Carbohydrate Polymers 94 (2013) 323–331

Contents lists available at SciVerse ScienceDirect

Carbohydrate Polymers

journal homepage: www.elsevier.com/locate/carbpol

Anionic ring-opening polymerization of ethylene oxide in DMF with cyclodextrin derivatives as new initiators

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ARTICLE INFO

Article history:
Received 11 September 2012
Received in revised form
13 December 2012
Accepted 26 December 2012
Available online 4 January 2013

Keywords:
Anionic polymerization
Star polymers
Cyclodextrin

ABSTRACT

Anionic polymerization initiated by cyclodextrins suffers from a poor solubility of those derivatives in standard polymerization solvents. The possibility to perform ethylene oxide polymerization initiated by monofunctional initiators (allyl alcohol, 2-methoxyethanol) by living ring opening polymerization in DMF, a good solvent for any CD derivative, was demonstrated by SEC, ^{1}H and ^{13}C NMR analyses. The study was extended to the use of native CD as initiator, leading to the synthesis of ill-defined structures, explained by the reactivity scale of the various hydroxyl functions. Two selectively modified CD derivatives are then used to synthesize a new family of star-shaped poly(ethylene oxide) polymers with CD core, having 14 or 21 arms. The polymerization was found to be living and DOSY experiments confirmed the well-defined structures for the synthesized star-polymers.

1. Introduction

Chemically modified cyclodextrins (CDs) allow numerous applications in several fields, such as drug delivery (Monnaert et al., 2004; Rajewski & Stella, 1996), catalysis (Badi et al., 2010), sensing (Ogoshi & Harada, 2008), and artificial channels (Bacri, Benkhaled, Guégan, & Auvray, 2005; Badi, Auvray, & Guégan, 2009; Jullien, Lazrak, Lacombe, Canceill, & Lehn, 1993; Tabushi, Kuroda, & Yokota, 1982). CDs offer the possibility to be selectively modified in order to synthesize new polymerization initiators. Various teams focused on the design of new CD-based initiators for the synthesis of star-shaped polymers using controlled polymerization (Yhaya, Gregory, & Stenzel, 2010). Seminal work was conducted by the group of Haddleton (Ohno, Wong, & Haddleton, 2001) and opened a new area in the design of star-shaped polymers by the use of modified CDs for ATRP polymerization. Styrene was successfully reported to be polymerized through this strategy, and various monomers such as (meth)acrylates, N-isopropylacrylamide were then used. In the mean time, Stenzel & Davis (2002) reported the synthesis of a heptafunctional trithiocarbonate β-CD derivative for controlled styrene polymerization by RAFT. Later on, Kakuchi et al. (2003) reported the synthesis of a TEMPO-modified β-cyclodextrin and reported limitation of such strategy for the synthesis of well-defined star-shaped polystyrene with a cyclodextrin core. Anionic ring-opening polymerization with a CD-based initiator was first reported by Topchieva et al. (1998): by using native cyclodextrin as initiator of ethylene oxide polymerization, ill-defined polymers were synthesized. Harada and co-workers reported the polymerization of lactones (β-butyrolactone, δ-valerolactone, ε-caprolactone) initiated by native cyclodextrin. Surprisingly, only one arm per cyclodextrin was evidenced (Osaki, Takashima, Yamaguchi, & Harada, 2007). Gou, Zhu, Xu, and Shen (2008) noticed that the use of stannous octoate Sn(Oct)$_2$ allowed the initiation of all the primary hydroxyl functions for the polymerization of ε-caprolactone. Using β-butyrolactone, Harabagiu and co-workers observed that all the hydroxyl functions of the CD could participate to the polymerization reaction, despite a transfer reaction leading to linear polymer that was not discussed in the previous works (Peptu et al., 2010). Lactide and glycolide were also polymerized in bulk using native CD as initiator in the presence of Sn(Oct)$_2$ (Mooguee, Omidi, & Davaran, 2010). Per-6-Tos-β-CD was synthesized by Adeli, Zarnegar, and Kabiri (2008) in order to initiate the polymerization of lactide using Sn(Oct)$_2$ as catalyst, then the tosylate functions of the CD primary face allowed the polymerization of 2-ethyl-2-oxazoline, through a cationic ring-opening polymerization (ROP). The ROP was also used by Pereira, Huin, Morariu, Bennevault-Celton, and Guégan (2012) to synthesize star poly(2-methyl-2-oxazoline) with 7 arms from β-cyclodextrin

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http://dx.doi.org/10.1016/j.carbpol.2012.12.062

permodified on the primary rim, using the core-first and the arm-first methods.

Anionic polymerization of ethylene oxide has been extensively studied (Boileau, 1989; Lapienis & Penczek, 2004; Taton et al., 2003). Selectively modified β-cyclodextrin, by grafting heptyl chains on the secondary face (Badi et al., 2006), was used as initiator for ethylene oxide polymerization, and living nature of the polymerization in THF was proved (Badi et al., 2009). In a general concern, anionic polymerization initiated by cyclodextrins suffers from a poor solubility of those derivatives in standard polymerization solvents. This solubility matter prevents that field from a large development, like the design of well-defined nanopores (Badi et al., 2009). Thus, in this work, we investigate the possibility to perform ethylene oxide polymerization by living anionic ring opening polymerization, in DMF, a good solvent for any CD derivative. It was already demonstrated that, in the case of acrylonitrile (Jiang, Zhang, Du, Zhang, & Wang, 2007), the polymerization in DMF followed a living mechanism. The study is then extended to the use of native CD as initiator, the reactivity scale of the various hydroxyl functions being revisited. Various selectively modified CD derivatives are used to synthesize a new family of star-shaped poly(ethylene oxide) polymers with CD core, having 14 or 21 arms. The living mechanism of the polymerization is then demonstrated.

2. Materials and methods

2.1. Materials

DMF (SDS-Carlo-Erba) and DMSO (SDS-Carlo-Erba) were dried over CaH_2 using the freeze drying thaw technique and then distilled under vacuum, using the so-called “cold-wall” technique.

β-Cyclodextrin was kindly provided by Roquette (France). Per-(2,3,6-tri-*O*-methyl)-β-CD, per(2,3,6-tri-*O*-(3-hydroxypropyl))-β-CD and per(2,6-di-*O*-(3-hydroxypropyl)-3-*O*-methyl)-β-CD were synthesized as previously described (Badi et al., 2006; Casu, Reggiani, & Gallo, 1968; Eskandani, Huin, & Guégan, 2011). CD or CD derivatives were first introduced in a 100 mL burette surmounted with a stopcock, then dried under vacuum (10^{-5} mmHg) at room temperature for 12 h. Then, 10 mL of heptane distilled from CaH_2 were introduced in the burette by distillation. An azeotropic distillation of heptane/H_2O was then conducted in order to eliminate the maximum of residual water from the CD (temperature of the azeotropic point: 79 °C). The same procedure was conducted using benzene. The CD initiator was then dried under high vacuum, 12 h, at 80 °C, and stored under vacuum.

2-Methoxyethanol (Aldrich) and allyl alcohol (Aldrich) were dried over molecular sieves (4 Å) for one night before being degassed and distilled in a 10 mL burette surmounted with a stopcock, and stored under vacuum.

Ethylene oxide (Aldrich) was dried on sodium films, until a pink color persisted, then the necessary amount of monomer was distilled in a 100 mL burette surmounted with a stopcock, and stored under vacuum.

The deprotonating agent, diphenylmethylpotassium (DPMK) in THF, was prepared as described previously (Normant & Angelo, 1960). Its concentration was determined by titration with acetanilide (Aldrich) in dried DMSO and was equal to 3.2×10^{-4} mol mL^{-1}. The required amount of DPMK was introduced in a 25 mL burette surmounted with a stopcock, and stored under vacuum.

2.2. Polymerization experiments

All vessels were flamed under high vacuum, prior to use. The solvent was vacuum-distilled in a 100 mL burette. Half of the solvent was distilled in the burette containing the DPMK and the other half in the burette containing the initiator (CD derivatives or monoalcohol). The burettes were maintained under high vacuum. The reactor, a 250 mL four-neck flask equipped with a magnetic stirrer was surmounted with three burettes containing each the ethylene oxide, the solutions of initiator (cyclodextrin derivatives or monoalcohol) and DPMK both in DMF, and put under high vacuum (after flaming the reactor wall). All the polymerization reactions were carried out at 40 °C, under high vacuum. CD derivative (typically 0.390 g for a native CD in 40 mL of DMF) was first introduced, followed by the slow addition of DPMK (20% compared to the [OH], typically 3.43×10^{-4} mol in 35 mL of DMF). The obtained homogeneous solution was stirred during 48 h at room temperature. The reactive mixture was then cooled to 0 °C in order to add the ethylene oxide monomer (typically 14.4 g), in a dropwise manner. The polymerization was then carried out at 40 °C and the reaction was quenched by addition of acidic methanol. After concentration of the polymerization medium, the polymer was precipitated successively in cold diethyl ether and pentane.

2.3. Characterizations

NMR spectra were recorded on a Bruker Advance AM300 spectrometer (^{1}H 300 MHz and ^{13}C 75 MHz) using DMSO-d_6 as solvent at 25 °C. The molar masses were determined by size exclusion chromatography (SEC) with THF or DMF as eluents, the concentration of the polymer being 3 mg mL^{-1}. The column is a Styragel column (type HR 4E) from Waters. SEC was calibrated using poly(ethylene oxide) standards. The software used for the data analysis was OmniSEC (Viscotek). The molecular weights of the star polymers were then calculated considering the functionality of the initiator (Grest, Fetters, & Huang, 1997). The molar masses reported in the tables (NMR and SEC) stand for the purified star polymers (free from linear PEO).

Dynamic Light Scattering analysis was performed using a dynamic light scattering detector (Zetasizer nano ZS, ZEN 3500, Malvern) operating at a wavelength of 532 nm. Measurements were made at 25 °C at a scattering angle of 173°. Each measurement was repeated triplicate.

For the Diffusion-Ordered SpectroscopY (DOSY) experiments, the maximum field gradient strength was calibrated using a home-made Plexiglas phantom (8 mm ± 0.01 length and a width equal to the inner diameter of the NMR tube) inserted in a H_2O filled NMR tube and using the pulse program calibgp (Bennevault-Celton et al., 2011; Seedhouse & Hoffman, 2008). The linear plot of the obtained gradient strengths against the gradient strength setting (GPZ1) used gave a maximum field gradient strength equal to 56.8 G cm^{-1}. The temperature calibration of the spectrometer was performed with a sample of 100% CH_3OH in the temperature range between 298 K and 313 K. The accuracy of the calibrations was checked by measuring the self-diffusion coefficient of a mixture H_2O/D_2O (10%/90% in moles) at 25 °C (Holz & Weingärtner, 1991). The DOSY experiments were carried out using the stegp1s pulse sequence with a linear gradient of 16 steps between 2% and 95%. Before each diffusion experiment, the proton relaxation times were determined in order to correctly set the D1 parameter of the DOSY sequence. The length of the gradient δ and the diffusion time Δ were optimized for each analyzed product. All the DOSY experiments were carried out at 25 °C and the concentration used for each sample was equal to 16 mg mL^{-1} in DMSO-d_6. The mathematical treatment of the data was performed as previously described (Bennevault-Celton et al., 2011).

Table 1
Polymerizations of ethylene oxide initiated by 2-methoxyethanol (Run 1) and allyl alcohol (Runs 2 and 3) carried out in DMF, using DPMK as deprotonating agent (20% of hydroxyl concentration), at 40 °C during 5 days, under vacuum.

Run	Initiators	[OH] (mol L^{-1})	[EO] (mol L^{-1})	Yield[a] %	$\bar{M}_{n,th}$[b] (g mol^{-1})	$\bar{M}_n$ NMR[c] (g mol^{-1})	$\bar{M}_n$SEC[d] (g mol^{-1})	PDI
1	2-Methoxyethanol	10.4×10^{-2}	4.1	98	1700	1600	1300	1.06
2	Allyl alcohol	9.9×10^{-2}	2	94	800	650	600	1.10
3	Allyl alcohol	9.9×10^{-2}	4	95	1700	1300	1100	1.10

[a] Polymerization yield = $m_{\text{polymer}}/m_{\text{EO}} \times 100$ (%).

[b] Theoretical molar mass $M_{n,th} = \frac{[\text{EO}]}{[\text{OH}]} \times \text{yield} \times M_{\text{EO}}$.

[c] Determined by ^{1}H NMR.

[d] Determined by SEC in THF using linear monodisperse PEO as standards.

3. Results and discussion

The major concern of polymerizations initiated by CD derivatives deals with the solubility of those initiators: standard solvents do not allow a full solubilization of CD-based initiator. We found out that DMF is the best solvent to solubilize the CD-based initiators used in this work, without aggregation (Fig. S1 in Supplementary data: dynamic light scattering performed on β-CD, showing only unimers).

To perform the anionic polymerization of ethylene oxide, strong nucleophilic derivatives are usually chosen as initiators, in order to obtain a fast initiating reaction. Multifunctional initiators are usually multialcohol derivatives that are partially deprotonated, allowing the formation of compound bearing in the mean time hydroxyl functions and alcoholate functions. Feng, Taton, Chaikof, and Gnanou (2005) have reported that a maximum of 30% of deprotonated alcohol is required to allow a complete solubilization of the multifunctional initiator (Feng et al., 2005). In this case, a fast exchange between alcoholate and hydroxyl groups, in comparison to the polymerization kinetics, allows for all these functions to take part in the ethylene oxide polymerization process and then allows the simultaneous growth of each star polymer arm.

3.1. Ethylene oxide polymerization using monofunctional initiator

In order to validate the use of DMF as a potential solvent for ethylene oxide anionic ring-opening polymerization, reactions were first initiated with monofunctional initiators (2-methoxyethanol, allyl alcohol). The polymerization of ethylene oxide initiated by allyl alcohol was first described by Cammas, Nagasaki, and Kataoka (1995) with potassium naphtalide, at 20–40 °C, during 48 h, in dry THF. The protocol was adapted to our reaction conditions.

Table 1 gives the experimental conditions used for the polymerizations and the characterization of the obtained polymers. Molar masses are determined by ^{1}H NMR and SEC (Figs. S2–S7 – Supplementary data).

The polymerization initiated by 2-methoxyethanol, using DPMK as deprotonating agent, gives polymer presenting a monomodal peak by SEC analysis (1300 g mol^{-1}), with a narrow distribution (Fig. S2). Such low molecular weight allows the use of ^{1}H NMR analysis to determine the PEO molar mass, by comparison between the integration of methoxy protons (3.2 ppm) and the one of the EO unit protons (3.4–3.7 ppm) (Fig. S3). Using quantitative ^{13}C NMR, the comparison of the integrations of methoxy carbon (58.5 ppm) and of EO unit carbons (70.2 ppm) gives a value for the molar mass of 1500 g mol^{-1}, in agreement with SEC and ^{1}H NMR results (Fig. S4 and Table 1). In addition, the integration ratio of the signals given by methoxy carbon and by carbon carrying hydroxyl function (60.6 ppm) is equal to 1, showing that the synthesized polymer is a telechelic α-methoxy-ω-hydroxy-PEO.

The same analyses (SEC, ^{1}H and quantitative ^{13}C NMR) were performed in the case of the polymerizations initiated by allyl alcohol, demonstrating the synthesis of a telechelic α-allyl-ω-hydroxy-PEO (Figs. S5–S7).

In conclusion, the experiments that we conducted in DMF with monofunctional initiators and DPMK give well-defined structures, with good yields, molar masses close to the expected ones and PDI around 1.06–1.10. EO polymerizations in DMF, with multifunctional initiators, are then encountered.

3.2. Ethylene oxide polymerization using multifunctional initiating systems

Among the various multihydroxyl molecules, cyclodextrin is a very versatile compound that can be used for the synthesis of star polymers, having discrete various numbers of arms. The experimental conditions that we used for β-CD derivatives took into account the experiments performed by Topchieva et al. (1998) and Badi et al. (2009) New series of polymerizations have been carried out using native β-cyclodextrin (βCD), per(2,3,6-tri-*O*-(3-hydroxypropyl))-β-CD (named $\beta\text{CD}'(\text{OH})_{21}$) and per(2,6-di-*O*-(3-hydroxypropyl)-3-*O*-methyl)-β-CD (named $\beta\text{CD}'(\text{OH})_{14}$) as initiators. Scheme 1 presents the different structures of the CD-based star-polymers targeted.

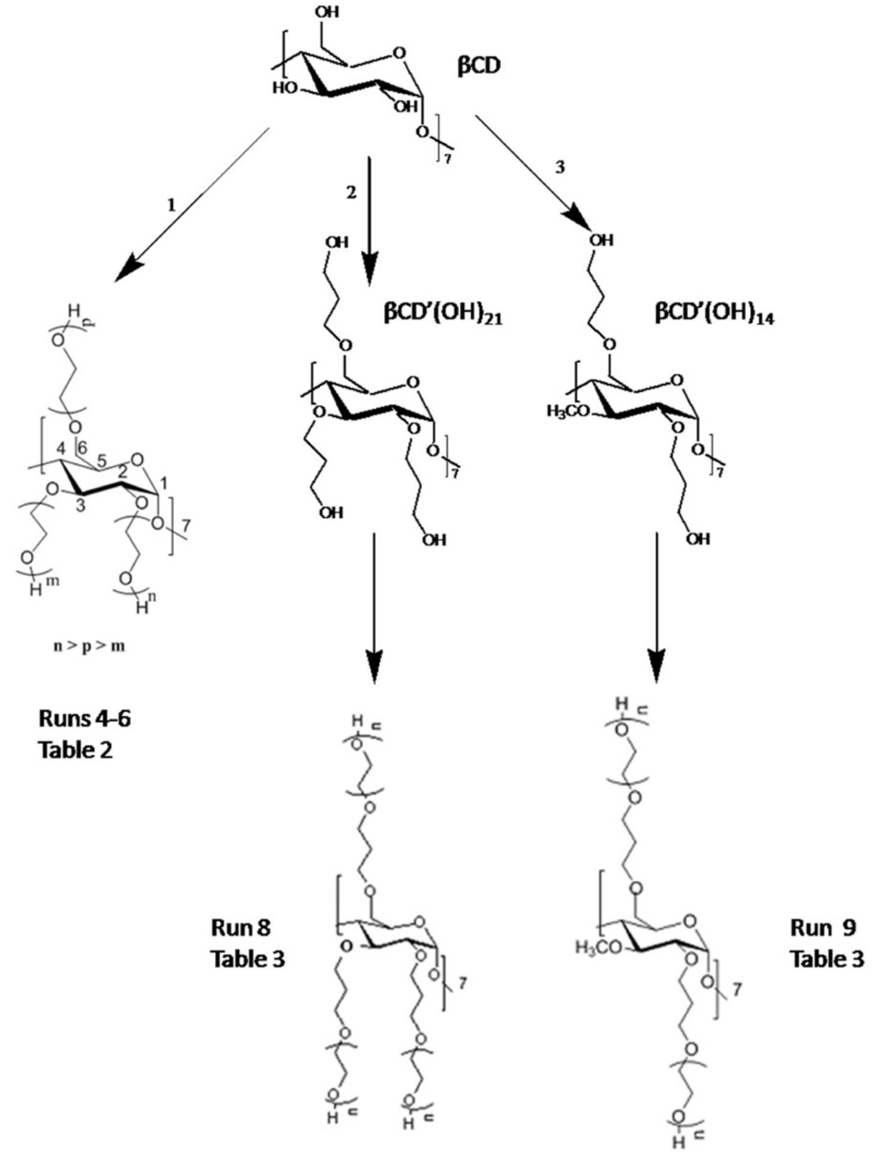
3.2.1. Native β-CD as initiator

Table 2 gives the experimental conditions used for the EO polymerization initiated by native β-CD. Characterization of the obtained polymers is provided. Molar masses are determined by ^{1}H NMR and SEC, after work-up.

Surprisingly, no polymerization occurred when the mixing time between CD and DPMK was lower than 24 h. Then, this time was set to 48 h for all the polymerizations.

First experiments (Runs 4 and 5, Table 2) led to the presence of two peaks in the SEC analysis, one being attributed to the star polymer and the other to linear PEO (Badi et al., 2009). For the SEC and NMR analysis, only the molar masses corresponding to the star polymer were reported in Table 2. The measured molecular weight of the star polymer was lower than the expected one, explained by the presence of linear PEO. The linear PEO has a $\overline{M_n}$ corresponding to at least the molecular weight of one branch of the star PEO, suggesting that water was already present at the beginning of the polymerization. In the first series of experiments (Runs 4 and 5, Table 2), the CD was only purified by a heptane azeotropic distillation. A further azeotropic distillation of benzene was carried out for Runs 6 and 7. This purification step does not allow a complete removal of water molecules, but allows the synthesis of star polymers with the lowest amount of linear PEO, leading then to a good agreement between theoretical masses and experimental results as shown by NMR and SEC (Run 6, Table 2).

Feng et al. (2005) suggested using 30% of DPMK per hydroxyl functions for the synthesis of star polymers initiated by multialcoholate initiators. In their system, this ratio leads to an average of one alcoholate per molecules, while it leads to about 6 alcoholates per cyclodextrin. In such ratio, precipitation of the initiator



Scheme 1. Structures of the different synthesized star polymers.

was encountered. Then only 20% of the hydroxyl functions of the CD were deprotonated in order to avoid precipitation of the initiator.

Polymerization kinetic is very slow: after 5 days, 30% of EO conversion was reached (Run 4, Table 2) and, after 12 days, only 56% of conversion was measured (Run 5, Table 2). The slow kinetic is explained by the experimental conditions used (dilution of the initiator and active species and deprotonation of only 20% of the hydroxyl functions).

The ^{1}H NMR spectrum (Fig. S8, Run 5) shows the appearance of the peaks corresponding to the EO units (between 3.3 and 3.7 ppm). The broad peak of EO overlaps the peaks corresponding to the protons H-2 to H-6 of the CD. However, the anomeric proton H-1 of the β-CD clearly appeared at 5.1 ppm. The signals between 5.5 and

Table 2
Polymerizations of ethylene oxide initiated by native β-cyclodextrin in DMF.[a]

Run	[OH] (mol L^{-1})	[EO] (mol L^{-1})	Time	Yield[b] (%)	$\bar{M}_{n,th}$[c] (g mol^{-1})	$\bar{M}_n$NMR[d] (g mol^{-1})	$\bar{M}_n$SEC[e] (g mol^{-1})	PDI
4	9.3×10^{-2}	4.1	5 days	30	13 500	12 500	11 000	1.13
5	9.6×10^{-2}	3.9	12 days	56	22 000	18 000	15 400	1.06
6	9.6×10^{-2}	4.0	11 days	59	24 000	nd[f]	23 500	1.14
7	9.4×10^{-2}	4.0	7 h	4	2700	–	–	–

[a] Using DPMK (20% of CD hydroxyl concentration) as deprotonating agent, with a deprotonation time of 2 days, at 40 °C, under vacuum, during different times.

[b] Polymerization yield = $(m_{\text{polymer}} - m_{\text{CD}})/m_{\text{EO}} \times 100$ (%).

[c] $\bar{M}_{n,th} = \frac{[\text{EO}]}{[\text{OH}]} \times \text{yield} \times 21 \times M_{\text{EO}} \times M_{\beta\text{-CD}}$.

[d] Determined by ^{1}H NMR.

[e] Calculated from SEC chromatogram in DMF, considering the 21 arms of the star-polymer obtained.

[f] Impossible to determine by ^{1}H NMR, due to a high $\bar{M}_n$.

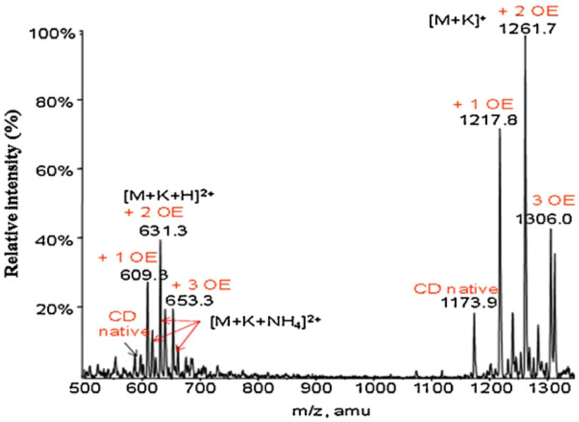


Fig. 1. ESIMS analysis of short PEO obtained from anionic polymerization of ethylene oxide initiated by native β-CD (Run 7, Table 2).

6 ppm, corresponding to OH-2 and OH-3, completely disappeared. Disappearance of the OH-6 functions is not ascertained due to the appearance of the PEO end-chain hydroxyl function. This question is solved by the ^{13}C NMR analysis, which demonstrates the disappearance of C bearing hydroxyl functions of the native CD: all the hydroxyl functions are involved in the polymerization initiation. However, well-defined structure of the star-polymers is not demonstrated at this stage, due to the various reactivity of the hydroxyl functions borne by the CD for a nucleophilic reaction (Khan, Forgo, Stine, & D'Souza, 1998).

In order to check the hydroxyl function reactivity order, a polymerization initiated by native β-CD was performed during 7 h (Run 7, Table 2). ESIMS analysis of run 7 (Fig. 1) shows that 0–3 EO units are linked to the β-CD. The main peaks are located at 1261.7 amu, corresponding to the fragment $[M_{CD}+K+2EO]^+$, and at 631.3 amu corresponding to $[M_{CD}+K+H+2EO]^{2+}$. According to the ^1H NMR performed in DMSO-d_6 (Fig. 2), it was possible to determine the average number of EO units present on one β-cyclodextrin (2.7 EO units), in accordance with the ESIMS analysis. Residual hydroxyl functions in the 5.5–6.0 ppm area are mainly attributed to OH-3 (Fig. 2). ^{13}C NMR analysis shows that the integration of the peak corresponding to the C bearing OH-3 is equal to the one measured for the anomeric C, whereas the ones corresponding to the C bearing OH-6 and OH-2 decreased. This result proves that the EO initiation by an alcoholate function borne by a CD occurred on the C-2, before the C-3 position of the β-CD, in agreement with the reaction order of the various hydroxyl functions of the CD (Khan et al., 1998).

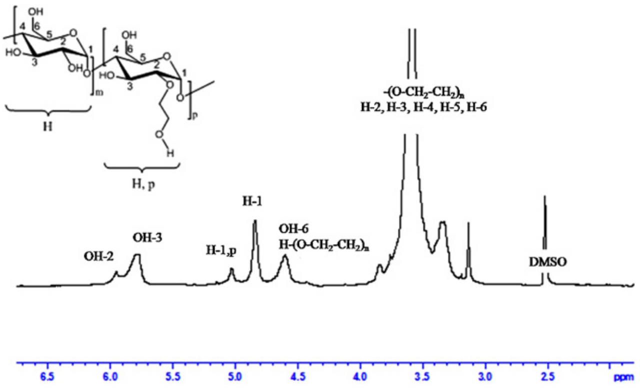


Fig. 2. ^1H NMR spectrum of a short PEO obtained from anionic polymerization of ethylene oxide initiated by native β-CD (Run 7, Table 2) in DMSO-d_6 (25 °C).

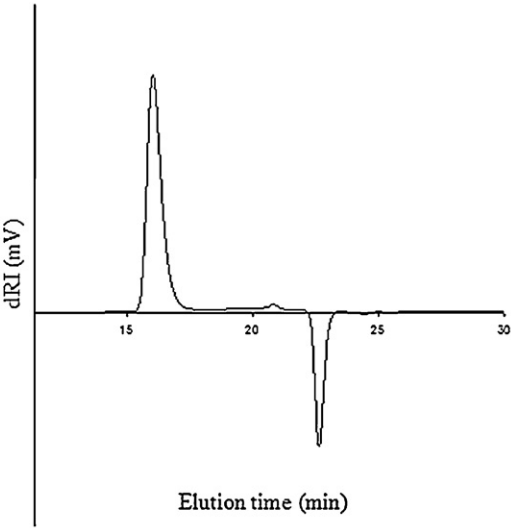


Fig. 3. SEC chromatogram of the purified star polymer initiated by $\beta CD'(OH)_{21}$ (Run 8, Table 3)(THF, 25 °C).

All these observations suggest that the structure of the star polymers obtained from an EO polymerization initiated by native CD is ill-defined and not controlled (Scheme 1, part 1). In order to have the same reactivity for the different hydroxyl functions, modifications of β-cyclodextrin were performed in order to obtain per(2,3,6-tri-*O*-(3-hydroxypropyl))-β-CD (named $\beta CD'(OH)_{21}$) presenting 21 hydroxyl functions of the same class, and per(2,6-(3-hydroxypropyl)-3-*O*-methyl)-β-CD (named $\beta CD'(OH)_{14}$) presenting 14 hydroxyl functions. The syntheses of those initiators were already discussed elsewhere (Badi & Guégan, 2007; Eskandani, Huin, & Guégan, 2011).

3.2.2. Per(2,3,6-tri-O-(3-hydroxypropyl))-β-CD as initiator

EO polymerization was initiated with $\beta CD'(OH)_{21}$ (Run 8, Table 3). After 10 days, only 18% of EO was converted into polymer. The molecular weight measured by SEC was surprisingly low, compared to the expected $\overline{M_n}$. This result was explained by the presence of two populations in SEC analysis, corresponding to the expected star polymer accompanied by linear PEO. Again, this linear α,ω-dihydroxy PEO was attributed to the presence of water entrapped in the CD derivative at the beginning of the polymerization.

Run 8 allows for the synthesis of star polymer with a narrow PDI (PDI = 1.07), a good argument for a controlled polymerization. The ^1H NMR spectrum of run 8 free from linear chains (eliminated by three precipitations in cold diethyl ether, as demonstrated by Fig. 3) shows the anomeric proton of the CD derivative (H-1, 5.0 ppm), the disappearance of the hydroxyl functions of the initiator at 4.4 ppm, the appearance of EO unit protons (3.5 ppm) and of the telechelic hydroxyl functions borne by the PEO chains (4.6 ppm) (Fig. 4). This last signal is integrated for 3, taking 1 anomeric proton as a reference. Each hydroxyl function was thus involved in the polymerization and a pure star polymer was obtained as witnessed by the disappearance of the $-\underline{C}H_2-OH$ signal at 58.0 ppm of $\beta CD'(OH)_{21}$ on the ^{13}C NMR spectrum of run 8 (Fig. S9 – Supplementary data) after polymerization, leading to a new peak at 60.2 ppm due to the $-\underline{C}H_2-OH$, of the PEO arms. The well-defined structure of the polymer from run 8 is ascertained by the SEC. Degradation of the glucopyranosyl functions in acidic medium was not undertaken to determine the number of EO units per branch (Fig. 3), since it is well known that PEO is also degraded at low pH.

Table 3
Polymerizations of ethylene oxide initiated by modified β-cyclodextrins in DMF[a] (Run 8: $\beta CD'(OH)_{21}$; Runs 9a–9c: $\beta CD'(OH)_{14}$).

Run	[OH] (mol L^{-1})	[OE] (mol L^{-1})	Time (days)	Yield[b] (%)	$\bar{M}_{n,th}$[c] (g mol^{-1})	$\bar{M}_n$ NMR[d] (g mol^{-1})	$\bar{M}_n$ SEC[e] (g mol^{-1})	PDI
8[g]	2.2×10^{-2}	4.1	10	18	33 000	10 000	8300	1.07
9a[h]	1.6×10^{-2}	2.4	7	11	12 000	6600	5600	1.14
9b[h]	1.6×10^{-2}	2.4	22	36	35 000	20 700	18 600	1.16
9c[h]	1.6×10^{-2}	2.4	32	44	43 000	nd[f]	22 500	1.01

[a] Using DPMK (20%) as deprotonating agent, at 40 °C, under vacuum, during different times.

[b] Polymerization yield = $(m_{polymer} - m_{CD})/m_{EO} \times 100$ (%).

[c] $\bar{M}_{n,th} = \frac{[EO]}{[OH]} \times \text{yield} \times M_{EO} + M_{CD\ derivative}$.

[d] Determined by ^{1}H NMR.

[e] Calculated from SEC chromatogram in DMF, considering the arm number of the star-polymers obtained.

[f] Only PEO visible, high molar mass hindering the determination of $\overline{M_n}$.

[g] $\beta CD'(OH)_{21}$ dried by an azeotropic distillation using heptane.

[h] $\beta CD'(OH)_{14}$ dried by an azeotropic distillation using heptane, followed by a freeze-drying in dried benzene.

3.2.3. Per(2,6-di-O-(3-hydroxypropyl)-3-O-methyl)-β-CD as initiator

Polymerizations of EO initiated by $\beta CD'(OH)_{14}$ were then performed (Runs 9a–9c, Table 3). The star polymers were separated from the linear polymers, after sonication of the crude product in diethyl ether at reflux and filtration, the linear polymer being soluble in this solvent, as shown by the SEC chromatograms of the different steps of purification (Fig. S10 – Supplementary data). The molar mass obtained was again far from the expected one, but the polydispersity was narrow, PDI values ranging from 1.01 to 1.16. We surprisingly found out that $\beta CD'(OH)_{14}$ was much more difficult to purify from water than native CD, which explains why targeted molecular weights are not obtained. The same statement holds for $\beta CD'(OH)_{21}$, discussed in the previous section.

Fig. 5 shows the ^{1}H NMR spectrum of the crude polymer of the run 9b, presenting the anomeric proton of the CD derivative (5.0 ppm), the disappearance of the hydroxyl functions of the initiator, the appearance of EO unit protons (3.5 ppm) and of the hydroxyl functions at the end of PEO chains (4.6 ppm). The analysis of the integrations of the purified polymer gave 2 hydroxyl functions for 1 anomeric proton. Same observations were carried out on the ^{13}C NMR spectrum (Fig. S11, Supplementary data). Slow initiation kinetic was observed since run 9a allowed synthesizing a star polymer with 12 arms only, as witnessed by the residual hydroxyl functions of the initiator identified in the ^{1}H and ^{13}C NMR analysis of the star polymer (Fig. S12, Supplementary data).

The EO polymerization in DMF, initiated by a CD derivative having 14 hydroxyl functions of the same reactivity, allowed us to obtain a well-defined star polymer of 14 branches, for conversion large enough, represented in Scheme 1, part 3.

Another matter to discuss at this point concerns the control of those polymerizations. It was not possible to perform kinetics on the same experiments, for safety reasons. Different experiments with different polymerization times were thus performed as described in Table 3 (Runs 9a–9c). Considering that DPMK was added in a proportion of 20% compared to the hydroxyl functions of the initiator and that the CD hydroxyl function concentration was constant, the concentration of active species at the beginning of the polymerization was considered constant. Fig. 6A shows $\ln([M]_0/[M]_t)$ plotted as a function of reaction time. The linearity of this curve demonstrates the absence of termination reactions during the polymerizations. The polymerization kinetic constant k_{app} was estimated by the slope of this plot, giving 5 mol^{-1} L days^{-1}, which is in agreement with the determination of the k_{app} found by Badi et al. (2009). In addition, Fig. 6B represents the molar masses obtained by SEC analyses of the star polymer peak versus yield of star polymer. The linear relationship between molar masses and yield shows the absence of transfer during the polymerization, demonstrating the controlled anionic EO polymerization in DMF.

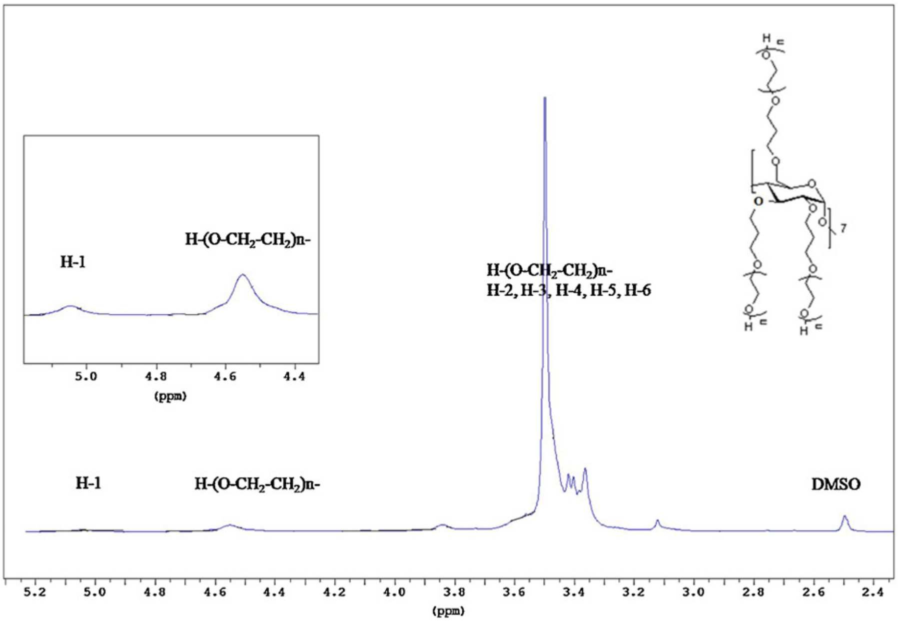


Fig. 4. ^{1}H NMR spectrum of the purified star polymer initiated by $\beta CD'(OH)_{21}$ (Run 8, Table 3) in DMSO-d_6 (25 °C).

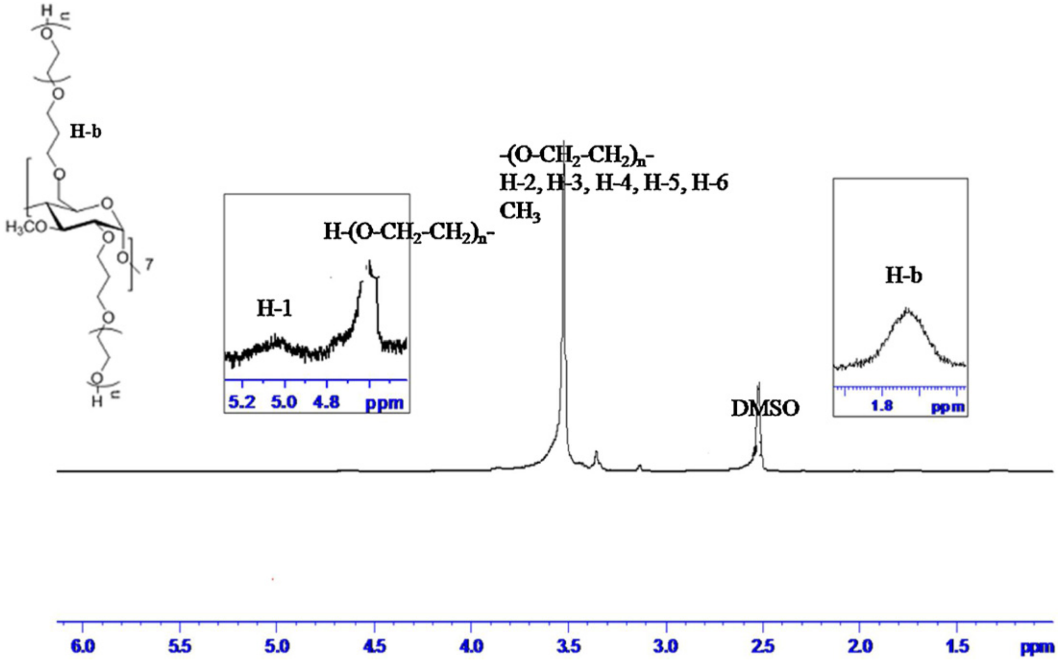


Fig. 5. ^{1}H NMR spectrum of the crude polymer initiated by $\beta CD'(OH)_{14}$ (Run 9b, Table 3) in DMSO-d_6 (25 °C).

3.3. *Characterization of the star polymers by DOSY NMR experiments*

DOSY experiments were attempted to confirm the star architecture of the polymers synthesized in this work. DOSY NMR is based on pulse-field gradient spin-echo NMR experiments, in which components are submitted to diffusion. This technique provides relevant information for the study of mixtures (Viel, Capitani, Mannina, & Segre, 2003) or for the structure characterization of polymers (Furukawa, Ishizu, & Yamane, 2005; Zhao & Beckham, 2003). All the DOSY experiments were performed at 25 °C, in DMSO-d_6. The diffusion coefficient values (Table 4) were determined by fitting the exponential decay of the resonance signals intensity against the gradient strength as previously described (Bennevault-Celton et al., 2011).

The synthesized polymers (Runs 9a and 9b, Table 3–Run 6, Table 2) were characterized by this technique and the results were compared to the CD initiators: native β-CD and $\beta CD'(OH)_{14}$. The ^{1}H NMR polymer spectra from Runs 9a and 9b were overlaid with the spectrum of the used CD initiator for comparison (Fig. 7). In the case of high molar mass polymers, the signals belonging to the cyclodextrin core decrease, until they disappear. Therefore, for the polymer 9b, calculation was only possible on the broad peak of EO units (pseudo 2D, Fig. 8).

Table 4
Diffusion coefficients of cyclodextrin derivatives and polymers, determined by DOSY experiments (DMSO-d_6, 25 °C).

Sample name	Kind of molecule	D (10^{10}) ($m^2\,s^{-1}$)
$\beta CD'(OH)_{14}$ (M = 2046 g mol^{-1})	Initiator	1.98 ± 0.03
9a	12 arm star polymer	1.18 ± 0.01
9b	14 arm star polymer	1.10
9b	Linear polymer	1.70 ± 0.03
Native β-CD (M = 1135 g mol^{-1})	Initiator	1.25 ± 0.03
Per(2,3,6-tri-*O*-methyl)-β-CD (M = 1430 g mol^{-1})	CD derivative	1.79 ± 0.09
6	21 arm star polymer	0.56 ± 0.01

The pseudo 2D of $\beta CD'(OH)_{14}$, given in Fig. S13, clearly shows that all the proton signals of the CD have the same diffusion coefficient ($1.98 \times 10^{-10} \pm 0.03\,m^2/s$), lower than the one of DMSO.

The diffusion coefficients of the star polymers initiated by this CD derivative (Runs 9a and 9b, Table 3) were respectively equal to $1.18 \times 10^{-10} \pm 0.01\,m^2/s$ and $1.10 \times 10^{-10}\,m^2/s$ (Table 4). These values confirm the presence of polymers, having a hydrodynamic volume higher than that of the CD initiator. In addition, concerning the polymer 9a with the lowest molar mass, the signals of cyclodextrin and EO units gave the same diffusion coefficient, confirming that the PEO is linked to the CD and that the polymerization

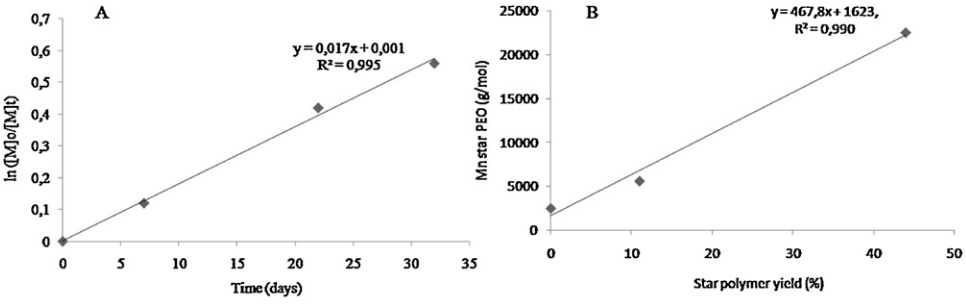


Fig. 6. Kinetics parameters studied for EO polymerization initiated by $\beta CD'(OH)_{14}$ (Run 9, Table 3).

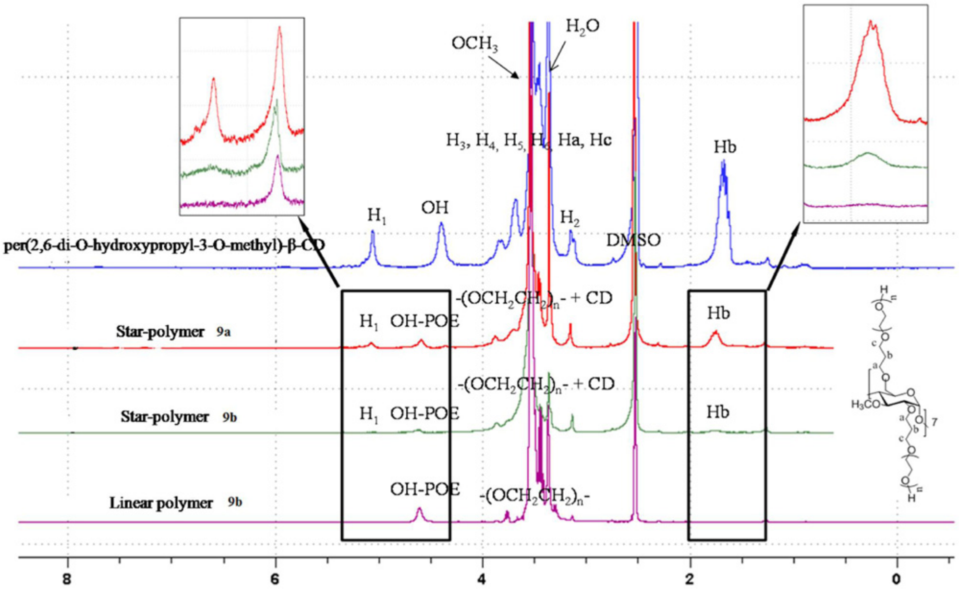


Fig. 7. ^{1}H NMR spectra of polymers and CD initiator in DMSO-d$_6$ (25 °C) (Runs 9, Table 3).

occurred from the hydroxyl functions of the cyclodextrin. This characterization allowed us to ascertain that the analyzed product was not composed from a mixture of cyclodextrin derivative and free PEO chains. Another comment concerns the difference between the D values of the two polymers, which is in agreement with their respective molar mass. The linear chains 9b, eliminated during the purification step of run 9, were also analyzed and conducted to a D value equal to $1.70 \times 10^{-10} \pm 0.03\ \mathrm{m^2/s}$, confirming the lower molar mass of these chains. The DOSY experiments showed the high efficiency of the purification process. For all the diffusants investigated in this study, monoexponential decays were observed (until disappearance of the signal), indicating that the samples were homogeneous and that the self-diffusion is monodisperse.

Concerning the star polymer initiated by the native β-cyclodextrin (Run 6, Table 2), the mathematical treatment of the DOSY gave a diffusion coefficient equal to $5.59 \times 10^{-11} \pm 0.10\ \mathrm{m^2/s}$, proving a high hydrodynamic volume of the star polymer. This value was compared to native β-CD and per(2,3,6-tri-*O*-methyl)-β-CD ones (Table 4 and Fig. S14). As expected, the star polymer D coefficient was lower than the ones of the cyclodextrin derivatives. However, the value obtained in the case of the native β-CD needs to deserve a comment. Indeed, the native β-CD diffusion coefficient was surprisingly lower than per(2,3,6-tri-*O*-methyl)-β-CD and βCD′(OH)$_{14}$ values. This result could be attributed to the formation of aggregates in the case of native β-CD favored by the presence of hydroxyl functions of the CD. When replaced the latters by methoxy functions, the interaction between the cyclodextrin was strongly reduced. The per(2,3,6-tri-*O*-methyl)-β-CD diffusion coefficient became coherent with the values of the other compounds.

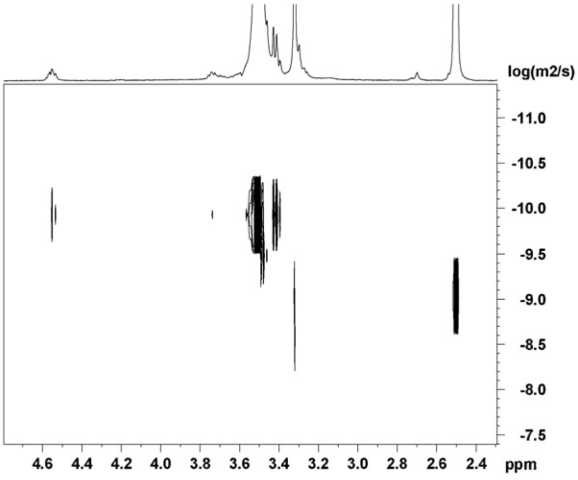


Fig. 8. 2D DOSY spectrum of star polymer (Run 9b, Table 3) in DMSO-d$_6$ (25 °C).

The comparison between polymers having either 14 arms (Run 9b, Table 3) or 21 arms (Run 6, Table 2), but with similar molar masses, shows that the star polymer with the higher arm number has a higher hydrodynamic volume, suggesting that latter was less compact in solution in DMSO. Furukawa et al. (2005) observed the same behavior for multi-arm star-shaped poly(tert-butyl methacrylate)s having high arm numbers.

4. Conclusions

In this work, the possibility to perform ethylene oxide polymerization by living anionic ring opening polymerization, in DMF, was demonstrated with monofunctional initiators, giving rise to linear PEO. Star polymers initiated by native β-cyclodextrin were also synthesized, the obtained polymers having ill-defined architectures, due to the various reactivities of hydroxyl functions. By using selectively modified cyclodextrin derivatives as initiators, new families of star-shaped poly(ethylene oxide) polymers, with 14 or 21 arms, were synthesized. Well-defined architectures were obtained, demonstrated by SEC, ^{1}H and ^{13}C NMR and DOSY experiments. The livingness of the ethylene oxide polymerization in DMF was demonstrated, opening the possibility to use this solvent for other controlled polymerizations.

Acknowledgment

The research leading to these results has received funding from the European Union’s 7th Framework Program (FP7/2007-2013) under grant agreement no. 264115-STREAM.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.carbpol.2012.12.062.

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