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# Synthesis of Colloidal Superparamagnetic Nanocomposites by Grafting Poly( $\epsilon$ -caprolactone) from the Surface of Organosilane-Modified Maghemite Nanoparticles

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**ABSTRACT:** Superparamagnetic and biodegradable/biocompatible core–corona nanocomposite particles were prepared by ring-opening polymerization of  $\epsilon$ -caprolactone initiated from the surface of maghemite. As was done in a previous work, an aminosilane coupling agent was chosen as the coinitiator and immobilized at the surface of the maghemite particles to allow the growth of the poly( $\epsilon$ -caprolactone) (PCL) chains from the solid surface. Two different catalytic systems based on aluminum and tin alkoxides were investigated. Whatever the catalyst used, diffuse reflectance Fourier transform spectroscopy brought evidence for polymer anchoring through a covalent bond, whereas thermogravimetric analysis attested to the presence of high amounts of PCL around the maghemite. Magnetization measurements proved that the nanocomposites kept their superparamagnetic properties after coating. The polymer contents obtained by this grafting-from route were compared with the results obtained by a more classical grafting-to process. © 2005 Wiley Periodicals, Inc. *J Polym Sci Part A: Polym Chem* 43: 3221–3231, 2005

**Keywords:** graft from maghemite; nanocomposites; polyesters; ring-opening polymerization

## INTRODUCTION

Ring-opening polymerization (ROP) of lactones and lactides has been widely investigated because of the properties of the resulting polyesters, such as biodegradability, biocompatibility, and miscibility with other polymers.<sup>1</sup> In particu-

lar,  $\epsilon$ -caprolactone (CL) is usually polymerized according to a coordination–insertion mechanism initiated from metal alkoxides like aluminum isopropoxide<sup>2</sup> and tin(II) octoate.<sup>3</sup> Because of various potential applications, particularly in the biomedical field, the grafting of poly( $\epsilon$ -caprolactone) (PCL) onto various surfaces has received increased interest in recent years. It was first shown by Miola et al.<sup>4</sup> that aluminum alkoxides supported on porous silica were able to initiate the ROP of CL. Later on, Carrot<sup>5</sup> and Joubert<sup>6</sup>

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succeeded in polymerizing CL from the surface of silylated silica nanoparticles with chemically anchored amino and hydroxyl functions as coinitiators, respectively. Silica silylation before polymerization has two objectives: first, it allows the introduction of initiating groups on the particle surface and, second, it ensures the formation of a nonhydrolyzable bond between the inorganic particle support and the polymer.

If silica were replaced by superparamagnetic iron oxide particles like maghemite or magnetite, such nanocomposites could find useful diagnostic or therapeutic applications. In particular, they could be used as drug carriers,<sup>7</sup> T2 contrast agents for magnetic resonance imaging, or colloidal mediators in magnetic hyperthermia for cancer treatment.<sup>8,9</sup>

To our knowledge, very little work has been done on the surface modification of iron oxide nanoparticles with the grafting-from technique,<sup>10</sup> whereas literature concerning the synthesis of magnetic nanocomposite colloids via emulsion<sup>11–13</sup> or dispersion<sup>14,15</sup> polymerizations is more abundant.

In a recent study, we reported the silylation of maghemite nanoparticles with amino and alcohol groups and showed that the resulting materials were able to coinstantiate the ROP of CL.<sup>16</sup> This preliminary study investigated the limits of the amino-modified system. Two catalytic systems based on either aluminum or tin alkoxides were investigated. The efficiency of each catalyst, estimated by measuring the monomer conversion and the amount of grafted polymer chains, was compared.

## EXPERIMENTAL

### Materials

Iron II chloride tetrahydrate (99%, Strem chemicals, 93-2632), iron III chloride hexahydrate (97%, Strem Chemicals, 93-2606), ammonia (28%, Carlo Erba, 314863), hydrochloric acid (37%, Riedel-de Haën, 07102), nitric acid (65%, Carlo Erba, 524536), ferric nitrate nonahydrate (>99%, Fluka, 44949), *N,N*-dimethylformamide (DMF, 99%, Acros Organics, 116220010), water (HPLC grade, Acros Organics, 268300025), and *N*-(2-aminoethyl)-3-aminopropyltrimethoxysilane (EDPS, 97%, ABCR, SIA0591.0) were used as received.

CL (99%, Aldrich, 16736-3) and benzyl alcohol (BzOH, 99%, Aldrich, 10800-6) were stored under

dry nitrogen over molecular sieves (3 Å, Aldrich, 20,857-4). Toluene (>99.5%, Fluka, 89681) was distilled over sodium and stored under dry nitrogen over molecular sieves. Aluminum isopropoxide ( $\text{Al}(\text{O}^i\text{Pr})_3$ , >98%, Aldrich, 22,041-8) and tin octoate ( $\text{SnOct}_2$ , 95%, Aldrich, 28,717-2) were dissolved in dry toluene at a concentration equal to 0.02 M and stored under dry nitrogen.

### Measurements

The diffuse reflectance Fourier transform (DRIFT) spectra were recorded on a Brücker IFS 66 FTIR instrument by the accumulation of 200 scans with a spectral resolution of  $4\text{ cm}^{-1}$ . Thermogravimetric analysis (TGA) was performed with a TGA/SDTA 851e apparatus from Mettler in the temperature range 30–800 °C with a scanning rate of 10 °C/min under an air stream. The total weight loss between 160 and 500 °C was taken into account to calculate the amount of PCL in the composite. Particle size in toluene was determined by light scattering with a Coulter N4+ apparatus working at 20 °C with a detection angle of 90°. Data were analyzed with the size distribution processor (SDP) weight peak mode. Differential scanning calorimetry (DSC) analyses were carried out with a PerkinElmer DSC-7 device. Aluminum pans containing about 10 mg of polymer were heated from –100 to 100 °C at  $20\text{ °C min}^{-1}$  under helium. Total iron concentrations in the aqueous dispersions were determined by the dissolution of maghemite nanoparticles in concentrated HCl, the complete reduction of iron (III) by a  $\text{SnCl}_2$  solution, the oxidation of excess  $\text{SnCl}_2$  by  $\text{HgCl}_2$ , and the titration of iron (II) by  $\text{K}_2\text{Cr}_2\text{O}_7$ , according to a method described elsewhere.<sup>17</sup> Magnetic properties were recorded on a SQUID MPMS-5S from Quantum Design at 300 K. The specific surface area of maghemite was determined by nitrogen adsorption according to the Brunauer–Emmett–Teller (BET) method. Transmission electron micrographs were acquired with a Philips EM 120 electron microscope operating at 120 kV. Drops of diluted dispersions were air-dried on carbon films supported by 200-mesh copper grids. The excess was then removed by absorption with filter paper. For negative staining, a droplet of 2 wt % uranyl acetate (99.9%, Electron Microscopy Sciences, Washington, United States) was deposited after drying of the sample and allowed to adsorb for 30 s. The excess was then removed by absorption.

### Preparation of the Maghemite Ferrofluid Suspension

The aqueous maghemite suspension was synthesized by precipitation from iron chlorides.<sup>18,19</sup> Briefly, 3.9 g of  $\text{FeCl}_2$  (19 mmol) and 10.9 g of  $\text{FeCl}_3$  (38 mmol) ( $\text{Fe}^{3+}/\text{Fe}^{2+} = 2$ ) were mixed at 80 °C with 435 mL of water and precipitated with 45 mL of a 28% ammonia solution. The resulting black dispersion of magnetite was separated and oxidized with 75 mL of  $\text{HNO}_3$  2 M for 10 min and then with 75 mL of a 0.33 M  $\text{Fe}(\text{NO}_3)_3$  solution at 100 °C during 30 min. The brown dispersion was centrifuged, washed three times with acetone, and peptized with 50 mL of  $\text{HNO}_3$  2 M for 15 min. After three additional washings with acetone, the red-brown paste was dispersed into 60 mL of water, and acetone traces were evaporated *in vacuo* at 60 °C. Finally, the total volume was brought to 60 mL by the addition of water, and the iron concentration was determined by volumetric titration. The average particle size, determined by transmission electron microscopy (TEM), was  $10 \pm 5$  nm, whereas dynamic light scattering indicated an average diameter of  $50 \pm 5$  nm, suggesting that the oxide particles were slightly aggregated. The specific surface area of the particles was  $130.0 \pm 0.5 \text{ m}^2 \text{ g}^{-1}$ , as determined by BET.

### Grafting of EDPS onto Maghemite

One hundred seventy milliliters of the aqueous ferrofluid ( $[\text{maghemite}] = 86 \text{ g} \cdot \text{L}^{-1}$ ) were

stripped by 170 mL of DMF. The resulting dispersion was sonicated for 15 min, and 19 mL (83.7 mmol) of EDPS was added. The mixture was stirred at 90 °C during 17 h. The excess silane was then removed by five centrifugation/dispersion cycles in DMF and the powder was cured *in vacuo* at 70 °C for 24 h. The amount of grafted silane was determined by TGA and was found equal to 1.1 mmol per gram of maghemite, which corresponds to  $111 \text{ mg} \cdot \text{g}^{-1}$ .

### ROP of CL from the Silylated Maghemite Surface Promoted by $\text{Al}(\text{O}^i\text{Pr})_3$

All the polymerizations were performed at 50 °C in Schlenk-type glassware under dry nitrogen and vigorous stirring. In a typical procedure, 0.5 g of the modified maghemite was dried *in vacuo* at 150 °C for 3 h to remove the physisorbed water. The maghemite powder was then dispersed in toluene and the required amounts of catalyst and monomer were introduced in the suspension medium. For example, sample 10 (Table 1) was synthesized by dispersing 0.5 g of silylated maghemite into 140 mL of toluene and adding 0.026 mmol (1.3 mL) of  $\text{Al}(\text{O}^i\text{Pr})_3$  and 187 mmol (20.7 mL) of CL.

After polymerization, the nongrafted polymer chains were removed by 10 centrifugation/dispersion cycles with tetrahydrofuran. Their degree of polymerization ( $\text{DP}_n$ ) and polymolecularity indices could not be determined because of the presence of residual maghemite particles

**Table 1.** Effect of the  $[\text{NH}_2]/[\text{Al}]$  Molar Ratio, Targeted  $\text{DP}_n$ , and Reaction Time on the Composite Polymer Content<sup>a</sup>

Sample	$[\text{NH}_2]/[\text{Al}]$	Targeted $\text{DP}_n$	Time (h)	Conversion (%) <sup>b</sup>	Weight Loss (%) <sup>c</sup>	$[\text{Grafted PCL}]^d$ mg/g Maghemite
1	4	180	48	100	11.1	35
2	8	180	112	100	10.7	30
3	10	180	112	61	23.1	210
4	12	180	112	21	26.4	270
5	18	180	112	18	34.2	430
6	10	130	91	100	9.6	20
3	10	180	112	61	23.1	210
7	10	320	137	15	25.8	260
8	10	360	137	5	28.4	310
9	17	350	137	6	33.4	415
10	19	320	835	17	49.1	855

<sup>a</sup> The polymerizations were performed in toluene at 50 °C.

<sup>b</sup> Determined after weighing the free polymer and neglecting the amount of grafted polymer.

<sup>c</sup> Determined by TGA.

<sup>d</sup> Determined using equation 1 ( $[\text{EDPS}] = 88 \text{ mg/g}$  except for sample 10, for which  $[\text{EDPS}] = 111 \text{ mg/g}$ ).

that could not be separated from the polymer, and this therefore prevented any size exclusion chromatography or nuclear magnetic resonance analysis. The polymer-grafted iron oxide particles were dried overnight *in vacuo* at 50 °C and analyzed by TGA.

Theoretical  $DP_n$ s were determined from the monomer and the total initiating group concentrations according to  $DP_n = [\text{monomer}]/([\text{alkoxide}] + [\text{amine}])$ .

The amount of PCL in the composite (expressed in  $\text{mg g}^{-1}$  of maghemite) was deduced from the weight loss between 160 and 500 °C with eq 1:

$$\text{Grafted PCL (mg/g)} = \left( \frac{\Delta}{100 - \Delta} - [\text{EDPS}] \right) \times 1000 \quad (1)$$

where  $\Delta(\text{wt}\%)$  corresponds to the TGA weight loss between 160 and 500 °C and  $[\text{EDPS}]$  is the amount of grafted EDPS expressed in  $\text{g g}^{-1}$  of maghemite.

To validate the efficiency of the washing procedure, a mixture of PCL-grafted maghemite dispersed into toluene and “free”, nongrafted PCL chains ( $M_n = 17,500 \text{ g mol}^{-1}$ ) was stirred for 90 h at 60 °C. After 10 centrifugations/dispersions with THF, the weight loss increased less than 2%, indicating that this washing procedure was able to remove adsorbed PCL from the composite. Unfortunately, it was not possible to dissolve the iron oxide core selectively in an acidic solution to determine the PCL molecular weight, as the polymer chains would hydrolyze under such conditions.

#### ROP of CL from the Silylated Maghemite Surface Promoted by $\text{SnOct}_2$

The principle was the same as for  $\text{Al}(\text{O}^i\text{Pr})_3$ , except that the Schlenk tube was equipped with a reflux condenser and heated to 110 °C under nitrogen. For example, sample 12 was prepared

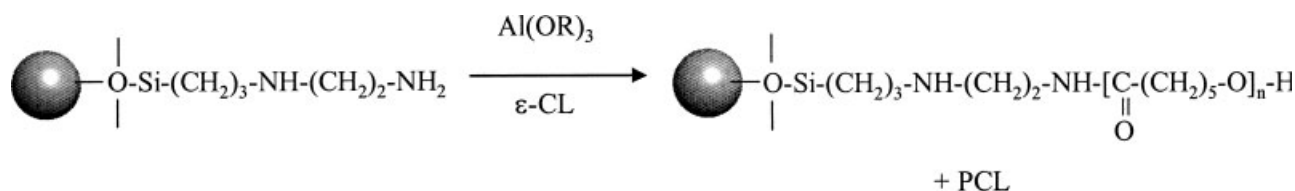
by the reaction of 0.52 g of silylated maghemite dispersed into 140 mL of toluene with 0.1 mmol (5 mL) of  $\text{SnOct}_2$  and 0.180 mol (20 mL) of CL.

## RESULTS AND DISCUSSION

The silylation step was the subject of a former study.<sup>16</sup> EDPS was immobilized on maghemite dispersed in DMF at 90 °C through condensation between the hydrolyzed silane and the maghemite superficial hydroxyl groups. It was concluded that EDPS was immobilized as multilayers around the maghemite particles. The silane grafting density was measured by TGA, and we concluded that a surface coverage of  $8.5 \mu\text{mol m}^{-2}$  was reached.

#### ROP of CL Catalyzed by Aluminum Isopropoxide

CL was first polymerized from the modified maghemite surface according to an anionic-coordinated process. The synthetic strategy is represented in Scheme 1. We decided to use aluminum isopropoxide instead of triethylaluminum, because we observed in a previous work<sup>6</sup> that the latter catalyst gives rise to an uncontrolled amount of free PCL chains through the presence of aluminoxanes. In a first step, CL coordinates onto aluminum isopropoxide, and the initiation is thought to proceed through the nucleophilic addition of the primary amine onto the carbonyl group of CL.<sup>5</sup> As a result, a first monomer unit is inserted, isopropyl alcohol is released, and an amide bond is formed. After this first step, the aluminum is linked to the particle through an Al—O bond, in which further monomer units will insert. Thus, PCL polymerizes by the so-called “coordination–insertion” mechanism. Concurrently, the aluminum alkoxide species are subject to interchange reactions with the released isopropyl alcohol,<sup>20</sup> competing with the monomer insertion and leading to the formation of isopropyl alcohol initiated PCL, which will be



**Scheme 1.** Synthetic strategy for the ROP of CL from EDPS-modified maghemite with aluminum isopropoxide as the catalyst.



referred to as free polymer. Thus, the propagating maghemite-PCL active species are temporarily converted into dormant alcohols in equilibrium with growing polymer. In other words, the primary amino groups play the role of coinitiators and are able to initiate the catalytic anionic coordinated ROP of CL leading to the simultaneous formation of grafted and free-polymer chains as depicted in Scheme 2.

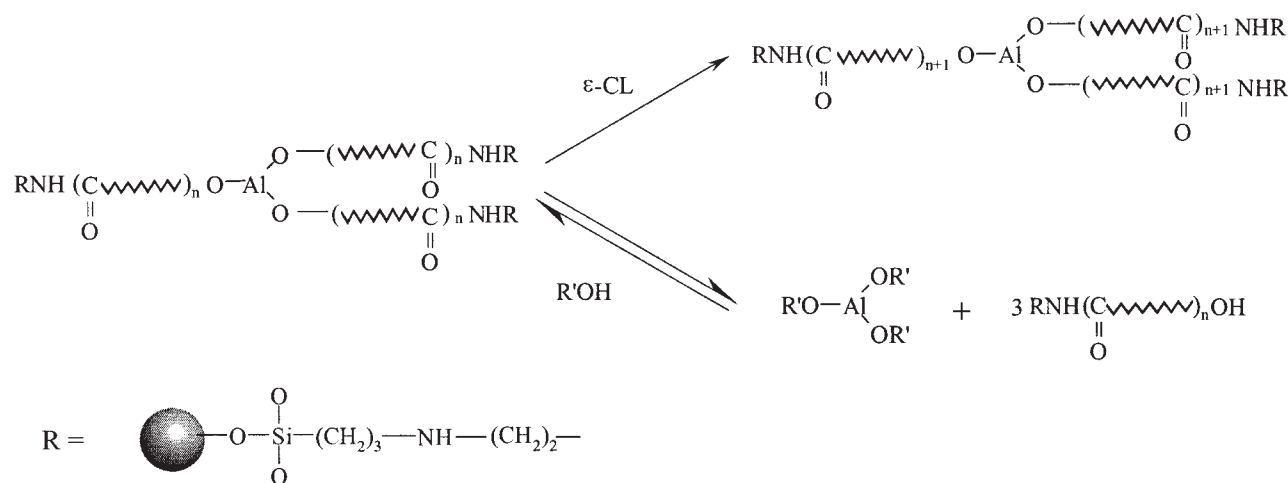
After polymerization, the free polymer was separated from the grafted maghemite particles by 10 successive centrifugation/dispersions into THF.

The composites were analyzed by DRIFT spectroscopy. The proof of grafting should be brought by the appearance of an amide function, created when the first monomer unit was grafted. However, because some DMF remained adsorbed on the maghemite surface after silylation even after a thermal treatment, the amide peak was hidden by the DMF signal around  $1670\text{ cm}^{-1}$ . Thus, to provide evidence of the grafting, the same polymerization experiment was performed from the surface of maghemite particles silylated into toluene.<sup>16</sup> To enhance the amide peak intensity, the polymerization was stopped to low conversions corresponding to 65 mg of grafted PCL per g of maghemite. The DRIFT spectra of silylated maghemite before

and after polymerization are presented in Figure 1.

The presence of the silane was evidenced by the following peaks<sup>21</sup> [Fig. 1(a)]:  $\nu$  (Si—OH) at  $926\text{ cm}^{-1}$ ,  $\nu$  (Si—O—Si) at  $1039$  and  $1117\text{ cm}^{-1}$ ,  $\omega$ (CH<sub>2</sub>) at  $1315\text{ cm}^{-1}$ ,  $\delta$  (Si—CH<sub>2</sub>) at  $1383\text{ cm}^{-1}$ ,  $\delta$  (CH<sub>2</sub>) at  $1475\text{ cm}^{-1}$ ,  $\delta$  (NH<sub>2</sub>) at  $1581\text{ cm}^{-1}$ ,  $\nu_s$  (CH<sub>2</sub>) at  $2870\text{ cm}^{-1}$  and  $\nu_{as}$ (CH<sub>2</sub>) at  $2932\text{ cm}^{-1}$ , besides the Fe—O signals characteristic of maghemite at  $634$  and  $580\text{ cm}^{-1}$ . After polymerization, peaks that can be ascribed to PCL appeared at  $1237\text{ cm}^{-1}$  ( $\nu_{as}$  C—O—C),  $1293\text{ cm}^{-1}$  ( $\omega$ CH<sub>2</sub>),  $1360\text{ cm}^{-1}$  ( $\tau$ CH<sub>2</sub>),  $1463\text{ cm}^{-1}$  ( $\delta$ CH<sub>2</sub>),  $1730\text{ cm}^{-1}$  ( $\nu_{C=O}$ ),  $2870\text{ cm}^{-1}$  ( $\nu_s$  CH<sub>2</sub>) and  $2932\text{ cm}^{-1}$  ( $\nu_{as}$  CH<sub>2</sub>). The peak at  $1658\text{ cm}^{-1}$  ( $\nu_{C=O}$  amide) as well as the shift of the signal corresponding to the amine from  $1581$  ( $\delta$  NH<sub>2</sub>) to  $1551\text{ cm}^{-1}$  ( $\delta$  NH amide) gave evidence of formation of an amide linkage, in agreement with an EDPS-initiated polymerization.

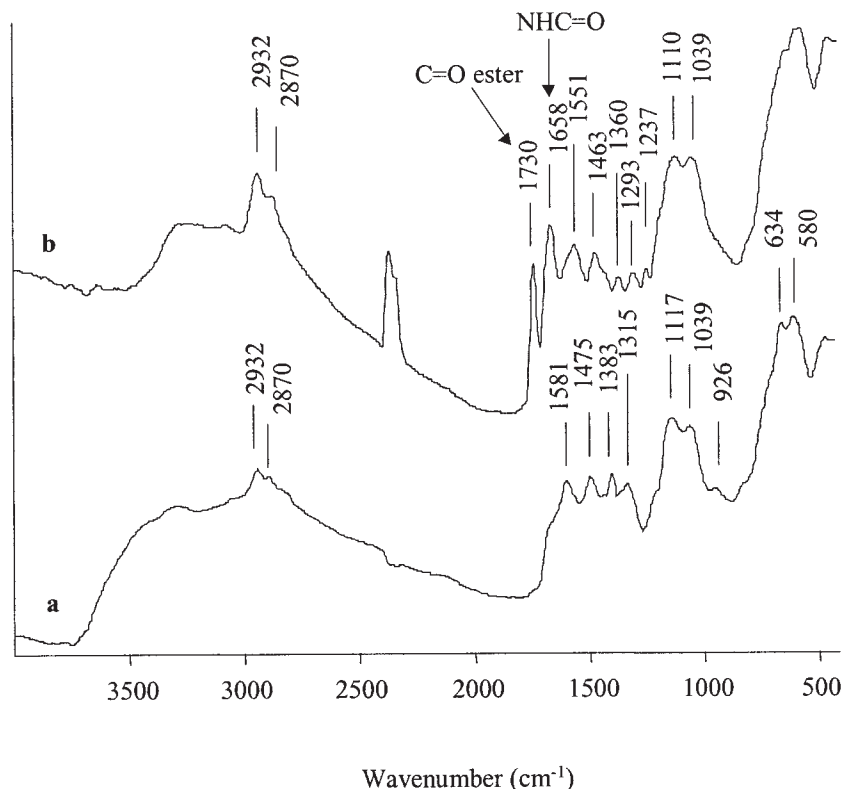
A series of experiments was performed to find optimal grafting conditions. In a first set of experiments, we investigated the effect of the [NH<sub>2</sub>]/[Al] molar ratio on the grafting of PCL while keeping the CL concentration constant. The polymerizations were quenched after 112 h by adding ethanol to the suspension medium. The variation of the polymer content in the composite versus the [NH<sub>2</sub>]/[Al] ratio is given in Table 1 and plotted in Figure 2.



R'OH = <sup>i</sup>PrOH or a growing polymer chain

~~~~~ PCL

**Scheme 2.** Competition between propagation and interchange reactions during the ROP of CL initiated from the surface of amine-functionalized iron oxide particles.



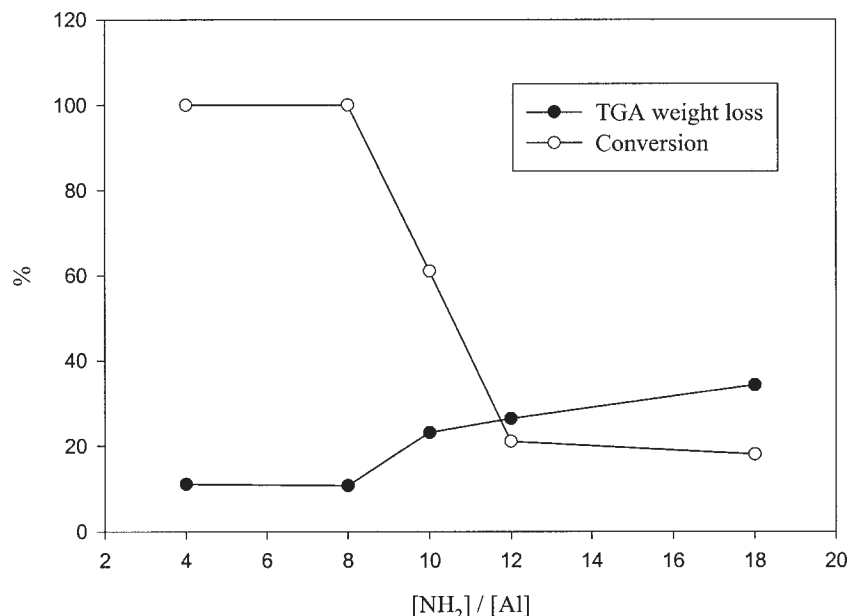
**Figure 1.** DRIFT spectra of silylated maghemite (a) before and (b) after polymerization.

It is apparent that the content of grafted polymer increased with the  $[\text{NH}_2]/[\text{Al}]$  ratio, while concurrently, the monomer conversion, determined by weighing the amount of free polymer formed and neglecting the grafted amount, decreased. The highest polymer contents were obtained for a high  $[\text{NH}_2]/[\text{Al}]$  ratio, that is, for low aluminum concentrations, indicating that the polymerization rate was the main factor governing the grafting efficiency. Similar results were obtained for the graft polymerization of CL from the surface of silica nanoparticles under similar experimental conditions.<sup>6</sup> Indeed, a controlled catalytic system requires fast alcohol-alkoxide interchanges compared with the propagation step. These interchange reactions are very fast during polymerizations performed in a homogeneous phase, leading to polymers with low polydispersity indices. However, because the alcohol groups are immobilized onto the iron oxide nanoparticles, they are less mobile and interchange reactions are not promoted. Therefore, if the propagation is too fast compared with these interchange reactions, free polymer will be produced in the majority. It is thus assumed

that lowering the polymerization rate by decreasing the aluminum concentration allows such interchange reactions between growing chains and dormant ones to proceed, resulting in a better grafting efficiency.

In a second series of experiments (samples 6 to 8), the  $[\text{NH}_2]/[\text{Al}]$  ratio was kept constant (equal to 10), and we varied the monomer concentration (i.e., the targeted  $\text{DP}_n$ s varied). The polymer content increased with increasing monomer concentration, while the conversion concurrently decreased (see Table 1). This can be explained by the steric hindrance provided by the grafted PCL chains around the metal catalyst. As the length of the grafted PCL chains increases, the reactive end groups that are entangled in the PCL corona become less and less accessible to the active species, resulting in a decrease in monomer conversion.

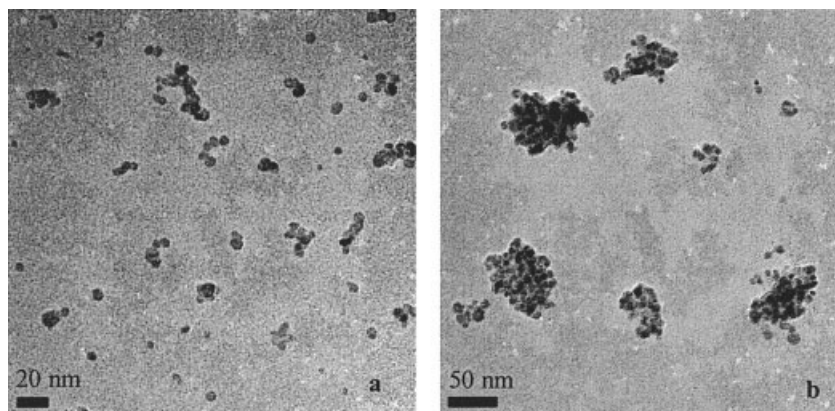
As before, increasing the  $[\text{NH}_2]$  to  $[\text{Al}]$  ratio from 10 to 13 (samples 8 and 9) enabled an increase in the polymer content, whereas the conversion remained unchanged. To reach higher monomer conversions and find optimal grafting conditions for a high  $[\text{NH}_2]/[\text{Al}]$  ratio



**Figure 2.** Effect of the  $[\text{NH}_2]/[\text{Al}]$  molar ratio on the composite polymer content.

and a high monomer concentration, an additional experiment was launched (sample 10), in which the reaction time was increased. As expected, the conversion slightly increased, which led to a higher polymer content in the composite. However, despite long polymerization times, the conversion remained quite low because of the low aluminum concentration. Nonetheless, we noted that a relatively high PCL amount equal to 855 mg/g of maghemite was grafted under these optimized conditions. It is also noteworthy that for PCL contents higher than 200 mg/g of maghemite, the nanocomposites had a filmy aspect after drying, suggesting that long chains were grafted. Below this value, a powder was obtained.

TEM pictures of uncoated and PCL-grafted maghemite are presented in Figure 3. A negative staining was accomplished with uranyl acetate. This compound adsorbs onto the organic shell and deflects the electron beam, sharpening the presence of the polymer. Unfortunately, the PCL-grafted maghemite particles are agglomerated; consequently, it is hard to observe the PCL film within these agglomerates, although it is possible to distinguish a diffuse white halo around the primary iron oxide particles that may correspond to the PCL corona [Fig. 3(b)]. In contrast, the raw maghemite particles [Fig. 3(a)] appear as nonagglomerated particles, because they did not undergo any thermal treatment that irretrievably leads to particle aggregation.



**Figure 3.** TEM pictures of (a) uncoated maghemite and (b) sample 10.



Either the thermal treatment performed on the silylated maghemite before polymerization or the existence of interparticular hydrogen bonds between the grafted PCL chains after air drying could explain the aggregation phenomenon that is observed in Figure 3(b).

The mean particle diameter of sample 10, as determined by dynamic light scattering (DLS) in THF, is equal to  $193 \pm 7$  nm, giving evidence that grafting was not performed from the surface of single particles, but for the most part from the surface of silylated maghemite aggregates that were also resistant to monomer diffusion and that did not break down upon polymerization. To preserve the colloidal properties of the iron oxide nanoparticles, it is thus clear that thermal treatments must be avoided.

### ROP of CL Catalyzed by Tin Octoate

Tin(II) octoate is a commonly used initiator/catalyst for ROP of lactides and lactones,<sup>22</sup> but the polymerization mechanism is still controversial. It is assumed by Penczek that the polymerization occurs via a coordination–insertion mechanism.<sup>3</sup> Two other important particularities of this catalyst are first that it is non toxic and therefore authorized in food and biological applications, and second that it allows almost complete conversions, even for monomer-to-catalyst ratios as high as  $10^4$ .<sup>23</sup> In the series of experiments shown in Table 2, we increased the  $[\text{NH}_2]/[\text{Sn}]$  molar ratio and maintained the monomer concentration as constant. In theory, no free polymer should be formed with tin octoate, because the tin alkoxide species are created only at the surface of the support. However, the presence of protic impurities inside the commercial catalyst causes the formation of free polymer in large proportions. As the reaction

rate was low, long polymerization times were necessary, but full monomer conversions were reached in every case. Because of the lowering of the polymerization rate compared with the previous catalytic system, interchange reactions were more effective, and significant amounts of PCL were grafted even for low  $[\text{NH}_2]/[\text{Sn}]$  ratios. However, contrary to what was observed for aluminum alkoxide, an increase in the  $[\text{NH}_2]/[\text{Sn}]$  ratio from 11 to 13 (samples 13 and 14) resulted in a decrease in the polymer content. This is presumably related to the long polymerization time used in these experiments. Indeed, sample 14 was allowed to react for a very long time, and it is well known that chain scissions due to intra- or intermolecular *trans*-esterifications occur after total monomer conversion.<sup>24</sup> These undesirable side reactions may account for the decrease in the polymer content. Consequently, the amount of grafted PCL was slightly smaller than with aluminum isopropoxide and did not exceed 600 mg/g of maghemite under optimized conditions.

### Comparison between Grafting-from and Grafting-to Routes

We recently reported on the coating of maghemite nanoparticles with PCL with a grafting-to route.<sup>25</sup> Briefly, the strategy consisted of functionalizing PCL chains of different molecular weights with a triethoxysilyl end group and condensing the modified PCL with the superficial hydroxyl groups of maghemite. The reaction time was set at 22 h. Nanocomposites containing up to 700 mg of PCL per gram of maghemite were synthesized with this method.

If we compare the PCL grafted amounts obtained by the grafting-from and grafting-to techniques, both strategies allow reaching

**Table 2.** Effect of the  $[\text{NH}_2]/[\text{Sn}]$  Molar Ratio on the Composite Polymer Content<sup>a</sup>

| Sample | $[\text{NH}_2]/[\text{Sn}]$ | Time (h) | Weight Loss (%) <sup>b</sup> | [Grafted PCL]<br>mg/g Maghemite <sup>c</sup> |
|--------|-----------------------------|----------|------------------------------|----------------------------------------------|
| 11     | 3                           | 135      | 23.7                         | 225                                          |
| 12     | 5                           | 255      | 34.4                         | 415                                          |
| 13     | 11                          | 864      | 41.5                         | 600                                          |
| 14     | 13                          | 1336     | 35.0                         | 430                                          |

<sup>a</sup> The polymerizations were performed in toluene at 110 °C. Targeted  $\text{DP}_n = 260$ . The conversion reached 100% for each experiment.

<sup>b</sup> Determined by TGA.

<sup>c</sup> Determined using equation 1.  $[\text{EDPS}] = 111$  mg/g except for sample 11, for which  $[\text{EDPS}] = 88$  mg/g of maghemite.

roughly similar contents of free and grafted polymer, but the second route is more convenient, because only short reaction times are necessary (22 h as compared with 835 h for sample 10). Moreover, with the grafting-to route, the nanocomposites are better characterized, because the length of the PCL chains is known and perfectly defined.

On the other hand, the advantage of the currently reported grafting-from route is that the PCL grafts wear a terminal hydroxyl group that allows further reactions like copolymerization with ethylene oxide to obtain a hydrophilic shell<sup>26</sup> or binding of any specific biological effector.<sup>9</sup>

## Composite Properties

### Magnetic Properties

The magnetization curves of raw maghemite powder, EDPS-silylated maghemite, and PCL-grafted maghemite (sample 10 of Table 1) are reported on Figure 4. Each sample exhibits a superparamagnetic behavior at room temperature, as evidenced by the absence of a hysteresis loop. The specific magnetizations are, respectively, equal to 53.3, 47.8, and 27.7 emu · g<sup>-1</sup> under an applied field of 10,000 Oe. If it is assumed that the magnetic properties of each maghemite core were not altered by the silylation and polymerization steps, the magnetization loss could be correlated to the relative weight of the nonmagnetic part of the materials.

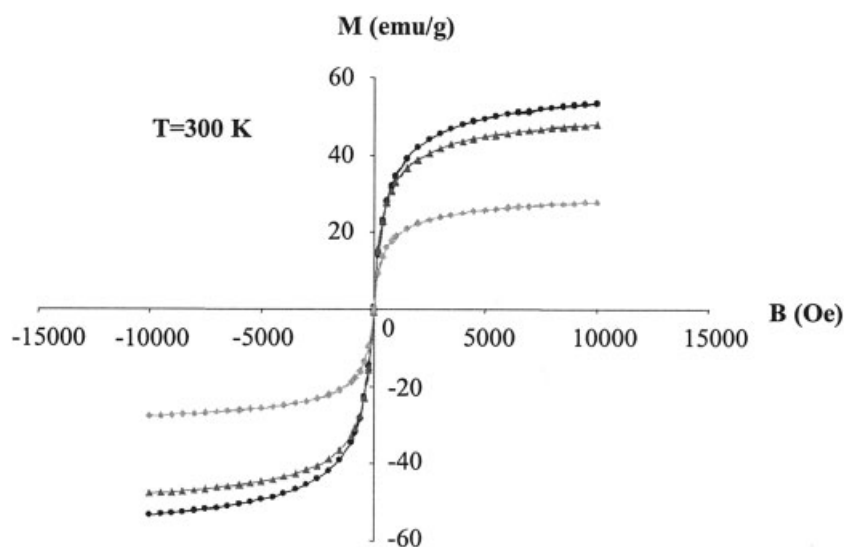
Such calculations led to 10.3 and 48 wt % for EDPS-silylated maghemite and PCL-grafted maghemite (sample 10), respectively. This last value matches with the weight loss of 49.1 wt % determined by TGA (Table 1).

### Thermal Properties

PCL degradation is known to occur involving two consecutive mechanisms<sup>27</sup> characterized, respectively, by a main degradation peak centered at 420 °C and a shoulder at 360 °C. First, the polyester chain is broken via an ester pyrolysis reaction, and then a depolymerization occurs in which the cyclic monomer is recovered. TGA and DSC analyses were performed on the surface-functionalized iron oxide particles to investigate the effect of grafting on the thermal degradation of PCL.

Analyses performed on PCL chains of  $M_n$  equal to 2800 g · mol<sup>-1</sup> showed a main degradation peak at 400 °C, a fusion temperature of 61 °C, and a fusion enthalpy of 113.1 J/g. Analyses performed after grafting are presented in Table 3.

It is obvious that the PCL degradation temperature is lowered after grafting. We have suggested in a previous work that the decrease in the degradation temperature is due to a loss of crystallinity of the polymer chains.<sup>25</sup> Indeed, increased amounts of amorphous chains could account for a better diffusion of the oxygen through the material, therefore resulting in a



**Figure 4.** Magnetic properties of raw maghemite (black), silylated maghemite (gray), and PCL-grafted maghemite (light gray).

**Table 3.** Thermal Properties of the Composites

| Sample | [Grafted PCL]<br>mg/g Maghemite | Degradation<br>Temperature (°C) <sup>a</sup> | Fusion<br>Temperature (°C) <sup>b</sup> | $\Delta H$ J/g <sup>b</sup> | Crystallinity<br>(%) <sup>c</sup> |
|--------|---------------------------------|----------------------------------------------|-----------------------------------------|-----------------------------|-----------------------------------|
| 3      | 210                             | 260                                          | 45                                      | 5.2                         | 4                                 |
| 4      | 270                             | 280                                          | 48                                      | 8.4                         | 6                                 |
| 8      | 310                             | 285                                          | 49                                      | 9.3                         | 7                                 |
| 5      | 430                             | 340                                          | 52                                      | 14.3                        | 10                                |
| 10     | 855                             | 340                                          | 54                                      | 29.1                        | 21                                |

<sup>a</sup> Determined by TGA.<sup>b</sup> Determined by DSC.<sup>c</sup> Determined by comparison with the heat of fusion of a fully crystalline PCL (139.5 J/g).<sup>28</sup>

lower degradation temperature. This assumption is supported by calculation (degrees of crystallinity were calculated from the ratio of the enthalpy of fusion of grafted PCL chains to that of the free nongrafted crystalline PCL),<sup>28</sup> which indicates that the PCL corona in the composite exhibits a weaker crystallinity compared with nongrafted PCL (Table 3). It is also noticeable that the degradation temperature increases with increasing PCL content in the composite, while concurrently the crystallinity increases. This suggests that when high amounts of PCL are grafted onto the surface, the effect of the inorganic support on chain disorganization becomes less important, resulting in a higher crystallinity of the grafted PCL chains. This brings us to the conclusion that the increase in the grafted PCL amounts is due to polymer chain extension rather than to the formation of a large number of short chains.

## CONCLUSIONS

Superparamagnetic nanocomposite materials were prepared by ROP of CL from a silylated maghemite surface. The polymerization was performed in the presence of aluminum isopropoxide or tin octoate. The covalent anchoring of the polymer was evidenced by the formation of an amide bond between the amino silane and the polymer. The grafting efficiency depends on the NH<sub>2</sub> to metal (Al, Sn) molar ratio. Furthermore, for a given ratio, the grafting efficiency also depends on the initial monomer concentration. Higher PCL grafted amounts were obtained with the aluminum-based catalytic system, which enabled grafting of up to 855 mg of PCL per g of maghemite, whereas tin octoate gave only 600 mg/g under optimized conditions.

Nevertheless, because tin octoate is a less reactive catalyst, the polymerization rate is lower, hence promoting interchange reactions between grafted and nongrafted polymer chains. Benefits of this effect are a full monomer conversion and effective grafting for lower metal to NH<sub>2</sub> ratios.

The reported grafting route produces nanocomposite colloids with PCL contents similar to those obtained with a grafting-to process, but with the advantage that the polymer grafts are terminated with an alcohol group. This function could be used for anchoring specific biological effectors or initiating the polymerization of another monomer, such as ethylene oxide. Such a strategy would lead to the creation of a superficial hydrophilic corona, which would surely improve colloidal stability and the stealthiness of the particles in, for example, administration through the blood compartment.<sup>9</sup>

TGA and DSC analyses seem to support the assumption that the increase in the amount of PCL at the maghemite surface is due to an increase in the length of the PCL chains and not the formation of large amounts of short chains. The superparamagnetic properties of such particles, together with the biodegradability of the corona, create interesting prospects for their use in therapeutic applications.

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