 8H, C***H***$_2CO_2$Me).

Tetraacid **5** (*Hydrolysis of tetramethylester **4**)*. Tetraester **4** (21g, 0.050mol) was mixed with 210 mL of an aqueous 3M NaOH solution for 24 h at room temperature. When the reaction was complete, the product was acidified and extracted with ethyl ether. Yield: 75%, 159 g (0.038 mol) of a white solid. Mp 91-92°C

^{13}C NMR (D_2O) δ (ppm)= 176.0(***C***OOH); 68.7 ($C_{4\circ}$ ***C***H_2O); 66.5 (O***C***H_2CH_2); 44.7 ($C_{4\circ}$); 34.1 (***C***H_2COOH). ^{1}H NMR (D_2O), δ (ppm)= 3.59 (t, 8H, OC***H***$_2CH_2$); 3.33 (s, 8H, $C_{4\circ}$C***H***$_2$O); 2.36 (t, 8H, C***H***$_2$COOH).

Hydroxylamine 8 (Diol protection of TRIS 6). Best yields were obtained when mixing TRIS **6** (12.7 g, 0.11 mol) with DMP **7** (41 mL, 0.33 mol) in 300 mL dry acetone, and 0.5 % (0.11mol, 21.0g) of *p*-TSA, during 3 h at room temperature. When the reaction was over, the solvent was vacuum removed and the product dissolved in water. The pH of aqueous solution was raised to 9 and the extraction performed with CH_2Cl_2. The product migrated into the organic phase whereas the unreacted **6** and the salt of *p*-TSA remained in the aqueous phase. Yield: 60%, 10.63g (0.066 mol). Melting point: 81-82ºC.

^{13}C NMR ($CDCI_3$) δ (ppm)= 97.5 (O-***C***$_{acetal}$-CH_3), 67.2 (C_{tris}***C***H_2OC_{acetal}), 64.8 (C_{tris}***C***H_2OH), 50.1 (***C***$_{tris}$), 24.8 and 22.2 (***C***H_3). ^{1}H NMR ($CDCl_3$) δ (ppm): 3.78 (d, 8H, C_{tris}-C***Ha***Hb-O-); 3.52 (d, 8H, C_{tris}-CHa***Hb***-O-); 3.49 (s, 8H, C_{tris}-C***H$_2$***-OH); 1,95 (N***H2***); 1.44 (s, 12H, C***H***$_3$); 1.41 (s, 12H, C***H***$_3$).

Dendritic monomer 1 (Esterification-Amidation of Tetraacid 5 with amine 8). Tetraacid **5,** 2.53g (0.006 mol) was dissolved in THF and activator 1,1´-carbonyldiimidazol (CDI) was added in a 1:1 equivalent relation. After 45 min. at room temperature amine **8** (1:1 equivalent ratio) was added and allowed to react to complete the reaction time. Then, the solvent was vacuum evaporated, the crude product was dissolved in chloroform and washed with water, the organic phase was dried with $CaCl_2$. Yield: 86%, 5.11g (0.005 mol).

FT-IR: 1735 cm^{-1} (ν C=O ester), 1660 cm^{-1} (ν C=O amide) and 1543 cm^{-1} (σ NH amide)

^{13}C NMR ($CDCI_3$) δ (ppm)= 171.8 (***C***OOR); 165.7 (***C***ONH); 98.7 (O-***C***$_{acetal}$-CH_3), 69.2($C_{4\circ}$ ***C***H_2O); 66.8 (O***C***H_2CH_2); 63.5 (C_{tris}***C***H_2OC_{acetal}), 62.2 (C_{tris}***C***H_2OH), 53.2 (C_{tris}), 44.5 ($C_{4\circ}$); 35.0 (***C***H_2COOR); 23.3 and 22.1 (***C***H_3). ^{1}H NMR ($CDCI_3$), δ (ppm): 4.12 (s, 8H, C_{tris}C***H***$_2$OCOR); 3.77 (d, 8H, C_{tris}-C***Ha***Hb-O-); 3.65 (t, 8H, OC***H***$_2CH_2$); 3.55 (d, 8H, C_{tris}-CHa***Hb***-O-); 3.31 (s, 8H, $C_{4\circ}$C***H***$_2$O); 2.58 (t, C_{tris}C***H***$_2$OCOR); 2.47 (t, CONHC_{tris}C***H***$_2$OH); 1,95 (N***H2***); 1.44 (s, 12H,

C***H***$_3$); 1.41 (s, 12H, C***H***$_3$). $C_{45}H_{80}N_4O_{20}$ (997.29): Calcd. C 54.19; H 8.10; N 5.62; O 32.09. Found: C 54.98; H 8.31; N 4.81; O 31.90.

II) Condensation reactions

Reactions were carried out using dendritic monomer **1** with dialdehydes (glutaraldehyde (GLU) and glyoxal (GLY)) in aqueous solution ([monomer] = 0.3M). They were acid catalyzed (HCl 0.4%) and at room temperature, in 1: 1 equivalent ratio, during 2 and 15 h. After the reaction time, the water was vacuum evaporated and the residue washed with chloroform, and the soluble and insoluble products separated.

Some experiments with toluendiisocyanate (TDI) were carried out in THF solution ([monomer] = 0.3M) while others were performed in bulk. All experiments were conducted under nitrogen atmosphere, without catalyst, and 1:1 equivalent ratio. Previously, the monomer **1** was dried in a vacuum dessicator at 30ºC for 24 h. The reactions were followed by the disappearance of isocyanate groups (2270-2240 cm^{-1}) using FT-IR spectroscopy.

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