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Analysis of Nitroxide-Mediated Polymerization of Styrene by Soft-Ionization-MS – A Challenging Task

*Wibke Dempwolf, Silke Flakus, Gudrun Schmidt-Naake**

Summary: A suitable method to synthesize well defined polymers with different architectures is the application of functionalized alkoxyamines in the controlled radical polymerization. The analysis of such nitroxide capped polymers by MALDI-TOF-MS is complex. Unexpected results of the mass analysis of our polymers lead us to study the influence of the structure of the analyte and the experimental conditions of the measurements in detail. In addition to common nitroxides like TEMPO, TEMPO-derivates, TIPNO and BIPNO, other alkoxyamines with special structure requirements were synthesized. These alkoxyamines were tested in different MALDI experiments. Supported by a comparison with other methods we postulate a fragmentation mechanism inside the nitroxide-group which takes place during the MALDI measurement. To the best of our knowledge such a fragmentation of the nitroxide-group itself during a MALDI-TOF experiment has not been described before.

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

Introduction

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 nitroxide capped polymers by MALDI-TOF mass spectrometry is complex, which was shown by various groups.[1–4] The detection of species depends on the analytical conditions of the measurement.[2,3]

Since the initial report by RIZZARDO,[5] who used the nitroxide TEMPO for controlled polymerization, 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.[6] While TEMPO and TEMPO derivatives are mainly used for styrene polymerization the use of nitroxides such as **B**,[7] **C**[8] and **D**[9] now permits the polymerization of a wide variety of monomers (Figure 1).

Unexpected results of the mass analysis of our styrene-polymers derived from nitroxide **C** and **D** lead us to study the influence of the structure of the analyte and the experimental conditions of the measurements in detail.[10]

The aim of this contribution is the investigation of different alkoxyamines with MALDI-TOF MS. Those are the commonly used unimolecular initiators for the NMRP. The MALDI technique is not considered to be designed for such small masses – that is true and some interfering signals derived from the matrix will be discussed later on – but this investigation should be seen as completion for the analysis of the corresponding polystyrenes.[10]

Institut für Technische Chemie, Technische Universität Clausthal, Erzstraße 18, 38678 Clausthal, Germany
Fax: (+49) 5323 72 3655;
E-mail: gudrun.schmidt@tu-clausthal.de

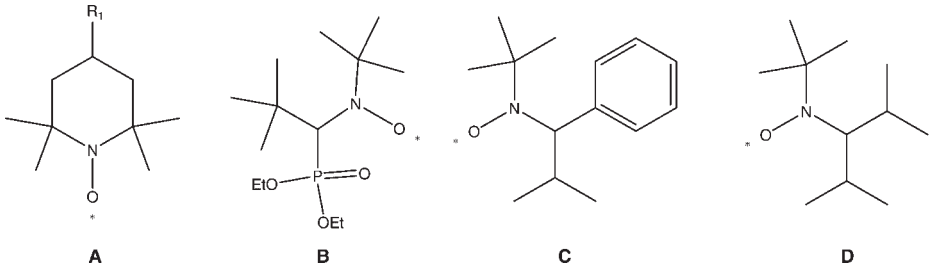

Figure 1.
Different nitroxides TEMPO and TEMPO-derivates (A), DEPN (B), TIPNO (C) and BIPNO (D).

Unfortunately, alkoxyamine **PhEt-NPPNO** (Figure 2b) was not suited to control a polymerization. This is another reason why also further alkoxyamines were investigated by means of MALDI-MS. In this way a comparison of different structures was possible and a deeper insight into fragmentation processes during the measurement could be made.

Experimental Part

Synthesis

Cl-BzEt-TIPNO *N*-tert-Butyl-*O*-[1-(4-chlormetyl-phenyl)-ethyl]-*N*-(2-methyl-1-phenyl- propyl)-hydroxylamine, **PhEt-BIPNO** *N*-tert-Butyl-*O*-(1-phenyl- ethyl)-*N*-(1-isopropyl-2-methyl-propyl)-hydroxylamine, **PhEt-DTBNO** *N*-di- tert-Butyl-*O*-(1-phenyl-ethyl)-hydroxylamine and **PhEt-NPPNO** Norpseudopelletierine-*O*-(1-phenyl-ethyl)-hydroxylamine were synthesized according to a procedure reported by HAWKER et al.[11] They were synthesized by mixing TIPNO and 4-Vinyl-benzyl-chloride in a ratio of 7 to 10 in isopropyl alcohol in case of Cl-BzEt-TIPNO or by mixing the according nitroxide with styrene in a ratio of 1 to 1 in isopropyl alcohol or a mixture of isopropyl alcohol, methanol and toluol.[12,13] 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).

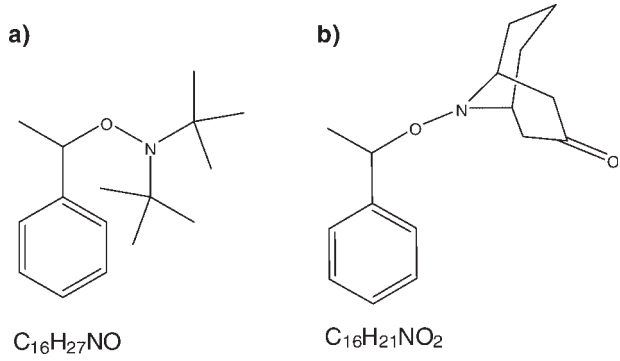

Figure 2.
Synthesized alkoxyamines derived from the nitroxides **a)** di-*tert*-butyl-*N*-oxyle and **b)** norpseudopelletierine-*N*-oxyle.

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. 2,5-Dihydroxybenzoic acid (DHB) (>99% purity; Fluka) 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. All spectra shown in this paper represent original data without any filtering or background subtraction.

Results and Discussion

Polymers which are capped with TEMPO [2,3] and TEMPO-derivates [15] are stable during the MALDI-TOF measurement by 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. The same can be found for the analysis of small alkoxyamine molecules derived from TEMPO and TEMPO-derivates.

Passing over from such cyclic structures without α-H-atom to acyclic nitroxides containing an α-H-atom like TIPNO and BIPNO the mass spectra look different. Besides the expected masses of the protonated complete alkoxyamine other lower masses can be detected (Figure 3). But it is shown by NMR data that no other side products have been present in the samples under investigation (not included in this short communication).

Taking this into account an interesting parallel can be drawn between the results of the alkoxyamines derived from TIPNO and BIPNO. Starting from the identified signal of the expected product, which is called **I** in both cases, the distance to **II** is 56 Da in each case.

As stated before, both molecules differ in the structure of the nitroxide-group, which are shown in Figure 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. **II** can then be assigned to (**Cl-BzEt-TIPNO** – *t*-butyl + H)H^+ with a mass of 318.16 Da (exp. 318.92 Da) in case of TIPNO as nitroxide and (**PhEt-BIPNO** – *t*-butyl + H)H^+ with a mass of 236.20 Da (exp. 236.90 Da) in case of BIPNO for instance (Table 1).

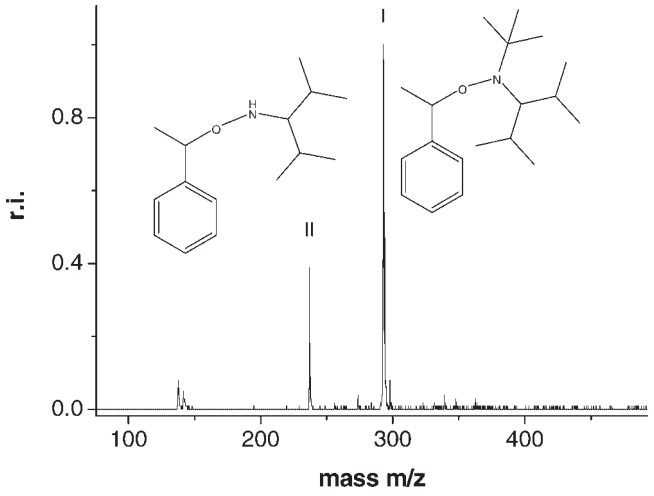

Figure 3.
MALDI mass spectrum of the alkoxyamine **PhEt-BIPNO**. Two signals can be clearly resolved, assumed structures are shown; exact data expressed in Table 1. Matrix: 2,5-dihydroxybenzoic acid.

Table 1.
Comparison of experimental and calculated values for the assumed structures. All displayed masses are monoisotopic masses (Da). For an explanation of variations between the calculated and the experimental observed masses see discussion

	Alkoyamine	Signals		Cation
		exp.	theor.	
I	PhEt-BIPNO	292.78	292.26	H^+
II	[PhEt-BIPNO – *t*-butyl + H]	236.87	236.20	H^+
I	Cl-BzEt-TIPNO	374.85	374.23	H^+
II	[Cl-BzEt-TIPNO – *t*-butyl + H]	318.92	318.16	H^+
I	PhEt-DTBNO	250.87	250.22	H^+
II	[PhEt-DTBNO – *t*-butyl + H]	194.92	194.15	H^+
I	PhEt-NPPNO	260.87	260.17	H^+
matrix	DHB^{+*}	154.79	154.03	
matrix	$[DHB - OH]^+$	137.71	137.02	
matrix	DHB	177.77	177.02	Na^+
matrix	DHB	193.70	192.99	K^+

It can be seen that there are variations between the calculated and the experimental observed masses. For verification of the interpretation the variation between the known mass of the matrix signals[18,19] and their experimental observed masses can be consulted which show the same variation (Table 1).

The formal loss of a *t*-butyl group has also been found by analyzing neat nitroxides.[16,17] In a recently published paper about nitroxide decomposition TIPNO was subjected to thermally decomposition experiments.[16] BRASLAU et al. proposed a new mechanism for the thermally decomposition of α-hydrogen nitroxides by a ''head-to-tail''-arrangement. Their result, the loss of the *t*-butyl-group, is the same as our finding. In another publication the photo excitation of the nitroxide DTBNO was analysed. The loss of the *t*-butyl-group was interpreted as a α-scission.[17]

To figure out which role is played by the α-H-atom in case of the assumed fragmentation during the MALDI analysis a systematic study of different nitroxides has been performed, Figure 4 shows the considerations. As stated before TEMPO and TEMPO-derivates are cyclic structures without α-H-atom. BIPNO and TIPNO are acyclic structures which content an α-H-atom. To round up the discussion two other structures are required: an acyclic structure without an α-H-atom and a cyclic nitroxide which includes such an α-H-atom. The prepared alkoxyamines which meet those demands are shown in Figure 2 and the results of the analysis in Table 1 respectively.

The **PhEt-DTBNO** also fragments during the MALDI analysis. As stated before in case of BIPNO and TIPNO a formal loss of the *t*-butyl-group accompanied by a proton transfer can be assumed resulting in a mass difference of 56 Da. The complete alkoxamine has a theoretical mass of 250.22 Da (exp. 250.87 Da) for the protonated analyte, the fragment has a mass of 194.15 Da (exp. 194.92 Da). The analysis of **PhEt-NPPNO** shows no lower masses compared to the complete alkoxyamine except to signals derived from the matrix material as is shown in Table 1.

The performed studies show that specific nitroxide structures tend towards fragmentation during the MALDI process. Due to a systematic investigation of different nitroxides with special structural requirements the influence of the structure on the properties could be displayed. It could be shown that not the presence of an α-H-atom is the essential criterion for the observed fragmentation behavior but rather if the structure is cyclic or acyclic. A related observation has been performed by KENTTÄMAA et al. by analyzing radical-radical recombination reactions in the gas

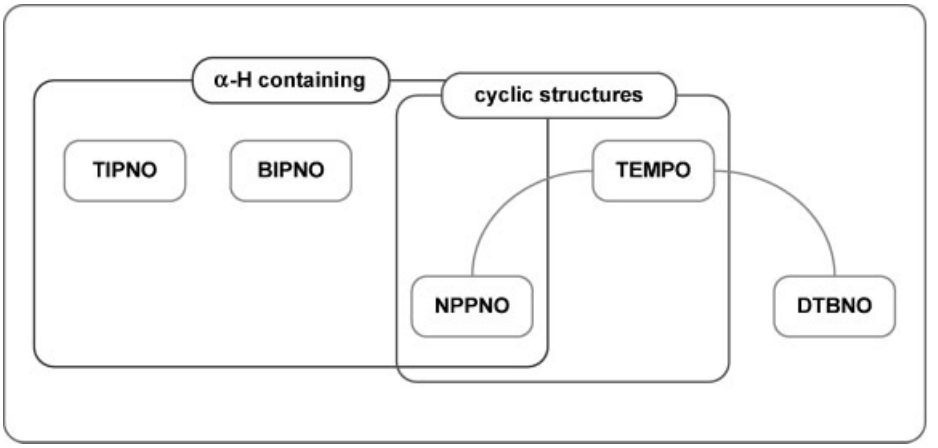

Figure 4.
Classification of different nitroxide structures which were analysed within this study. The results of the MALDI analysis are shown in Table 1.

phase of nitroxides and substituted phenyl-radicals by using FT-ICR mass spectrometry.[20]

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 formal loss of a *t*-butyl-group in case of acyclic nitroxides BIPNO, DTBNO and TIPNO. However cyclic structures like TEMPO, TEMPO-derivates and NPPNO are stable under the applied conditions.

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[1] C. B. Jasieczek, D. M. Haddleton, A. J. Shooter, A. Buzy, K. R. Jennings, R. T. Gallagher, *Polymer preprints* **1996**, *37*, 845.
[2] M. A. Dourges, B. Charleux, J. P. Vairon, J. C. Blais, G. Bolbach, J. C. Tabet, *Macromolecules* **1999**, *32*, 2495.
[3] A. Bartsch, W. Dempwolf, M. Bothe, S. Flakus, G. Schmidt-Naake, *Macromol. Rapid Commun.* **2003**, *24*, 614.
[4] T. Schulte, K. O. Siegenthaler, H. Luftmann, M. Letzel, A. Studer, *Macromolecules* **2005**, *38*, 6833.
[5] E. Rizzardo, *Chem. Aust.* **1987**, *54*, 32.
[6] [6a] E. E. Malmström, C. J. Hawker, *Macromol. Chem. Phys.* **1998**, *199*, 923; [6b] C. J. Hawker, A. W. Bosman, E. Harth, *Chem. Rev.* **2001**, *101*, 3661.
[7] [7a] D. Benoit, S. Grimaldi, J. P. Finet, P. Tordo, M. Fontanille, Y. Gnanou, *Polym. Prepr.* **1997**, *18*, 729; [7b] D. Benoit, S. Grimaldi, J. P. Finet, P. Tordo, M. Fontanille, Y. Gnanou, *ACS Symp. Ser.* **1998**, *685*, 225.
[8] D. Benoit, V. Chaplinski, R. Braslau, C. J. Hawker, *J. Am. Chem. Soc.* **1999**, *121*, 3904.
[9] S. Flakus, K. Mandel, M. Bartsch, G. Schmidt- Naake, *Macromol. Rapid Commun.* **2005**, *26*, 1698–1703.
[10] W. Dempwolf, S. Flakus, G. Schmidt-Naake, *Macromol. Rapid. Commun.* submitted.
[11] V. Dao, D. Benoit, C. J. Hawker, *Journal of Polymer Science: Part A: Polymer Chemistry* **1998**, *36*, 2161.
[12] S. Flakus, Dissertation **2006**, TU Clausthal.
[13] W. Dempwolf, Dissertation **2007**, TU Clausthal.
[14] M. Bothe, G. Schmidt-Naake, *Macromol. Rapid Commun.* **2003**, *24*, 609.
[15] B. Lepoittevin, X. Perrot, M. Masure, P. Hemery, *Macromolecules* **2001**, *34*, 425.
[16] A. Nilsen, R. Braslau, *Journal of Polymer Science: Part A: Polymer Chemistry* **2006**, *44*, 697.
[17] D. R. Anderson, T. H. Koch, *Tetrahedron Letters* **1977**, *35*, 3015.
[18] K. Strupat, M. Karas, F. Hillenkamp, *Int J of Mass Spectrom and Ion Processess* **1991**, *111*, 89.
[19] V. Bokelmann, B. Spengler, R. Kaufmann, *Eur. Mass. Spectrom.* **1995**, *1*, 81.
[20] J. L. Heidbrink, F. S. Amegayibor, H. I. Kenttämaa, *Int J Chem Kinet.* **2004**, *36*, 216.

