Published in: Polymer (1996), vol. 37, iss. 17, pp. 3983-3987
Status: Postprint (Author's version)

A new poly(ε-caprolactone) containing hybrid ceramer prepared by the sol-gel process

D. Tian, Ph. Dubois, R. Jérôme

Center for Education and Research on Macromolecules (CERM), University of Liège, Sart-Tilman, B6,
4000 Liège, Belgium

Abstract

A new inorganic-organic hybrid material, known as ceramer, has been prepared by the sol-gel process. α,ω-Hydroxyl poly(ε-caprolactone) (PCL) has been used as an organic reagent, as such or after conversion of the hydroxyl end-groups into triethoxysilane end-groups. The novelty has to be found in the biocompatibility and biodegradability of the organic constitutive component. Since the hydroxyl end-groups of PCL are less reactive than the triethoxysilane counterparts, the preliminary reaction of the hydroxyl end-groups with 3-isocyanatopropyltriethoxysilane is recommended for decreasing the gelation time and the amount of PCL extractable from the final hybrid material. In this respect, it has been observed that the amount of PCL incorporated into the network is limited by the early vitrification of the reactive system. This drawback can be alleviated by curing the sample at a high enough temperature (100°C). TEM observations have shown that the organic and inorganic phases are intimately mixed when the weight composition in SiO_2 and PCL is close to 50%.

Keywords: sol-gel process; poly(ε-caprolactone); bioglass

Introduction

During the last decade, special attention has been paid to the synthesis and characterization of inorganic-organic hybrid materials prepared by the sol-gel process [1-7]. This interest relies upon the unique opportunity of combining in a controlled way the most remarkable properties of inorganic glasses and organic polymers, for instance flexibility of synthetic polymers and high modulus, high thermal stability and good optical properties of inorganic glasses. The main physical, mechanical and optical properties of these composite materials, known as ceramers, are strongly dependent on phase continuity, average phase size, molecular mixing at the phase boundaries and intrinsic properties of the constitutive components.

Poly(ε-caprolactone) (PCL) is known for a unique set of properties, i.e. biocompatibility, permeability and biodegradability [8]. The range of these properties is furthermore increased by copolymerization with lactides and glycolide, which accounts for widespread applications in medicine as biodegradable sutures, artificial skin, resorbable prostheses and containers for sustained drug release [8-12]. Depending on the polymerization mechanism, PCL can be end-capped with a hydroxyl group at both ends [13,14], which is reactive toward alkoxysilane [4b]. The sol-gel process has thus the potential of combining valuable properties into a novel type of ceramer, such as non-toxicity for living organisms, resorption after an appropriate period of implantation time and good ultimate mechanical properties.

This paper reports a preliminary study of the synthesis of aliphatic polyester-silica hybrid ceramers by the sol-gel technique. This hybrid ceramer may be envisioned as a novel type of degradable bioglass. It could also be used as a coating material for bone implants and prosthetic devices. Due to an expectedly high scratch resistance, it would also be a valuable coating for organic polymers, particularly for polymer compatible with PCL, such as bisphenol A polycarbonate and PVC. This type of ceramer could also be used as support for enzyme immobilization.

Experiment

Materials. High purity tetraethoxysilane (TEOS) (Janssen, Geel, Belgium), *a,ω*-hydroxyl PCL of a 2000 molecular weight (Aldrich, Bornem, Belgium), 3-isocyanatopropyltriethoxysilane (Lancaster, Strasbourg, France), hydrochloric acid (12 N) (Lab Chemistry, Geer, Belgium), tetrahydrofuran (THF) (Janssen) and ethanol (Riedel-de Haën, Seelz, Germany) were used as received. Toluene (Janssen) was dried by refluxing over calcium hydride and distilled under nitrogen atmosphere. 1,4-Diazobicyclo(2,2,2)octane (DABCO) (Aldrich) was dried by repeated (three times) azeotropic distillation of toluene just before use.

Procedure. (1) Triethoxysilane end-capped PCL. Hydroxyl end-capped PCL was dried by repeated (three times) azeotropic distillation of toluene just before use. In a carefully-dried pyrex flask, equipped with a rubber septum, PCL and 3-isocyanatopropyltriethoxysilane were dissolved in dry toluene in a 1:1.2 molar ratio and added with DABCO as a catalyst (1 equiv.). This reactive mixture was stirred and maintained at a constant temperature of 50°C for 24 h. The triethoxysilane end-capped PCL was then precipitated into cold methanol.
(2) PCL containing hybrid ceramer. The sol-gel technique was applied to PCL/TEOS mixtures of various compositions used at a 20 wt% concentration in THF. The reaction conditions were kept constant except for the PCL end-groups, i.e. hydroxyl or triethoxysilane. A stoichiometric amount of water (based on the number of hydrolysable alkoxide substituents) was added to initiate the hydrolysis reaction. HC1 was used as a catalyst in a 0.05/1 HCL/TEOS molar ratio. A representative synthesis was as follows: 1.5 g TEOS was added to the PCL (0.5 g) solution in THF (10.0 ml) and thoroughly mixed until a homogeneous solution was formed. Then deionized water (0.52 ml), ethanol (0.80 ml) and HCl (0.01 ml) were added under rapid stirring at ambient temperature for *ca.* 10 min. The clear solution was then cast into a plastic Petri dish and covered with a Parafilm. Based on a preliminary series of gelation experiments it was shown that, after several days depending on the PCL end-groups (hydroxyl or triethoxysilane) (see gelation time I in *Tables 1* and *2*), the Parafilm was to be removed. The total gelation (see gelation time I + II in *Tables 1* and 2) was the time requested for the flow becoming unobserved by the naked eye. The gelified material was then dried under ambient conditions for one week prior to testing.

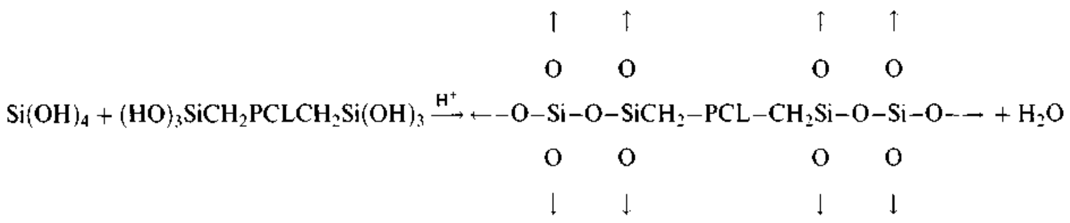
Characterization. I.r. analysis was performed with a Perkin—Elmer 106 *FT*i.r. spectrometer. Samples were analysed as thin films cast on NaCl windows. ^{1}H n.m.r. spectra were recorded in $CDCl_3$ at 400 MHz in the *FT* mode with a Brüker AN 400 superconducting magnet system. Glass transition temperature (T_g), melting temperature (T_m) and melting enthalpy (ΔH_m) were measured by differential scanning calorimetry (d.s.c.) with a DuPont 910 d.s.c. thermal analyser. The heating rate was 20°C min^{-1}. PCL was tentatively extracted from hybrid materials in a standard Soxhlet apparatus, with THF for at least 24 h until no further weight loss was observed. The sol fraction was calculated from the initial and final weight of the sample. Some samples were directly cast on a copper grid for observation by transmission electron microscopy (TEM). Observations were carried out with a Philips CM100 microscope. There was enough contrast between the organic polymer and the inorganic phase to avoid any specific staining.

Results and discussion

Equations (l)-(3) [equation (3) is unbalanced] are an oversimplified view of the reaction pathway envisioned for the synthesis of PCL containing ceramers. Indeed hydrolysis of the ethoxysilane groups whatever their origin (TEOS or PCL end-groups) is assumed to be complete before polycondensation occurs. Undoubtedly, the actual network forming process is much more complex due to the interplay of hydrolysis and condensation. Even though the actual stepwise reaction mechanism cannot be detailed, it is clear that PCL chains must be end-capped by ethoxysilane groups for them to be possibly incorporated into the final network. For this purpose, a commercially available α,ω-hydroxyl PCL has been reacted with an excess of 3-isocyanatopropyltriethoxysilane (20 mol% excess) in toluene, in the presence of 1,4-diazabicyclo (2,2,2) octane, as a catalyst.

$$Si(OEt)_4 + 4H_2O \xrightarrow{H^+} Si(OH)_4 + 4CH_3CH_2OH \qquad (1)$$

$$(EtO)_3SiCH_2{-}PCL{-}CH_2Si(OEt)_3 + 6H_2O \xrightarrow{H^+} (HO)_3SiCH_2{-}PCL{-}CH_2Si(OH)_3 + 6C_2H_5OH \qquad (2)$$



$$Si(OH)_4 + (HO)_3SiCH_2PCLCH_2Si(OH)_3 \xrightarrow{H^+} \leftarrow{-}O{-}\underset{\underset{\downarrow}{O}}{\overset{\overset{\uparrow}{O}}{Si}}{-}O{-}\underset{\underset{\downarrow}{O}}{\overset{\overset{\uparrow}{O}}{Si}}CH_2{-}PCL{-}CH_2\underset{\underset{\downarrow}{O}}{\overset{\overset{\uparrow}{O}}{Si}}{-}O{-}\underset{\underset{\downarrow}{O}}{\overset{\overset{\uparrow}{O}}{Si}}{-}O{-}\rightarrow + H_2O \qquad (3)$$

Table 1 Data for α,ω-triethoxysilane PCL (M_n = 2000) containing creamers

Entries	H23	H25	H30	H24	H36	H37	H62	H44	H26
TEOS:PCL (wt. ratio)	50:50	50:50	50:50	60:40	60:40	70:30	75:25	80:20	90: 10
THF:EtOH (vol. ratio) Gelation^a	100:0	100:4	100:16	100:0	100:16	100: 16	100:4	100:8	100:0
I	2d	3d	2d	2d	2d	3d	6d	3d	3d
II	2d	2d	2d	2d	2d	2d	2d	2d	2d
Appearance^b	O	S	S	S	T/S	T	T	T	T
T_m^c	53.0 C	47.5°C	50.0 C	54.5 C	45.5 C				
ΔH_m(Jg^{-1})^d	24.0	5.9	5.8	7.8	0.7	0	0	0	0

[a] *Gelation time (day): Step I, the solvent evaporation at room temperature is slowed down by a covering parafilm (I); Step II, solvent evaporation occurs at room temperature and air atmosphere*
[b] *T stands for transparent; O for opaque; and S for translucent*
[c] *T_m, melting temperature of PCL*
[d] *ΔH_m, melting enthalpy of PCL*

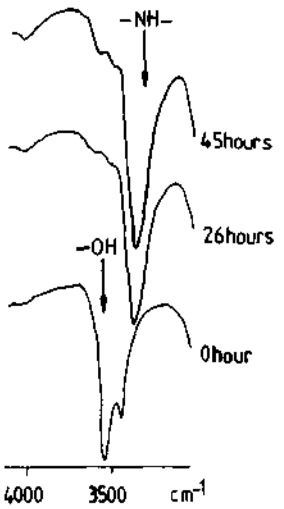
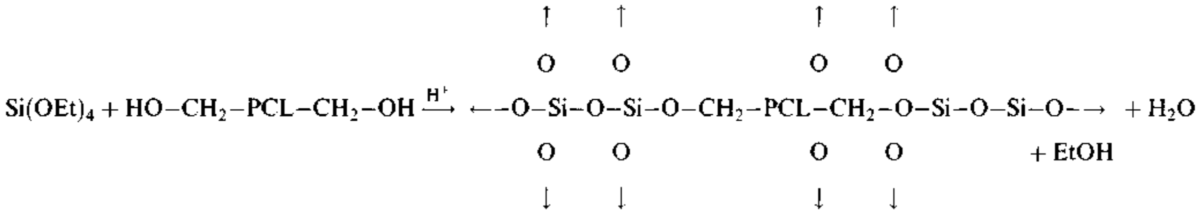


Figure 1 I.r. spectra of the reaction product of PCL-diol with 3-isocyanatopropyltriethoxysilane in the presence of DABCO as a catalyst in toluene at 50°C for different reaction times

The reaction progress has been followed by *FT*i.r. The hydroxyl groups at *ca.* 3500 cm^{-1} have been observed to disappear completely in favour of urethane linkages (3384 cm^{-1}) *(Figure 1).* When the reaction is complete *(ca.* 24 h), the polymer is recovered and purified by precipitation into cold methanol, in which the catalyst and the excess of 3-isocyanatopropyltriethoxysilane (even after reaction with methanol) are soluble. Furthermore, no carboxylic acid end-group can be detected by *FT*i.r. supporting that no chain degradation has occurred during the end-capping reaction.

Although the gelation time is essentially independent of the PCL content, this content has an effect on the final material, which is opaque at a high PCL content but becomes transparent when this content is decreased (see *Table 1,* entries H30, H36, H37). It is also clear that the ethanol content in the solvent mixture also affects the appearance of the ceramer. At PCL contents higher than 40 wt%, opacity steadily increases as the ethanol content is decreased *(Table J,* entries H23, H25 and H30, or H24 and H36). At a lower PCL content, the final film remains transparent however even in the absence of ethanol *(Table 1,* entry H26). In the traditional sol-gel systems, alcohol is currently used as solvent. However, as shown in the reaction scheme [equations (1)-(3)], alcohol is also a by-product of the hydrolysis reaction. Therefore, the ethanol content must be kept as small as possible for not adversarily affecting the hydrolysis reaction rate, while preserving transparency of the final material when possible. Since the PCL oligomers used in this study are prone to crystallize at room temperature, it is worth analysing the final hybrid material by d.s.c. *Table 1* shows that no crystallinity is detected when the samples are transparent, i.e. when 30 wt% PCL or less is used in the PCL: TEOS starting feed. This observation indicates that the PCL chains are so intimately incorporated into the silica network that they are prevented from crystallizing. When the PCL content is increased beyond 40 wt%, the final hybrid materials become more and more opaque and a melting endotherm is observed, from which the melting temperature and the melting enthalpy can be extracted. PCL crystallinity depends on the THF : EtOH ratio. The melting enthalpy rapidly drops upon the addition of even a small amount of ethanol *(Table 1*, entries H23, H25, H30 and H24, H36) and accordingly transparency of the final product is improved. Thus, ethanol appears to perturb the hydrolysis-condensation balance in such a way that incorporation of the PCL chains into the silica network is favoured. This observation is consistent with a hydrolysis reaction faster than the polycondensation reaction, so that probability for silica to be formed independently of the PCL component is decreased.

As shown in *Table 2,* α,ω-hydroxyl PCL can also be used as such in the sol-gel process, i.e. without the previous conversion of the hydroxyl end-groups into triethoxysilane groups. Ethanol has again a beneficial effect on the material transparency as previously discussed. Transparency is once more observed when the PCL content is smaller than 30 wt% (PCL : TEOS). This observation indicates that the following polycondensation reaction can occur:



$$\mathrm{Si(OEt)_4 + HO{-}CH_2{-}PCL{-}CH_2{-}OH} \xrightarrow{H^+} \leftarrow{-}\mathrm{O}{-}\underset{\underset{\downarrow}{\mathrm{O}}}{\overset{\overset{\uparrow}{\mathrm{O}}}{\mathrm{Si}}}{-}\mathrm{O}{-}\underset{\underset{\downarrow}{\mathrm{O}}}{\overset{\overset{\uparrow}{\mathrm{O}}}{\mathrm{Si}}}{-}\mathrm{O{-}CH_2{-}PCL{-}CH_2{-}O}{-}\underset{\underset{\downarrow}{\mathrm{O}}}{\overset{\overset{\uparrow}{\mathrm{O}}}{\mathrm{Si}}}{-}\mathrm{O}{-}\underset{\underset{\downarrow}{\mathrm{O}}}{\overset{\overset{\uparrow}{\mathrm{O}}}{\mathrm{Si}}}{-}\mathrm{O}{-}\rightarrow \; + \mathrm{H_2O} \; + \mathrm{EtOH} \tag{4}$$

Although this polycondensation reaction is possible, its reaction rate is much slower than that schematized by equation (3). Indeed, the gelation time requested for the formation of a transparent film is much longer, in agreement with a lower reactivity of the PCL hydroxyl end-groups compared to silanol (or silanolate) end-groups. It must also be stressed that there is only one hydroxyl group per chain end, in contrast to three silanolates in the case of equation (3).

A typical d.s.c. curve is illustrated in *Figure 2* (entry H62 in *Table 1*). The first scan shows an endotherm at about 80°C which is commonly attributed to the vaporization of volatile compounds, such as water, ethanol and solvent [15]. The very broad endotherm centred at *ca.* 150°C is the signature for a further progress of the sol-gel reaction. Interestingly enough, the two endotherms at *ca.* 80°C and 150°C have completely disappeared when the sample is rescanned after cooling from 200°C down to -150°C. Furthermore, the glass transition of PCL at -56.5°C is less visible. All these observations support that the reaction is not complete as long as it is carried out at 25°C.

Table 2 Data for α,ω-hydroxyl PCL (M_n = 2000) containing creamers

Entries	H46[e]	H48	H53	H52	H50	H49	H57
TEOS:PCL (wt. ratio)	50:50	60:40	60:40	70:30	75:25	80:20	90: 10
THF:EtOH (vol. ratio)	100:20	100: 16	100:20	100:9.6	100:4	100:8	100:0
Gelation[a] I	l0d	7d	11d	11d	11d	11d	11d
Time (day) II	2d	2d	2d	2d	2d	2d	2d
Appearance[b]	O	O	S	T	T	T	T
T_m[c]	24.0 C 49.3 C	52.5' C	54.2 C				
ΔH_m(J g^{-1})[d]	36.2 7.2	24.2	8.1	0	0	0	0

[a] *Gelation time, see Table I*
[b] *T stands for transparent; O for opaque; and S for translucent*
[c] *T_m, melting temperature of PCL*
[d] *ΔH_m, melting enthalpy of PCL*
[e] *Two melting peaks are observed*

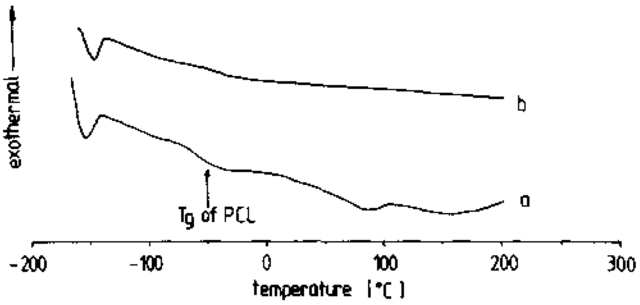


Figure 2 D.s.c. traces of PCL ceramers (sample H62 in Table 1). (a) First scan; (b) second scan after quenching

Table 3. Soxhlet extraction of functional endcapped PCL from ceramers prepared from a 75:25 TEOS:PCL wt ratio (entries H50 and H62 in Tables 1 and 2)

Curing time at 100°C (h)	PCL wt%[a]	
	α,ω-hydroxyl PCL[b] (H50)	α,ω-triethoxysilane PCL[c] (H62)
0	11.5% (21.5%)	20.5% (39.4%)
6	32.0% (59.7%)	35.0% (67.3%)
24	42.5% (79.3%)	45.0% (86.5%)
48	41.0% (76.5%)	42.0% (80.8%)

[a] PCL wt% left in the composite after Soxhlet extraction (see Experimental section) and compared to the theoretical PCL content (noted in brackets)
[b] Theoretical PCL wt% = 53.6%
[c] Theoretical PCL wt% = 52.0%

Transition from a liquid to a glassy material more likely limits the reaction progress by reducing the probability for the reagents to enter into efficient collisions. This drawback seems to be at least partly overcome by thermal treatment up to 200°C. Annealing above 200°C is however prohibited due to the poor thermal stability of PCL [16].

In order to know to which extent PCL chains are incorporated into the silica network, PCL has been extracted in a Soxhlet apparatus with THF. Data listed in *Table 3* show that *ca.* 20.5% PCL is part of the hybrid material when the reaction is carried at 25°C and PCL is end-capped with triethoxysilane.

Figure 3 Transmission electron micrograph (magnification of 205 000) for a PCL ceramer containing 54 wt% SiO_2. The length of the bar corresponds to 500 Å. SiO_2 is observed as black spots

The incorporation yield is less by 12% when the PCL hydroxyl end-groups are not reacted with 3-isocyanatopropyltriethoxysilane in a preliminary step. Whatever the PCL end-groups, hydroxyl or triethoxysilane, *Table 3* shows that an annealing at 100°C has a very beneficial effect on the PCL conversion. For instance, the fraction of incorporated PCL in the H62 sample increases from 20.5% up to 35.0% when the hybrid material is annealed at 100°C for 6h. A longer annealing time at 100°C, e.g. 2 days, is not recommended, since the fraction of soluble PCL tends to increase with time. This effect might indicate a partial degradation of PCL with release of soluble fragments. This hypothesis is assessed by ^{1}H n.m.r. analysis of the sol fraction, which shows the presence of carboxylic acid end-groups. After annealing at 100°C, the amount of extractable

PCL remains higher when α,ω-hydroxyl PCL has been used rather than the triethoxysilane derivative.

The TEM of a PCL ceramer is shown in *Figure 3* at a magnification of 205 000. This preliminary observation suggests some degrees of co-continuity in the phase structure when the weight composition is close to 50%. More information about the phase morphology of PCL ceramers as analysed by TEM (and image analysis), SAXS, d.m.a., AFM and SEM-EDXA will be reported in the near future.

Preliminary results on cells culture are encouraging, since 46 wt% PCL containing ceramer allows glial cells to grow onto the surface. These cells are also growing on pure SiO_2 in sharp contrast to what happens on a PCL surface. More details will also be reported on the bioactive properties of PCL ceramers in the future.

Acknowledgement

The authors are grateful to the 'Services Fédéraux des Affaires Scientifiques, Techniques et Culturelles' for financial support in the frame of the 'Poles d'Attraction Interuniversitaires: Polymères'.

References

[1] For most recent reviews, see:
(a) Wilkes, G.L., Huang, H.H. and Glaser, R. H., 'Silicon-Based Polymer Science', Advances in Chemistry Series 224, American Chemical Society, Washington DC, 1990, pp. 207-226. (b) Novak, B. M. *Adv. Mater.* 1993, 5, 422
[2] Phillip, G. and Schmidt, H. *J. Non-Cryst. Solids* 1984, 63, 283
[3] (a) Mark, J. E., Jiang, C. and Tang, M. Y. *Macromolecules* 1984, 17, 2616. (b) Wang, S. H., Ahmad, Z. and Mark, J. E. *Polym. Bull.* 1993, 31, 323
[4] (a) Brennan, A. B. and Wilkes, G. L. *Polymer* 1991, 32, 733. (b) Wang, B., Brennan, A. B., Huang, H. and Wilkes, G. L. *J. Macromol. Sci.* 1990, A27, 1447
[5] (a) Chujo, Y., Ihara, E., Kuse, S., Suzuki, K. and Saegusa, T. *Macromol. Chem. Macromol. Symp.* 1991, 42/43, 303. (b) Toki, M., Chow, T. Y., Ohnaka, T., Samura, H. and Saegusa, T. *Polym. Bull.* 1992, 29, 653
[6] (a) Surivet, F., Lam, T. M., Pascault, J. P. and Mai, C. *Macromolecules* 1992,25, 5748. (b) Girard-Reydet, E., Lam, T. M. and Pascault, J. P. *Macromol. Chem. Phys.* 1994, 195, 149
[7] (a) Ellsworth, M. W. and Novak, B. M. J. *Am. Chem. Soc.* 1991. 113, 2756. (b) Ellsworth, M. W. and Novak, B. M. *Polym. Prep. (Am. Chem. Soc. Div. Polvm. Chem.)* 1993, 34, 356
[8] Pitt, C. G., Marks, T. A. and Schindler, A. in 'Controlled Release of Bioactive Materials' (Ed. R. Baker), Academic Press, 1980
[9] Schindler, A., Jeffcoat, R., Kimmel, G. L., Pitt, C. G., Wall, M. E. and Zweidinger, R. in 'Contemporary Topics in Polymer Science' (Eds J. R. Pearce and E. M. Schaefger), Vol. 2, Plenum, New York, 1977, p. 251
[10] Vert, M. *Makromol. Chem.. Macromol. Symp.* 1986, 6, 109
[11] Pak, J. Ford, J. L., Rostron, C. and Walters, V. *Pharm. Acta Helv.* 1985, 60, 160
[12] Grijpma, D. W., Zondervan, G. J. and Penning, A. J. *Polym. Bull.* 1991,25,327
[13] Dubois, Ph., Degée, Ph., Jérôme. R. and Teyssié, Ph. *Macromolecules* 1993, 26, 2730
[14] Duda, A. *Macromolecules* 1994, 27, 576
[15] Lemoine, C, Gilbert, B., Michaux, B., Pirard, J. P. and Lecloux, A. J. *Non-Cryst. Solids* 1994, 175,1
[16] Dubois, Ph., Barakat, I., Jérôme, R. and Teyssié, Ph. *Macromolecules* 1993, 26, 4407