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# Anionic Polymerization of *para*-(1-Ethoxy ethoxy)styrene: Rapid Access to Poly(*p*-hydroxystyrene) Copolymer Architectures

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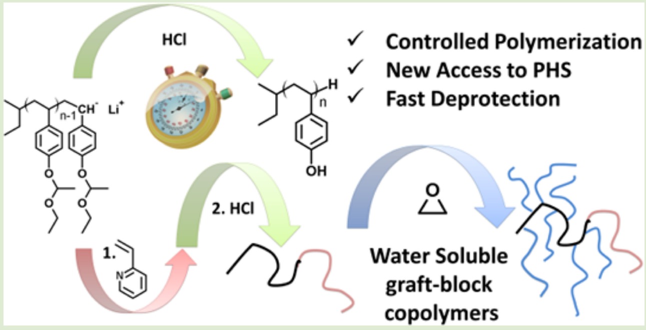
*Supporting Information*

**ABSTRACT:** Living anionic polymerization of *para*-(1-ethoxy ethoxy)styrene (*p*EES) resulting in molecular weights between 2700 and 69 000 g $mol^{-1}$ and polydispersity indices ≤1.09 is introduced. P*p*EES can be used as a precursor for the synthesis of well-defined poly(*p*-hydroxystyrene) (PHS) architectures, enabling facile and rapid acidic deprotection at room temperature within a few minutes. In addition, a series of block copolymers containing *p*EES and 2-vinylpyridine (2VP) have been synthesized by anionic block copolymerization, with varied block ratios ($X_{2VP}$) between 0.13 and 0.83. Characterization by $^1$H NMR spectroscopy, size exclusion chromatography (SEC), and differential scanning calorimetry (DSC) was carried out, and all polymers have been deprotected, leading to the respective PHS-*b*-P2VP block copolymers. Furthermore, PHS-*b*-P2VP has been used as a macroinitiator for the anionic ring-opening polymerization of ethylene oxide (EO) to generate ((PHS-*g*-$PEO_{51})_{13}$-*b*-$P2VP_{40}$) graft-block copolymers.



Despite the enormous success of controlled radical polymerization techniques in recent years, living anionic polymerization still plays an important role for the synthesis of well-defined macromolecules, especially with regard to block copolymers, terminally functionalized polymers, and complex polymer architectures.[1−5] However, it is often challenging to prepare functional polymers by living anionic polymerization due to the high reactivity of the living carbanion toward most functional groups located at monomers,[6−9] initiators,[10−12] or termination reagents.[13−16] Thus, protected monomers have to be employed for the polymerization. Facile removal of the protective groups is a key feature in this context.

Poly(4-hydroxy styrene) (PHS) represents an interesting hydroxyl-functional analogue of polystyrene, especially with regard to polymer modification reactions. For instance, Grayson et al. utilized PHS in several works as a macroinitiator for the synthesis of dendronized architectures.[17,18] At present, 4-*tert*-butoxystyrene (*t*BuOS) is generally used as the favored protected precursor monomer for the synthesis of PHS by carbanionic or living radical polymerization techniques.[19−21] On the other hand, acetal protected glycidyl ethers (ethoxy ethyl glycidyl ether, EEGE) have been frequently used in oxyanionic epoxide polymer chemistry.[2,15,22−24]

In analogy to this class of monomers, Endo et al. recently introduced *p*-(1-ethoxy ethoxy)styrene (*p*EES) for the free radical polymerization as an alternative to 4-*tert*-butoxy styrene (*t*BuOS).[25] This structure may be viewed as a styrene-based, EEGE-analogous monomer, since it possesses the same acetal protecting group. To the best of our knowledge, Endo's work represents the first report on the *p*EES monomer.

Our current work describes the first anionic polymerization of *p*EES and also introduces block copolymers containing *p*EES and 2-vinylpyridine (2VP) (see Supporting Information for experimental details). Subsequent acidic hydrolysis of the acetal protecting group at the *p*EES results in PHS or the corresponding block copolymers, respectively. Remarkably, deprotection of P*p*EES is achieved at room temperature in less than 5 min, as will be detailed below. In addition, the PHS-*b*-P2VP block copolymers have also been applied as macroinitiators for the ring-opening polymerization of ethylene oxide (EO) to generate amphiphilic poly(*p*-hydroxystyrene-*g*-poly(ethylene oxide))-*b*-poly(2-vinylpyridine) ((PHS-*g*-PEO)-*b*-P2VP) graft-block copolymers (Scheme 1).

A series of different homopolymers, block copolymers, and graft-block copolymers consisting of a P*p*EES-block and a P2VP-block have been prepared by living anionic polymerization to demonstrate the versatility of the approach presented here. P*p*EES was synthesized in THF at −90 °C. To the best of our knowledge, this polymer has not been synthesized with any controlled polymerization technique to date. The homopolymers prepared showed molecular weights in the range of 2700−69 000 g·$mol^{-1}$, with low polydispersity (PDI) (see Table 1).

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**Scheme 1. Synthetic Strategy for PHS-*b*-P2VP and Amphiphilic ((PHS-*g*-PEO)-*b*-P2VP) Graft-Block Copolymers**

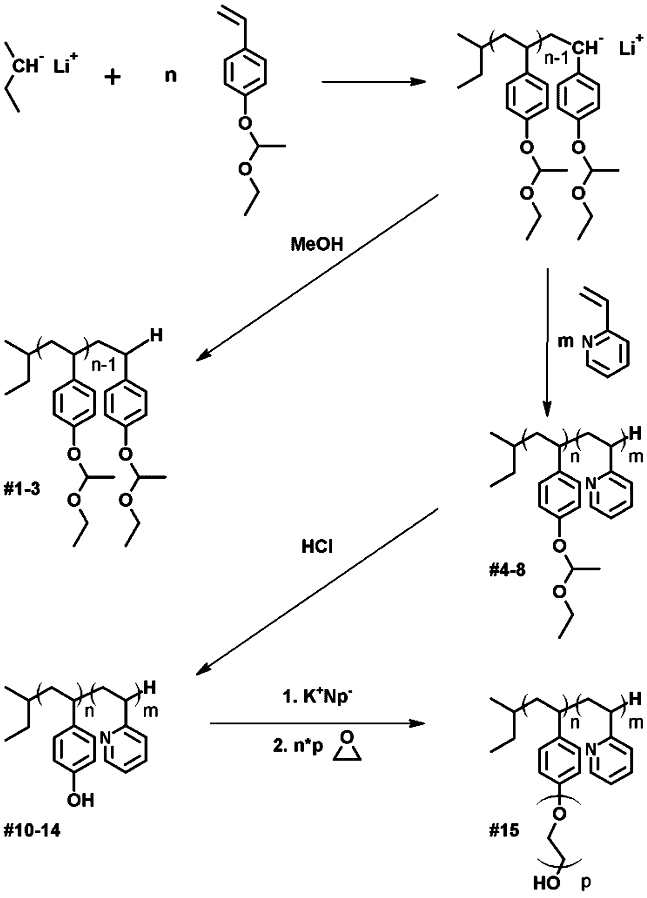

**Table 1. Characterization Data for Homo and Block Copolymers Containing *p*EES and 2VP**

| no. | polymer[a] | $X_{(2VP)}$[a] | Mn[a] | Mn[b] | PDI[b] | $T_g$/°C |
|---|---|---|---|---|---|---|
| 1 | P*p*EES$_{14}$ | 0 | 2700 | 3100 | 1.09 | 6.1 |
| 2 | P*p*EES$_{22}$ | 0 | 4000 | 4100 | 1.06 | 8.7 |
| 3 | P*p*EES$_{360}$ | 0 | 69000 | 68500 | 1.03 | 26.6 |
| 4 | P*p*EES$_{33}$-*b*-P2VP$_5$ | 0.13 | 6900 | 6700 | 1.09 | 17.8 |
| 5 | P*p*EES$_{17}$-*b*-P2VP$_8$ | 0.33 | 4200 | 3900 | 1.07 | 21.1 |
| 6 | P*p*EES$_{13}$-*b*-P2VP$_{37}$ | 0.74 | 6800 | 5900 | 1.11 | 48.4 |
| 7 | P*p*EES$_{13}$-*b*-P2VP$_{40}$ | 0.77 | 7100 | 5800 | 1.16 | 54.5 |
| 8 | P*p*EES$_{13}$-*b*-P2VP$_{58}$ | 0.83 | 9200 | 6900 | 1.14 | 60.8 |
| 9 | P2VP$_{34}$ | 1 | 3900 | 3500 | 1.16 | 66.3 |

[a] Molecular weight in g·mol$^{-1}$, calculated from $^1$H NMR. [b] MWD characterized by size exclusion chromatography (SEC) in differential scanning calorimetry (DSC) (PS standard).

It is an important issue in this context, in which way the properties of P*p*EES differ from P*t*BuOS commonly used for the preparation of PHS, especially with regard to the ensuing acidic hydrolysis step. On the one hand, anionic synthesis in THF is feasible for both polymers under the same conditions. On the other hand, the resulting polymers exhibit completely different properties. After precipitation, P*t*BuOS with a molecular weight of 4000 g·mol$^{-1}$ is obtained as a solid with a glass transition of around 73 °C.[20] In the case of P*p*EES (#2, Mn = 4000 g·mol$^{-1}$), the glass transition is 9 °C, which translates to a highly viscous sample at room temperature. In addition, the acetal protection group should be easier hydrolyzed to generate PHS than the *tert*-butoxyl group. Investigation of the cleavage of the acetal group confirmed extremely fast hydrolysis. Acidic cleavage was carried out in an NMR tube to directly follow the kinetics of the deprotection step. The $^1$H NMR spectrum of P*p*EES (Figure 1, red line) in DMSO-$d_6$ (400 MHz) shows three characteristic signals that can be assigned to the acetal protecting group at 5.43−5.18, 3.74−3.53, and 3.27−3.53 ppm. One drop of DCl (20% in $D_2O$) was added, and the reaction mixture was shaken for 20 s before measuring the next spectrum. As can be seen from the $^1$H NMR spectrum (Figure 1, black line), full cleavage of the protective groups was achieved by this facile procedure. Due to the deprotection reaction, additional signals from ethanol (EtOH) and acetaldehyde (MeCHO) arise. As a result, all deprotection reactions were carried out at room temperature for a maximum of 5 min in an acidic solution.

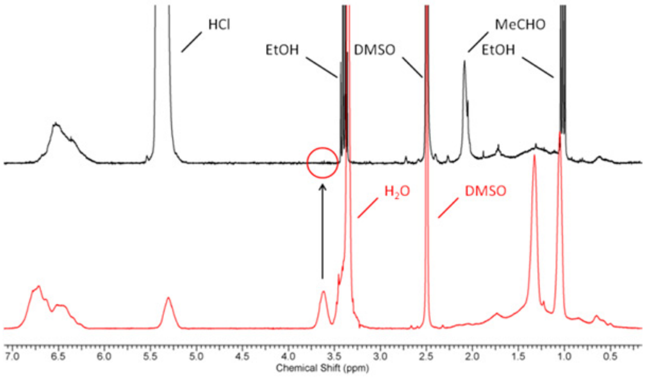

**Figure 1.** $^1$H NMR spectra demonstrating cleavage of the protecting acetal by acidic hydrolysis (#2); red spectrum represents the protected precursor compound and the black spectrum the deprotected PHS.

Poly(2-vinylpyridine) (P2VP) is pH-sensitive and has been used for a large variety of complex polymer architectures.[13,26−29] In recent work, our group developed a new double termination strategy to provide EEGE-end functionalized poly(2-vinylpyridine) (P2VP). Subsequent acidic hydrolysis of the functionalized P2VP resulted in two hydroxyl end groups, which were used as macroinitiators for the synthesis of amphiphilic AB$_2$-miktoarm star polymers consisting of one P2VP and two poly(ethylene oxide) (PEO) segments.[30] Up to date, there are a variety of elegant works dealing with the combination of P2VP and PHS, but never combined in one polymer.[31−35]

On the basis of these promising results concerning P*p*EES, a series of new P*p*EES-*b*-P2VP block copolymers with different block ratios were synthesized by sequential anionic polymerization and characterized by SEC, $^1$H NMR, and DSC. Introduction of the second block provides a new platform for potential applications and post modifications, especially with regard to pH-dependent properties and stabilization of nanoparticles. Characterization data of the block copolymers are summarized in Table 1. The difference between molecular weights determined by SEC and $^1$H NMR increased with molecular weight and increasing 2VP incorporation. $^1$H NMR spectroscopy turned out to be the most reliable method for the determination of the molecular weight. By comparing the integrals of the initiator, the H3 of the aromatic P2VP system and the characteristic signal of the acetal-protected PHS molecular weight, composition, and consequently the block ratio can be calculated. The SEC traces are important with regard to the extent of control of the reaction. As can be seen in the Supporting Information, all synthesized block copolymers exhibit monomodal SEC traces (Figures S7, S9, S11, and S13, Supporting Information), indicating quantitative block copolymer formation. To attain unequivocal evidence for block formation, a diffusion-ordered NMR spectrum (DOSY NMR) of block copolymer sample 5 has been measured. All $^1$H NMR resonances can be assigned to the same diffusion signal at 2.21 $\times 10^{-6}$ m$^2$/s, confirming quantitative block formation (Figure S8, Supporting Information). Nevertheless, the polydispersity increased to some extent with higher 2VP ratios, due to the high reactivity of the 2VP monomer. It is challenging to synthesize well-defined P2VP by living anionic polymerization without the addition of salts, like lithium chloride to reduce the reactivity of the living chain ends.[36] Consequently 2VP was distilled to the cooled living P*p*EES solution (−90 °C) over a period of approximately 30 min to reduce the concentration of 2VP in the reaction mixture to generate narrowly distributed block copolymers, showing polydispersity indices (PDI) of 1.09−1.16.

Differential scanning calorimetry has been employed to study the thermal properties of the block copolymers. It is striking that increasing 2VP content in block copolymers leads to higher glass transition temperature from 6 to 9 °C for P*p*EES (Mn $\leq$ 4000 g·mol$^{-1}$) up to 66 °C for the P2VP homopolymer (Mn = 4000 g·mol$^{-1}$), which additionally supports successful block formation. On the basis of these results, a desired $T_g$ can be adjusted via the block ratio in a broad temperature range.

Similar to the rapid and efficient deprotection of the homopolymers (see Figure 1), all block copolymers (P*p*EES-*b*-P2VP, #4−8) have been deprotected in acidic dioxane at room temperature as well. Dioxane is a good solvent for the precursor as well as for the deprotected polymer, and fast and quantitative deprotection was achieved. Furthermore all deprotected polymers have been characterized by $^1$H NMR as well as SEC (Supporting Information, see Figures S3 and S10−S 23). $^1$H NMR characterization evidenced successful acidic hydrolysis of the protected PHS in all cases. As an example for this reaction, both $^1$H NMR spectra as well as the SEC trace of the deprotected block copolymer (#7 → #13) are shown in Figure 2. In analogy to Figure 1 the red spectrum represents the protected block copolymer. As can be seen in the black spectrum obtained after acidic hydrolysis, there are no acetal protons remaining in the region of 5.2−5.4 ppm. A new signal occurs between 9 and 9.5 ppm, which can be assigned to the hydroxyl groups of the hydroxystyrene units. Taking into account both measurements, it can be concluded that less than 5 min treatment with acidic dioxane at room temperature is sufficient for quantitative deprotection without any side reactions.

To demonstrate a possible application of the new PHS-*b*-P2VP, we used it as a macroinitiator for the anionic ring-opening polymerization of EO to prepare amphiphilic water-soluble (PHS-*g*-PEO)-*b*-P2VP. Linear AB-block copolymers and AB$_2$-miktoarm star polymers containing P2VP and PEO segments have been studied in numerous important works, especially with regard to their behavior in aqueous solutions and with respect to their pH sensitivity.[26,30,37−39] This work describes the synthesis of a new amphiphilic graft-block copolymer containing water-soluble PEO grafted arms and a pH-sensitive P2VP block. It is important for this transformation that all phenolic hydroxyl groups are rapidly deprotonated with potassium naphthalide.[21] Starting with PHS$_{13}$-*b*-P2VP$_{40}$ the deprotected PHS backbone has been used as a macroinitiator for the anionic ring-opening polymerization of EO leading to the desired graft-block copolymer monitored by SEC and $^1$H NMR (see Figure 3). The expected increase of the molecular weight is confirmed by SEC (Mn = 28600 g·mol$^{-1}$, in DMF using PS standard). A slight increase of the polydispersity was observed for this step (PDI = 1.23). The additional PEO signals at 3.3−3.8 ppm in the $^1$H NMR spectrum demonstrate the

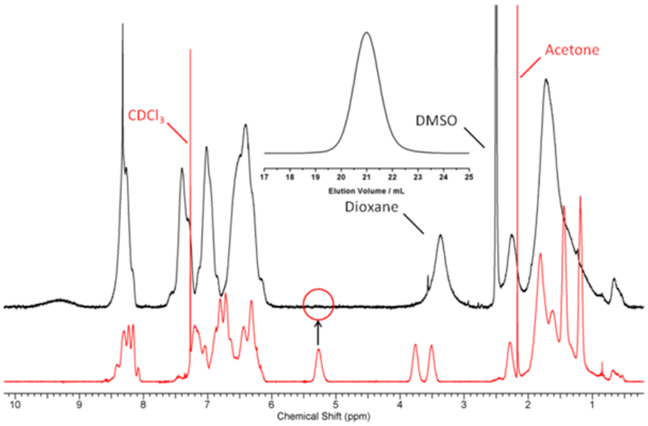

**Figure 2.** $^1$H NMR spectra of the cleavage of the protecting acetal groups by acidic hydrolysis at room temperature for 5 min in dioxane; red spectrum represents protected precursor compound (#7) and black spectra the deprotected species (#13).

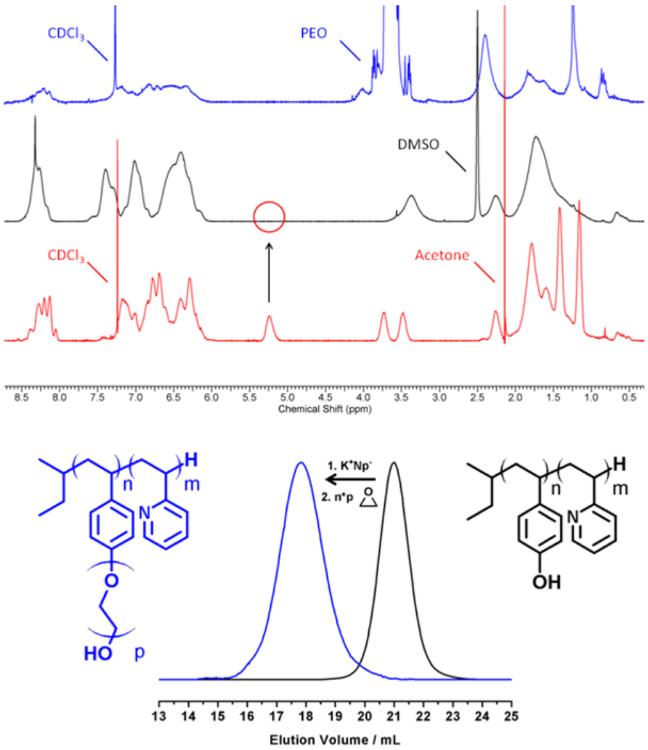

**Figure 3.** Bottom: SEC diagrams of the PHS$_{13}$-*b*-P2VP$_{40}$ precursor (#13, black line, right) and the (PHS-*g*-PEO$_{51}$)$_{13}$-*b*-P2VP$_{40}$ block-grafted copolymer (#15, blue line, left, PDI = 1.23), top: $^1$H NMR of P*p*EES$_{13}$-*b*-P2VP$_{40}$ (#7, red line), PHS$_{13}$-*b*-P2VP$_{40}$ (#13, black line), and (PHS-*g*-PEO$_{51}$)$_{13}$-*b*-P2VP$_{40}$ block-grafted copolymer (#15, blue line).

success of the "*grafting from*" synthesis. The molecular weight and the composition of the block-grafted polymer have been calculated by comparing the integrals of the aromatic system with the integrals of the PEO signals. In consideration of the utilized PHS precursor block, the resulting block-grafted polymer has 13 PEO chains per polymer, each with 51 EO repeating units leading to the structural formula $(\mathrm{PHS}\text{-}g\text{-}\mathrm{PEO}_{51})_{13}\text{-}b\text{-}\mathrm{P2VP}_{40}$, with a calculated molecular weight of 35 000 $\mathrm{g \cdot mol^{-1}}$. The discrepancy between the molecular weights calculated by $^1$H NMR and measured by SEC can be explained with the block-grafted polymer architecture having a smaller hydrodynamic radius compared to common block copolymers. The resulting water-soluble block-grafted polymer is the focus of further studies, especially with regard to its pH-dependent aggregation behavior and nanoparticle stabilization.

In summary, we have introduced the living anionic polymerization and block copolymerization of the readily available *p*(1-ethoxy ethoxy)styrene (*p*EES) monomer. P*p*EES represents a highly suited precursor for the synthesis of well-defined poly(4-hydroxy styrene) (PHS) by carbanionic polymerization. Compared with the frequently used poly-4-*tert*-butoxystyrene (P*t*BuOS), the experimental effort for the removal of the acetal protecting group is considerably reduced, and extremely rapid removal is achieved. In contrast to P*p*EES, the deprotection of PtBuOS is often carried out at 60 °C in acidic dioxane for several hours. In contrast, the deprotection of P*p*EES can be achieved at room temperature and is quantitative within minutes. Consequently, this polymer may be used for in situ applications requiring a fast change of polymer properties depending on the pH value. In addition, we have synthesized block copolymers containing P*p*EES and P2VP. The block copolymers were deprotected with the same procedure within minutes. The resulting poly(4-hydroxy styrene)-*b*-poly(2-vinyl pyridine) (PHS-*b*-P2VP) is of interest due to its amphoteric pH properties. The PHS block possesses an acidic proton and the P2VP block a basic nitrogen atom. Finally the PHS-*b*-P2VP has been employed as a macroinitiator for the anionic ring-opening polymerization of ethylene oxide (EO) to generate an amphiphilic water-soluble block-grafted ((PHS-*g*-PEO)-*b*-P2VP) polymer. These novel polymer architectures comprising P2VP may be useful for a variety of applications, especially with respect to the pH-sensitive behavior of P2VP.[26,37,39] Further studies on nanoparticle stabilization using (PHS-*g*-PEO)-*b*-P2VP and their properties as well as studies of the pH-dependent aggregation are in progress.

## ■ ASSOCIATED CONTENT

### Ⓢ Supporting Information

Detailed experimental procedures as well as analytical and spectral characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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### Notes

The authors declare no competing financial interest.

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