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PREPARATION AND CHARACTERIZATION OF WATER SOLUBLE HIGH MOLECULAR WEIGHT β-CYCLODEXTRIN–EPICHLOROHYDRIN POLYMERS

E. RENARD, A. DERATANI, G. VOLET and B. SEBILLE
Laboratoire de Physico-Chimie des Biopolymères, U.M.R. 27, C.N.R.S., Université de Paris, XII, 2 rue Henri Dunant, 94320 Thiais, France

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Abstract—Water soluble β-cyclodextrin polymers were prepared from β-cyclodextrin crosslinked with epichlorohydrin under basic conditions. The influence of preparation conditions on the molecular weight distribution has been investigated. The knowledge of this relationship allows for the choice of reaction parameters according to the desired weight distribution of the β-cyclodextrin polymer. A procedure was developed for the preparation of high molecular weight water soluble polymer (*M*w higher than 10^4). Copyright © 1996 Elsevier Science Ltd

INTRODUCTION

Water soluble cyclodextrin polymers have been the subject of previous investigations [1, 2]. Indeed, these polymers have a large number of potential applications. For example, control of the release of a soluble substance across a membrane [3] and partitioning of organic compounds in an aqueous two-phase system [4]. The usefulness of the water soluble cyclodextrin (CD) polymers lies mainly in their ability to form an inclusion with lipophilic guests. The polymeric form can increase the stability constant of these complexes [5, 6] and can explain their enhanced catalytic effect on esterolyse [5, 7]. The main applications of these polymers are related to chromatographic techniques as supports either in thin layer chromatography [4, 8, 9] or in liquid column chromatography [10–13].

Two different ways have been reported to produce water soluble CD-polymers and two kinds of macromolecular structure can be distinguished: polymers containing CD pendant groups, or polymers having CD units as a part of the skeleton. The first type was prepared by radical polymerization of acryloyl cyclodextrin monomers (acryloyl-CD, *N*-acryloyl-6-aminocaproyl-CD) [14, 15]. The synthesis of these monomers was carried out by acylation according to the Bender method [16] starting from *m*-nitrophenylacrylate derivative and CD, and proceeded by nucleophilic attack on one secondary alcohol group. These monomers were also copolymerized with other water soluble monomers (acrylamide, acrylic acid, *N*-vinylpyrrolidone) to give water soluble copolymers.

An alternative way to synthesize such CD-polymers is to chemically modify a pre-existing polymer. Mono-6-(*p*-tolylsulfonyl)-β-CD was covalently linked, by nucleophilic substitution, to poly(allylamine) [17] or to poly(ethylenimine) [18]. Recently, the chemical grafting of poly(1-vinylimidazole) by 6-O-(3-chloro-2-hydroxypropyl)-β-CD derivative was reported [19].

The second type of polymer can be prepared by coupling the CD with proper bifunctional agents. Many papers have reported the preparation of soluble polymers from limited polycondensation of CD or CD derivatives with epichlorohydrin or other epoxy compounds such as ethylene glycol bis-(epoxypropyl) ether [20] or butylene glycol bis(epoxypropylether) [21] in aqueous solution. This type of polymer has a structure more branched than the first one based on CD pendant groups from main chain. Other reagents (chloroacetic acid or γ-aminobutyric acid) can be employed in addition to epichlorohydrin, leading to polymers containing ionic groups [22].

The preparation of water soluble polymers by carefully controlling polycondensation has also been described [23–25]. It is claimed that this synthesis is the simplest way to prepare such polymers, but generally it concerns only low molecular CD oligomers. The main problem is how to control the reaction in order to avoid the formation of insoluble polymers. In this study, we focussed on the synthesis of water soluble β-CD–epichlorohydrin polymers in order to obtain high molecular weight chains. Moreover, we have investigated the relationship between preparation conditions and properties of the end products. Furthermore, the polymers obtained were characterized by physico-chemical measurements.

EXPERIMENTAL

β-CD was provided by Orsan (France). Epichlorohydrin was purchased from Prolabo (France). Both reagents were used without further purification.

Synthesis

For this purpose, a reaction vessel of 250 mL volume was used equipped with a U-shaped mechanical stirrer from Bioblock Scientific, model 94349.

A typical synthesis procedure for a molar ratio EP/β-CD = 10 and NaOH = 33% w/w is described below: a mixture of 5 g of β-CD (0,44 mmol.) in 8 mL of NaOH solution was mechanically stirred overnight at room temperature. The mixture was heated to 30°C and EP was added (3,445 mL) rapidly. The temperature was monitored during polymerization and kept at 30°C. The stirring (600 rpm) was kept constant during the reaction. The reaction was stopped after 3 hr 50 min by addition of acetone. After decantation, acetone was removed. The pH of the aqueous solution was decreased to 12 with hydrochloric acid 6 N. The solution obtained was kept at 50°C overnight. After cooling, the solution was neutralized with HCl 6 N and diafiltrated (molecular weight cut-off 1000) under pressure (2 bars). The solution obtained was evaporated and the solid triturated with acetone. The white product was isolated by filtration and dried under vacuum.

Analysis

NMR spectroscopy analysis were carried out in D_2O on a Brücker A2000 spectrometer.

The polymers were characterized by the ratio of both components (EP/β-CD) included in the polymer and by the CD content. These values were determined by two different methods. The first one was the procedure described by Wiedenhof [1]. The product was hydrolysed by hydrochloric acid. The liberated reducing sugar content was determined by iodometry. The calculation takes into account the water content which was determined by Karl Fisher titration (Mettler DL 18). The second method is based on ^1H NMR spectroscopy. The spectrum of β-CD shows two types of signals: one peak near 5 ppm assigned to the anomeric proton attached to the C-1 of the glucose unit, and two broadened peaks between 3 and 4 ppm corresponding to the hydrogen atoms of the pyranose rings. The chemical modification gives no significant shift in the spectrum signals. However, the signal assigned to the resonance of the hydrogen atoms of the 2-hydroxypropyl ether segment is shifted below the two broadened peaks of the pyranose units. Consequently, the increase of five hydrogen atoms by one EP molecule appears in the integration value of these peaks. The ratio of peak integration enables a determination of the substitution degree.

Intrinsic viscosity measurements of β-CD–EP polymers were performed in a thermostatted water bath at 25°C with an Ubbelohde viscometer. The intrinsic viscosity $[\eta]$ was estimated as a common intercept at $C = 0$ of the η_{sp}/C and the $(\ln \eta_r)/C$ vs C plots.

Size exclusion chromatography (SEC) was carried out with the pump Spectra–Physics (Isochrom LC pump) and with an gel column from Beckman (30 × 0,75 cm). $LiNO_3$ = 0,1 M with NaN_3 0,05% w/w was used as eluent and the flow rate was of 0,5 mL/mn. The molecular weight distribution was determined by refractive index measurements on a Waters apparatus, R401. The column was calibrated with standard Pullulan samples (P-82 from Shodex).

Preparative SEC was carried out with the Ultraspherogel SEC 4000 with pure water as eluent.

Refractive index increment measurements were determined on a differential refractometer model RI-71 from Shodex.

Low-angle laser light scattering (Wyatt Technologies Mini DAWN) was used to measure the average molecular weights of both fractions of the high β-CD–EP polymer. The three detection angles are 45°, 90° and 135°. The wavelength of incident light is 690 nm. Polydispersity was determined using two kinds of SEC column: a PL aquagel-OH 40 from Polymer Laboratories and a TSK G3000 SW from Toyo Soda. The differential refractomer detector was a model RI-71 from Shodex. Temperature was controlled at 35°C. The eluent used was the same as described above for the standard SEC study.

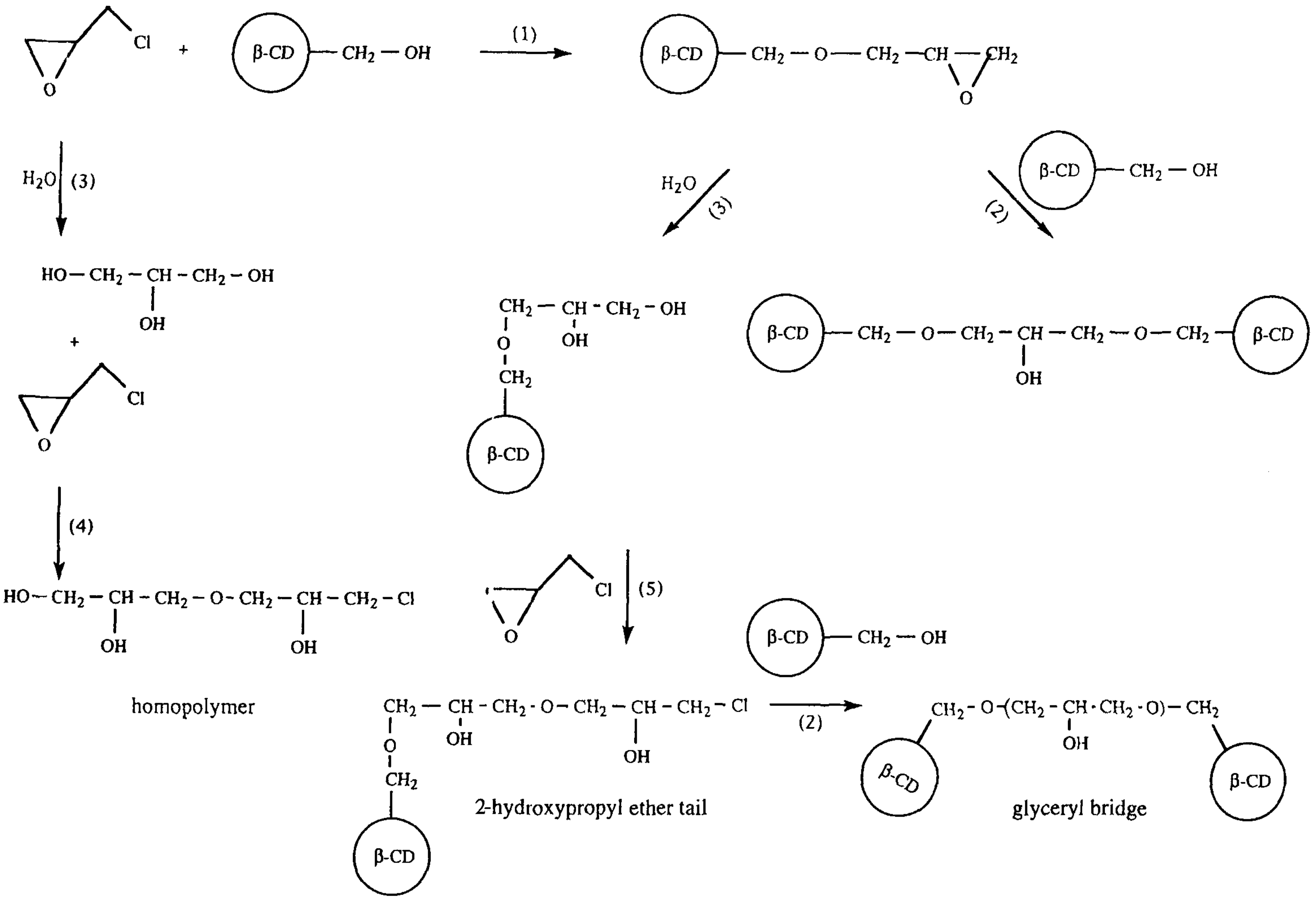
RESULTS AND DISCUSSION

Synthesis

Preparation of water soluble β-CD polymers was achieved by the reaction of β-CD with epichlorohydrin (EP) in an alkaline medium by a two step procedure. First the β-CD was stirred with an excess of NaOH in order to form alcoholate sites. Then, EP was added to the suspension obtained. All the possible reactions are presented in Scheme 1. Hydroxyl groups can react with one reactive group of the bifunctional agent (Reaction 1). The side chain obtained can further react in two different ways: the epoxyde ring can react with another hydroxyl group of a second β-CD molecule (Reaction 2), resulting in a glyceryl bridge connecting two CD cavities, or, the epoxyde ring is hydrolysed (Reaction 3). In this last case, the end result is a β-CD molecule with a glycerol moiety. Moreover, EP has the capability to react on itself (Reaction 4) to form homopolymers of epichlorohydrin. Consequently, the glyceryl bridges and the glycerol tails can have different lengths.

Several reaction parameters have been set in order to develop the conditions of a reproducible synthesis. For example, the size of the reaction vessel, the speed of the stirrer and the volume of the reaction mixture were kept constant. All these parameters have been mentioned previously as essential in the preparation of calibrated beads of polymers [26]. We have verified that they have a deep influence on the preparation of water soluble β-CD–EP polymers. Furthermore, authors generally produced water soluble polymers at high temperature (above 50°C) in a few minutes [4, 27–29]. However, we chose to work at lower temperature (30°C) to reduce the rate of the polymerization in order to more easily control the reaction and avoid gel formation.

A series of polymers was prepared with different molar ratio of EP and β-CD. The results are summarized in Table 1. The use of a molar ratio of EP/β-CD lower than 10 gave soluble polymers, even for a reaction time as long as 60 hr. From our results, the occurrence of insoluble polymers is observed for an EP/β-CD ratio >7. For these high EP/β-CD ratios, it is possible, however, to obtain soluble polymers by stopping the reaction before gelation. Yields of soluble polymer were about 80%, in the conditions where polycondensation gave no insoluble gel. In the other cases, yields in soluble polymers were lower and about 50%. The compositions of polymers obtained from an initial EP/β-CD ratio of between 1 and 5 indicate that EP has been incorporated into the chains in the same proportion as at the initial stage. This suggests that few or no EP homopolymers have been synthetized. For larger ratios of EP/β-CD (up to 10), the number of 2-hydroxypropyl ether segments per β-CD appears independent of the initial EP quantity. Composition values obtained by both methods of analysis (NMR or iodometry) are generally in good agreement. Nevertheless, it can be noticed that the EP value determined from



Scheme 1. Reaction scheme of the polycondensation of the β-CD with EP. For the sake of clarity, only reactions on the primary alcohols are shown.

Table 1. Effect of the EP/β-CD molar ratio on the polycondensation

EP/β-C D in reaction mixture	1	3	5	7	10	12	15
Reaction time	60 hr	60 hr	60 hr	60 hr	3 hr 50 min	4 hr 40 min	4 hr 20 min
Gelation time	—	—	—	—	4 hr	4 hr 45 min	4 hr 30 min
Chemical yield (%)	36	76	86	75	50^{d}	52^{d}	54^{d}
EP/β-CD in the polymer	1.6^{a} 0.9^{b}	3^{a} 4.33^{b}	5.5^{a} 6.8^{b}	11.6^{a} 10.8^{b}	16^{a} 14.3^{b}	16.2^{a} 12.7^{b}	14.5^{a} 13.7^{b}
β-CD content^{c} (%)	94	77	69	58	58	54	53

[a] Ratio determined by the Wiedenhof method [1].
[b] Ratio determined by ^{1}H NMR.
[c] Based on the ^{1}H NMR.
[d] Polymers soluble isolated before gelation.

iodometric CD determination is higher than the one determined by NMR when the intial EP/β-CD ratio is larger than 7. These results suggest that the hydrolysis of the CD in the polymer is not complete for highly substituted CD-polymers. Thus, it was concluded that EP values obtained from NMR are safer to use for the determination of the CD content.

The effect of the temperature on polymer synthesis was investigated. The role of temperature was studied with the ratio EP/β-CD = 3. The results are listed in Table 2. Polycondensation is not significantly dependent upon temperature. Indeed, the EP/β-CD ratio in the polymer is generally the same as that of the initial mixture. However, for the highest temperature (90°C) the EP polymer content is increased. This result suggests that EP reacts better at high temperature.

The effect of NaOH concentration was also investigated. A ratio of EP/β-CD = 10 was used. Results (Table 3) point out that NaOH concentration has a dramatic influence on the reaction. When NaOH concentration is higher than 33%, no polycondensation occurs. It must be stressed that the use of 50% NaOH solution instantaneously induces the precipitation of β-CD. The decrease of NaOH concentration favours the EP–β-CD polycondensation. When it is carried out in the presence of 22% or 16% NaOH, the reaction rate is twice as fast as with 33% NaOH. Moreover, the use of 10% NaOH solution restricts the reaction of β-CD with EP to water soluble polymers. Yields obtained are in agreement with previously reported results (Tables 1 and 2). The EP/β-CD ratio of the polymer is influenced by NaOH concentration. The use of a low NaOH concentration (16% and 22%) leads to a EP/β-CD ratio in the polymer near to the initial quantities of both monomers, while EP content in the polymer is increased for higher initial NaOH concentrations.

Table 2. Influence of the reaction temperature on the polycondensation

Temperature (°C)	30	50	74	90
Gelation time	—	—	—	—
Reaction time (hr)	60	60	60	60
Chemical yield (%)	76	80	62	45
EP/β-CD in the polymer	4.3^{a} 4^{b}	4^{a} 4.8^{b}	4.1^{a} 4.6^{b}	5^{a} 5.6^{b}
β-CD content^{c} (%)	79	76	77	73

[a] Ratio determined by the Wiedenhof method [1].
[b] Ratio determined by ^{1}H NMR.
[c] Based on the ^{1}H NMR.
Polycondensation conditions: EP/β-CD = 3, NaOH = 33%.

Structural characterization

Previous synthesis of β-CD–EP polymers often referred to the work of Szejtli [6, 27] in which soluble β-CD–EP polymers were prepared with an EP/β-CD ratio of 10. This ratio can vary from 10 to 15 according to various authors. With such experimental conditions, authors obtained between 10 and 17 2-hydroxypropyl ether segments per β-CD [23, 28–31]. These results are comparable with ours. However, these authors did not precisely describe the NaOH concentration used. Two authors studied the influence of EP quantity on polycondensation and they proposed two methods of preparation, for either soluble or insoluble polymer [28, 29]. The EP/β-CD ratio corresponding to the borderline between those two kinds of polymer is different for both authors (3 and 15). We have found the intermediate value to be 7. These differences could be explained by the use of different experimental parameters, namely the NaOH concentration. Indeed, we have shown that NaOH concentration had a dramatic effect mainly on the polycondensation rate. This can be explained by the relative reactivities of the three hydroxyl groups at C-2, C-3 and C-6. The reactivity of the hydroxyl groups of β-CD is dependent on the NaOH concentration [32–34]. Thus, we can assume that the position of attachment of the 2-hydroxypropyl ether segments is governed by the NaOH concentration. ^{13}C NMR provides a very sensitive method for determining the substitution site. Our assignments are based on those made previously for β-CD derivatives [35]. Figure 1 presents information about the location of the EP residues. Resonances C-2′, C-3′ and C-1′ are the result of C-2 and C-3 substitution. These substitutions produce a downfield chemical shift (~5 ppm) of the carbon bearing the substituent, whereas a small upfield shift is observed for the β carbon (C-1′). Resonance C-6′ is the result of substitution taking place at C-6. A downfield chemical shift of about 9 ppm is produced. Resonance C-9 is due to the terminal carbon of the 2-hydroxypropyl ether segment. Other substituent carbon atoms have chemical shifts corresponding to the peak *a* of Fig. 1. The assignments C-8″ and C-9″ show the existence of the glycidyl group which can be responsible for gelation of the polymer after prolonged storage (as sometimes observed). The chemical shifts of different carbon atoms in the ^{13}C NMR of β-CD-polymer are listed in Table 4. For NaOH concentration lower than 33%, our data are consistent with substitution reactions taking place at all three positions (hydroxyls on C-2, C-3 and C-6) on

Table 3. Influence of the NaOH concentration on the polycondensation

NaOH solution (% w/w)	50	33	22	16	10
Reaction time	—	3 hr 50 min	2 hr 30 min	2 hr 35 min	60 hr
Gelation time	—	4 hr	2 hr 45 min	2 hr 45 min	—
Chemical yield (%)	—	50^{d}	59^{d}	40^{d}	86
EP/β-CD in the polymer	— —	16^{a} 14.3^{b}	14.1^{a} 11.6^{b}	12.4^{a} 9.5^{b}	9^{a} 7.6^{b}
β-CD content^{c} (%)	—	52	57	62	67

[a] Ratio determined by the Wiedenhof method [1].

[b] Ratio determined by ^{1}H NMR.

[c] Based on the ^{1}H NMR.

Poycondensation conditions: EP/β-CD = 10, $T = 30°C$, NaOH solution = 8 mL.

[d] Polymers soluble isolated before gelation.

the two sides of the cavity. In the literature it is well known that under weak basic conditions (NaOH < 5%), only the most acidic hydroxyl groups at C-2 and C-3 give rise to anions. However, our conditions are intermediate and a part of the C-6 hydroxyl groups can react with EP. This assumption could explain the observed rate of the reaction (see Table 3). Under strong alkaline conditions, the resonances of C-1, C-2 and C-3 are unaffected but the resonance of C-6 is shifted. This fact constituted evidence that most of the substitution is occurring on the primary alcohols. This result is in agreement with previous findings obtained for β-CD derivative synthesis [35–37] and supports the conclusion that an NaOH concentration of 33% favours the reactivity of the more accessible primary hydroxyls at C-6, restricting the polycondensation.

It is interesting to note that when the average degree of substitution (D.S.) is lower than 10, the end product is always soluble. For D.S. = 12, the

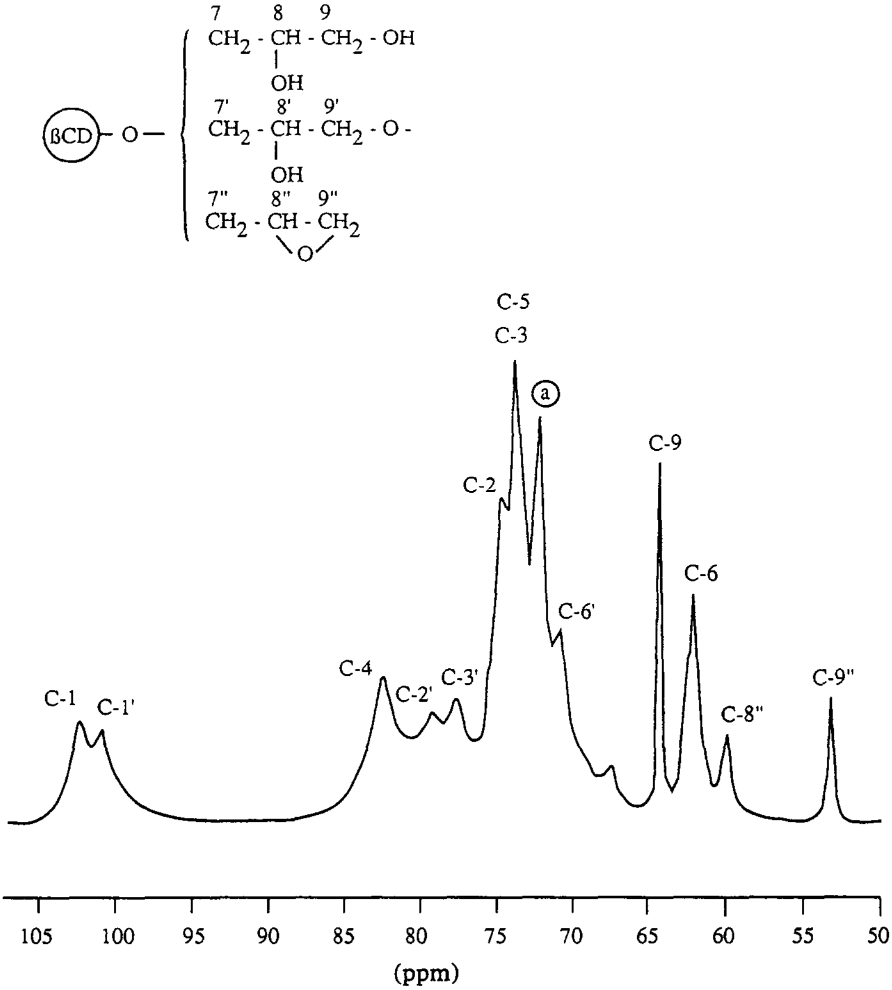


Fig. 1. ^{13}C NMR spectrum and the proposed structure of β-CD–EP motif. (D_2O, 4000 accumulations).
a = C-7, C-8, C-7', C-8', C-9'.

Table 4. Spectral assignments for ^{13}C NMR for a series of β-CD–EP polymers

	Chemical shift (ppm) for polymers obtained under different reaction conditions						
Assignments	β-CD/EP = 1/1 NaOH = 33%	β-CD/EP = 1/5 NaOH = 33%	β-CD/EP = 1/7 NaOH = 33%	β-CD/EP = 1/10 NaOH = 33%	β-CD/EP = 1/10 NaOH = 22%	β-CD/EP = 1/10 NaOH = 16%	β-CD/EP = 1/10 NaOH = 10%
C-1	101.3	101.8	101.5	101.4	101.9	101	100.4
C-1′	—	—	—	—	99.4	100	99
C-4	80.5	80.8	80.7	81	81.2	80.3	80.6
C-2′	—	—	—	—	79.2	77.4	78
C-3′	—	—	—	—	75.8	75.2	76
C-2	73	72.8	72.6	73.7	73.2	72.3	72.3
C-3	71.8	71.9	71.6	71.7	71.9	71.5	71.7
C-5	71.3	71.9	71.6	71.7	71.9	71.5	71.7
a	70[a]	70.3	69.4	71.7	70.8	70	70
C-6′	68.9[a]	70	68.4	68.5	69	68.6	69
C-9	62.2[a]	63.2	62.2	62.2	62.4	62	62.2
C-6	60	60.2	60	60	60	60	60

[a] Resonance of low intensity.

polycondensation gives rise to cross-linked polymer. Nevertheless, between 10 and 12, the two structures are possible, the proportion of which is strongly dependent upon the NaOH concentration. We can conclude that the final structure depends on the position of the OH groups of β-CD molecules where the substitutions occur. When the 2-hydroxypropyl ether segments are attached on both sides of the CD cavity (NaOH < 33%), each side is easily accessible for another β-CD. On the contrary, when the chain branches are located mainly on one single side (NaOH > 33%), the approach of two β-CD molecules is sterically hindered. In this case, the linkage between several β-CD molecules could be explained by the presence of longer 2-hydroxypropyl ether segments, which is observed from the higher ratio of EP/β-CD. In the case of a very high NaOH concentration solution, β-CD precipitation prevents any polycondensation.

Polymer characterization

The molecular weight distribution of the polymers was determined by SEC with water compatible high performance columns. The SEC profiles depend strongly on the degree of substitution (Fig. 2). Two kinds of elution diagram are observed, corresponding to the polymer products obtained after polycondensation from different initial conditions: soluble

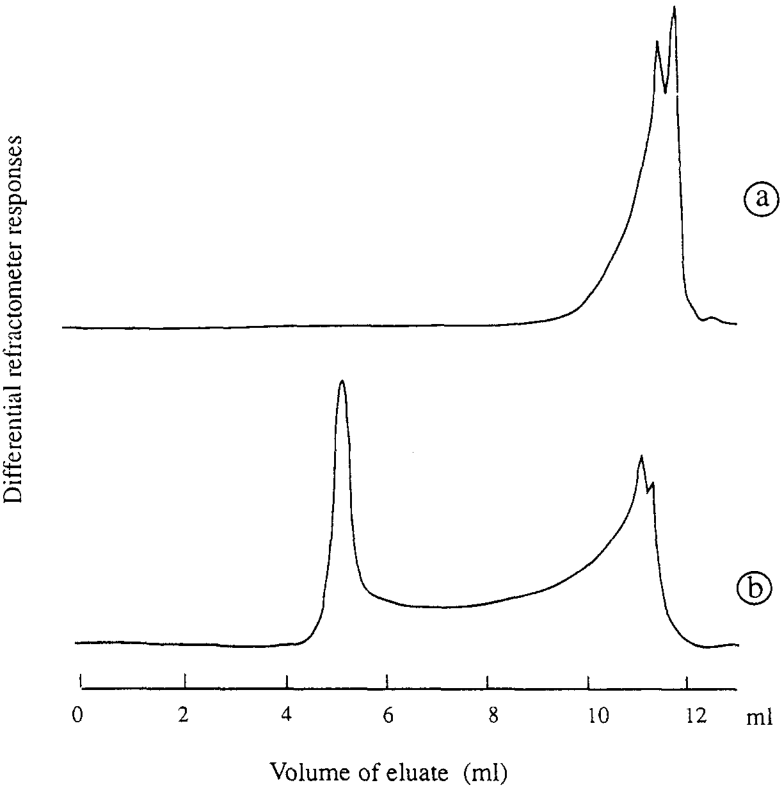


Fig. 2. Elution diagrams of β-CD–EP polymers. Polycondensation conditions: a: EP/β-CD = 7, NaOH = 33%, $T = 30°C$, time reaction = 60 hr; b: EP/β-CD = 10, NaOH = 33%, $T = 30°C$, time reaction = 3 hr 50 min.

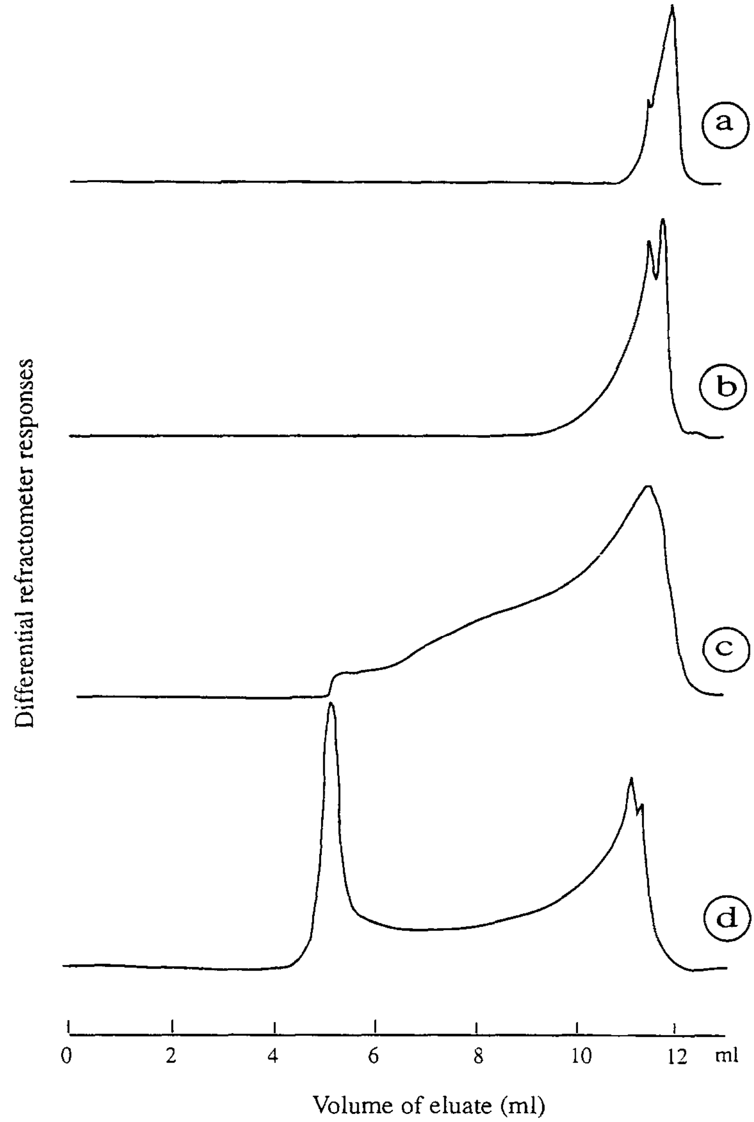


Fig. 3. Elution diagrams of β-CD–EP polymers vs polycondensation time. Polycondensation conditions: EP/β-CD = 10, NaOH = 33%, $T = 30°C$, time reaction = 1 hr for a, 2 hr 30 min for b, 3 hr 30 min for c and 3 hr 50 min for d.

polymers or soluble fractions of sample containing cross-linked polymers. For a final EP/β-CD ratio in the polymer lower than 12, i.e. for the polymers which never cross-link, the chromatographic profile corresponds to several low molecular weight compounds [Fig. 2(a)]. The average molecular weight calculated on the basis of this elution diagram from the pullulan calibration is between $\bar{M}w = 5000$ D and $\bar{M}w = 6000$ D. The chromatogram 2b is observed for a compound isolated just before gelation which corresponds to a highly substituted β-CD (final EP/β-CD ratio higher than 12). The product appears highly polydispersed. The elution diagram suggests that the polymer is in fact a mixture: high molecular weight polymers (HP), low molecular weight polymers (LP) and a fraction of largely polydispersed polymers. The first fraction corresponds to a product which is excluded from the gel matrix (up to 400.000 D from pullulan standards). The second peak in the low molecular weight region is similar to the 2a profile. In order to investigate these two components, we have isolated the main two fractions using preparative SEC. The HP fraction (corresponding to the excluded peak) was found to be about 30% of the total mixture. The other fraction was collected between 10 mL and 11,4 mL, corresponding to molecular weights from pullulan calibration between 12.000 and 4400. The LP fraction was found to be about 40% of the total mixture. The $\bar{M}w$ values were studied using dual detection SEC with a light scattering detector (LS) and a differential refractometer. For the LS investigations, we have determined the refractive index increments (d*n*/d*c*) of both isolated fractions (0,137 mL/g for the LP and 0,146 mL/g for the HP). The $\bar{M}w$ of the LP and the HP fractions from the dual detection were

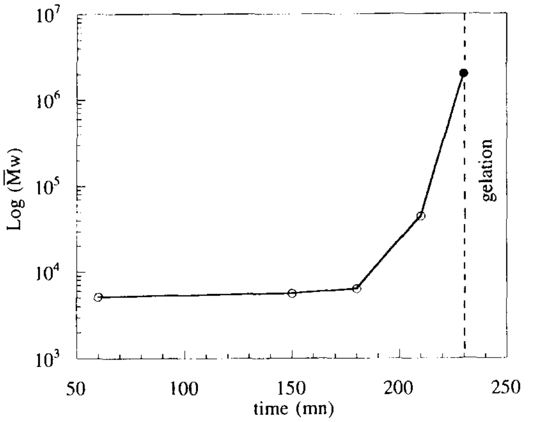


Fig. 4. Variation of the $\bar{M}$w values vs time reaction. Polycondensation conditions: EP/β-CD = 10, NaOH = 33%, $T = 30°C$. ○: $\bar{M}$w determined from pullulan standards; ● $\bar{M}$w determined from MALLS detection.

12.000 D and 2 × 10^6 D, respectively. This last value can be considerated as the upper limit of molecular weight for water soluble β-CD–EP polymers because polymers of higher weight are insoluble gels.

In order to analyse the growth of the polymer during polycondensation, we have examined the variations of the molecular weight distribution and intrinsic viscosity as a function of polymerization time. Figure 3 represents the profile of polymer samples obtained after different times of reaction with identical initial conditions. It appears clearly that the condensation gives rise to a high molecular weight in the period of time just preceding the gelation step. For example, the profile of curve 3c corresponds to a mean molecular weight $\bar{M}$w = 44.000 D (pullulan standards) for a reaction time of 3 hr 30 min. The profiles 3a and 3b corresponding, respectively, to 1 hr and 2 hr 30 min reaction time show evidence of the presence of small molecular weight compounds. After 3 hr 30 min the curve 3c reveals the occurrence of a polymer, the mean molecular weight of which is measured as $\bar{M}$w = 44.000 D (pullulan standards). Ten min after, the molecular size grows strongly and polymer fractions of $\bar{M}$w up to 400.000 D appear at the excluded volume. Nevertheless, even for conditions leading to high molecular weight polymer, the fraction of small molecular compounds is always present in the final product as usual for an ordinary polycondensation reaction. Figure 4 summarizes the $\bar{M}$w values of the different products for increasing reaction time.

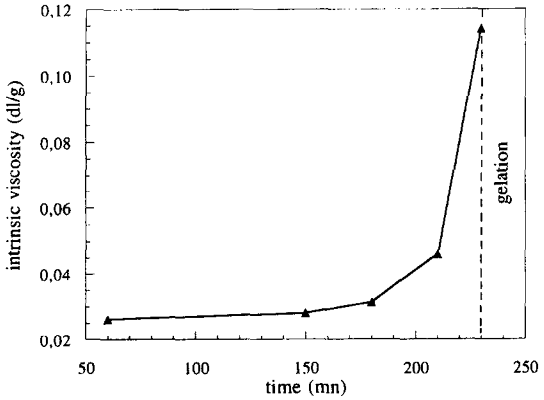


Fig. 5. Variation of the intrinsic viscosity vs time reaction. Polycondensation conditions: EP/β-CD = 10, NaOH = 33%, $T = 30°C$.

Figure 5 shows the intrinsic viscosity of the same products and also illustrates the dramatic increase of viscosity close to the gelation point that is observed for a precise range of reaction times.

In previous results [23, 27, 30, 36] several authors claimed that the upper limit is about 10,000 D and that over 10,000 D these polymers are swelling gels. Our results show that high molecular soluble polymer can be obtained. Indeed, EP–β-CD adducts are a mixture of very different molecular weight compounds. The mean value is poorly informative and a precise SEC anaylsis is essential to estimate the molecular weight. Moreover, when achieving the polycondensation time reaction very close to gelation, it is possible to obtain very high molecular weight compounds. These conditions necessitate a very accurate control of the reaction.

The present results permit us to propose a mechanism of polycondensation. The condensation of EP with β-CD in a basic aqueous medium proceeds by successive steps. Initially the β-CD reacts with EP molecules to produce β-CD–EP polymers of low molecular weight, which contain a maximum of ten β-CDs. Then, when both polymer concentration and substitution degree of the β-CD increase, EP displays a tendency to homopolymerize and to increase the size of the arms. The consequence allows a higher probability of oligomer linkage together. The proposed structure is probably a hyperbranched structure made of short-chain and long-chain branches, loops of β-CD molecules or only 2-hydroxypropyl ether segments. The complete structure of the polymer is presently under investigation.

CONCLUSION

The reaction of EP with β-CD leads to water soluble polymers, the molecular weight of which depends on several features: initial ratio EP/β-CD, NaOH concentration and reaction time. We have given evidence for the formation of very high molecular weight polymer (2 × 10^6) by stopping the reaction just before gelation. Nevertheless, it is possible to obtain only polymers of small molecular weight, using an NaOH concentration or an initial ratio EP/β-CD at low levels. NMR analyses have allowed us to characterize the substitution sites on the β-CD cage. It has been shown that a low NaOH concentration favours the substitution on the two sides of the cavity, while a high NaOH concentration leads to substitution mainly on one side, leading to a long 2-hydroxypropyl ether segment and high molecular weight compounds.

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