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IV. Polymer Characterization

Different Nitroxide-Capped Polystyrenes and their Behavior During an Analysis via MALDI-TOF Mass Spectrometry

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Summary: Different nitroxide-terminated polystyrenes are characterized using matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS). Careful MS analysis reveals that in contrast to TEMPO-capped chains which can be analyzed without fragmentation, a fragmentation of the *N*-oxyle group occurs in case of TIPNO and BIPNO. A fragmentation resulting in the loss of a *t*-butyl-group is proposed as consequence of the treatment during the measurement.

Keywords: matrix-assisted laser desorption/ionization mass spectrometry (MALDI-MS); nitroxide; polystyrene; radical polymerization

Introduction

A lot of approach about free radical polymerization techniques has been made during the past few years. The three main methods which are used to produce well-defined polymers by radical polymerization are nitroxide-mediated radical polymerization (NMRP),[1,2] atom transfer radical polymerization (ATRP)[3] and reversible addition-fragmentation chain transfer polymerization (RAFT).[4] With aid of the controlled radical polymerization it is possible to obtain narrow molar mass distributions of well-defined polymers with different architectures. This work deals with the characterization of polymers which were polymerized via NMRP.

Since the initial report by Rizzardo,[5] who used TEMPO as nitroxide, much progress has been made in the field of NMRP. A good overview about the history of the nitroxide development is given in some special reviews.[1,2] While TEMPO and TEMPO derivatives are mainly used for styrene polymerization the use of nitroxides such as **B**,[6,7] **C**[8] and **D**[9] now permits the polymerization of a wide variety of monomers (Scheme 1).

The modern MALDI-TOF mass spectrometry is a powerful technique for the fast and accurate determination of a variety of polymer characteristics. The determination of absolute molecular weights of individual polymer chains provides much information, such as the repeat unit and the kind of end groups.

The analysis of *N*-oxyl capped polymers by MALDI-TOF mass spectrometry is complicated. A discrimination of species occurs depending on the analytical conditions of the measurement.[10,11]

The aim of this paper is the investigation of different nitroxide-capped polystyrenes with MALDI-TOF MS. Styrene was chosen as monomer for a better comparability of the results. Thus it is possible to see the differences between nitroxides of type **A** on the one hand and **C** or **D** on the other hand.

Experimental Part

Synthesis

C-BzEt-OH *N*-tert-Butyl-*O*-[1-(4-hydroxymetyl-phenyl)-ethyl]-*N*-(2-methyl-1-phenyl-

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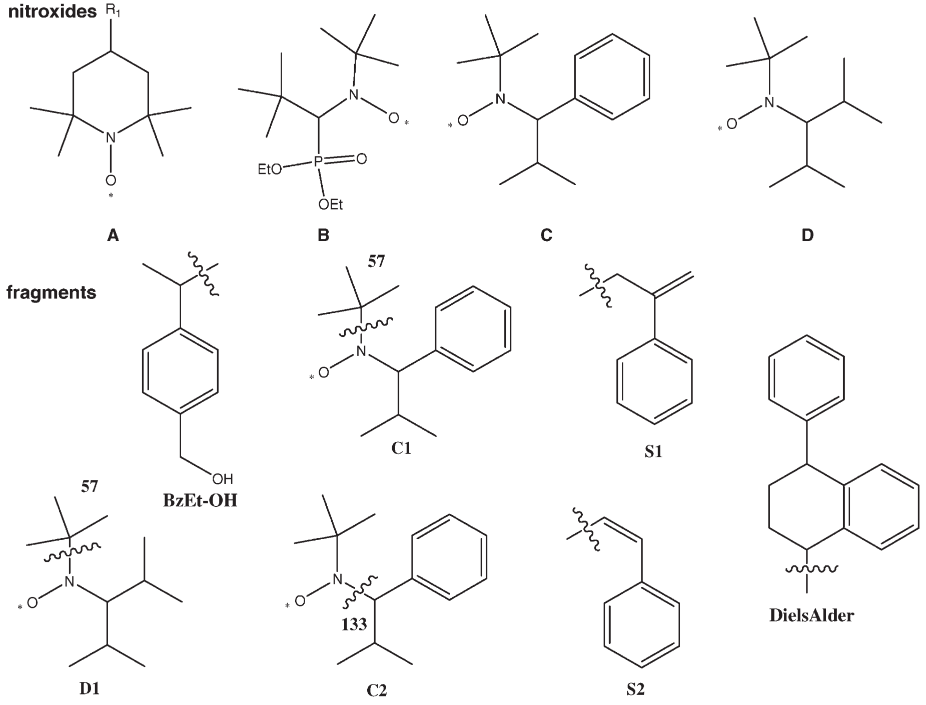

Scheme 1.
Different nitroxides TEMPO and TEMPO-derivates (**A**), DEPN (**B**), TIPNO (**C**) and BIPNO (**D**); and their corresponding module assignment for the shortcut of the interpretation of results in the tables.

propyl)-hydroxylamine and **D-BzEt-OH** *N*-tert-Butyl-*O*-[1-(4-hydroxymetyl-phenyl)-ethyl]-*N*-(1-isopropyl-2-methyl-propyl)-hydroxylamine were synthesized according to the procedure reported by Hawker et al.[12] They were synthesized by mixing the nitroxide and 4-Vinyl-benzyl-alcohol in a ratio of 7 to 10 or 6 to 8 respectively in isopropyl alcohol.[13] To this mixture the Mn(salen)Cl catalyst[14] and sodium borohydride were added in small amounts. The reaction mixtures were stirred for 24 h at room temperature and chloroform was added. Hydrochloric acid (0.5 M) was added as long as the catalyst and sodium borohydride were removed. After that the mixture was washed with water until the solution became acid-free. The organic phase was dried over sodium sulfate and the solvent was removed under reduced pressure. Purification occurs by column chromatography (20:1 petrol ether/ethyl acetate).

Procedure for Polymerizations

Exact data of each sample are given in Table 1. Polymerizations were carried out in sealed glass ampoules at 125 °C under a nitrogen atmosphere. Samples were taken after 15 minutes, cooled down in a refrigerator, and dissolved in THF. The

Table 1.
Experimental Conditions for Styrene NMRP Carried out at 125 °C and GPC Characterization of the Polystyrene Samples.

	[alkoxyamine] (mmol* L^{-1})	Time (min)	Conversion %	M_n	M_w	PDI
C-BzEt-OH	40	15	6	3700	4700	1.29
C-BzEt-OH	20	15	6	5100	7000	1.37
D-BzEt-OH	40	15	16	4800	6000	1.27

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product was precipitated into methanol and dried in vacuum to constant mass.

Characterization

MALDI-TOF MS measurements were performed on a Bruker Biflex III equipped with a 337 nm nitrogen laser. Positive ion spectra were acquired in linear mode and 20 kV acceleration voltages. DHB was chosen as matrix and no salt was added. Samples were prepared from THF solution by mixing matrix (16 mg/mL) and sample (10 mg/mL) in a ratio of 10:1. When using the matrix dithranol silver trifluoroacetat was added. Samples were prepared from THF solution by mixing matrix (20 mg/mL), sample (10 mg/mL) and salt (10 mg/mL) in a ratio of 10:1:1. The matrices DHB ($>$ 99% purity) and dithranol ($>$ 99% purity) were used as provided by Fluka. Polystyrene standards were used for external calibration of the mass spectra. All spectra shown in this paper represent original data without any filtering or background subtraction.

Molecular mass distributions were determined by size exclusion chromatography (SEC) on a Knauer instrument equipped with SDV columns of PSS and nucleogel columns of Machery-Nagel with THF as eluent (flow rate of 1 mL/min) and refractive index detection. A calibration curve based on polystyrene standards was used.

Results and Discussion

TEMPO and TEMPO-Derivates

Polymers which are capped with TEMPO[10,11] and TEMPO-derivates[15] are stable during the MALDI-TOF measurement using DHB as matrix without any additives. Using this preparation method protonated chains can be detected which is an unusual behavior in the analysis of synthetic polymers. During the matrix-assisted laser desorption/ionisation process the ionisation of synthetic polymers is usually achieved by an attachment of cations.[16] In case of the DHB matrix sodium adducts are usually detected even without the addition of sodium salts, because of the unavoidable traces of sodium from the sample preparation.

The protonated chains which can be detected are the intact ‘‘dormant’’ chains which have the nitroxide group on the one side of the chain and the initiating group on the other. By using DHB as matrix the nitroxide end group will be protonated selectively and no ionization of the dead chains will occur.[10] The adaptability of this method to functionalized TEMPO-capped polystyrenes was also demonstrated.[11] The list of TEMPO-capped polystyrenes is rounded of by the discussion of 4-hydroxy-TEMPO.[15] We also analyzed other TEMPO derivates with the same results mentioned above but which should not be discussed here in detail.[17]

As soon as a salt is added the spectra look different. The matrix dithranol with an addition of silvertrifluoroacetat, a commonly used method to analyze polystyrenes via MALDI-TOF MS, leads to chain-end degradation in case of TEMPO-capped polystyrenes. No ‘‘dormant’’ species could be observed.

Studer et al.[18] synthesized some new sterically hindered styryl-TEMPO derivates. One of them, 2,2,6,6-Tetraethylpiperidin-4-one-*N*-oxyl, was used in a polymerization of *N*-isopropylacrylamide. After careful MS analysis they suggested a new mechanism of chain-end degradation during MS analysis.[19] The matrix DHB was applied with an addition of $NaBF_4$ for an improved ionization. Under these conditions and by applying low laser intensity it was possible to observe the protonated oligomer containing the alkoxyamine, the whole ‘‘dormat’’ species. Using higher laser intensity additionally chain-end degradation took place, resulting in protonated chains of methylene-terminated PNIPAMs and also their corresponding Na^+ adducts effected by the added salt.

To commemorate, protonated intact alkoxyamine-capped chains can be analysed using the matrix DHB. Chain-end degradation occurs when a salt is added and higher laser intensities are used.

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However, we expected similar results when analyzing polystyrenes capped with other nitroxides. But our results did not correspond to our expectations which will be discussed in the following.

TIPNO and BIPNO

Different TIPNO- and BIPNO-capped polystyrenes were analyzed by means of MALDI-TOF MS. Within this communication we would like to discuss polystyrenes derived from TIPNO- and BIPNO-alkoxyamines with (4-hydroxymetyl-phenyl)-ethyl as starting fragment, the generality of our finding will be discussed in detail in a forthcoming publication. The measurements were carried out using two different matrices. DHB was used for protonation of the whole "dormant" species, for other experiments we used dithranol as matrix with an addition of silvertrifluoroacetat. At first we would like to discuss the results using dithranol as matrix.

Dithranol: Figure 1 shows an enlargement of structure **D-BzEt-OH** and **C-BzEt-OH**. Two series can be observed in each spectrum. The difference between the peaks inside a series is 104 m/z corresponding to styrene. Interestingly the absolute mass of the signals are congruent. Both spectra seem to show the same structures. The molar mass values for the experimentally observed series are reported and compared with the theoretical values (Table 2).

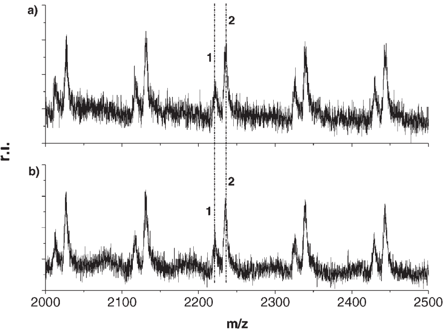

Figure 1.
Enlargement of the measurement with the matrix Dithranol and Silvertrifluoracetate as additive; a) Polystyrene synthesized with the alkoxyamine **D-BzEt-OH**, b) Polystyrene synthesized with the alkoxyamine **C-BzEt-OH**.

Series 2, here represented by a signal at 2235 m/z, can be calculated for a product of a fragmentation of polystyrene during the MALDI-TOF measurement, which was described by Davis et al.[20] It is obviously the same structure which will be obtained following the chain-end degradation mechanism described by Studer et al.[19] In case of our nitroxide-capped polystyrene both mechanisms are possible. However, which mechanism really is responsible for the occurrence of this species should not be the object of discussion.

The other peak at 2221 m/z, corresponding to series 1, can be calculated for the corresponding second styrene fragment according to the fragmentation described by Davis et al.[20] as well as for a β-H abstraction induced by the nitroxide itself as side reaction.[21] It is evident, that no intact "dormant" chains can be detected using this preparation conditions, which was also described by other groups.

DHB: The MALDI-TOF spectrum of **C-BzEt-OH** and **D-BzEt-OH** is shown in Figure 2. Obviously not only one peak

Table 2.
Comparison between the experimental and theoretical values of the products. Molar Masses of the Ag^+-ionized polystyrenes (Dithranol/Silvertrifluoracetate).

Product	u_{exp} a)	u_{calc} b)	Assumed possible structure	n
C-BzEt-OH	2235 c)	2235 c)	S1-St$_n$-BzEt-OH,Ag$^+$	18
C-BzEt-OH	2221 c)	2221 c)	S2-St$_n$-BzEt-OH,Ag$^+$	18
D-BzEt-OH	2235 c)	2235 c)	S1-St$_n$-BzEt-OH,Ag$^+$	18
D-BzEt-OH	2221 c)	2221 c)	S2-St$_n$-BzEt-OH,Ag$^+$	18

a) Value of the experimentally observed peak (u); b) value of the calculated peak (u); c) average mass; no isotopic peak.

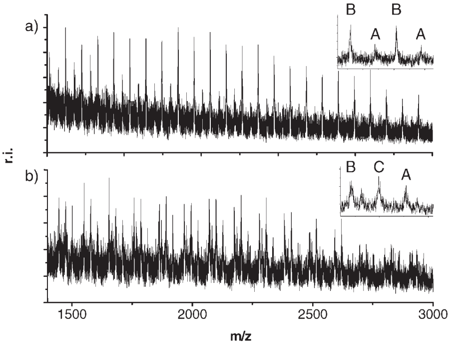

Figure 2.
Enlargement of the measurement with the matrix DHB without any additives; a) Polystyrene synthesized with the alkoxyamine **D-BzEt-OH**, b) Polystyrene synthesized with the alkoxyamine **C-BzEt-OH**.

series remains. In fact two or in case of TIPNO-capped chains at least three series could be resolved. The difference between the peaks inside a series is again 104 m/z corresponding to styrene. No identical signals can be observed between the two spectra, although the two samples are structural identical, except of the nitroxide-group.

In each case series **A** corresponds to the expected product, where one extremity is the nitroxide-group and the other is the starter-group. This means that e. g. the signal at 2127 Da (Figure 2b) is in good agreement with the calculated mass of 2127 Da. The molar mass values for the experimentally observed series using DHB as matrix are reported and compared with the theoretical ones (Table 3).

But apart from a thermal initiation via a Diels-Alder product no other side products were expected. Based on the fact that only nitroxide-capped chains can be detected using the soft ionization with DHB as matrix, the other series should also belong to structures containing nitrogen. Taking this into account an interesting parallel can be drawn between the both samples presented in Figure 2. Starting from the identified signal of the expected product, which is called series **A** in both cases, the distance to series **B** is 56 Da in each case. As stated before, both products differ only in the structure of the nitroxide-group, which are shown in Scheme 1. The structural element which is present in both structures **C** and **D** is the *t*-butyl-group with a mass of 57 Da. Thus we suppose a fragmentation inside the nitroxide-group resulting in the loss of the *t*-butyl-group with a subsequent addition of a hydrogen atom. Series **B** can than be assigned to (H-C1-St_{17}-BzEt-OH)H^+ with a mass of 2071 Da (exp. 2071 Da) in case of TIPNO as nitroxide and (H-D1-St_{19}-BzEt-OH)H^+ with a mass of 2245 Da (exp. 2245 Da) in case of BIPNO.

In a paper about nitroxide decomposition TIPNO was subjected to thermally decomposition experiments.[22] Braslau et al. proposed a new mechanism for the thermally decomposition of α-hydrogen nitroxides (Scheme 2). Their result, the loss of the *t*-butyl-group, is the same as our finding.

But there are significant differences between both studies. We analyzed nitroxide-capped polystyrenes and Braslau et al.[22] the pure nitroxide. Therefore the

Table 3.
Comparison between the experimental and theoretical values of the products. Molar Masses of the H^+-ionized polystyrenes (DHB, no additives).

Product	u_{exp} [a)]	u_{calc} [b)]	Assumed possible structure	n
C-BzEt-OH	2127 [c)]	2127 [c)]	C-St_n-BzEt-OH,H^+	17
C-BzEt-OH	2071 [c)]	2071 [c)]	H-C1-St_n-BzEt-OH,H^+	17
C-BzEt-OH	2099 [c)]	2099 [c)]	H-C2-St_n-BzEt-OH,H^+	18
D-BzEt-OH	2301 [c)]	2301 [c)]	D-St_n-BzEt-OH,H^+	19
D-BzEt-OH	2245 [c)]	2245 [c)]	H-D1-St_n-BzEt-OH,H^+	19

[a)] Value of the experimentally observed peak (u); [b)] value of the calculated peak (u); [c)] average mass; no isotopic peak.

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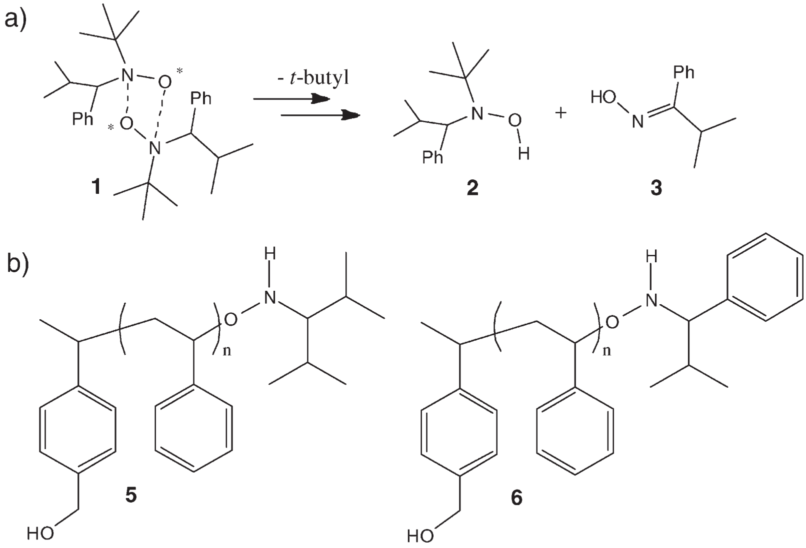

Scheme 2.
"Head-to-tail"-arrangement of the nitroxide TIPNO **1** results in formation of a hydroxylamine **2** and an oxime **3**.[22] Assumend possible structures obtained as result of MALDI analysis from **D-BzEt-OH 5** and **C-BzEt-OH 6**.

bimolecular reaction involving the formation of a "head-to-tail"- dimer can not be the explanation for the loss of the *t*-butyl-group in our case. The nitroxide group is attached to the polymer chain, so no dimer formation is possible.

That is why we suppose another fragmentation mechanism, a simple α-scission process, like it was found as result of photo excitation of the nitroxide DTBN.[23] Another indication for that explanation is series **C** of the TIPNO-sample **C-BzEt-OH**. Starting again from series **A**, which assignment is indisputable, the distance to series **C** is 132 Da. If we perform the scission at the other α-bond in nitroxide **C** (Scheme 1), we will loose a phenylisobutyl-group with a mass of 133 Da, the exact data are given in Table 3.

At this point it must be mentioned that we have only a mass as result of our measurements, so that the real structure of the fragmentation product must be regarded as uncertain. Other nitroxides with different structural requirements have been investigated in form of the neat alkoxyamines.[24] By analyzing the unimolecular initiators themselves in addition to different nitroxide-capped polystyrenes a classification of different nitroxide structures regarding their fragmentation behavior in a MALDI-experiment under the applied conditions could be made.[17,24]

Conclusion

Due to careful MS analysis we suppose a fragmentation inside the nitroxide-group during the analysis via MALDI TOF mass spectrometry resulting in the loss of a *t*-butyl- or a phenylisobutyl-group respectively in case of the α-hydrogen nitroxides BIPNO and TIPNO. That way a parallel can be drawn between our finding during soft ionization mass spectrometry and thermally decomposition experiments or photochemical processes investigated by other groups.

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