Star Shaped Polyglycidols End Capped with Vinyl sulfonate Groups and Conjugation Reaction with Dodecylamine

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Summary: The synthesis of six arm star shaped polyglycidols followed by end capping with vinyl sulfonate groups is reported. The obtained multifunctional polymers show excellent reactivity towards amines. The addition of amines to the vinyl sulfonate groups was proven via NMR spectroscopy.

Keywords: star shaped polyglycidols; vinyl sulfonate functional groups

Introduction

Polyglycidols and their derivates have gained much attention in biomedical applications due to their high functionality, solubility in aqueous media and biocompatibility. Starting with polyglycidols biomimetic polymers were prepared by attaching various building blocks to the hydroxymethyl side chains. Several groups have studied the anionic and cationic polymerization of glycidol leading to branched polymers.[1,2] The obtained polyglycidols show no toxicity in cell culture experiments while oligoglycidols are already approved as food and pharmaceutical additives by FDA.[3,4] To increase the number of reactive end groups the architecture of the polymer was changed to star shaped instead of linear polymers.

To obtain polyglycidols with well-controlled architecture, molecular weight and molecular weight distribution, the hydroxy group of the monomer has to be protected with a suitable protecting group and a multifunctional initiators have to be used.[5,6]

For multifunctional polyglycidols the hydroxymethyl side groups were converted by polymer analogous reactions: (i) via carboxy methylation carboxylic acid groups were introduced, (ii) via esterification polyglycidols with long alkyl chains were obtained, and (iii) via cyano ethylation followed by hydrogenation amine groups were achieved.

By reaction of the hydroxyl group in the side chain with phenylchloroformate polyglycidols with active carbonate groups in the side chain were obtained and a variety of functional groups have been introduced by reactions with functional amines.[6]

Another possibility for the synthesis of multifunctional polyglycidols is the use of highly reactive vinyl sulfonate groups. These groups are showing an orthogonal functionality compared to the hydroxy groups and are known to readily react with amines.[7]

In this communication we present the synthesis of six arm star shaped polyglycidols end capped with vinyl sulfonate groups and their further reaction with amines.

Synthesis

Star shaped polyglycidols were synthesized using dipentaerythritol as multifunctional initiator and ethoxyethyl glycidyl ether (EEGE) as monomer. The end groups of the obtained polymer were further functionalized by reaction with 2-chloroethylsulfonylchloride to form vinyl sulfonate groups (Figure 1). To prove the reactivity of the multifunctional polymers a model

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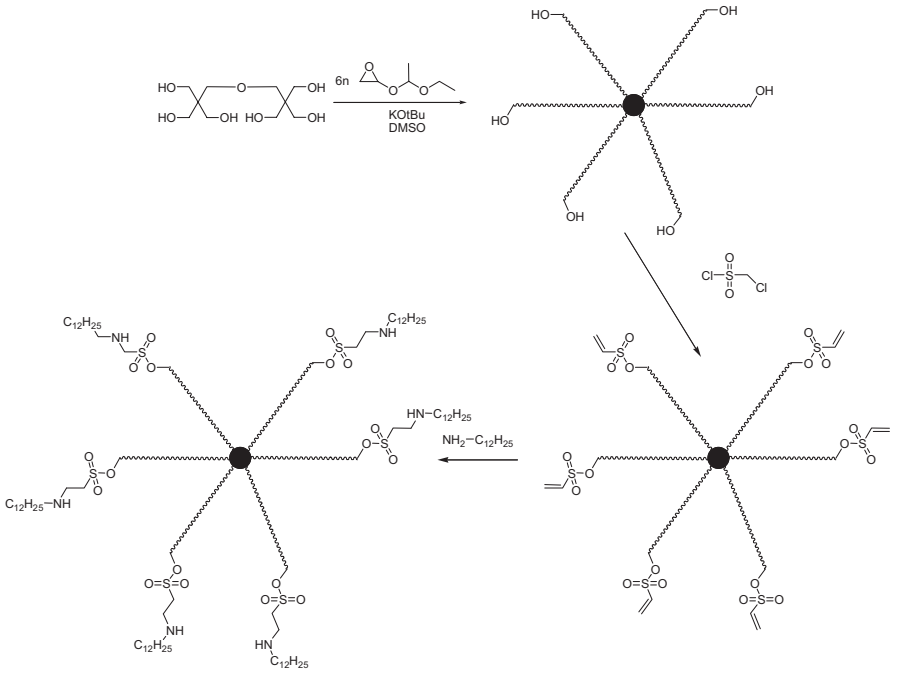

Figure 1.
Synthesis of six arm star shaped poly(ethoxyethyl glycidyl ether) (PEEGE) end capped with vinylsulfonyl groups and consecutive reaction with dodecylamine.

reaction with dodecylamine was carried out followed by removal of the protection group under acidic conditions.

In the first step dipentaerythrithiol (566 mg, 2.26 mmol) was activated with 0.1 eq. per hydroxy group of potassium tert. butoxide (1.36 mL, 1.36 mmol) and then ten eq. per hydroxy group of EEGE (20 mL, 136 mmol) had been added resulting in a polymer with a molecular weight of 8,500 g mol^{-1} and a molecular weight distribution of 1.08 determined by size exclusion chromatography (SEC) relative to PMMA standards. The formation of the star shaped polymer was verified by quantitative carbon NMR spectroscopy which showed that all six hydroxy groups successfully initiated the polymerization.

In the second step the obtained polymer (10 g, concentration of end groups 6.6 mmol) (was treated with four eq. per end group of triethylamine (3.4 mL, 26 mmol) and two eq. of 2-chlorosulfonylchloride (1.2 mL, 12 mmol) forming the vinyl sulfonate end capped polymer. End group analysis via NMR spectroscopy showed one group per eleven EEGE repeating units (Figure 2).

Furthermore IR spectroscopy verified the end capping of the polymer by the vinyl sulfonate functionality ($\lambda = 1366\,\mathrm{cm}^{-1}$, asymmetrically SO_2 stretching vibration).

SEC-Measurements of the end capped polymer showed no broadening of the molecular weight distribution to 1.09.

In the last step the reactivity of the end capped polyglycidol was proven by reaction with dodecylamine. The polymer was combined with three eq. of dodecylamine forming the expected conjugate without any additional base at room temperature. Afterwards the acetal protecting group of the PEEGE was removed under acidic conditions. The addition of the amine could be clearly confirmed by the disappearance of the vinyl groups ($\delta = 6$-7 ppm) (Figure 3).

Furthermore the obtained polyglycidol functionalized with dodecylamine showed a

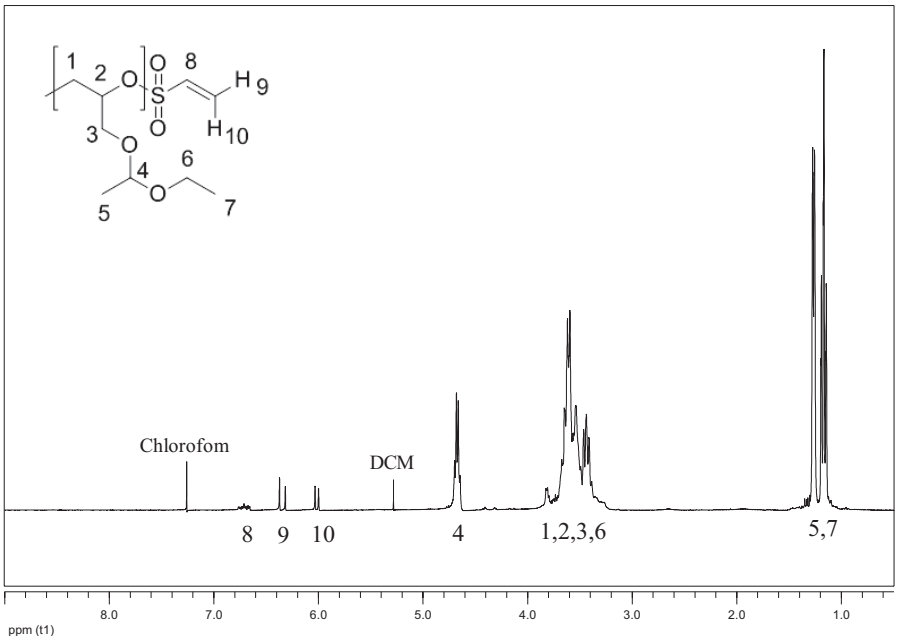

Figure 2.
[1]H-NMR spectrum of a six arm star shaped PEEGE end capped with vinylsulfonyl groups.

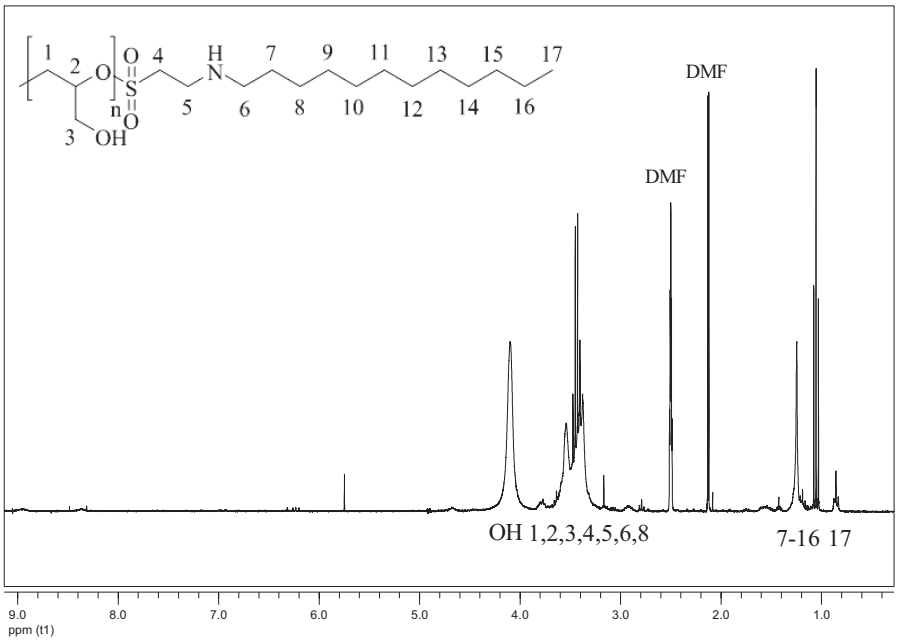

Figure 3.
[1]H-NMR spectrum of a six arm star shaped polyglycidol functionalized with dodecylamine.

good solubility in non-polar solvents like $CHCl_3$ in difference to non-functionalized polyglycidol which is only soluble in highly polar solvents like water or DMF. This change in behavior showed the successfully addition of the long alkyl chain on the highly hydrophilic polymer.

Conclusion

It has been shown that the end capping of six arm star shaped polyglycidols with vinyl sulfonate groups is possible via a polymer-analogous reaction. A 100% functionalization degree was determined by NMR spectroscopy. The reactivity of the introduced functional groups was proven by reaction of the multifunctional polymers with dodecylamine as a model reaction monitored by NMR spectroscopy.

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