Synthesis of Boc Protected Block Copolymers Based on para-Hydroxystyrene via NMRP

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Summary: Nitroxide mediated free radical polymerization (NMRP) was used for the preparation of orthogonally protected block copolymers based on para-hydroxystyrene. The polymers have a low polydispersity and an active chain end. By a series of polymer analogous reactions, a partly deprotected block copolymer was synthesized consisting of a block with unprotected phenolic OH groups and a further block which is protected by the thermolabile Boc group.

Keywords: diblock copolymers; p-hydroxystyrene; macroinitiators; NMRP; protecting groups

Introduction

A characteristic feature of block copolymer systems is the repulsion between unlike blocks causing microphase separation at mesoscopic length scales.[1] The size and type of ordering can be controlled varying the molecular weight, chemical structure, molecular architecture and composition of the block copolymers. Understanding and controlling the morphology of a block copolymer is essential for any application.[2]

Here we employ block copolymers based on p-hydroxystyrene. They consist of a block with protected phenolic OH groups and a further block with unprotected phenolic OH groups. The big difference in the polarity of the two blocks causes a strong incompatibility which result in a phase separation even for blocks of low molecular weight. The gradual removal of a protecting group leads to a change of the composition of the block copolymer which should also affect the morphology. This coherence is of great interest especially for phase investigations in thin films (thickness <100 nm). The formation of a defined nanostructure requires usually block copolymers

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with a very low polydispersity.[2,3] Therefore the synthesis of the block copolymer was carried out applying nitroxide mediated free radical polymerization (NMRP).[4] As the phenolic OH group act as a transfer reagent the direct polymerization of unprotected p-hydroxystyrene is not practicable.[5] To overcome this problem orthogonally protected p-hydroxystrene derivatives were employed. Selective removal of only one protecting group leads to the desired partly deprotected, phase-separated block copolymer. Of special interest was the preparation of block copolymers with one Boc protected block since those protecting groups can be removed by simple thermal treatment.

Experimental

Characterization:

^{1}H NMR measurements were performed in 5 mm diameter tubes with a Bruker DRX 500 NMR spectrometer at 500.13 MHz. Acetone-d_6 has been used as solvent for the polymers as well as for internal calibration of the spectra.

GPC measurements were carried out on a Knaur modular equipment with two different columns and solvents. The homopolymers and the protected block copolymers were measured with a MERCK LiChrogel PS 40 column and with chloroform as solvent. Polystyrene standards were applied for calibration. The partly deprotected block copolymers were measured with two Zorbax Trimodal-S columns in dimethyl acetamide which contained also 2 vol% water and 3.0 g/L LiCl. Here PVP standards were used for calibration.

TGA measurements were performed on a Perkin Elmer TGA 7 with a heating rate of 10 K/min.

Materials

When not specified all employed chemicals were purchased form Fluka, Aldrich and Merck and were also of analytical grade.

Synthesis of monomer and polymers

The synthesis of the monomer TBDMS-OSt and the procedure of the polymerization was performed similar as already described in literature.[6]

Synthesis of the initiators and polymerization

Initiator 1 and initiator 2 have been synthesized similar to literature.[7-10] The homopolymers as well as the block copolymer **A** were synthesized via NMRP similarly as described previously.[6]

Polymer analogous reactions

Synthesis of block copolymer **B**

In a mixture of 60 mL dioxane and 12 mL methanol 2 g of block copolymer **A** was dissolved. After addition of 4 mL of hydrazine monohydrate the reaction was stirred for 48 h. The polymer was precipitated in 400 mL water, recovered by filtration, dissolved in a mixture of ethyl acetate and methanol (1:3) and precipitated in water again. After filtration, the polymer was dried at 70 °C in a vacuum oven and amounted to 1.4 g of block copolymer **B.**[12]

Synthesis of block copolymer **C**:

1 g of block copolymer **B** was dissolved in 10 mL ethyl acetate followed by the addition of 1.8 g potassium carbonate and 2 g of di-tert-butyl dicarbonate. After stirring for 24 h the polymer was precipitated in 400 mL methanol and recovered by filtration. The obtained precipitate was purified by reprecipitation in methanol and dried in vacuum at 40 °C to give 1.2 g of block copolymer **C.**[13,14]

Synthesis of block copolymer **D**:

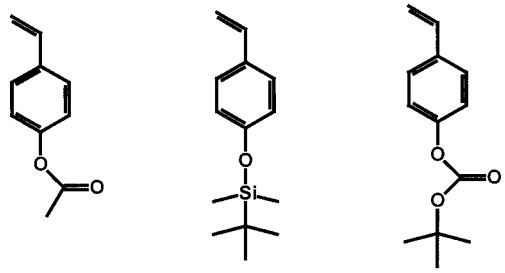
0.8 g of block copolymer **C** and 4 mL of a 1 M solution of tetra(n-butyl) ammonium fluoride in THF were mixed in 6 mL of dry THF at room temperature. After stirring for 4 h, the polymer was precipitated in 400 mL of a 1:1 mixture of water and methanol. Precipitation was repeated several times to remove impurities, yielding 0.5 g of block copolymer **D.**[13]

Polymerization of protected p-hydroxystyrene derivatives via NMRP

For this study, the following orthogonally protected p-hydroxystyrene derivatives were used as monomers for NMRP: p-acetoxystyrene (Ac-OSt), p-tert-butyldimethylsilyloxystyrene (TBDMS-OSt) and p-tert-butoxycarbonyloxystyrene (Boc-OSt).

Figure 1 shows the applied monomers and also the appropriate reagent for the selective removal

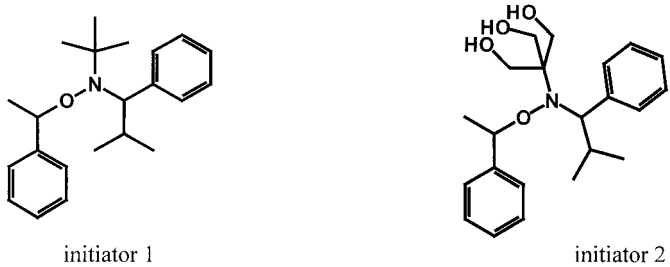
of the protecting group.



Abbreviation:	Ac-OSt	TBDMS-OSt	Boc-OSt
Removal by:	hydrazine monohydrate	fluoride	heat or H^+

Figure 1: Protected p-hydroxystyrene derivatives

Figure 2 show the two different initiators which were applied for NMRP. They were synthesized very similar as already described in literature[7-10] and are known as "Hawker-adducts". In contrast to initiator 1, initiator 2 contains three hydroxyl groups which are able to stabilize the free nitroxide radical. Hence it follows that the polymerization can be conducted at much lower temperatures. This can be very important for polymerizations of monomers which contain a thermolabile group like the Boc group.



initiator 1 initiator 2

Figure 2: Applied initiators for NMRP

Table 1 summarizes some results of the polymerizations carried out with initiator 1 and

initiator 2. All polymerizations with initiator 1 were run in bulk at 120 °C for approximately 16 hours. In respect of the amount of the initiator two equivalents of acetic anhydride were additionally added as it works as a rate accelerating additive.[11] In contrast to Ac-OSt and TBDMS-OSt, which resulted in well controlled homopolymers with narrow molar mass distribution, Boc-OSt could not be polymerized under these conditions.

Polymerizations with initiator 2 were run without addition of acetic anhydride as it most likely reacts with the OH groups of the initiator which results in a high polydispersity (PD). Firstly we polymerized Ac-OSt also at 120 °C but only over a period of 195 minutes. Despite the short reaction time we achieved already 56 % conversion and the molecular weight of the obtained poly(Ac-OSt) is 9900 g/mol. This is in good agreement with the theoretical value ($M_{n,cal}$ = 9100 g/mol, conversion implemented). Moreover the PD of poly(Ac-OSt) is only 1.16 which is comparable with those obtained for the polymerizations with initiator 1. These results underline the high efficiency of this initiator for NMRP. Due to the thermal lability of the Boc group, the polymerization of Boc-OSt was conducted at only 85 °C but over a period of 9 days. Under these conditions it was possible to polymerize Boc-OSt in a controlled fashion but about 7 % of the Boc groups were degraded. These results told us that the preparation of Boc group containing block copolymers cannot be accomplished by the direct polymerization of Boc-OSt. In order to achieve our goal anyhow we decided to apply a series of polymer analogous reactions.

Table 1: Results of the polymerization of protected p-hydroxystyrene derivatives

Initiator	**Homopolymer**	**M_n [g/ mol]**	**$M_{n,cal}$ [g/ mol]**	**PD**	**Yield [%]**
1	poly(Ac-OSt)	11150	11600	1.18	85
1	poly(TBDMS-OSt) macroinitiator (**MI**)	9800	11900	1.16	82
2	poly(Ac-OSt)	9900	9100	1.16	56
2	poly(Boc-OSt)	16500	6600	1.38	26

Polymer analogous reactions on block copolymers based on p-hydroxystyrene

The starting point was the preparation of the block copolymer poly(TBDMS-OSt)-b-poly(Ac-OSt) **A**. In order to achieve this, the homopolymer poly(TBDMS-OSt) was taken as macroinitiator **MI** and the second block was formed by sequential monomer addition of Ac-OSt. The block copolymer formation was also conducted at 120 °C and also with the addition of two equivalents of acetic anhydride in respect to the amount of macroinitiator. Diglyme was additionally added to dissolve all poly(TBDMS-OSt). After polymerization for approximately 24 hours we obtained block copolymer **A** in 81 % yield and with a molar mass of 42700 g/mol and a polydispersity of 1.19. Scheme 1 gives an overview over the subsequent single reaction steps while the corresponding ^{1}H NMR spectra are presented in Figure 3. After formation of block copolymer **A** all acetyl groups were removed using hydrazine monohydrate giving block copolymer **B**.[12] Block copolymer **C** was obtained by the reaction of block copolymer **B** with di-tert-butyl dicarbonate.[13, 14] The following treatment of **C** with tetrabutylammonium fluoride (TBAF) resulted in the orthogonal removal of the TBDMS groups leading to the desired block copolymer **D**.[13]

Table 2: Results of the preparation of the orthogonally protected block copolymers

block copolymers	**macroinitiator MI**		**block copolymers**		
	Mn [g/mol]	**PD**	**M_n [g/mol]**	**$M_{n,cal}$ [g/mol]**	**PD**
Poly(TBDMS-OSt)-b-poly(Ac-OSt) **A**	9800	1.16	42700	40000	1.19
Poly(TBDMS-OSt)-b-poly(H-OSt) **B**	—	—	46900	40000	1.63
Poly(TBDMS-OSt)-b-poly(Boc-OSt) **C**	—	—	48700	40000	1.20
Poly(H-OSt)-b-poly(Boc-OSt) **D**	—	—	51500	40000	1.52

All ^{1}H NMR (Figure 3) spectra were recorded in acetone-d_6 as solvent and show clearly that all polymer analogous reactions are orthogonal and highly effective.

In Table 2 the molecular weight (M_n) and the polydispersity (PD) of the macroinitiator and the derived block copolymers **A**, **B**, **C** and **D** are summarized. The molecular weight and the polydispersity was determined by GPC. The GPC measurements of the protected block copolymers **A** and **C** and the macroinitiator **MI** were carried out in chloroform while for the partly deprotected block copolymers **B** and **D** dimethyl acetamide was used. However in the GPC curve of the partly deprotected block copolymer **B** and also in the curve of block copolymer **D** a shoulder in the range of increasing molecular weight is clearly discernible. This means that under the conditions of the GPC measurement a fraction of a higher molecular weight is present. Since this higher molecular fraction is not observable in the GPC curve of block copolymer **C** we assumed that this fraction is caused by a simple physical association of at least two single molecules. This assumption is also corroborated by the fact that hydrogen bonding caused by phenolic OH groups are significantly stronger than those of normal aliphatic alcohols. Therefore the preparation of a molecular dispersed solution of a partly deprotected and thus, amphiphilic block copolymer like **B** and **D** is presumably much more difficult than for protected polymers like **A** and **C**. This would also explain the higher polydispersity of the block copolymers **B** and **D** compared with those of **A** and **C**.

In Figure 4 the GPC eluation peaks of the macroinitiator poly(TBDMS-OSt) **MI** and the derived block copolymers **A** and **C** are presented. All GPC curves are monomodal and have no shoulders. This implies that the initiation by the macroinitiator is highly efficient and the formation of well controlled and pure block copolymers is verified.

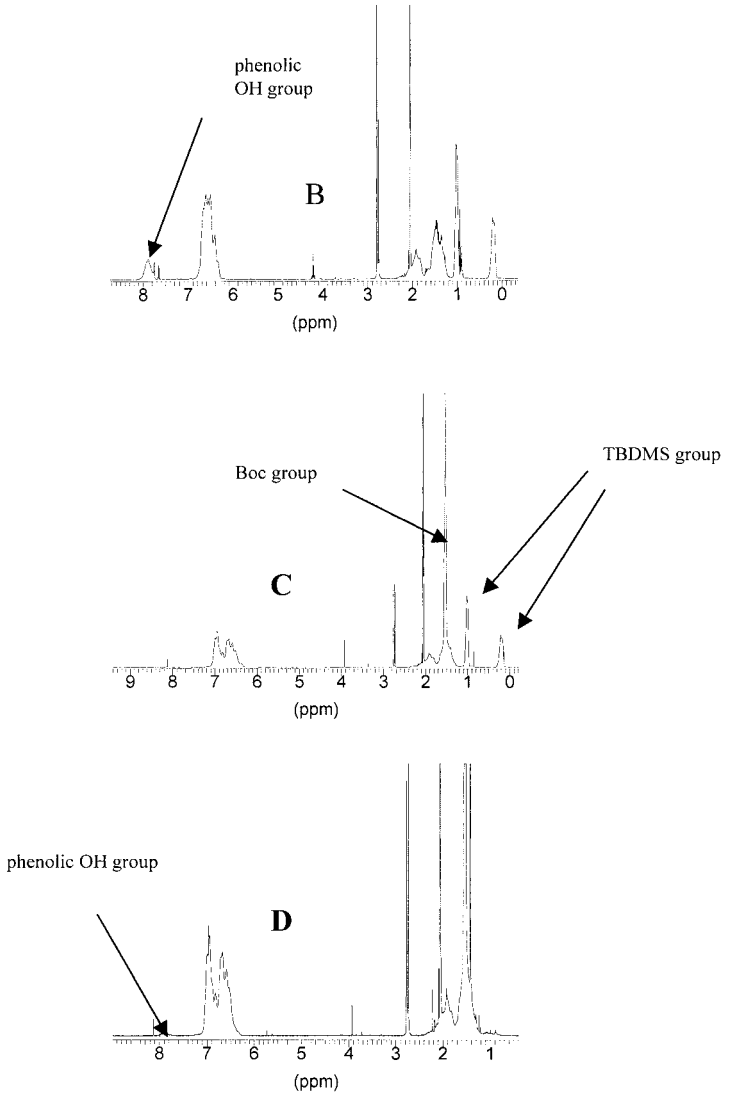


Figure 3: Proton NMR spectra of the block copolymers **B**, **C** and **D** measured in acetone-d_6

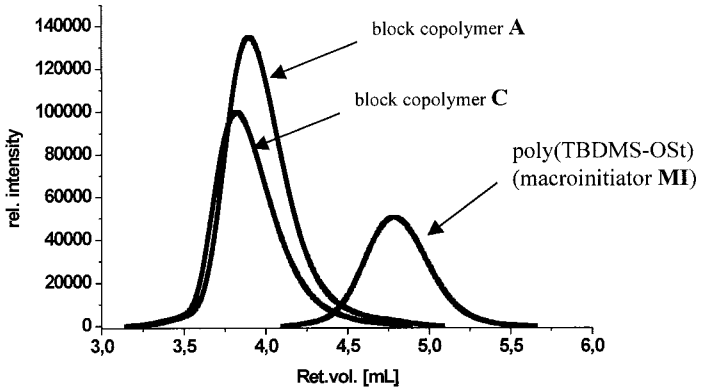


Figure 4: GPC eluation curves of the macroinitiator poly(TBDMS-OSt) **MI** and the derived block copolymers **A** and **C** measured in chloroform

TGA investigations of the block copolymers C and D

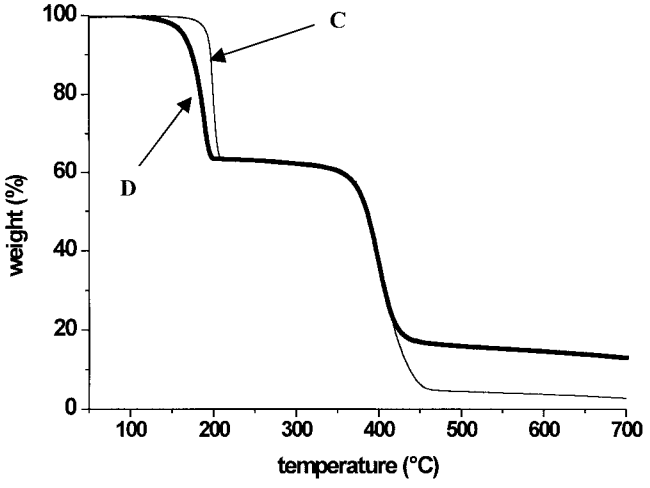


Figure 5: TGA curves of the polymer **C** and **D**

Figure 5 shows the TGA curves of the block copolymers **C** and **D**. While heating up with 10 °C per minute all Boc groups were removed near to 200 °C which is in good agreement with results already presented in literature.[15] But it is worthwhile to mention that the degradation of the Boc groups in the partly deprotected block copolymer **D** (thick line) started at least 10 K earlier than in block copolymer **C** (thin line).

Conclusion

Orthogonally protected block copolymers based on p-hydroxystyrene were successfully prepared with high control over molar mass and narrow molar mass distribution using NMRP. A quantitative and orthogonal removal of the acetyl groups, the TBDMS groups and the Boc groups was accomplished by employing hydrazine monohydrate, TBAF and heat, respectively. Using series of polymer analogous reactions a partly deprotected block copolymer consisting of a block with unprotected phenolic OH groups and a second block protected with Boc groups was synthesized.

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