Synthesis of Poly(ferrocenylsilane) Polyelectrolyte Hydrogels with Redox Controlled Swelling

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Introduction. Stimulus-responsive hydrogels[1] are attracting much attention due to their potential use in controlled release systems[2] where drugs or cosmetics can be released upon receiving a specific stimulus, or as actuators, artificial muscles or valves.[3,4] Typical stimuli used to date include temperature, pH, ionic strength, light and to a much lesser extent redox stimuli.[5] Redox stimuli may offer fast and reversible switching between states and can be applied externally. In addition, due to access to nanofabricated electrodes or metallic lines, redox-responsive systems can be addressed at the nanoscale. Redox-responsive hydrogels reported in the literature include a ferrocenyl surfactant system showing controlled fluid viscoelasticity,[6] polyaniline-based gels as, e.g., actuators for controlled release[7] or catalysis,[8] an ionically cross-linked polyphosphazene,[9] and a poly(acrylic acid) system comprising *β*-cyclodextrin/ferrocenecarboxylic acid cross-links.[10] In the case of the latter two, cross-links were broken and restored by redox reactions, which led to reversible swelling-contraction or sol- and gel-like behavior.

We have been interested to form redox-responsive poly(ferrocenylsilane) (PFS)[11] polyion hydrogels based on water-soluble PFS polyelectrolyte chains.[12] PFS chains are composed of alternating ferrocene and silane units and can be reversibly oxidized and reduced by chemical and electrochemical means.[13] PFS hydrogels may undergo redox-induced volume changes or changes in viscoelastic properties due to alterations in chain conformation, charge density and polarity of the constituent polymer chains. Redox-responsive PFS polyions in the form of polyelectrolyte multilayers have already shown their potential in colloidal photonic crystals where a reversible tuning of the intergap transmitting state was achieved by switching the redox states of the PFS multilayer.[14]

While poly(ferrocenylsilane) networks based on PFS chains soluble in regular organic solvents have been reported,[15] there are to our knowledge no accounts of PFS polyion hydrogels in the literature. Here we report on the synthesis of two distinct types of poly(ferrocenylsilane) polyion network, featuring permanent positively or negatively charged side groups.

Results and Discussion. A cationic poly(ferrocenylsilane) hydrogel was obtained in two steps. First, high molar mass poly(ferrocenyl(3-iodopropyl)methylsilane) **1** chains[16] were cross-linked with *N*,*N*,*N*′,*N*″,*N*″-pentamethyldiethylenetriamine at room temperature to a lightly cross-linked network (Scheme 1). Subsequently, remaining iodopropyl side groups were converted into positively charged side groups by quaternization using *N*,*N*-dimethylethylamine, resulting in a permanently charged cationic network. Finally, iodide counterions were exchanged to chloride ions.

A polyanionic poly(ferrocenylsilane) hydrogel was also obtained by side group modification of poly(ferrocenyl(3-iodopropyl)methylsilane) **1**. To introduce negatively charged side groups, the carbon nucleophile α-lithio isobutyl methanesulfonate was used.[17] Sulfonate ester carbanions are of interest as nucleophiles, as they enable the introduction of alkanesulfonate ester moieties which, after deprotection, are turned into alkanesulfonate functionalities. Alkylalkane sulfonates are conveniently α-metalated by *n*-butyllithium and can subsequently be alkylated by alkyl halides.[18] Alkylations are especially efficient when alkyl iodides are employed. Reaction of poly(ferrocenyl(3-iodopropyl)methylsilane) **1** with one equivalent of α-lithio isobutyl methanesulfonate led to the formation of PFS network **4** (Scheme 2).

Previously, the use of 3.2 equiv of α-lithio isobutyl methanesulfonate with respect to iodopropyl side groups yielded PFS with isobutyl sulfonate side groups without any cross-linking.[16] An explanation for the cross-linking observed using just 1 equiv of $LiCH_2SO_3$*i*-Bu is shown in Scheme 2. The basic $LiCH_2SO_3$*i*-Bu anion may abstract a proton from the α-position of isobutylsulfonate groups attached to PFS. The resulting carbanion could attack a PFS iodopropyl side group, thus forming a covalent bond between PFS chains. When an excess of $LiCH_2SO_3$*i*-Bu is used, iodopropyl side groups are consumed much more quickly and intramolecular alkylations are not observed.

The isobutyl protecting groups were removed by heating network **4** with tetrabutylammonium iodide in THF.[17] Exchange of the tetrabutylammonium counterions with sodium ions in aqueous NaCl produced the polyanionic network **5** (Scheme 2).

To prove that hydrogels were formed, water-uptake measurements were performed. Gel samples were subjected to several drying and hydration cycles to establish the swelling ratio[19] (by weight) SW which was calculated as follows: $SW = (W_h - W_d)/W_d$, where W_h and W_d are the hydrated and dry sample weights, respectively (Table 1). The difference in swelling ratio is likely caused by a lower cross-link density of the PFS polyanion network. The obtained swelling ratios are typical of ionic networks.[19] For instance, pH sensitive polymers incorporating *N*-acryloyl-*N*′-ethyl piperazine[19a] or *N*,*N*-dimethylaminoethyl methacrylate[19b] showed a strongly pH dependent swelling behavior, with a markedly higher water uptake under conditions when the amine groups were protonated.

Upon swelling in deionized water, the ionic PFS networks **3** and **5** became amber transparent elastic hydrogels. The hydrogels could be reversibly oxidized and reduced electrochemically. Cyclic voltammograms obtained after swelling of cationic network **3** in aqueous $NaClO_4$ show the two oxidation and reduction waves typical of poly(ferrocenylsilanes)[13,20] at maxima of $E_{ox} = -27$ mV and $E_{ox} = +173$ mV. Reduction waves were found at $E_{red} = +47$ mV and $E_{red} = -176$ mV. For the anionic hydrogel **5**, the typical oxidation waves were observed at $E_{ox} = -18$ mV and $E_{ox} = +86$ mV, and reduction waves at $E_{red} = +52$ mV and at $E_{red} = -50$ mV. Ferrocene units at alternating positions are oxidized first, followed by ferrocene units located between ferrocenium sites at a higher potential.[13] Upon electrochemical oxidation, the hydrogels changed color from amber to green-blue and turned back to amber upon reduction. Oxidation of the anionic hydrogel was accompanied by a clear

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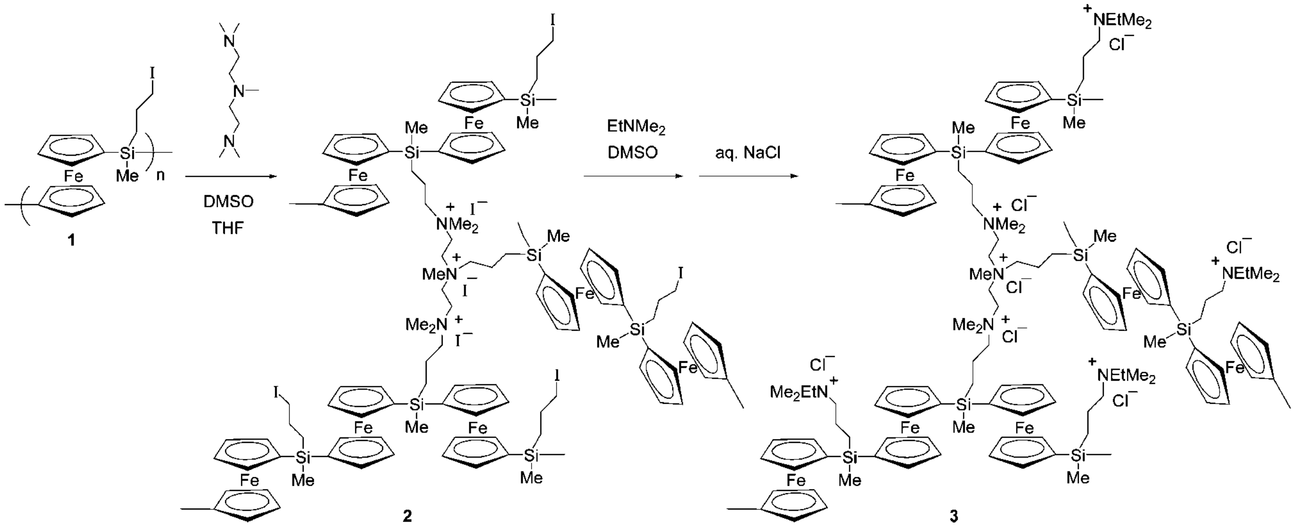
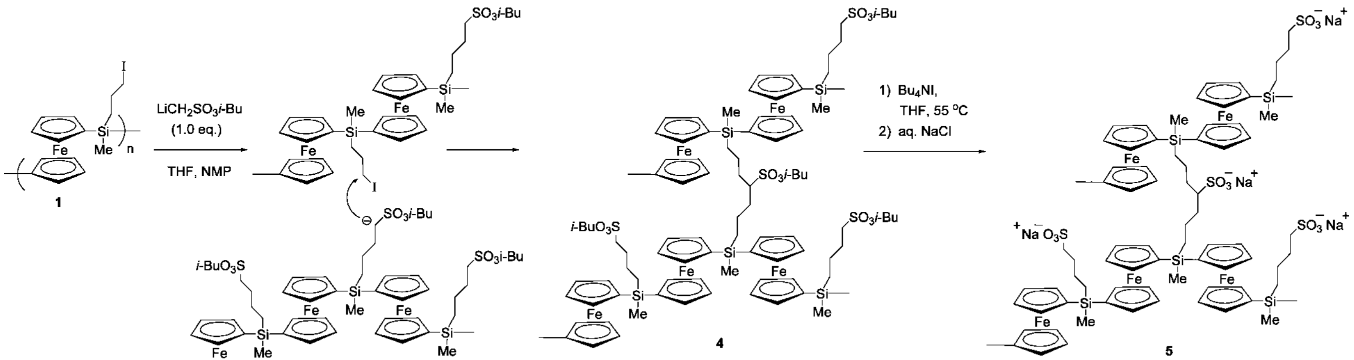
Scheme 1. Synthesis of a Polycationic Poly(ferrocenylsilane) Hydrogel[a]



[a] Poly(ferrocenyl(3-iodopropyl)methylsilane) **1** was lightly cross-linked, using a triamine, to network **2**. Unreacted iodopropyl moieties in **2** were then converted into positively charged side groups using *N*,*N*-dimethylethylamine (EtNMe$_2$). Ion exchange led to the cationic PFS hydrogel **3**.

Scheme 2. Synthesis of a Polyanionic Poly(ferrocenylsilane) Hydrogel[a]



[a] PFS **1** was converted into a PFS featuring isobutylsulfonate side groups using α-lithio isobutyl methanesulfonate. Proton abstraction in the α position of some of these groups led to intermolecular alkylation, producing network **4**. Cleavage of the isobutylsulfonate side groups using tetrabutylammonium iodide (Bu$_4$NI) and ion exchange of the resulting Bu$_4$N$^+$ counterions to Na$^+$ gave PFS hydrogel **5**.

Table 1. Polyion Network Swelling Measurements in Water

	cationic network **3** mass (mg)		anionic network **5** mass (mg)	
	1st swelling	2nd swelling	1st swelling	2nd swelling
dry network	13.3	14.4	3.3	10.1
hydrogel	882	1021	413	1260
swelling ratio	65.3	69.9	124.2	123.7

change in mechanical behavior: the gel collapsed and lost its elastic nature. Upon reduction the network reswelled and regained its elasticity. We ascribe the observed collapse to electrostatic attraction between the positively charged ferrocenium units in the PFS main chain and the negatively charged sulfonate side groups of the polymer. Work in progress includes studies of mechanical properties and actuator response of hydrogels exhibiting controlled degrees of oxidation.

In summary, hydrogels of cationic and anionic poly(ferrocenylsilane) strong polyelectrolytes were obtained by covalent cross-linking approaches.[21] The networks showed a strong swelling in water and could be reversibly hydrated and dehydrated. The extent of charging could be controlled by the redox voltage. In case of the polyanionic hydrogel, oxidation–reduction cycles led to a reversible collapse and reswelling of the network.

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Supporting Information Available: Text discussing the cyclic voltammetry and a figure showing cyclic voltammograms of **3** and **5**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(21) **Materials.** Poly(ferrocenyl(3-iodopropyl)methylsilane) **1** ($M_w = 5.8 \times 10^5$ g/mol, $M_n = 2.0 \times 10^5$ g/mol, $M_w/M_n = 2.9$) was synthesized as described earlier.[16] ^{1}H NMR ($CDCl_3$): δ 0.46 ($SiCH_3$, s, 3H); 1.00 (1-CH_2, m, 2H); 1.87 (2-CH_2, m, 2H); 3.22 (3-CH_2, m, 2H); 3.99 + 4.23 (Cp, m, 8H). ^{13}C NMR ($CDCl_3$): δ −3.12 ($SiCH_3$); 12.15 (1-CH_2); 18.16 (2-CH_2); 28.80 (3-CH_2); 69.97 (Cp−Si); 71.36 + 73.39 (Cp). Dimethylsulfoxide (DMSO) and methanol were obtained from Biosolve and used without further purification. *N,N,N′,N″,N″*-Pentamethyldiethylenetriamine (PMDETA), *N,N*-dimethylethylamine and 1-methyl-2-pyrrolidinone (NMP, anhydrous, 99.5%), were obtained from Aldrich and used as received. Tetrahydrofuran (THF) was distilled from sodium-benzophenone under argon. **Techniques.** ^{1}H NMR spectra were recorded on a Varian Unity Inova (300 MHz) instrument at 300.3 MHz. The chemical shift of the solvent peak at $\delta = 7.26$ ppm was used as a reference. GPC measurements were carried out in THF (flow rate 2.0 mL/min) at 25 °C, using microstyragel columns (bead size 10 μm) with pore sizes of 10^5, 10^4, 10^3 and 10^6 Å (Waters) and a dual detection system consisting of a differential refractometer (Waters model 410) and a differential viscometer (Viscotek model H502). Molar masses were determined relative to narrow polystyrene standards. **Polycation Hydrogel 3.** High molar mass poly(ferrocenyl(3-iodopropyl)methylsilane) **1** (0.5044 g, 1.273 mmol repeat units) was dissolved in THF (2 mL), and subsequently DMSO (1 mL) was added. To the solution was added PMDETA (28 mg, 0.161 mmol) in THF (0.2 mL). After 3 h at 20 °C, a gel had formed. After agitation on a shaking platform for another h, *N,N*-dimethylethylamine (0.54 g, 7.4 mmol) was added and the gel was left for 24 h. Upon conversion of the iodopropyl side groups into quaternary ammonium groups, the gel shrinks due to polymer precipitation. DMSO (3 mL) and *N,N*-dimethylethylamine (0.50 g, 6.8 mmol) were added which caused the cross-linked PFS to swell again, since the polycation is fully compatible with DMSO. After another 24 h, the gel was immersed in NaCl solution (0.1 M, 100 mL) to exchange the iodide counterions with chloride counterions. The NaCl solution was replaced after 6 h for in total six times. The gel was then immersed in Milli-Q which was replaced repeatedly to remove excess NaCl from the gel. **Polyanion Hydrogel 5.** A solution of isobutyl methanesulfonate (0.76 g, 5.0 mmol) in dry THF (10 mL) was cooled under argon to −90 °C, and *n*-BuLi (2.4 mL, 3.8 mmol) was added dropwise. After this was stirred for 20 min, a solution of **1** (1.51 g, 3.8 mmol r.u.) in THF (15 mL) and NMP (6 mL) was added dropwise using a syringe. Traces of **1** in the syringe were taken up with dry THF (5 mL) and also added. The solution was brought to −50 °C and stirring was continued at that temperature for 8 h. After subsequent stirring overnight, the temperature of the reaction mixture reached room temperature. By then, the polymer solution had turned into a gel. Removal of NMP was achieved by adding methanol (100 mL) which caused the gel to collapse. The methanol was replaced three times and finally decanted. To cleave the isobutylsulfonate groups, NBu_4I (2.2 g, 6.0 mmol) in THF (30 mL) was added and the gel was heated at 55 °C for 16 h. The ionic nature of the gel caused it to collapse, allowing the THF to be decanted. Deprotection was continued in methanol (30 mL) containing NBu_4I (2.2 g, 6.0 mmol) at 55 °C for 48 h. The gel was immersed in MeOH/Milli-Q water (75/150 mL) which was replaced several times to remove NBu_4I. Exchange of the NBu_4^+ ions into Na^+ counterions was performed against 0.05 M NaCl (3 × 200 mL). Excess NaCl was finally removed by immersion in Milli-Q water. **Swelling Measurements.** Gel samples were dried under a slow stream of nitrogen to a constant weight and then immersed in Milli-Q water for 6 h. Excess water was removed and the weight of the hydrated gel was established. Drying and rehydration was repeated several times. **Cyclic Voltammetry.** Electrochemical measurements were carried out on hydrogels swollen in aqueous $NaClO_4$ (0.1 M). Cyclic voltammograms were recorded between −0.5 and +0.5 V at a scan rate of 50 mV/s, using a Hg/Hg_2SO_4 reference electrode, a Pt counter electrode, and an indium-tin oxide (ITO) surface, supporting the hydrogel, as a working electrode.

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