

## FUNCIONALIZACIÓN DE POLIPROPILEN GLICOL HIDROXITERMINADO CON GRUPOS NITRÓXIDO.

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Resumen – A new, simple and general approach for the end-functionalization with nitroxide moieties, of polypropylene glycol hydroxyl-terminated (PPG) using for the first time oxoammonium salts (Br-TEMPO) in the presence of Et<sub>3</sub>N in solution under mild reaction conditions is discussed. As far we know the oxoammonium salts has not been used before for this end in polymers. The functionalization process is carried out using only one synthetic pathway in where high levels of functionalization (98%) measured by <sup>1</sup>H-NMR and titration (as indirect test) were found. A functionalization reaction mechanism is proposed, in where peroxides groups are formed. The structure of the difunctional macroalkoxyamine containing peroxide bonds at the ends of each chain was confirmed by <sup>1</sup>H-NMR.

**Introducción.** Great interest has been focused on functional polymers as building blocks for the synthesis of block and graft copolymers, polymer networks, and chain-extended polymers<sup>1,2</sup>. Block copolymers exhibit unique and useful properties in both solution and solid state due at the thermodynamic incompatibility between each block, given as results novel morphologies (highly ordered domains) depending of the block copolymer composition and the microphase separation. In particular, amphiphilic block copolymers such as polystyrene-*block*-polypropylene glycol (PSt-*b*-PPG) are very attractive materials from both the scientific and the industrial point of view, due at their hydrophobic/hydrophilic behavior, which could be used in potentials applications in drug delivery systems<sup>3</sup>, biomedical applications<sup>4</sup>, compatibilizers<sup>5</sup> and as templates to synthesize inorganic nanoparticles<sup>6</sup>. Considerable efforts have been committed for the synthesis of this kind of diblock copolymers: i) by a free radicals process<sup>7</sup>; ii) anionic polymerization<sup>8,9</sup>. In the context of controlled radical polymerization (CRP) technique by nitroxide mediated polymerization (NMP), some works have explored the synthesis of diblock copolymers of PPG-*b*-PSt using a macroalkoxyamine (modifying one chain end of PPG with an alkoxyamine derivative from SG1) in the presence of St.<sup>10,11</sup> According with our knowledge few works have disclosed the synthesis of triblock copolymers of PSt-*b*-PPG-*b*-PSt using a prepolymer of PPG functionalized at the ends of each chain with nitroxide moieties (bifunctional macroalkoxyamines) in the presence of St. On the other hand, nitroxides are free stable radicals that in the presence of a specific counter-ion could lead to oxoammonium salts (OS)<sup>12</sup>. This kind of salts are powerful, selective and nonmetallic oxidants extensively used for the oxidation of primary and secondary alcohols to aldehydes and ketones, respectively<sup>13-15</sup>. Several scientific studies using (OS) like oxidants have been developed until our days, since that Guluve *et al.*,<sup>16</sup> reported for first time the use of this salts like oxidant agents. However, we have found that the (OS) not only are excellent oxidant agents but that, in the presence of a basis (ej. triethylamine, Et<sub>3</sub>N), the chemistry of oxidation radically changes towards chemistry of functionalization, which is not an obvious result. Thus, on this basis, in principle practically any substrate, molecule or chemical

compound containing hydroxyl groups could be functionalized with nitroxide moieties in only one step.

In summary, some strategies of synthesis have been developed in order to obtain amphiphilic diblock copolymers of PSt-*b*-PPG or PSt-*b*-PPG-*b*-PSt, using difunctional macroalkoxyamine for NMP. However, all these novel approaches involve numerous synthetic pathways and sophisticated methods of purification. In this study we disclose a simple, robust and general approach for the end-functionalization with nitroxide moieties, of polypropylene glycol hydroxyl-terminated (PPG) using for the first time oxoammonium salts (Br-TEMPO) in the presence of Et<sub>3</sub>N in solution. Notice that as far we know the oxoammonium salts has not been used before for this end in polymers. The functionalization process is carried out using only one synthetic pathway in where high levels of functionalization measured by <sup>1</sup>H-NMR and titration (as indirect test) were found. A functionalization reaction mechanism is proposed, in where peroxides groups are formed. The structure of the difunctional macroalkoxyamine containing peroxide bonds at the ends of each chain was characterized by <sup>1</sup>H-NMR and ATR-FTIR.

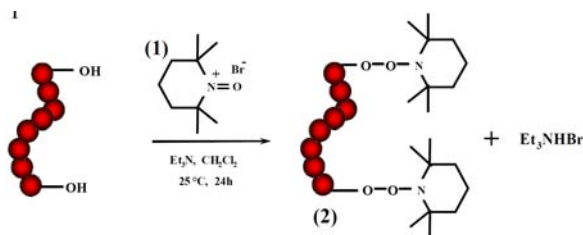
**Experimental.** <sup>1</sup>H NMR experiments were recorded using an FT-NMR Jeol Eclipse 300 instrument at 300 MHz in CDCl<sub>3</sub> at room temperature. ATR-FTIR spectra were recorded on a Thermo-Nicolet 6700 spectrometer of 4000–400 cm<sup>-1</sup> using 42 scans and 4 cm<sup>-1</sup> of resolution.

**Purification of poly(propylene glycol) hydroxyl-terminated (PPG)** 30 g of PPG (130–190 ppm of phenolic antioxidant) was purified on a chromatographic column which was previously slurry-packed with silica gel. The column was eluted using 300 mL of CH<sub>2</sub>Cl<sub>2</sub> in order to remove the antioxidants. The fractions containing pure poly(propylene glycol) hydroxyl-terminated without antioxidants, PPG\_w/a) were combined and dried on a vacuum oven at room temperature overnight. PPG\_w/a (30 mg) was characterized by <sup>1</sup>H NMR and ATR-FTIR spectroscopy.

**Synthesis of oxoammonium bromide salt: Br-TEMPO.** In a typical experiment<sup>17</sup> bromine, was added slowly to a solution of TEMPO (5 g, 0.032 mol in 100 mL of CCl<sub>4</sub>). A brown solid was formed instantaneously and was purified by soxhlet extraction system using CCl<sub>4</sub>. The Br-TEMPO salt was dried over vacuum at room temperature overnight (yield = 95%). <sup>1</sup>H-NMR (CDCl<sub>3</sub>): δ(ppm): 2.3–2.7 (m, 6H), 1.7–2.0 (s, methyl, 12H).

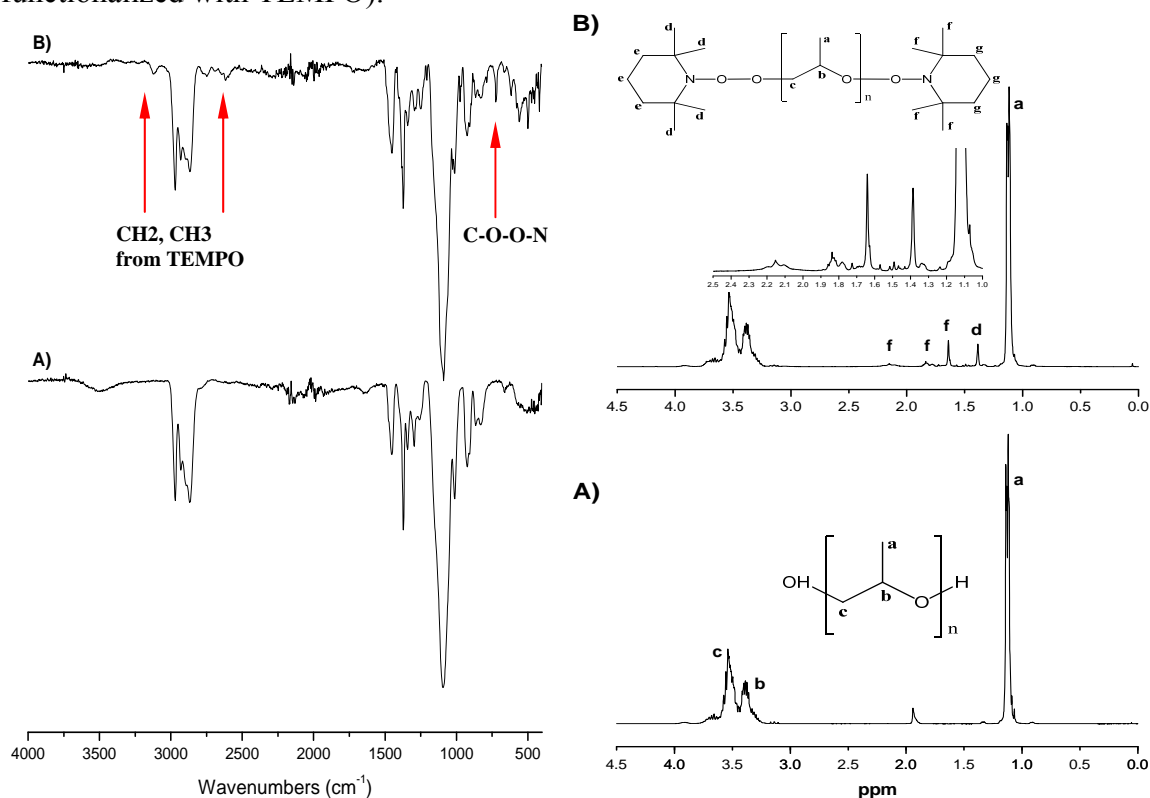
**Synthesis of the bifunctional macroalkoxyamine TEMPO-PPG-TEMPO** 25 g of PPG without antioxidants (PPG\_w/a, 0.041 mol of –OH groups) were dissolved in 20 mL of CH<sub>2</sub>Cl<sub>2</sub> in the presence of triethylamine (Et<sub>3</sub>N, 4.58 g, 0.045 mol) in a 100 mL glass reactor. After that, 9.71 g (0.041 mol) of Br-TEMPO salt were dissolved into 80 mL of CH<sub>2</sub>Cl<sub>2</sub> and were added drop-wise to the reactor. A solid was formed instantaneously (Et<sub>3</sub>NHBr) indicating indirectly that the functionalization reaction have being carried out. The functionalization reaction proceeded during 12 h at 60 °C under nitrogen atmosphere. The solution was filtered and the solid (Et<sub>3</sub>NHBr) obtained was characterized by <sup>1</sup>H-NMR. The solution filtered containing TEMPO-PPG-TEMPO was purified on a chromatographic column using CH<sub>2</sub>Cl<sub>2</sub>. TEMPO-PPG-TEMPO (30 mg) was characterized by <sup>1</sup>H NMR and ATR-FTIR spectroscopy.

**Results and Discussion.** The new and simple synthetic route to obtain functionalized polymers with TEMPO moieties using Br-TEMPO salts is shown in Scheme 1.



**Scheme 1.** Schematic representation of the functionalization of PPG-hydroxy terminated with TEMPO mediated by oxoammonium bromide salt.

The reaction mechanism to obtain (2) involves a nucleophilic substitution mechanism by a free-radical process. In this reaction it is proposed that the hydroxyl groups at the end-chain of the polymer are potential sites for attack by a nucleophile such as bromine. This strategy takes advantage of the inherent existence of an equilibrium in (1) between the salt and radical species (bromine and TEMPO) which has been proposed previously.<sup>17</sup> In this way, a bromine radical is produced from (1), which abstract a hydrogen atom from hydroxyl group to generate hydrobromic acid (HBr) and an oxygen-centered radical site at the end of the chain, which is then quickly capped by the nitroxide radical to form (2). The HBr formed during this synthesis is trapped by Et<sub>3</sub>N to form triethylamine hydrobromide (Et<sub>3</sub>NHBr). Figure 1 shows <sup>1</sup>H-NMR spectra corresponding to: A) PPG virgin, B) PPG-T (PPG functionalized with TEMPO).



**Figure 1.** ATR-FTIR: A) PPG-OH, B) PPG-T (PPG functionalized with TEMPO)

**Figure 2.** <sup>1</sup>H-NMR: A) PPG-OH, B) PPG-T (PPG functionalized with TEMPO)

Figure 1A shows typical bands from PPG-OH at 3500 cm<sup>-1</sup> corresponding to stretch intermolecular hydrogen bonding (–OH), C–H stretch:  $\nu_s$  2969 cm<sup>-1</sup> and  $\nu_{as}$  2867 cm<sup>-1</sup> both of –CH<sub>3</sub>,  $\nu_{as}$  2923 cm<sup>-1</sup> of –CH<sub>2</sub>–; C–H bend:  $\nu_s$  1452 cm<sup>-1</sup> and  $\nu$  924 cm<sup>-1</sup> out-of-plane both

of  $-\text{CH}_2-$ ,  $\nu_s$  1372  $\text{cm}^{-1}$  of  $-\text{CH}_3$ ;  $\nu$  1342  $\text{cm}^{-1}$  corresponding to wag intermolecular  $\text{C}-\text{H}\cdots\text{OH}$ ;  $\text{C}-\text{O}-\text{C}$  stretch  $\nu_s$  1094  $\text{cm}^{-1}$  and  $\nu_s$  1012  $\text{cm}^{-1}$  corresponding to primary alcohol. Figure 1B shows a new band at 700  $\text{cm}^{-1}$  attributed to peroxide bond<sup>18</sup>. Also at 2600  $\text{cm}^{-1}$  and 3100  $\text{cm}^{-1}$  new vibrations were observed and attributed to aliphatic groups  $\text{CH}_2$  and  $\text{CH}_3$ , respectively, from TEMPO. In Figure 2A characteristic chemical shifts from PPG-OH are shown:  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta(\text{ppm})$ : 1.02-1.2 (m, 3H,  $-\text{CH}_3$ ), 3.2-3.45 (m, 1H,  $-\text{CH}-$ ), 3.45-3.7 (m, 2H,  $-\text{CH}_2-$ ). Figure 2B shows a new chemical shifts at 1.4-1.6 ppm and 1.8-2.1 ppm assigned to  $\text{CH}_3$  and  $\text{CH}_2$  groups, respectively, of the piperidine ring from TEMPO. The efficiency was measured by titration and confirmed by  $^1\text{H}$ -NMR (90%) on basis at the new chemical shifts.

**Conclusiones.** For the first time, PPG-OH was functionalized with TEMPO moieties using OS (Br-TEMPO). The results lead to the following conclusions: i) The OS are strong candidates for the functionalization of PPG containing hydroxyl groups. This new approach of synthesis opens up several possibilities of applications in the generation of novel materials (block copolymers) following a facile chemistry pathway. ii) High efficiencies of functionalization were found. iii) Spectroscopic evidences by  $^1\text{H}$ -NMR for the functionalization of PPG with TEMPO was provided and the presence of the peroxidic bond was confirmed and quantified by titration.

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