Notes

Improved Synthesis and Characterization of ω-Primary Amino-Functional Polystyrenes and Polydienes

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Polymers bearing reactive functional end groups are interesting materials with application in the fields of colloid chemistry, surface modification, catalysis, and drug delivery and also for the preparation of block and graft copolymers.[1] We are in particular interested in block copolymers comprising a synthetic segment (polystyrene or polybutadiene) and a polypeptide segment, so-called molecular chimeras, in view of their phase behavior and emulsifying properties.[2] Linear polypeptide block copolymers are usually obtained via the ring-opening polymerization of *N*-carboxyanhydrides of protected α-amino acids initiated by primary amino-end-functionalized macroinitiators.[3] For this purpose, it is preferable to use well-defined polymers with a high degree of functionalization, and a method to achieve this goal is ionic living polymerization which, however, demands high-purity experimental conditions and a suitable masking/protection of functional groups.[4] Up to the present, numerous procedures have been reported employing either functionalized initiators or termination agents to synthesize end-functionalized polymers—an overview is given in ref 1.

I. Monoamino-Functional Polymers

The most general and efficient procedures for the ω-end-functionalization of styrene and diene polymers include the capping of living polymeric anions with 1,1-diphenylethylene derivatives[5] or the termination with ω-functional-α-haloalkanes[6] or -chlorosilanes.[7] The primary amino groups are usually masked as silazanes and are subsequently released by an acid-catalyzed hydrolysis of the Si−N bond. By any of these methods, highly functionalized polymers can be obtained, but sometimes, the awkward synthesis and purification of the functionalization agents limits their applicability. We chose to employ the quenching of living polymeric anions with a chlorosilane bearing a bis(trimethylsilyl)amino group to prepare ω-amino-functional polystyrenes and polybutadienes. DeSimone et al.[7] described a three-step procedure producing these termination agents in less than 40% yield. To improve their availability, we worked on a more convenient synthetic procedure toward such chlorosilane derivatives. As a result, we were able to prepare 1-(chlorodimethylsilyl)-3-[*N*,*N*-bis(trimethylsilyl)amino]propane from readily available reagents (high-purity grade reagents from Aldrich) in just two steps in a 46% yield—the reaction process is outlined in Scheme 1. However, the yields reported in the literature for the two reaction steps (see below) suggest that the product could be obtained in a yield as high as 60%.

Synthesis of 1-(Chlorodimethylsilyl)-3-[*N,N*-bis(trimethylsilyl)amino]propane. First, we prepared 3-[*N*,*N*-bis(trimethylsilyl)amino]-1-propene by nucleophilic substitution of allyl bromide with potassium *N*,*N*-bis(trimethylsilyl)amide as described by Bestmann and Wölfel:[8] To a stirred ice-cold solution of 15.0 g (75 mmol) of potassium *N*,*N*-bis(trimethylsilyl)amide in hexamethyldisilazane (HMDS) was added dropwise a solution of 8.5 g (70 mmol) of allyl bromide in 10 mL of HMDS under a dry argon atmosphere. The mixture was stirred at room temperature for 8 h. The precipitated inorganics were removed by filtration through Celite 500, and the residual solution was fractionated by vacuum distillation. The product was obtained as a clear, colorless liquid in a 66% yield (lit.: 73%), bp 82 °C (30 mbar). ^{1}H NMR:[9] δ/ppm = 0.0−0.3 (m, 18H, Si(CH_3)$_3$), 3.44 (d, J = 4.6, 2H, CH_2N), 5.04 (dd, J = 10.1, 17.2, 2H, CH_2=), 5.78 (m, 1H, =CH).

This intermediate *N*-allyl disilazane was hydrosilylated with chlorodimethylsilane according to DeSimone et al.:[7] 9.0 g (45 mmol) of 3-[*N*,*N*-bis(trimethylsilyl)amino]-1-propene, 8.5 g (90 mmol) of chlorodimethylsilane, and a catalytic amount of chloroplatinic acid were slowly heated to 60 °C with stirring under dry argon. As soon as an exotherm was observed, the heat was removed and the greenish mixture was stirred at room temperature for 2 h. The 1-(chlorodimethylsilyl)-3-[*N*,*N*-bis(trimethylsilyl)amino]propane was obtained by fractional vacuum distillation as a clear, colorless liquid in 69% yield (lit.: 83%), bp 104 °C (1 mbar). ^{1}H NMR: δ/ppm = 0.0−0.3 (m, 18H, NSi(CH_3)$_3$), 0.43 (s, 6H, ClSiCH_3), 0.72 (m, 2H, ClSiCH_2), 1.45 (m, 2H, CH_2), 2.75 (m, 2H, CH_2N) (partial hydrolysis of the product).

Scheme 1. Synthesis of 1-(Chlorodimethylsilyl)-3-[*N,N*-bis(trimethylsilyl)amino]propane Used to Prepare ω-Amino-Functional Polystyrenes and Polydienes

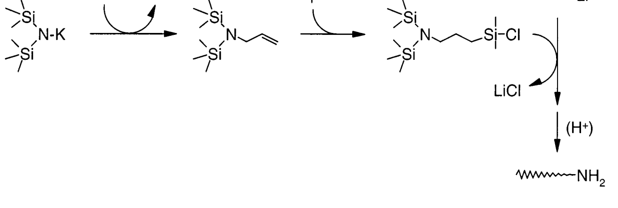

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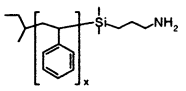
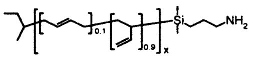
Table 1. Chemical Structures and Molecular Characteristics of the Prepared ω-Amino-Functional Polymers[a]

	sample	$\bar{x}$	*y*	PDI
	**PS-1**	57	0.94 >0.95 #	1.04
	PS-2	217	0.90 #	1.03
	**PB-1**	27	0.95	1.10
	PB-2	85	0.87	1.08
	PB-3	119	0.95	1.08

[a] Key: $\bar{x}$, number-average degree of polymerization (SEC); *y*, amino-functionality (NMR, #LACCC); PDI, polydispersity index (SEC).

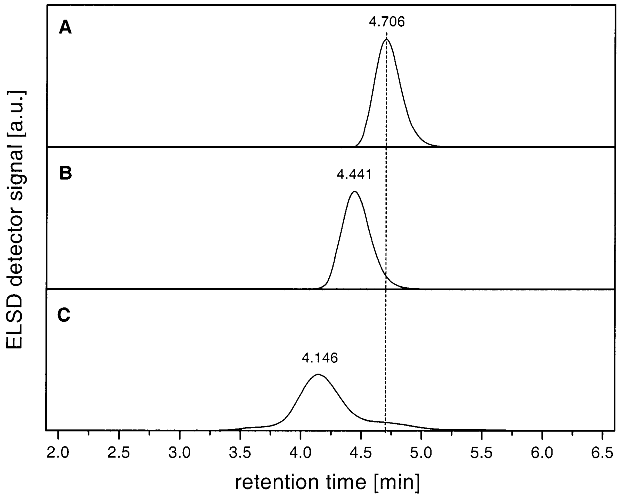


Figure 1. LACCC chromatograms of a H-terminated polystyrene (A) and the ω-amino-functional polystyrene samples **PS-1** (B) and **PS-2** (C). Note that under the given critical conditions for polystyrene, the functionalized polymer chains elute faster in the SEC mode.

Synthesis and Characterization of ω-Primary Amino-Functional Polystyrenes and Polybutadienes. Anionic polymerizations were performed employing standard high-vacuum techniques; all glassware was flame-dried and purged with argon as the inert gas. Solvents and monomers were purified according to standard procedures described elsewhere in the literature;[10] *sec*-butyllithium (*s*BuLi) was purchased as a 1.3 M solution in hexane (Aldrich) and was used as received. It should be noted that the polymerization of styrene and 1,3-butadiene can be performed in either cyclohexane or tetrahydrofuran (THF) as well as in mixtures of the two solvents. Here, for example, we performed the polymerization of styrene in cyclohexane at +50 °C while that of butadiene was carried out in THF at −78 °C to give preference to a 1,2- vs 1,4-monomer addition.

The ~20 wt % solutions of a poly(styryl)lithium in cyclohexane were quenched with a solution of the freshly distilled 1-(chlorodimethylsilyl)-3-[*N*,*N*-bis(trimethylsilyl)amino]propane (1.2 mol equiv with respect to the initiator, + 5 mol % *s*BuLi to remove last traces of impurities) in THF, and the mixtures were stirred overnight at room temperature (in the course of the reaction, the initially orange-red solution decolorized and a precipitate of LiCl was formed). The solvent was evaporated and the residue redissolved in THF/1 N HCl (9:1 v/v). The solutions were stirred for 2 h at room temperature, neutralized with NaOH, concentrated, and filtered. Finally, the polymers were precipitated in a 5-fold excess of aqueous ethanol (96%), filtered, redissolved in benzene, and freeze-dried. ^{1}H NMR: δ/ppm = −0.2−0.1 (m, $CH_2Si(CH_3)_2$), 0.5−1.0 (m, CH_2, CH_3, *s*-butyl), 1.1−1.7 (m, CH_2), 1.7−2.7 (m, CH), 6.2−6.9 (m, *m*-CH, phenyl), 6.9−7.6 (m, *o*/*p*-CH, phenyl). MALDI−TOF MS (**PS-1**):[11] $\Delta m = 104.05$ Da (molar mass of the styrene repeating unit, $M_{\text{styrene}} = 104.15$ Da); r.m. = 69.3 Da (residual mass expected: $M(C_9H_{23}NSi) - M_{\text{styrene}} = 69.04$ Da).

The ~2 wt % solutions of a poly(butadienyl)lithium in THF were quenched at −78 °C with 1-(chlorodimethylsilyl)-3-[*N*,*N*-bis(trimethylsilyl)amino]propane. The reaction mixtures were slowly heated to room temperature and stirred overnight, during which the bright yellow color of the living polymer solutions vanished completely. The solvent was evaporated to dryness and replaced by petroleum ether and aqueous HCl. After the mixtures were vigorously stirred for 2 h at room temperature and neutralized with NaOH, the organic layer was separated and the solvent was evaporated. The polymeric residues were dried in a vacuum at 35 °C to constant weight. ^{1}H NMR: δ/ppm = −0.1−0.1 (m, $Si(CH_3)_2CH_2$), 0.5−0.9 (m, CH_2, CH_3, *s*-butyl), 1.0−2.2 (m, CH, CH_2), 4.7−5.0 (m, $=CH_2$, 1,2-adduct), 5.2−5.6 (m, =CH, 1,2-adduct), CH=CH, 1,4-adduct).

We prepared two polystyrenes (**PS**) and three polybutadienes (**PB**) (microstructure = 90% 1,2- and 10% *trans*-1,4; ^{1}H NMR) with molecular weights in the range of 1.5−23 kDa, all having a narrow molecular weight distribution (polydispersity index, PDI = 1.03−1.09) as indicated by size exclusion chromatography (SEC).[12] The ^{1}H NMR spectra of the final products were in accordance with the expected chemical structure, and the lack of trimethylsilyl signals at δ ~ 0.2 ppm confirmed the complete removal of protecting groups. The amino-functionality of the polymers was calculated from the ratio of the areas beneath the signals of the end groups at δ = 0.5−1.0 (*s*-butyl, 8H) and −0.2−0.1 ppm ($Si(CH_3)_2CH_2$, 8H) to be usually greater than 90%; see Table 1. However, NMR did not allow the accurate measurement of the functionality of the high-molecular weight polystyrene sample (**PS-2**), and we therefore applied liquid adsorption chromatography at critical conditions (LACCC) which enables the sensitive tracing of chemical heterogeneities or functional groups independent of the molecular weight of the sample.[13] From the peak areas in the LACCC chromatograms[14] depicted in Figure 1, the amino-functionality of **PS-2** was determined to be 90% (**PS-1**: >95%).

II. Polyamino-Functional Polymers

Besides monofunctional macroinitiators, we are also interested in ω-polyamino-functional polymers, aiming

Scheme 2. Synthesis of 4-[*N*,*N*-Bis(trimethylsilyl)aminomethyl]styrene Used to Prepare ω-Polyamino-Functional Polystyrenes

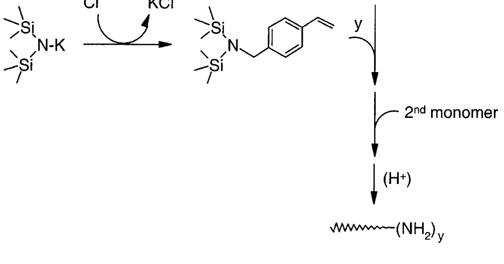
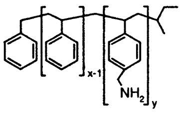


Table 2. Chemical Structure and Molecular Characteristics of the Prepared ω-Polyamino-Functional Polystyrenes[a]

	sample	$\bar{x}$	$\bar{y}$	PDI
	**PS-1***	182	4.3	1.13
	PS-2*	63	8.0	1.08
	PS-3*	193	7.7	1.14
	PS-4*	188	12.6	1.14

[a] Key: $\bar{x}$, number-average degree of polymerization (NMR); $\bar{y}$, number-average amino functionality (MALDI−TOF MS); PDI, apparent polydispersity index (SEC).

to prepare star-shaped polypeptide block copolymers.[2] Due to the difficult availability of initiators or termination agents having more than one masked functional group, we chose an alternate route which is the synthesis of block copolymers with an amino-functional segment (see Scheme 2). The synthesis of, e.g., polystyrene-*block*-poly(4-aminomethylstyrene)s by sequential anionic polymerization of styrene and 4-[*N*,*N*-bis(trimethylsilyl)aminomethyl]styrene is known from the work of Nakahama et al.[15] However, the better availability of block copolymers is at the expense of a perfect control over the amino-functionality; i.e., these macroinitiators exhibit an average degree of amino-functionality with a Poisson distribution at best.

Synthesis of 4-[*N*,*N*-Bis(trimethylsilyl)aminomethyl]styrene. Nakahama et al.[15] obtained 4-[*N*,*N*-bis(trimethylsilyl)aminomethyl]styrene from (*N*,*N*-bis(trimethylsilyl)aminomethyl)methyl ether (prepared from chloromethyl methyl ether and lithium *N*,*N*-bis(trimethylsilyl)amide) and 4-vinylphenylmagnesium chloride in less than 50% yield. We instead employed the recipe of Bestmann and Wölfel[8] which enables the direct synthesis of 4-[*N*,*N*-bis(trimethylsilyl)aminomethyl]styrene from 4-chloromethylstyrene and potassium *N*,*N*-bis(trimethylsilyl)amide; see Scheme 2. Note that this reaction pathway considerably facilitates the synthesis of amino-functional monomers. The styrene derivative could be isolated as a clear, colorless liquid in a 43% yield after fractionated vacuum distillation,[16] bp 72 °C (0.05 mbar). ^{1}H NMR: δ/ppm = 0.07 (s, 18H, $Si(CH_3)_2$), 4.08 (s, 2H, CH_2N), 5.18, 5.70 (2d, J = 11, 18 Hz, 2H, $CH_2{=}$), 6.69 (dd, $-CH{=}$), 7.20, 7.33 (dd, 4H, arom).

Synthesis and Characterization of Poly(4-aminomethylstyrene)-*block*-polystyrenes. The sequential anionic polymerization of 4-[*N*,*N*-bis(trimethylsilyl)aminomethyl]styrene and styrene was performed in THF at −78 °C using *s*BuLi as the initiator.[15] Before the styrene was added to the dark green solution of the living poly(4-[*N*,*N*-bis(trimethylsilyl)aminomethyl]styryl)lithium, a sample of the precursor polymer was withdrawn from the reactor. The removal of the protecting groups and the purification of copolymers was carried out as described above, ^{1}H NMR: δ/ppm = 0.5−1.0 (m, CH_2, CH_3, *s*-butyl), 1.3−2.4 (m, CH, CH_2), 3.8−4.2 (m, NCH_2), 6.2−6.9 (m, *m*-CH, phenyl), 6.9−7.3 (m, arom).

We prepared four copolymer samples (**PS***) with molecular weights in the range of 7.6−21.2 kDa (PDI = 1.08−1.14; SEC) and average amino-functionalities of 4.3−12.6; see Table 2. ^{1}H NMR analyses confirmed the chemical structure of the copolymers, and SEC showed the absence of any precursor residuals. MALDI−TOF MS was used to determine the absolute number-average degree of polymerization of the poly(4-aminomethylstyrene) precursor (Δm = 133.4 Da, r.m. = 58.3 Da; expected, 133.1 and 58.0 Da, respectively) (cf. Figure 2)[17] which is equal to the average amino-functionality of the copolymer. From these data and the chemical composition of the copolymers obtained from ^{1}H NMR, the number-average molecular weights of the copolymers were calculated. It should be noted that the so obtained products are much easier to characterize and to purify as if the reverse sequence of monomer addition had been chosen. However, all attempts failed to achieve a living/controlled polymerization of 1,3-butadiene as the second monomer.

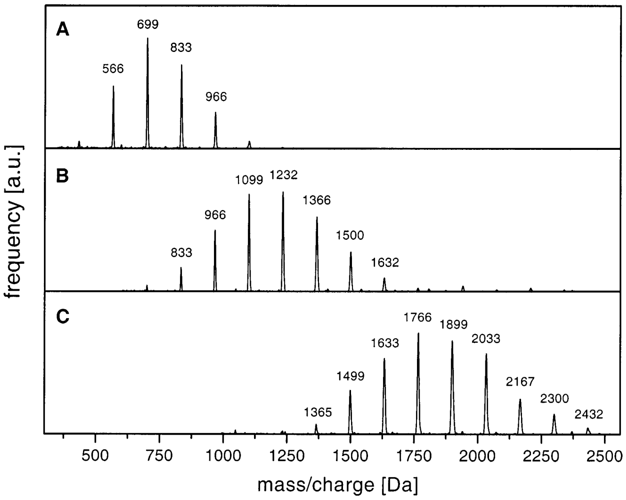


Figure 2. MALDI−TOF mass spectra of the oligo(4-aminomethylstyrene) precursors ($[M - Ag]^+$) of the copolymer **PS-1*** (A), **PS-3*** (B), and **PS-4*** (C).

In summary, we were able to facilitate the synthesis of chlorosilane and styrene derivatives bearing a silazane functional group and thus to improve the availability of well-defined primary amino-functional polymers.

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References and Notes

(1) (a) Goethals, E. G., Ed. *Telechelic Polymers: Synthesis and Applications*; CRC Press: Boca Raton FL, 1989. (b) Abhimanyu, O. P.; Schulz, D. N.; Novac, B. M., Eds.; *Functional Polymers: Modern Synthetic Methods and Novel Structures*; ACS Symposium Series 704, American Chemical Society: Washington, DC, 1998. (c) Hirao, A.; Hayashi, M. *Acta Polym.* **1999**, *50*, 219−231. (d) Hong, K.; Uhrig, A.; Mays, J. M. *Curr. Opin. Solid State Mater. Sci.* **1999**, *4*, 531−538. (e) Quirk, R. P.; Yoo, T.; Lee, Y.; Kim, J.; Lee, B. *Adv. Polym. Sci.* **2000**, *153*, 67−162. (f) Jagur-Grodzinski, J. *React. Funct. Polym.* **2001**, *49*, 1−54.

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(9) ^{1}H NMR spectra were recorded at 25 °C in $CDCl_3$ with a Bruker DPX-400 spectrometer operating at 400.1 MHz. Signals were referenced to that of the solvent at $\delta = 7.24$ ppm and assigned with the aid of literature data reported elsewhere.

(10) Förster, S.; Krämer, E. *Macromolecules* **1999**, *32*, 2783−2785.

(11) MALDI−TOF mass spectra were recorded with a Bruker Reflex III and a Kratos MALDI 3 employing a nitrogen laser source ($\lambda = 337$ nm) in the reflectron or linear mode, respectively. Either 1,8-dihydroxy-9[10*H*]-anthracenone or 2,5-dihydroxybenzoic acid was used as the matrix and silver trifluoroacetate as the cation source. Bovine insulin was used to calibrate the equipment.

(12) SEC was performed on Thermo Separation Products setups being equipped with UV (TSP UV1000) and RI (Shodex RI-71) detectors. THF was used as the eluent at 30 °C at a flow rate of 1.0 mL/min. The employed column set consisted of three 300 × 8 mm MZ-SD*plus* (spherical polystyrene gel with 5 μm average particle size) columns with pore sizes of 10^3, 10^5, and 10^6 Å, respectively. Polystyrene and poly(1,2-butadiene) standards (PSS GmbH) were used for calibration.

(13) The liquid chromatographic fractionation of polymers is driven by entropic and/or enthalpic interactions inside the pores of a separation material. When both effects are compensating each other at the so-called critical conditions of adsorption, i.e., the value of the free enthalpy is equal to zero ($\Delta G = 0$), a homologous series of polymer samples elute at the same retention time independent of molecular weight. For polymer chains with a different chemical or topological structure, it is $\Delta G \neq 0$, and these chains will therefore elute in either the size exclusion or the adsorption mode. This effect can be used to separate functionalized polymer chains from nonfunctionalized ones with the same molecular weight. For further information, see: Pasch, H.; Trathnigg, B. *HPLC of Polymers*; Springer: Heidelberg, Germany, 1997.

(14) LACCC measurements were conducted on a Hewlett-Packard HPLC system (HP1090) using a an evaporative light scattering detector (SEDEX 45, ERC) at 45 °C. The flow rate was 0.5 mL/min and 10 μL of about 1.5 wt % polymer solutions were injected. The eluent with the critical solvent composition for polystyrene at 45 °C was THF/*n*-hexane 60/40 (w/w), and the column used was a 250 × 4 mm SGX NH_2 (silica gel modified with aminopropyl-triethoxysilane, Separon) with a 120 Å pore size and 7 μm average particle size.

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(16) Despite of the presence of a radical inhibitor, a considerable amount of the crude monomer was lost due to thermal polymerization.

(17) It should be noted that for all precursors the determined value of the PDI was considerably lower than what one would expect for a Poisson-distributed sample. This might be attributed to some discrimination of higher oligomers in the course of the MALDI process.

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