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Silicone Nano/Microstructures Obtained in Ionic Polymerization

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Summary: This work presents a novel surfactant-free method of preparation of silicone hollow nano/microstructures in water. New silicone monomer was synthesized by attaching the unsaturated fatty acid ester – methyl 10-undecenoate (UDM) to the commercial silicone monomer - 1,3,5,7-tetramethylcyclotetrasiloxane (D_4^H) using hydrosilylation reaction. The reaction was catalyzed by Karstedt's catalyst [Pt(0)-divinyltetramethyldisiloxane complex]. That modified monomer, tetra(11-methoxy-11-oxoundecyl)-tetramethylcyclotetrasiloxane ($D_4^{undecyl}$), undergoes self-organization in water. The anionic ring-opening polymerization of $D_4^{undecyl}$ resulted in formation of the silicone polymer (poly-$D_4^{undecyl}$). Both, the silicone monomer and the polymer were dispersed in aqueous medium using sonication. The structures in the dispersions were visualized by cryo-transmission electron microscopy (Cryo-TEM) and optical microscopy. The size of the particles was also determined from dynamic light scattering (DLS) measurements.

Keywords: anionic ring-opening polymerization; Cryo-TEM; hydrosilylation; nanocapsules

Introduction

Hollow nano/microcapsules are interesting structures because of their potential applications as drug carriers, penetration enhancer in cosmetics, solubilizers, protective shells for enzymes or catalyst.[1,2] Liposomes are among the most intensively studied nanosystems.[3,4] That is due to their unique properties such as nontoxicity, biodegradability, as well as simplicity of preparation and control over the composition and size. Unfortunately, the major problem with liposomes is their low stability during storage which is due to their strong tendency for degradation, aggregation, and fusion leading to uncontrolled leakage of the entrapped compounds, e.g., a drug before administration.[3] The well-known method for preparation of more stable structures with controlled size is the polymerization/crosslinking process of the appropriate silicone precursors within vesicle templates.[5–7] However, this technique has also some disadvantage related to inconvenient removal of the surfactant templates.

In this paper we present an innovative method of preparation of silicone hollow structures of controlled sizes without necessity of a surfactant presence. Silicones find a wide variety of healthcare applications due to their unusual properties. For example they are used in many pharmaceutical formulations or in the construction of medical devices.[8] Silicones are well-known for their very high permeability to many biologically active substances as well as for the exceptional chemical and thermal stability. Their low chemical reactivity and

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low surface energy makes them biocompatible. Silicones in conjunction with fatty-acid derivatives create a new hybrid organic-inorganic material. The main idea of this work was to use the ability of fatty acids to self-organize in water and their biocompatibility.[9] For that reason the unsaturated fatty acid ester, methyl 10-undecenoate (UDM), was chosen to modify commercial silicone monomer, 1,3,5,7-tetramethylcyclotetrasiloxane (D_4^H). The modified monomer, tetra(11-methoxy-11-oxoundecyl)-tetramethylcyclotetrasiloxane ($D_4^{undecyl}$) was obtained in hydrosilylation reaction between the unsaturated fatty acid ester and D_4^H in the present of Karstedt's catalyst [Pt(0)-divinyltetramethyldisiloxane complex]. The anionic ring-opening polymerization of the synthesized monomer with concomitant hydrolysis of the ester group yielded the polysiloxane chains with pendant undecanoic acid groups.

Materials and Methods

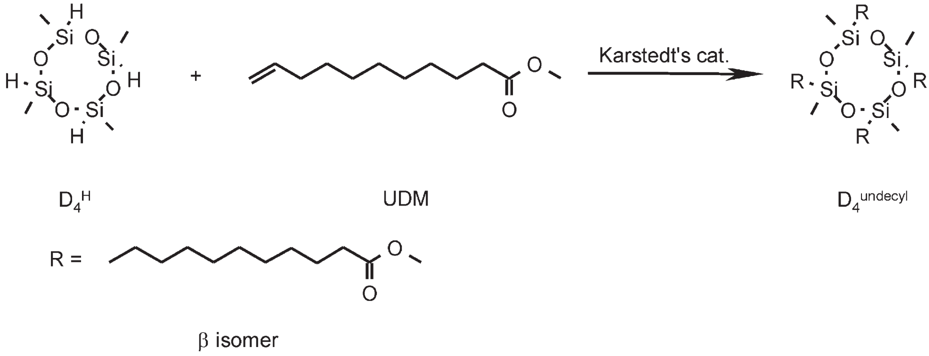
1,3,5,7-Tetramethylcyclotetrasiloxane (D_4^H, ABCR), Karstedt's catalyst (platinum-divinyltetramethyldisiloxane complex in xylene, 2.1-2.4% platinum concentration, ABCR), methyl 10-undecenoate (UDM, Aldrich, 96%) and toluene (Aldrich, anhydrous) were used as received. Millipore-quality water was used for all solution preparations. ^1H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$, on a Bruker AMX 500 Hz instrument. IR spectra were obtained using a Bruker Equinox 55 spectrometer. Liquid substances were deposed between two KBr plates. An inverted microscope Nikon Eclipse TE2000-E (Japan) equipped with a halogen lamp and a 100× objective lens (Nikon Plan Apo VC /1.40 oil) were used for optical microscopy.

Synthesis of the Silicone Monomer

The monomer, tetra(11-methoxy-11-oxoundecyl)tetramethylcyclotetrasiloxane ($D_4^{undecyl}$), was obtained according to a modified procedure published by G. Lligadas [10] (see Scheme 1). The UDM (3.68 g, 0.0178 mol) and D_4^H (1.04 g, 0.0043 mol) were dissolved in anhydrous toluene (9 g). The mixture was bubbled with nitrogen and after 30 minutes 150 μL of Karstedt's catalyst was added at 35 °C. The reaction was carried out at 60 °C for 2 h. The reaction mixture turned light brown when reaching the end of the hydrosilylation. Toluene was then removed under the high vacuum. Crude product was purified by column chromatography using CH_2Cl_2/SiO_2. Obtained viscous oil (3.0 g, yield 65.6%) was characterized by IR, ^1H NMR and ^{13}C NMR spectroscopy.

Anionic Ring-Opening Polymerization

The polymer (poly-$D_4^{undecyl}$) was obtained according to a modified procedure pub-



Scheme 1.
Synthesis of the monomer ($D_4^{undecyl}$).

lished by Lottner[11] (see Scheme 2). 300 mg (0,29 mmol) of $D_4^{undecyl}$ was dissolved in 40 mL of CH_2Cl_2, 73 mL of a 20% methanolic KOH solution and 3 mL of millipore-quality water were added. The mixture was refluxed for 3h and stirred for 17h at room temperature. The resulting white precipitate was filtered off and the filtrate was evaporated. The obtained powder was dissolved in water and acidified with a 7% aqueous HCl solution (pH 1.5). After few hours the formed precipitate was filtered off and washed with water. The obtained polymer was dried at 90 °C for 12h and next, was characterized by IR, ^{1}H NMR and ^{13}C NMR spectroscopy.

Dynamic Light Scattering Measurements

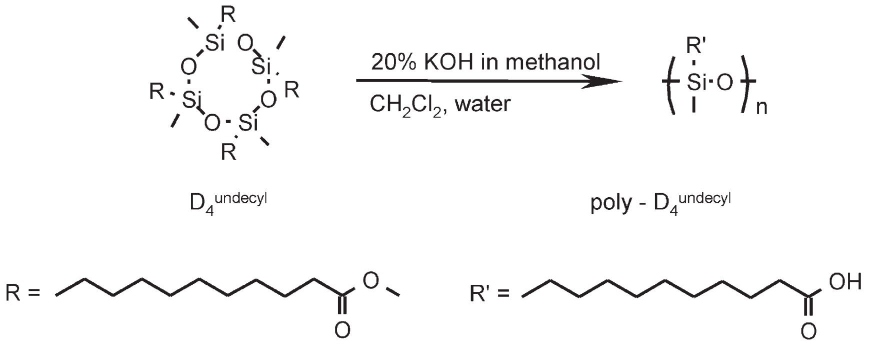
A Malvern Nano ZS light-scattering apparatus (Malvern Instrument Ltd., Worcestershire, UK) was used for dynamic light scattering (DLS) measurements. The z-average diameter (d_z) and dispersity (PD) of the samples were automatically provided by the instrument using cumulant analysis.

Cryo-Transmission Electron Microscopy (Cryo-TEM)

Cryo-TEM was used to visualize the formation of the objects in solutions. This technique allows the least perturbing and direct imaging of the hydrated sample. The samples for cryo-TEM were prepared as described earlier.[12] The sample was vitrified in liquid ethane held at -183 °C and then transferred without reheating into Tecnai Sphera G^{20} electron microscope using Gatan 626 cryo-specimen holder. The images were recorded at 120 kV accelerating voltage and microscope magnification typically of 14 500× using Gatan UltraScan™ 1000 slow scan CCD camera and low dose mode with a dose not exceeding 15 electrons per square Å. Typical value of applied underfocus ranged between 1.5 to 2.3 μm. The applied blotting condition resulted in specimen with thickness ranging from 100 to ca 300 nm.

Results and Discussion

The silicone monomer, tetra(11-methoxy-11-oxoundecyl)tetramethylcyclotetrasiloxane ($D_4^{undecyl}$), was successfully obtained in the hydrosilylation reaction (see Scheme 1). According to the spectral analysis (FTIR, ^{1}H and ^{13}C NMR), the reaction was completed in 2 hours. In the FTIR spectrum of $D_4^{undecyl}$, the bands characteristic for Si-H groups vanished (2164, 890 cm^{-1}) and new bands appeared. They were assigned to the created $Si{-}CH_2$ bonds (1198 and 1172 cm^{-1}). The NMR spectra also confirmed that the hydrosilylation reaction was ended in 2 hours (see Special Data of $D_4^{undecyl}$). In general, the hydrosilylation reaction leads to formation of two different isomers of the hydrosilylated compound: $-Si-CH_2-CH_2-$ (isomer β) and $-Si-CH(CH_3)-$ (isomer α). The molar ratio of isomers α and β strongly



Scheme 2.
Anionic ring-opening polymerization of the monomer ($D_4^{undecyl}$).

depends on the type of catalyst, solvent and structure of the unsaturated compound.[7,13] The analysis of ^{1}H NMR spectrum of our product showed that only isomer β was obtained under our experimental conditions.[14]

Special Data of $D_4^{undecyl}$: ^{1}H NMR (500 MHz, $CDCl_3$, δ): 0.015 (m, 12H, Si$-$C$\underline{H}_3$), 0.485 (m, 8H, C$\underline{H}_2$$-$Si), 1.238 (m, 56H, C$\underline{H}_2$), 1.568 (m, 8H, C$\underline{H}_2$), 2.251 (t, 8H, C$\underline{H}_2$$-$CO), 3.615 (s, 12H, C$\underline{H}_3$-O); ^{13}C NMR (500 MHz, $CDCl_3$, δ) 0.03 (Si$-$$\underline{C}H_3$), 17.8 (Si$-$$\underline{C}H_2$), 23.6 (Si$-CH_2-$$\underline{C}H_2$), 25.6 ($\underline{C}H_2-CH_2-CO$), 30.2 ($\underline{C}H_2$), 34.8 ($\underline{C}H_2-CO$), 52.1 ($\underline{C}H_3-O$), 175 ($\underline{C}=O$); IR (film): 2924, 2855 cm^{-1} (C$-$H); 1743 cm^{-1} (C$=$O); 1258 cm^{-1} (Si$-CH_3$); 1198, 1172 cm^{-1} (Si$-CH_2$); 1080 cm^{-1} (Si$-$O$-$Si).

Preparation of Vesicles

The $D_4^{undecyl}$ (1 wt.%) was dispersed in water at pH 7.1 using vortexing. The structures formed in the dispersion were visualized using the optical microscopy. Figure 1 shows the presence of vesicles with good spherical morphology in the system. The light scattering measurements (DLS) (see Figure 2) was used to determine the size of the vesicles. The monomer dispersed in water formed structures of hydrodynamic diameter in a micro-scale (the diameter in the range 1 - 3 μm). To reduce the size of the objects, the sample was sonicated for 10 minutes at 4 °C with a probe sonicator (Sonics VC 130, Newtown, CT USA). The sonication led to the formation of two populations of vesicles of much smaller sizes (the hydrodynamic diameter around 35 and 190 nm).

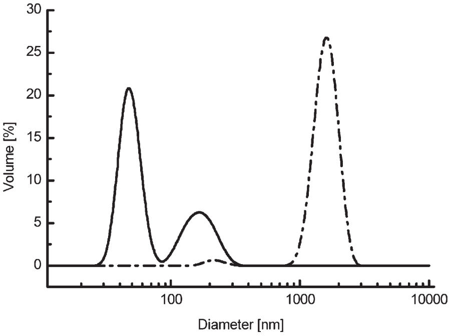


Figure 2.
The light scattering measurements (DLS) of $D_4^{undecyl}$ dispersed in water before (dash dotted line) and after sonication (solid line).

Anionic Ring-Opening Polymerization

The anionic ring-opening polymerization of the synthesized monomer with concomitant hydrolysis of the ester group resulted in formation of polysiloxane chains with pendant undecanoic acid groups (see Scheme 2). The FTIR spectra of the initial monomer and poly-$D_4^{undecyl}$ are shown in Figure 3. Several differences in the spectra can be noticed. The band at 1080 cm^{-1}, present in the monomer spectrum and assigned to the asymmetric Si$-$O$-$Si stretching vibration in small ring cyclosiloxanes splits into two absorption maxima: the first at 1094 cm^{-1} and the

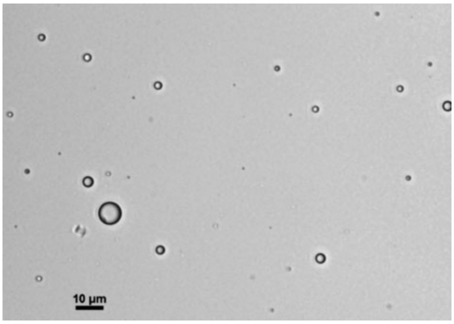


Figure 1.
The object formed by the $D_4^{undecyl}$ dispersed in water before sonication seen by optical microscope.

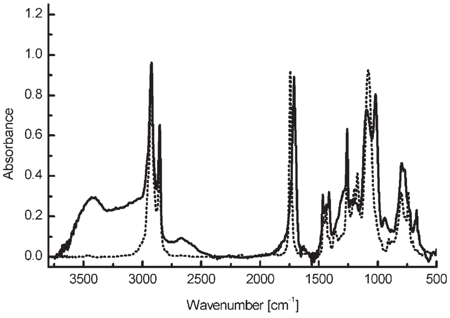


Figure 3.
Infrared spectra of $D_4^{undecyl}$ (dotted line) and the silicone polymer (solid line).

second at 1018 cm^{-1}, which corresponds to formation of longer and linear polysiloxane chains.[15] The new broad bands centered at 3573 and 2656 cm^{-1} appeared, which were assigned to the stretching vibration of OH bond in carboxylic acids and to the hydrogen-bounded carboxylic OH groups in O−H···O=C system. Moreover, the band at 1742 cm^{-1} in the monomer spectrum, characteristic of the C=O stretching vibration in esters move to 1712 cm^{-1}, typical of that in associated carboxylic acids. The analysis of IR spectra showed that the monomer underwent polymerization by anionic ring opening polymerization mechanism with concomitant hydrolysis of ester bonds. Anionic polymerization of cyclosiloxanes is well-established in literature.

IR: cm^{-1} 3573 ν(COOH), 2924, 2853 ν(C−H), 1712 ν(C=O), 1258 ν(Si−CH$_3$), 1229, 1201 ν(Si−CH$_2$), 1092, 1018 ν(Si−O−Si).

Preparation of Nanocapsules

The poly-D_4^{undecyl} (0.5 wt.%) was dispersed in water at pH 8.1 using vortexing. The sample was sonicated for 10 minutes at 4 °C with the probe sonicator. The cryo-TEM micrographs of the structures formed in the sonicated dispersion are presented in Figure 4. The poly-D_4^{undecyl} in aqueous solution creates hollow nanocapsules of disperse sizes. The DLS measurements were performed to determine the size distribution profile of the poly-D_4^{undecyl} nanocapsules. Figure 5 shows the typical profile. Two population of the objects are present in the dispersion with the hydrodynamic diameter around 50 and 120 nm.

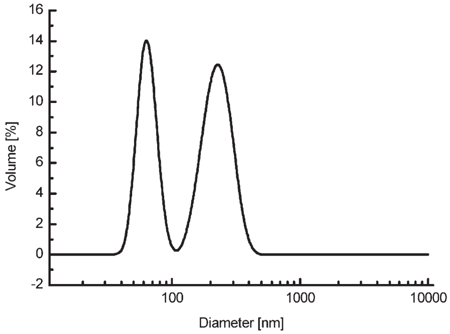


Figure 5.
The light scattering measurements (DLS) of poly-D_4^{undecyl} dispersed in water after sonication.

Conclusion

Novel, surfactant-free method for synthesis of silicone nanacapsules was developed. The hybride monomer D_4^{undecyl} which self-organize in water with a formation of hallow nanostructures was synthesized. Anionic ring-opening polymerization of

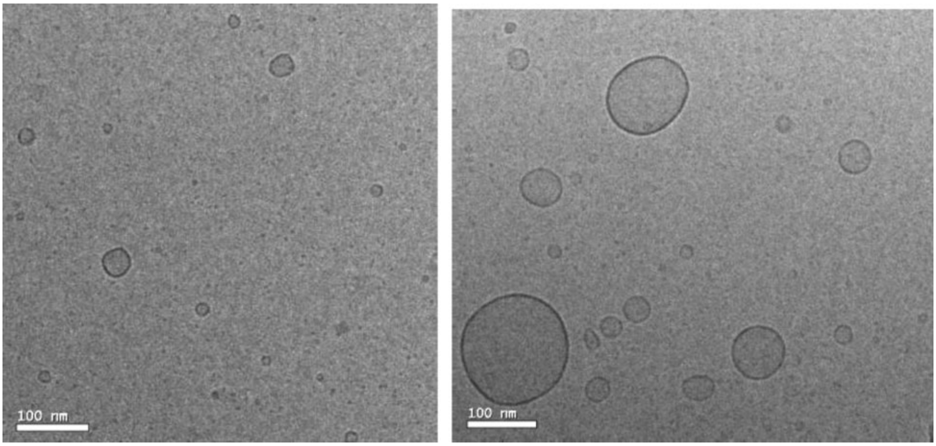


Figure 4.
The cryo-TEM micrographs of the objects formed in the sonicated dispersion of poly-D_4^{undecyl} at pH 8.1.

that monomer results in formation of poly-$D_4^{undecyl}$. It was shown that silicone nano/microcapsules can be easily prepared from $D_4^{undecyl}$ and poly-$D_4^{undecyl}$. Both, the silicon monomer and the polymer are able to self-organize in water with creation of hollow structures. Using sonication, the size of the formed structures can be reduced to nanoscale.

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