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Nitroxide-Mediated Copolymerization of MMA with Styrene: Sequence Analysis of Oligomers by Using Mass Spectrometry

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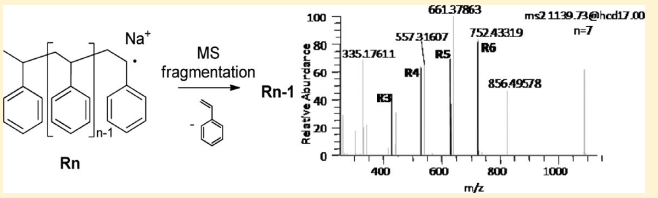
Supporting Information

ABSTRACT: The application of a sterically hindered alkoxyamine initiator for the nitroxide-mediated copolymerization (NMP) of methyl methacrylate (MMA) and styrene is presented. Working under the assumption that addition of a styrene monomer as the last embedded monomer of each dormant nitroxide-terminated copolymer will bypass the β-H-transfer (disproportionation, hydroxylamine elimination) that leads to termination of the living polymerization as observed for MMA polymerization, we successfully developed a method for the sequence analysis of oligomers by applying ESI mass spectrometry by using an orbitrap. With this method we were able to analyze chain end composition. To learn about the mass spectrometry fragmentation behavior of these nitroxide-terminated copolymers, we first analyzed different homo-oligomers and then went on with examples of co-oligomers. Oligomers consisting of styrene, *n*-butyl acrylate, and *N*-isobutylacrylamide (NIPAM), copolymers prepared from MMA and styrene, and alternating co-oligomers prepared from maleic acid anhydride and styrene were investigated. With the premise that oligomers containing 5−10 monomers are representative models for high molecular weight polymers, we could prove the validity of the assumptions made above.



INTRODUCTION

Controlled living radical polymerization has received great attention during the past 10 years, leading to the development of several methods that allow controlled polymerization of various monomers by radical chemistry.[1] ATRP (atom transfer radical polymerization),[2] RAFT (reversible addition−fragmentation chain transfer polymerization),[3] I-group transfer polymerization,[4] Te-, Sb-, and Bi-group transfer polymerization,[5] Co-mediated polymerization,[6] and NMP (nitroxide-mediated polymerization)[7] are all very promising methods that allow the synthesis of various polymers with defined molecular weights and polydispersities below the theoretical limit (PDI < 1.5). ATRP, NMP, and some cobalt-mediated polymerizations are controlled by the persistent radical effect (PRE).[8,9] However, it is important to note that, in contrast to ATRP and the cobalt-mediated polymerization, no metal is used in NMP.[10,11]

While NMP has reached a stage where a wide range of monomers like styrene, *n*-butyl acrylate, other secondary acrylates, and NIPAM can be polymerized with high control, a controlled homopolymerization of the family of methacrylic acid esters remains difficult.[11−15]

Using 2,2,6,6-tetramethylpiperidine-*N*-oxyl radical (TEMPO) as the initiator/regulator for the NMP of methyl methacrylate (MMA), the terminating β-H-transfer from the growing radical chain to the nitroxide or direct hydroxylamine elimination from the corresponding alkoxyamine becomes the major reaction pathway (Scheme 1). In addition to the formation of hydroxylamine, a polymer chain with a terminal alkenyl function is formed which does not react further in the polymerization process. This prevailing chain termination event prevents high conversions and a controlled polymerization.

By using nitroxides such as *N-tert*-butyl-*N*-(1-diethylphospho-2,2-dimethylpropyl) nitroxide (SG1) or 2,2,5-trimethyl-4-phenyl-3-azahexane 3-nitroxide (TIPNO) and their corresponding alkoxyamines, β-H transfer could be largely suppressed.[16] However, also with these sophisticated regulators the homopolymerization of MMA remained uncontrolled. The equilibrium constant between activation and deactivation is too large, meaning that the concentration of the propagating macroradical is high, leading to irreversible radical couplings.

Benoit et al. showed that a controlled radical copolymerization of MMA is possible in the presence of styrene.[17] Moreover, new work by Charleux et al. has demonstrated controlled living copolymerization of MMA with only a few mol % styrene.[18−20] More specifically, they theoretically calculated and could prove experimentally that the copolymerization of MMA with SG1, Blockbuilder, and a few mol % of styrene at 90 °C is a controlled and living process.[18,21]

To explain this phenomenon, they assumed that the last embedded monomer had to be a styrene monomer or else the above-mentioned termination reactions must take place (Figure 1). ESR, ^{1}H NMR, and ^{31}P NMR experiments on such copolymers supported this hypothesis.[19]

Along with the established methods for determining average molecular weights like gel permeation chromatography (GPC), vapor pressure, membrane osmometry, viscometry, light scattering, and ultracentrifugation, mass spectrometry methods such as

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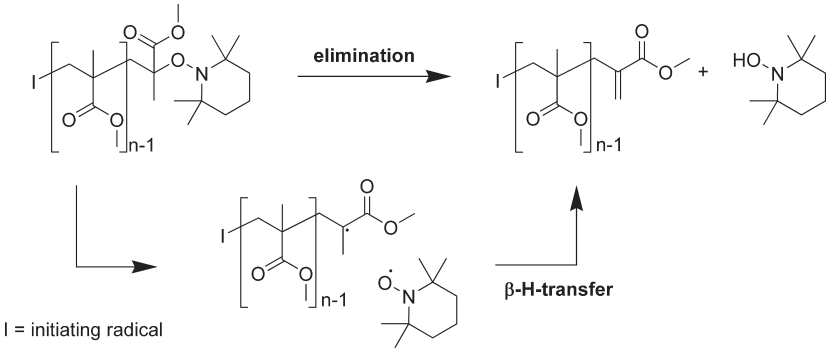
Scheme 1. Termination of the NMP with MMA via Direct Elimination or β-H Transfer



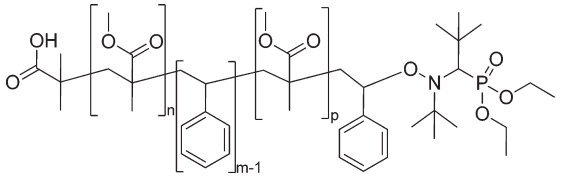


Figure 1. Assumed structure of a copolymer with styrene as the ultimate monomer.

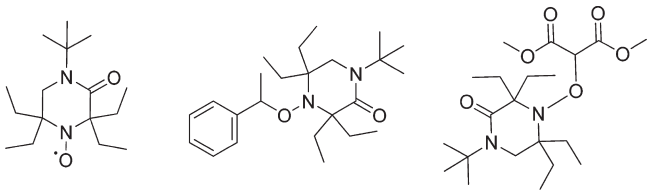


Figure 2. Nitroxide **1** and corresponding alkoxyamine initiators **2** and **3**.

electrospray ionization (ESI) or matrix-assisted laser desorption/ionization (MALDI) mass spectrometry are becoming more useful for polymer analysis.[22]

Additionally, the use of MS-MS can complement MS experiments.[23−25] By using ESI-ion trap instruments to analyze the fragmentation pathways generated by collision-induced dissociation (CID), Adamus et al. were able to elucidate the monomer arrangement in copolyester chains of poly[(*R*,*S*)-3-hydroxybutyrate-*co*-L-lactide] prepared by ring-opening copolymerization. Many studies on the degradation of polymers have appeared in the literature.[26,27] However, the utilization of high-resolution instrumentation or extensive MS experiments has not been fully explored. The majority of MS-based polymer investigations have been conducted in the area of free radical polymerization to deepen the knowledge of reaction mechanisms. All aspects of the general radical polymerization, initiation, propagation, termination, and chain transfer processes have been covered.[28] With respect to NMP, examples include MS studies (ESI as well as MALDI) that confirmed the chain end-capping mechanism by a nitroxide and the observation of unsaturated polymer end groups, which ultimately led to the conclusion that chain termination events were dominated by β-H transfer.[29,30]

Here we present the controlled and living nitroxide-mediated copolymerization of MMA with a few mol % styrene by using initiator **2**, which is derived from nitroxide **1**. Polymerization studies of styrene, *n*-butyl acrylate, and *N*-isopropylacrylamide with initiator **2** were previously reported.[31]

To analyze the sequence and composition primarily at the terminal ends of the polymeric structures, different MS-MS methods were applied. To this end, we first prepared a number of different oligomers using NMP and subsequently analyzed them by ESI-MS with MS experiments. The results of the sequential analysis of different oligomers provide new insights into polymer composition and degradation and provide direct evidence that styrene is always the ultimate monomer of a MMA−styrene copolymer.

EXPERIMENTAL SECTION

Materials. All reactions were performed under an argon atmosphere using the standard Schlenk technique. Size exclusion chromatography (SEC) was carried out with degassed tetrahydrofuran as eluent at a flow rate of 1.0 mL/min at room temperature (rt) on a system consisting of a HPLC pump 64 (Knauer), a set of two PLgel 5 μm MIXED-C columns (300 × 7.5 mm, Polymer Laboratories, linear range of molecular weight: 200−2 × 10^6 g/mol), and a Knauer RI differential refractometer detector. Data were analyzed with PSS WinGPC Compact V.7.20 software (Polymer Standards Service) based on calibration curves constructed using poly(methyl methacrylate) standard (Medium MW calibration kit M-M-10) to determine the molecular weight of poly(methyl methacrylate) with peak molecular weights ranging from 1660 to 1 000 000 g/mol. Styrene (Acros, 99%) *n*-butyl acrylate (Acros, 99%), and methyl methacrylate (Acros, 99%) were distilled under reduced pressure from CaH_2 to remove stabilizer. *N*-Isopropylacrylamide (Acros, 99%) was recrystallized from pentane. 1,2-Dichloroethane was distilled from CaH_2. Nitroxide **1** and alkoxyamines **2** and **3** were synthesized according to published procedures (Figure 2).[31,32]

Mass Spectrometry. ESI spectra were measured on a Quattro LCZ (Waters-Micromass) and on a LTQ Orbitrap XL (Thermo Scientific) with both CID (collision induced decomposition) and HCD (high-energy decomposition) capabilities. The resolution on the Quattro was set to be better than unit. On the orbitrap R = 30 000 routinely, 100 000 if necessarily. Fragmentation conditions are optimized for each compound. Spectra are averaged to improve signal-to-noise ratio. Samples (0.2 mg) are dissolved in 1 mL of methanol or chloroform/methanol (1:1). To improve the sodiation, 10 μL of a saturated methanolic $NaBF_4$ solution was added. All samples were introduced by static nanospray with internal electrical contact. The capillary voltage was adjusted to provide a stable spray (0.8−1.4 kV).

Scheme 2. Copolymerization Initiated by Alkoxyamine 2

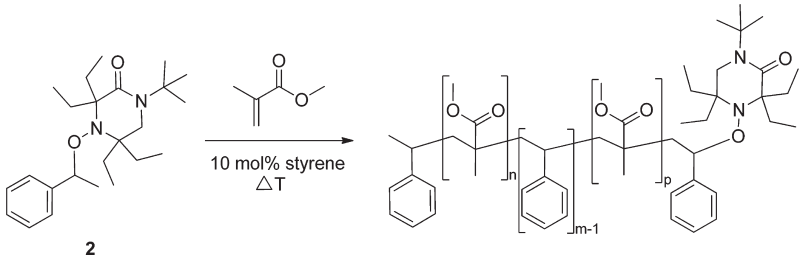


Table 1. Copolymerization of MMA (9.29 mmol) and Styrene (10 mol %) Initiated by 2

entry	initiator [mol %]	temp [°C]	time [h]	conv [%]	$M_{n,theo}$ [g/mol]	$M_{n,exp}$ [g/mol]	PDI
1[a]	0.1	90	2.5	38	37 800	65 900	1.55
2	0.1	90	1	13	14 300	18 700	1.32
3	0.1	90	1	8[b]	8 600	21 900	1.34
4	0.1	90	2	13[b]	14 100	27 800	1.26
5	0.1	90	3	20	22 300	26 000	1.23
6	0.1	90	3	21[b]	23 700	31 400	1.22
7	0.1	90	6	23	25 900	35 600	1.20
8	0.1	90	6	22[b]	24 200	35 400	1.18
9	0.1	90	9	26	29 200	45 300	1.14
10	0.1	90	12	53	58 300	68 700	1.15
11	0.1	90	24	61	67 400	84 600	1.13
12	0.1	90	37	73	91 100	112 300	1.13
13	0.3	90	0.5	8	2 800	10 600	1.35
14	0.3	90	2	25	8 700	16 400	1.23
15	0.3	90	4	41	14 700	23 000	1.23
16	0.6	90	0.25	22	7 700	9 000	1.25
17	0.6	90	3	46	8 400	15 000	1.19
18	0.6	90	6	67	12 200	17 000	1.21
19	1.0	60	24	8	800	3 400	1.23
20	1.0	90	3	51	5 700	14 700	1.25
21	1.0	125	0.5	46	5 100	10 400	1.25
22	1.0	125	3	60	6 700	13 200	1.22

[a] Reaction conducted with 0 mol % styrene. [b] Polymer dissolved in dichloromethane and then precipitated in pentane.

Example Procedure for a Copolymerization of Methyl Methacrylate with Styrene. A Schlenk tube was charged with alkoxyamine **2** (3.6 mg, 0.1 mol %), methyl methacrylate (1.00 mL, 9.29 mmol), and styrene (0.10 mL, 0.93 mmol, 10 mol %). The tube was subjected to three freeze−thaw cycles and then sealed. The polymerization was carried out under argon at 90 °C for 24 h. The resulting mixture was cooled to rt and dissolved in CH_2Cl_2 (2 mL). The solvent was removed *in vacuo*, and residual monomer was removed in a vacuum-drying cabinet at 60 °C for at least 12 h. Conversion was determined gravimetrically. Molecular weight and polydispersity index (PDI) were determined by size exclusion chromatography. The polymer was obtained as colorless solid (626 mg, 61%, $M_{n,theo}$ = 67 400 g/mol, M_n = 84 600 g/mol, PDI = 1.13).

Example Procedure for the Preparation of a Oligomer Used in Mass Analysis. A Schlenk tube was charged with alkoxyamine **2** (19 mg, 0.05 mmol, 1.0 equiv) and styrene (50 μL, 0.50 mmol, 10.0 equiv) in 1,2-dichloroethane (0.5 M, 0.1 mL). The reaction was carried out under argon at 125 °C for 2 h. The resulting mixture was cooled to rt by using a water/ice bath and was analyzed by mass spectrometry without further purification.

Procedure for the Preparation of Co-oligomers of Methyl Methacrylate and Styrene Used in Mass Analysis. A Schlenk tube was charged with alkoxyamine **2** (36 mg, 0.093 mmol, 1.0 equiv), methyl methacrylate (0.20 mL, 1.9 mmol, 20.0 equiv), and styrene (21 μL, 0.19 mmol, 2.0 equiv) in 1,2-dichloroethane (0.5 M, 0.2 mL). The reaction was carried out under argon at 125 °C for 30 min. The resulting mixture was cooled to rt by using a water/ice bath and was analyzed by mass spectrometry without further purification.

Procedure for the Preparation of Co-oligomers of Maleic Acid Anhydride and Styrene Used in Mass Analysis. A Schlenk tube was charged with alkoxyamine **2** (11 mg, 0.026 mmol, 1.0 equiv), maleic acid anhydride (13 mg, 0.13 mmol, 5.0 equiv), and styrene (15 μL, 0.13 mmol, 5.0 equiv) in 1,2-dichloroethane (0.5 M, 0.2 mL). The reaction was carried out under argon at 115 °C for 2 h. The resulting mixture was cooled to rt by using a water/ice bath and was analyzed by mass spectrometry without further purification.

RESULTS AND DISCUSSION

Copolymerization of MMA with a Small Amount of Styrene by Using Initiator 2. Reaction conditions were chosen according to those reported for the copolymerization initiated by

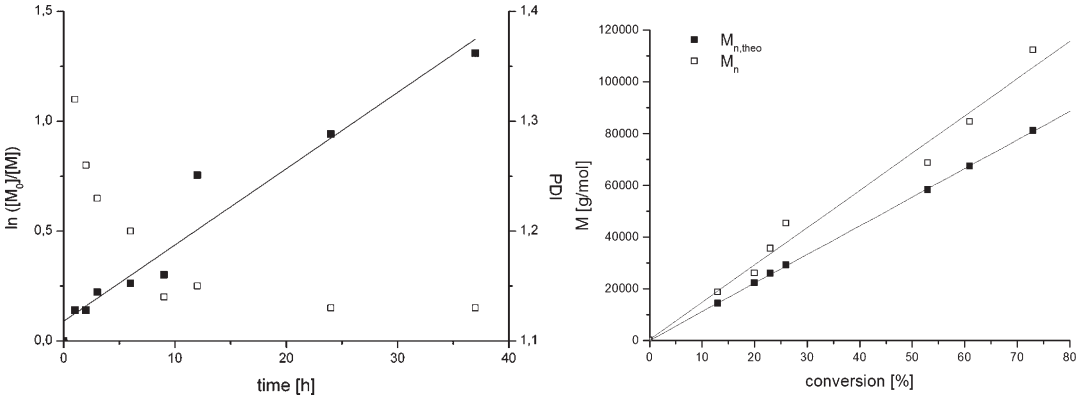


Figure 3. Monomer conversion vs time (■, left); PDI evolution vs time (0.1 mol % **2**) (□, left); theoretical molecular weight (■, right) and experimental molecular weight (□, right) vs monomer conversion.

Table 2. Block Copolymerization of Styrene Initiated by Macroinitiators Resulting from Copolymerizations of MMA with Styrene

entry	macroinitiator (entry Table *1*)	M_n (initiator) [g/mol]	initiator PDI	conv [%]	M_n [g/mol]	PDI
1[a]	3	21 900	1.34	30	39 400	1.17
2[a]	4	27 800	1.26	32	45 700	1.18
3[a]	6	31 400	1.22	33	65 500	1.15

[a] With 6.39 mmol of styrene and 0.05 mol % macroinitiator for 4 h at 105 °C.

SG1 and Blockbuilder. In contrast to the work of Charleux et al., no additional free nitroxide was necessary using initiator **2** in order to get a controlled copolymerization.[19] As shown in Scheme 2 and Table 1, the copolymerization of MMA with 10 mol % styrene initiated by 0.1−1.0 mol % alkoxyamine **2** at 90 °C exhibited conversions up to 73%.

Entry 1 shows the homopolymerization of MMA using initiator **2**. A PDI of 1.6 clearly documents that this polymerization does not correspond to a controlled living process. Entries 2−12 describe results obtained for polymerization reactions of MMA in the presence of 10 mol % styrene for 1−37 h using 0.1 mol % of initiator. Longer reaction times resulted in smaller PDI values. Conversions were between 13% and 73% with $M_{n,exp}$ ranging between 18 700 and 112 300 g/mol. Entries 13−15 show the results for the copolymerization initiated with 0.3 mol % of **2**. Under these conditions, higher conversions were achieved. After 4 h reaction time, a conversion of 41% was noted. Entries 16−18 show the results for the copolymerization initiated with 0.6 mol % of initiator **2**. In this case, 43% of monomer was converted after 3 h, and a copolymer with a molecular weight of 17 000 g/mol and a PDI of 1.2 resulted. Entries 19−22 present the results obtained for copolymerizations with 1.0 mol % of initiator loading at different reaction temperatures. Entry 19 clearly documents that copolymerization at 60 °C is possible. However, reaction time had to be extended. Only 8% conversion was achieved after 24 h. As expected, higher temperatures resulted in higher conversions (3 h, 60% at 125 °C; 51% at 90 °C). All PDI values were between 1.25 and 1.22.

We confirmed the controlled character of the MMA/styrene copolymerizations by determining conversion as a function of time and by analyzing molecular weight (M_n and $M_{n,theo}$) as a function of monomer conversion (M_0). The linear rise of $\ln([M_0]/[M])$ vs time at higher conversions and the ratio of molecular weight to conversion are typical characteristics for a controlled living polymerization. A plot of PDI vs time reveals

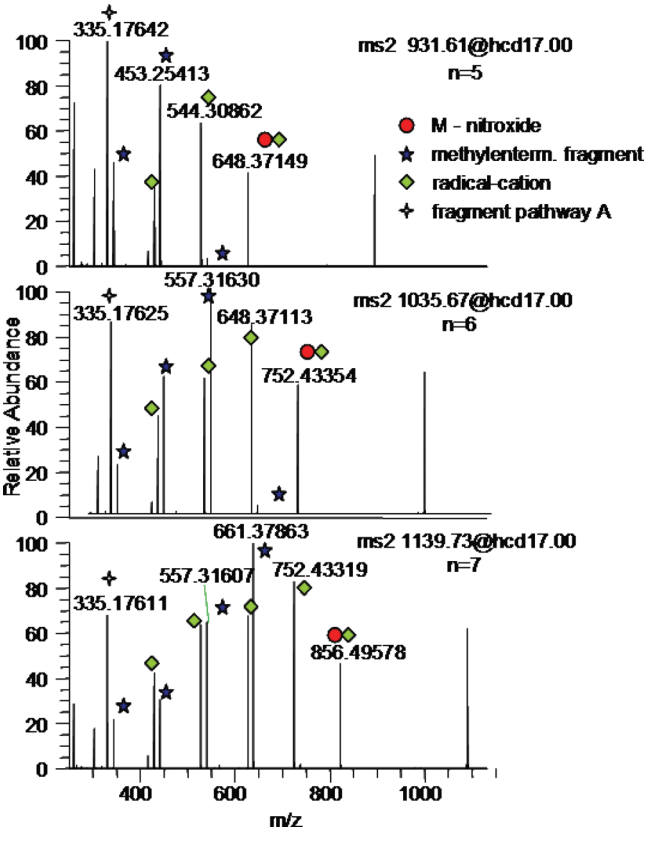


Figure 4. ESI spectra: HCD fragmentation of the styrene oligomers with $n = 5$, 6, and 7 (m/z = 932, 1036 and 1140, Na^+ addition) regulated by initiator **2**.

that the PDI levels off between 1.10 and 1.15 after a 9 h polymerization time (Figure 3).

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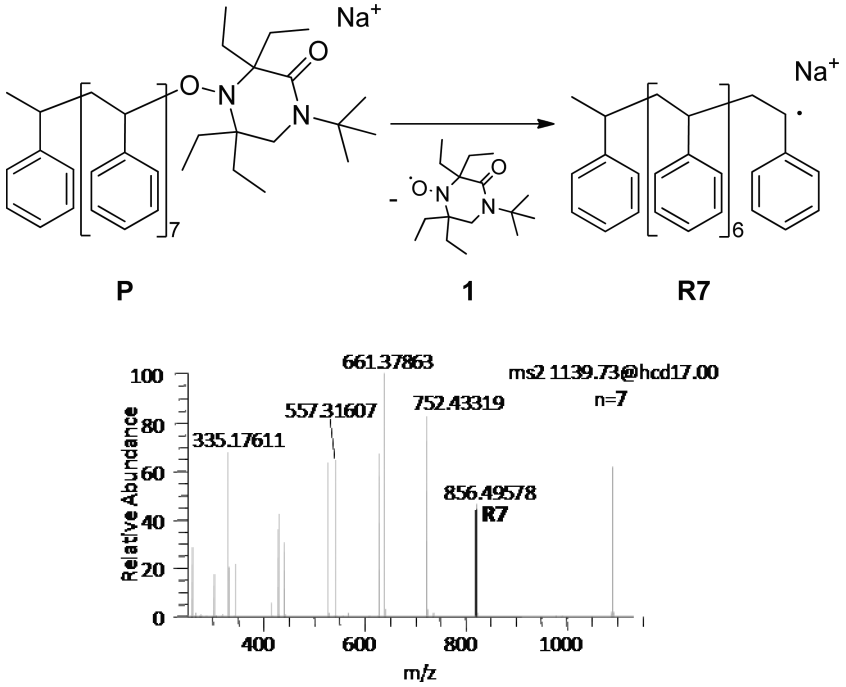
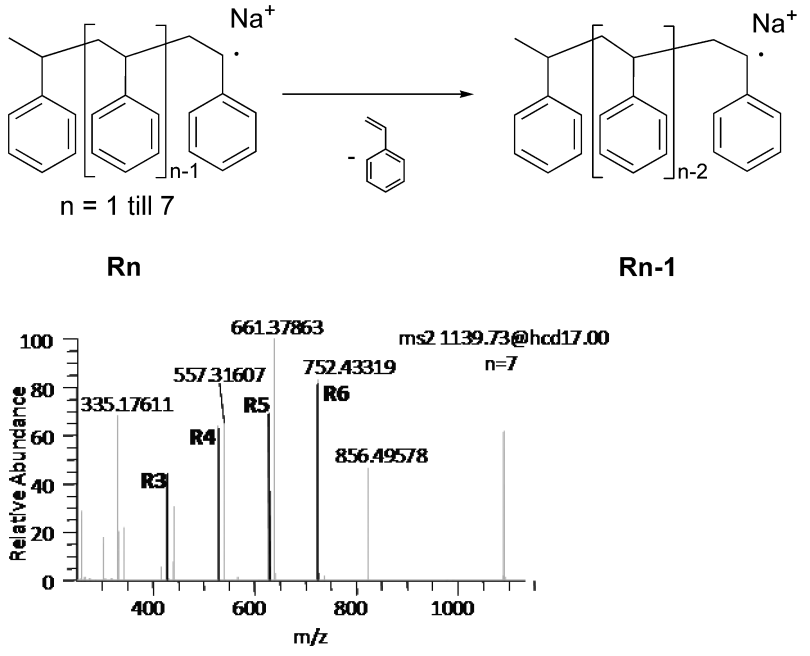
Scheme 3. C−O Bond Homolysis and ESI Spectrum: HCD Fragmentation of Styrene Oligomers with $n = 7$ ($m/z = 1140$, Na^+ Addition) Regulated by Initiator 2 (Radical R7 Is Accented in Black)



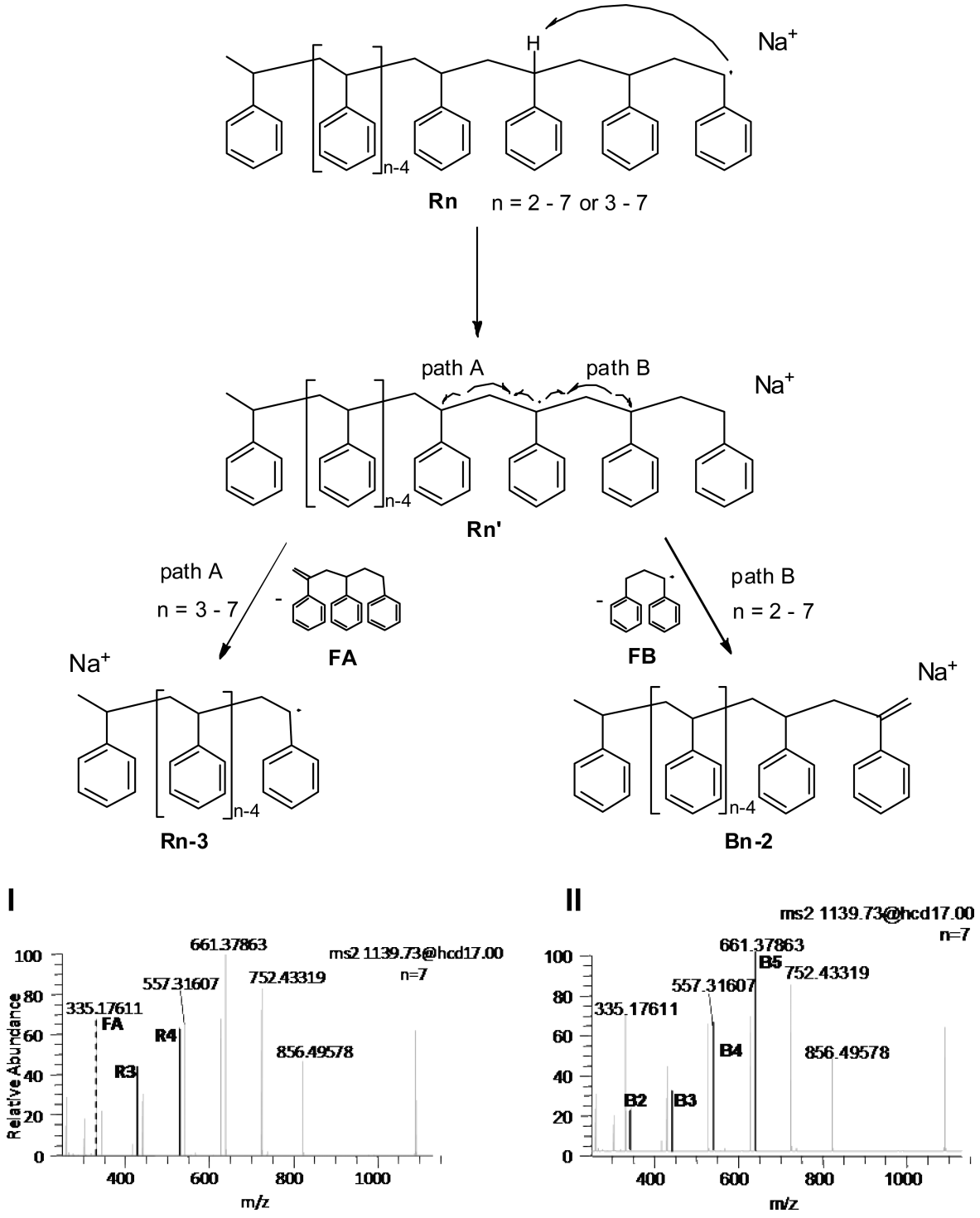
Scheme 4. Depolymerization and ESI Spectrum: HCD Fragmentation of Styrene Oligomers with $n = 7$ ($m/z = 1140$, Na^+ Addition) Regulated by Initiator 2 (Radical Cations Rn-1 Are Accented in Black)



Chain Extension. To prove the living character of the copolymerization, alkoxyamine-terminated copolymers (Table 1, entries 3, 4, and 6) were used as macroinitiators for the synthesis of block copolymers with styrene as a monomer. At 105 °C and a reaction time of 4 h, block copolymers with PDIs smaller than 1.2, molecular weights up to 65 500 g/mol, and conversions of around 30% were obtained providing evidence that the copolymerization regulated with **2** is a living process. For an example of SEC curve, see the Supporting Information.

ESI-Mass Spectrometric Sequence Analyses of Oligomers. The analyses of daughter ion spectra were accomplished by using

Scheme 5. 1,5-H Shift Followed by Fragmentation; ESI Spectra: HCD Fragmentation of Styrene Oligomers with $n = 7$ (m/z = 1140, Na^+ Addition) Regulated by Initiator 2 Following Path A (I) and Path B (II) (Fragments Are Accented in Black)



an orbitrap mass spectrometer which provides precise high-resolution detection which makes it possible to unequivocally determine the elemental composition of ions. Two MS-MS methods were used: CID (collision-induced decomposition) and HCD (high-energy decomposition). Characteristic for CID is the specific excitation of the mother ion; the corresponding daughter ions are unaffected. Therefore, the fragmentation stops after the initial step. The HCD excitation works on precursors as well as on product ions. Therefore, isomerizations and fragmentations under mass spectrometry conditions can readily be followed (sequential fragmentation of a polymer can be detected in the same spectrum).

For the mass spectrometric analyses, oligomers with a degree of polymerization of up to 10 with masses not exceeding m/z =

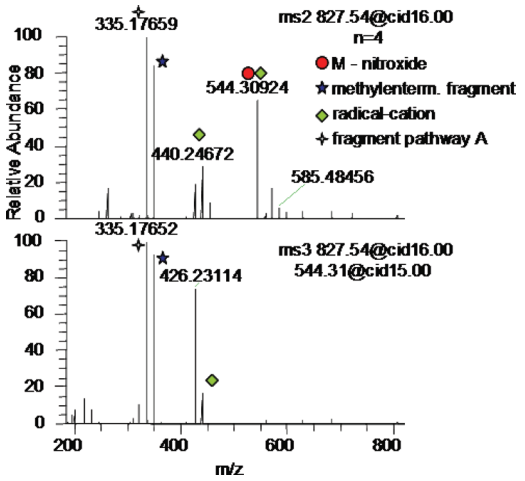


Figure 5. ESI spectra: CID fragmentation of the styrene oligomers regulated by initiator **2** with $n = 4$ ($m/z = 828$, Na^+ addition) and of the daughter ion with $m/z = 544$.

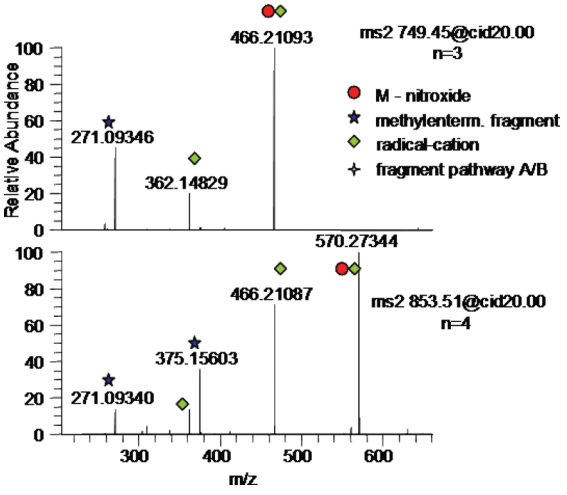


Figure 6. ESI spectra: CID fragmentation of styrene oligomers with $n = 3$ and 4 ($m/z = 749$ and 854, Na^+ addition) regulated by initiator **3**.

1500 g/mol were synthesized and analyzed. These oligomers were considered to be model systems for the corresponding polymers. In general, the fragmentation of protonated oligomers provides less sequence information. These ions predominantly yield fragments containing heterocycles of the nitroxyl residue and/or nonspecific loss of alcohol from the esters. The M + Na^+ fragmentation gave much better sequence information as will be shown below.

Oligostyrene. To identify proper conditions, oligostyrenes prepared by NMP using alkoxyamine **2** as initiator/regulator were studied first. The full ESI spectra of the H^+ and Na^+ adducts of styrene oligomers are provided in the Supporting Information. The daughter ion spectra of the Na^+ adducts of oligostyrene with 5, 6, and 7 styrene moieties (Figure 4) reveal a rather complete fragmentation pattern that is observed for all three polymers selected (n = 5, 6, 7). The spectra show the cleavage of the C−O bond, liberating the nitroxide **1**, as the initial event (●, M - nitroxide). To assign each peak of the series, additional MS experiments were performed.

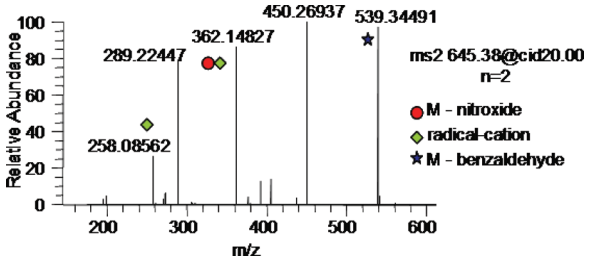
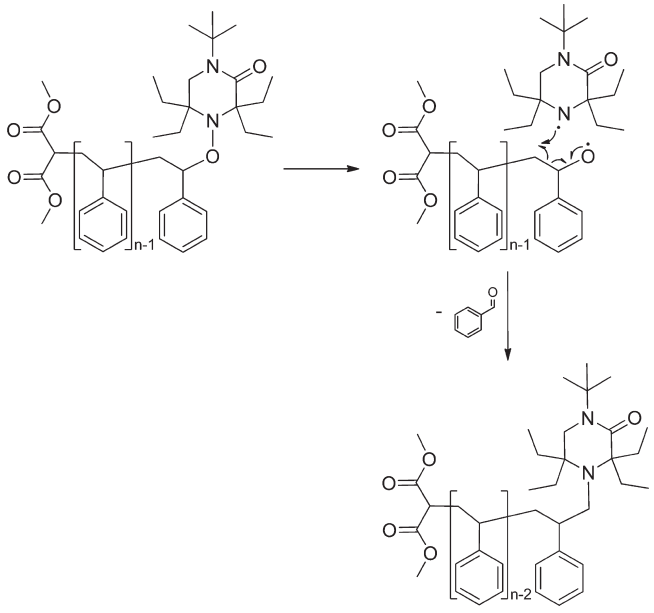


Figure 7. ESI spectra: CID fragmentation of sodiated styrene oligomer with $n = 2$ ($m/z = 645 \rightarrow$) regulated by initiator **3**.

Scheme 6. Proposed Mechanism for the Elimination of Benzaldehyde



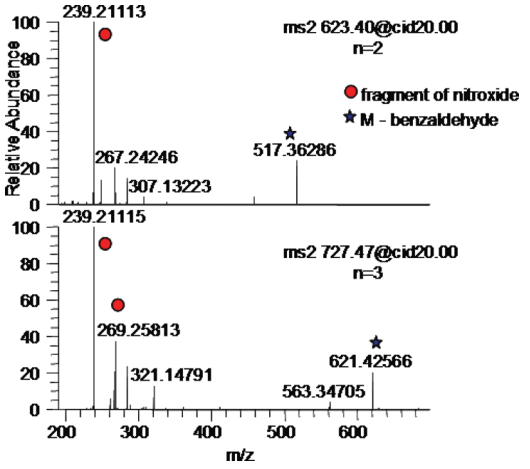


Figure 8. ESI spectrum: CID fragmentation of the protonated styrene oligomer with $n = 2$ and 3 ($m/z = 623$ and 727) regulated by initiator **3**.

By adding $NaBF_4$ to the sample solution, it was possible to promote Na^+ addition to the nonpolar oligomer chain which

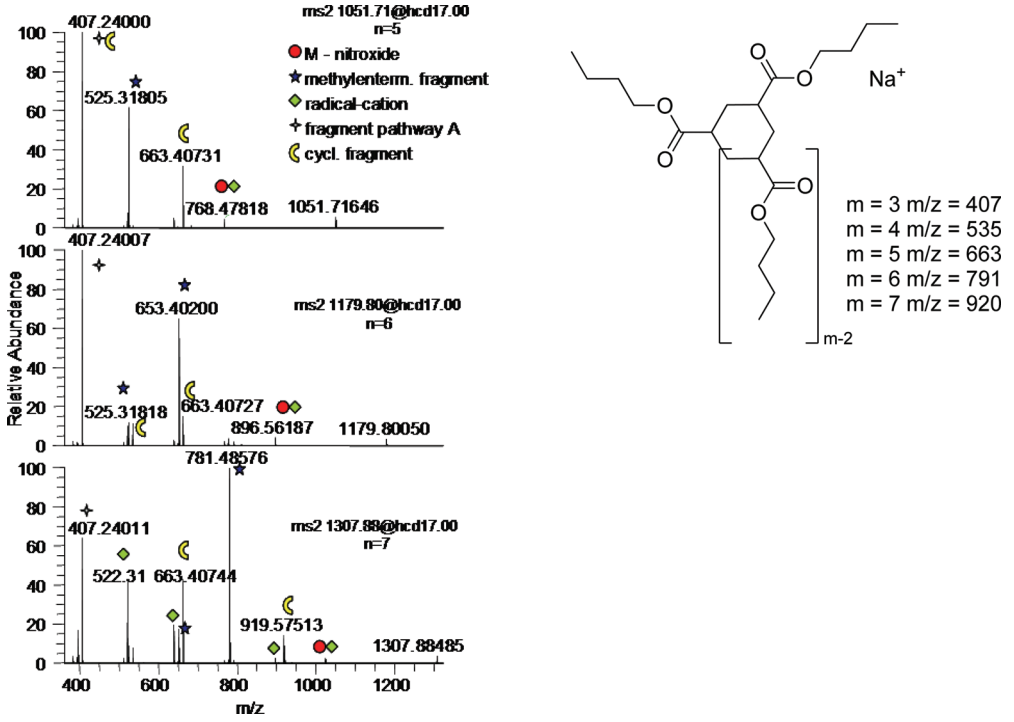


Figure 9. ESI spectra: HCD fragmentation of *n*-butyl acrylate oligomers with $n = 5$, 6, and 7 (m/z = 1052, 1180, and 1309, Na^+ addition) regulated by initiator **2**. The structure shows examples for possible cyclic fragments.

allowed to accurately analyze gas phase depolymerization by styrene fragmentation during MS analysis in the form of radical cations (for example, for $n = 7$, $m/z = 856 \rightarrow 752 \rightarrow 648 \rightarrow 544 \rightarrow 440$). In Figure 4 the corresponding peaks are tagged with ◆. Additionally, fragments with a terminal methylene unit were detected (m/z = 661, 557, 453 and 349), tagged as ★ (methylene-terminated fragments). To get a better understanding on the processes occurring during MS analysis, the peaks of the fragments in the fragmentation spectra of an oligostyrene and their origin (with $n = 7$, $m/z = 1140$) are further discussed in detail below.

Scheme 3 shows the mass-selected styrene polymer **P** with seven embedded styrene units, fragmentation of the nitroxyl radical and the resulting radical **R7**, which can be detected as a Na^+ addition in the fragmentation spectra.

Because of depolymerization by liberation of styrene monomers, new radical fragments derived from **R7**, smaller radical cations (**Rn-1**), appeared as shown in Scheme 4.

For certain chain lengths, we observed the loss of 2 or 3 styrene units in a single fragmentation step. After initial homolysis of the C−O bond, the thus-generated benzylic radical **Rn** can react along with the depolymerization in a 1,5-H shift. This radical transposition leads to a new more stable tertiary benzylic radical cation **Rn′**. **Rn′** can then further react via two different β-elimination pathways A and B, leading to **Rn-3** and **Bn-2**. Since both fragments bear the same substituents that are energetically similar, charge retention is observed for both sides and both products are readily detected by MS analysis (Scheme 5).

In the case that the radical remains on the polymer chain, a fragment (**FA**) built up by originally three monomer units will be eliminated. This fragment will either be cyclic or linear and bears a terminal methylene unit (path A). **FA** can be observed as Na^+ addition with m/z = 335, and the radical polymer fragment (M−nitroxide−**FA**−x styrene) is equal to the peaks of radicals **Rn** deriving from the stepwise depolymerization fragmentation. For the case that the radical remains on the other fragment, the polymer chain loses a phenyl(phenylethyl)-methyl radical fragment **FB** (path B) and the methylene-terminated polymer chain **Bn** (M−nitroxide−**FB**) is formed which is two monomer units shorter than the original polymer. Every radical polymer chain fragment can follow either pathway.

With a MS experiment ($827 \rightarrow 544 \rightarrow$) it was proven that the formation of the ions m/z = 335 and 349 are indeed formed via a stepwise process according to Scheme 4 (Figure 5). The MS-Quattro spectrum is essentially identical but additionally shows fragment **FB** (m/z = 218, see Supporting Information).

To check whether these mechanisms are also operative on polymers bearing other initiating groups, initiator **2** was replaced by **3**, which carries a dimethylmalonyl moiety instead of the benzyl moiety and should therefore enhance the propensity of cations such as Na^+ to add to the polymer chain (see Supporting Information).

Because of the fact that CID excitation results only in mother ion excitation, a genealogy can be investigated through consecutive experiments (Figure 6). In the case of $n = 3$ and 4 (m/z = 749 and 854), CID-MS-MS experiments reveal the loss of the nitroxyl radical upon simultaneous formation of the first radical cation. This is followed by the depolymerization of discrete styrene monomers upon formation of further radical cations. As expected, fragments containing the dimethylmalonyl substituent (radical as well as the methylene terminated) win the competition for Na^+-ion adduct formation against the pure styrene fragments.

In addition to the discussed fragmentation series, the loss of benzaldehyde from the parent nitroxide-terminated polymer was

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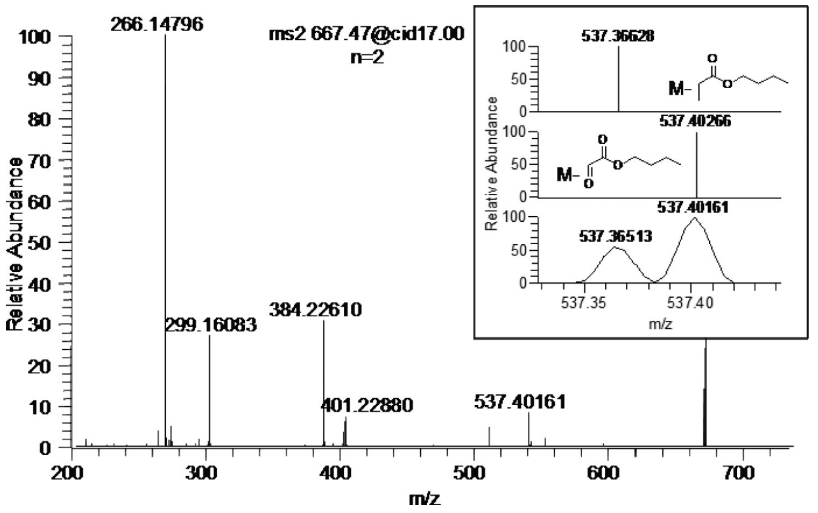

Figure 10. ESI spectrum: CID fragmentation of *n*-butyl acrylate oligomers with $n = 2$ ($m/z = 667$, Na^+ addition) regulated by initiator **2**. Box shows zoom of $m/z = 537$ and calculated masses.

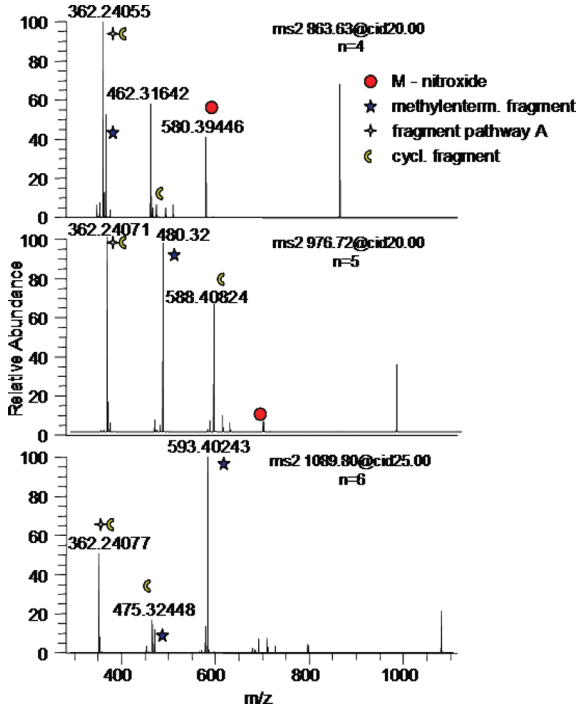

Figure 11. ESI spectra: CID fragmentation of NIPAM oligomers with $n = 4$, 5, and 6 ($m/z = 864$, 977, and 1090, Na^+ addition) regulated by initiator **2**.

also observed. This is designated as ★ (M−benzaldehyde) in Figure 7 for the first members of the oligomer series, the example $n = 2$ ($m/z = 645$).

This fragment suggests a N−O bond homolysis at the nitroxyl group (fragmentation of the piperidine moiety), release of benzaldehyde by β-fragmentation, followed by recombination with the piperidyl radical (Scheme 6). The heterocyclic residue remains in the oligomer chain. The release of benzaldehyde was even more prominent in the spectra of the H^+ addition−fragmentations in which fragments of the nitroxyl residue were also detected (Figure 8).

***n*-Butyl Acrylate Oligomers.** For a full series of the H^+ and Na^+ addition experiments on butyl acrylate oligomers, we refer to the Supporting Information. The expected degradation of oligoacrylate by C−O bond homolysis followed by depolymerization was observed. However, we were also able to observe fragmentation by initial C−O bond homolysis, 1,5-H shift, followed by the loss of dimer or trimer structures as also observed for oligostyrene (see Scheme 5).

Figure 9 shows the radical cations and the corresponding fragment **FA** as well as the methylene-terminated fragments which are formed by the loss of 1,5-dibutylglutaric acid ester. Aside from the fragmentation of dimer and trimer structures, the fragmentation of larger butyl acrylate units is also possible. In many of these cases, the entire acrylate chain remains as fragment liberated by the loss of the nitroxyl and the styrene unit. These fragments will not persist as diradicals and will either form olefinic or cyclic structures.

The expulsion of an aldehyde from the oligomer chain was also observed. N−O bond homolysis, release of aldehyde ($C_6H_{12}O_3$), and subsequent recombination with the piperazinone fragment resulted in a piperazinone-terminated oligomer. In addition to the release of the aldehyde, the appearance of propionic acid butyl ester ($C_7H_{14}O_2$) was noted (Figure 10).

Except for the end-group information, the fragmentation spectra of the protonated oligomers gave no further insights into the structure of the oligomer since mainly fragmentations of butanol from the ester substituents were observed.

NIPAM Oligomers. For a series of additions of weak intensity H^+ and strong intensity Na^+ to oligomers composed of NIPAM monomers, see Supporting Information.

The usual regular depolymerization that follows C−O bond homolysis was not observed for NIPAM oligomers. Rather, fragmentation via 1,5-H shift followed by a loss of a radical or a methylene-terminated trimer was identified (Figure 11). The methylene-terminated oligomers that are formed in this process are formally the same kind of fragments that were previously reported in 2005 by Schulte et al.[33]

Co-oligomers Made of MMA and Styrene. As mentioned in the Introduction, MMA can be polymerized by NMP in the

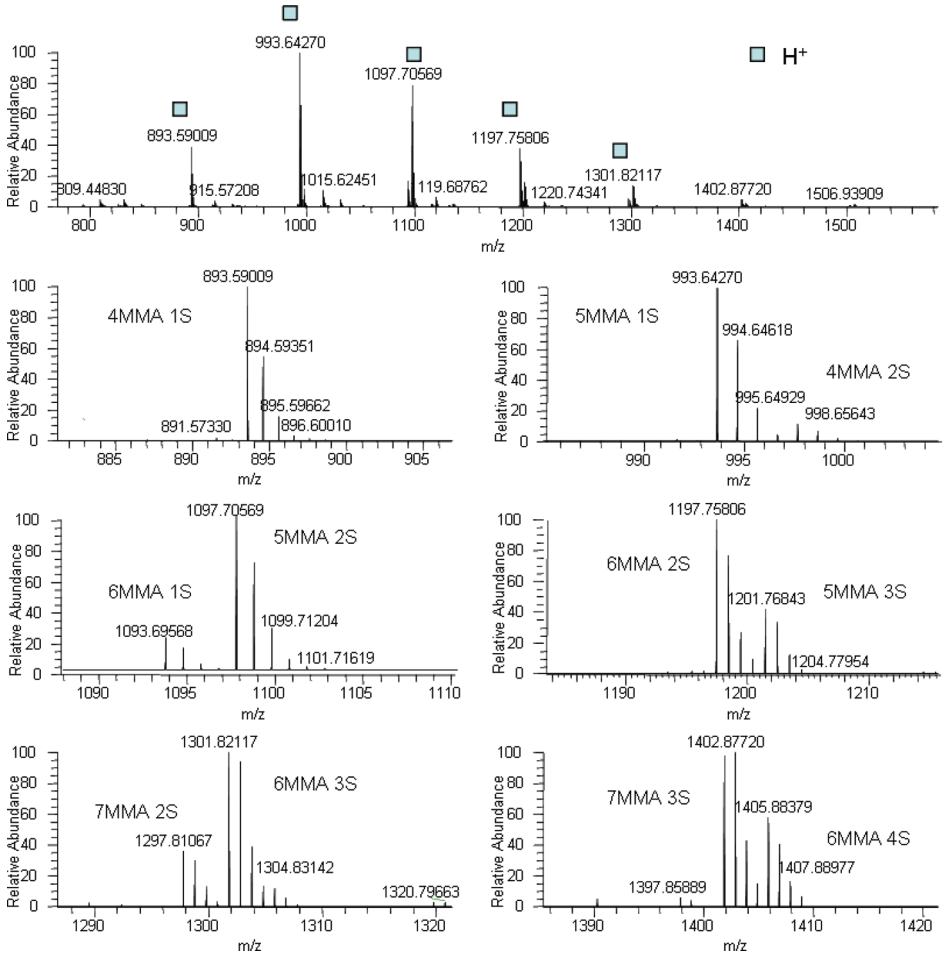

Figure 12. Entire ESI spectrum of H^+ addition series of the co-oliogmers of MMA and styrene regulated by initiator **2** with detailed example spectra.

presence of small amounts of styrene. We decided to analyze such copolymers/oligomers by MS analysis to get a proper picture on the composition and the end group of such oligomers. The mass spectra of the protonated co-oligomers enabled the determination of the overall composition (MMA/styrene) of each individual compound (Figure 12). We found that the co-oligomers mainly consist of several units of MMA and one or two units styrene in addition to the initiating styryl moiety (Figure 13).

The assumption already discussed in the Introduction that the last embedded monomer in such co-oligomers must be a styrene monomer was validated.

In the case of $m/z = 1094$ ($n = 6$) the MS-MS experiments on the H^+ adduct showed the release of benzaldehyde as also observed for styrene oligomers (see Supporting Information). The release mechanism is likely to be the same as postulated above for the pure styrene oligomers. In other words, the oxygen in the benzaldehyde originates from the nitroxyl substituent at the terminus of the oligomer chain. The fact that the co-oligomer contains only one styrene moiety provides unambiguous evidence that the terminal monomer in the selected polymer chain must be a styrene moiety. In addition to the release of benzaldehyde, fragmentations of hydroxylamine, methanol, and the heterocycle are also observed.

Co-oligomers with two styrene monomers embedded within the oligomer chain should have one styrene adjacent to the nitroxide. The fragmentation of the oligomers from H^+ addition showed the same results as those obtained for oligomers bearing only one styrene moiety. In the case of $m/z = 898$ ($n = 3$, $m = 2$), the release of benzaldehyde and elimination of hydroxylamine, followed by fragmentation of methanol were observed (Figure 14).

The addition of Na salts during MS analysis promotes formation of Na^+ adducts. As compared to the experiments conducted on protonated oligomers, fragmentation of these Na^+ adducts gives more detailed structural information (see Supporting Information).

The fragmentation of oligomers containing only one styrene unit showed a depolymerization sequence which begins with the fragmentation of the nitroxide, followed by one styrene monomer and then several monomers of MMA. Examples for mass selected oligomers with $n = 4$, 5, 6, and 7 ($m/z = 916$, 1016, 1116, and 1216) are shown in Figure 15.

The spectra for the fragmentation of co-oligomers containing two embedded monomers of styrene showed basically the same fragmentation pattern (Figure 17). These spectra clearly showed the M−nitroxide radical cation that is initially released by homolysis of the C−O bond. In the second step, a styrene monomer is fragmented. Importantly, release of a MMA monomer as second step was not observed in any case, which clearly proves that only styrene occurs as ultimate monomer in such oligomer chains. The third fragmentation step shows liberation

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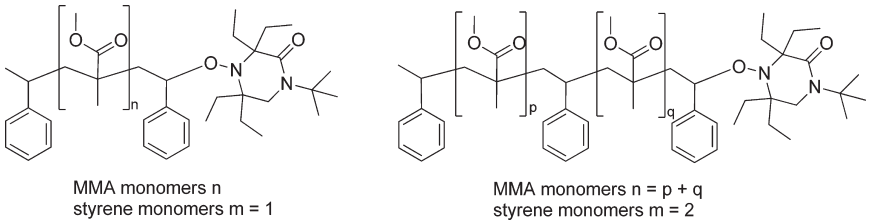

Figure 13. Co-oligomer made of several MMA and only one or two styrene monomers in addition to the initiating styryl moiety.

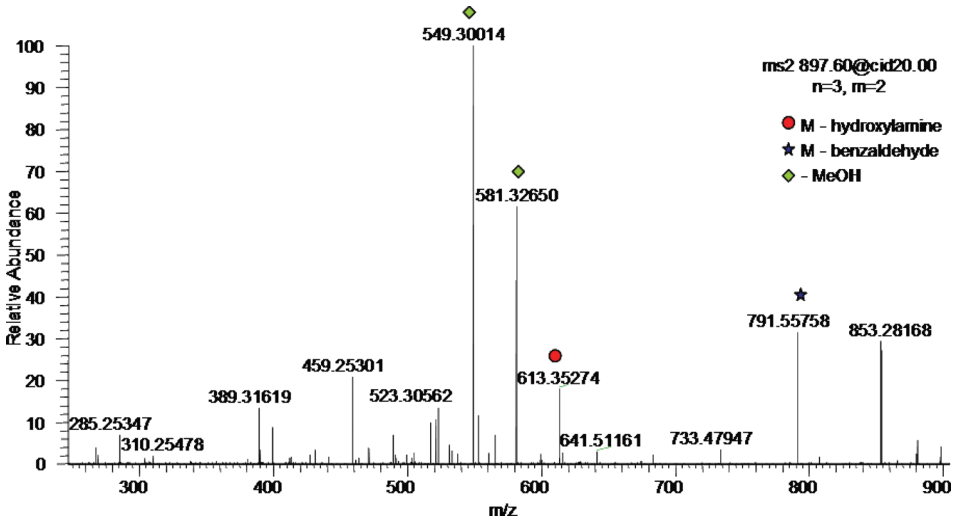

Figure 14. ESI spectrum: CID fragmentation of co-oligomer with $n = 3$, $m = 2$ ($m/z = 898$, H^+ addition) regulated by initiator **2** (853.28168 is a peak derived from background impurity).

of either styrene or MMA. This experiment indicates a statistical distribution of the second styrene monomer within the chain structure. Accordingly, for the following monomer expulsions, fragmentation of either a MMA monomer or a styrene monomer was observed.

These results further support the suggestion that styrene is the terminal embedded monomer in a NMP controlled copolymerization of MMA/styrene mixtures and demonstrate that the suppression of termination by β-H-transfer for polymers containing styrene as ultimate monomer enables a living copolymerization process.

Alternating Co-oligomers Made of Maleic Acid Anhydride and Styrene. The copolymerization of maleic acid anhydride and styrene by nitroxide-mediated polymerization has already been reported.[34,35] The alternating structure is caused by the different electronic nature of the monomers. We prepared such copolymers by NMP using alkoxyamine **2** as initiator/regulator and decided to analyze such co-oligomers by mass spectrometry to experimentally clarify if the alternating structure suggested can be validated by ESI-MS. For series of H^+ and Na^+ adducts of such co-oligomers, see Supporting Information.

A close analysis of the spectra revealed the perfect alternating structure of the oligomers. The formation of Coloumb dimers under MS conditions complicated the analysis of smaller oligomers. Two kinds of structures were observed. In one case, a series of signals containing the same amount of maleic acid anhydride and styrene monomers added to the initiator with the sum formula $C_8H_9(C_4H_2O_3)_n(C_8H_8)_nC_{16}H_{31}N_2O_2Na^+$ were

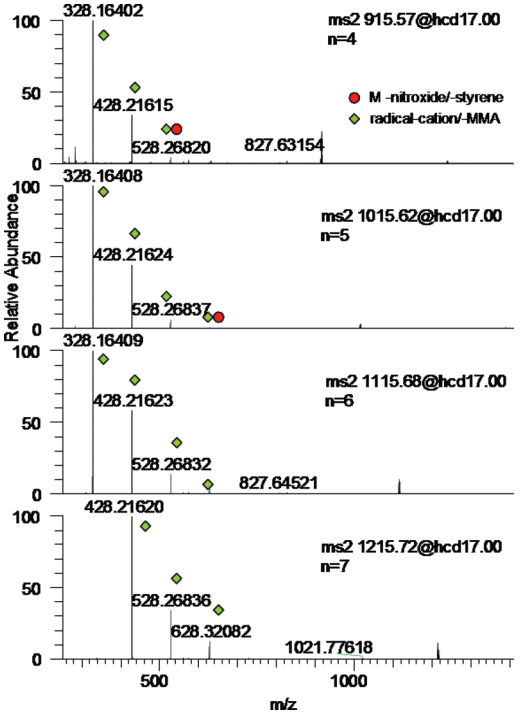

Figure 15. ESI spectra: HCD fragmentation of co-oligomers with $n = 4$, 5, 6, and 7 ($m/z = 916$, 1016, 1116 and 1216, Na^+ addition) regulated by initiator **2**.

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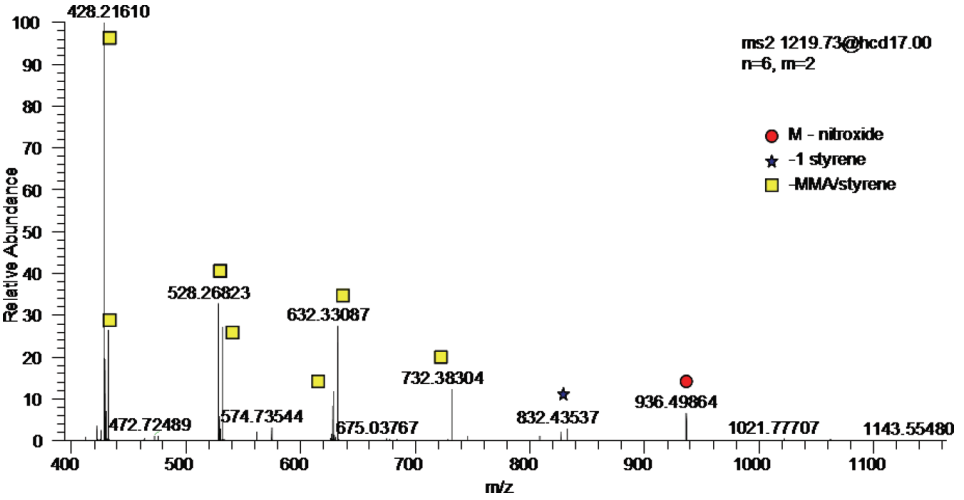

Figure 16. ESI spectrum: HCD fragmentation of co-oligomer $n = 6$, $m = 2$ ($m/z = 1220$, Na^+ addition) regulated by initiator **2**. All marked ions are radical cations.

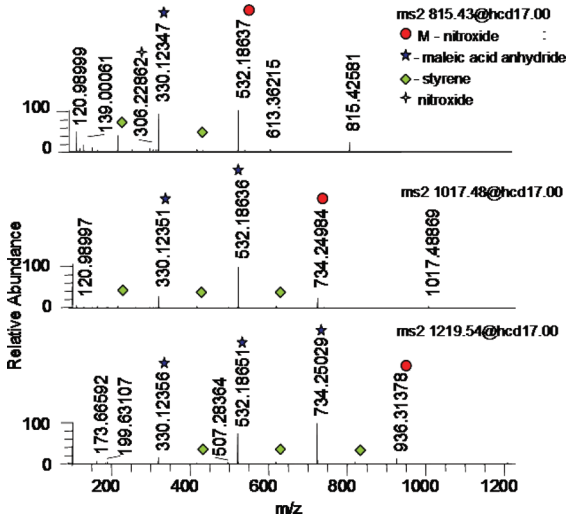

Figure 17. ESI spectra: HCD fragmenation of alternating oligomers with $n = m = 2$, 3, and 4 (m/z = 815, 1017 and 1220, Na^+ addition) regulated by initiator **2**.

observed. If the addition of monomers is strongly alternating, then styrene should be the last added monomer in the oligomer chain since the maleic acid anhydride as ultimate monomer would induce fragmentation of the hydroxylamine in the corresponding macroalkoxyamine and hence would lead to termination of the polymerization process.

On the contrary, the other series that was observed revealed a sum formula $C_8H_9(C_4H_2O_3)_n(C_8H_8)_{n+1}C_{16}H_{31}N_2O_2Na^+$ with an additional monomer of styrene. To answer the question of where that extra styrene monomer lies, an additional fragmentation experiment was conducted. After fragmentation of the nitroxide from the chain, a radical cation remains that eliminates alternating units of styrene and maleic acid anhydride, starting with a monomer of styrene. The fragmentation sequence clearly showed that the co-oligomer has a strongly alternating structure and is not a random 1:1 mixture of the two monomers. For a copolymer containing a statistical mixture of monomers, the fragmentation of each monomer would be observed in every fragmentation state (Figure 17).

The fragmentation of oligomers containing an additional styrene monomer showed a similar fragmentation pattern (Figure 18). Initially, the C−O bond is homolyzed and thereby releasing the nitroxide. This is followed by an alternating release of monomers starting with a styrene fragmentation. Caused by the strongly alternating structure the extra embedded monomer styrene must sit at the initiating styryl unit as first embedded monomer. m/z = 330 consists of one styrene unit from the initiator and one unit of each monomer. This indicates that the benzylic radical initiating the polymerization can add either to maleic acid anhydride or to styrene. Obviously, there is little selectivity for addition of the first monomer. However, the second monomer adds in a strongly alternating fashion with perfect selectivity.

For both radical oligomer species, a 1,5-H shift is possible. If a 1,5-H shift occurs to the styryl terminus, a tertiary benzylic radical inside the chain will be formed. This radical has two possibilities for fragmentation as shown in Scheme 7. If it follows decomposition path A, a methylene-terminated fragment is generated consisting originally of one monomer of maleic acid anhydride and two monomers of styrene ($m/z = 329$ for $M + Na^+$). This fragment was observed only in the fragmentation spectra for $n = 2$, $m = 3$.

If path B is followed (opening of the five-membered ring), the process corresponds to an isomerization and the product has the same mass. The 1,5-H-shift starting from a radical containing a maleic acid anhydride terminus should release a fragment ($m/z = 323$, $M + Na^+$) of originally two monomers of maleic acid anhydride and one monomer of styrene if path A is followed (see Scheme 7, right-hand side). This fragment could not be observed. A reaction following path B should give a fragment deriving from one monomer maleic acid anhydride and one monomer styrene. The oligomer chain should terminate with a methylene residue. However, none of these products were identified. Because the signals for the fragments containing a terminal maleic acid anhydride unit are not very prominent in the fragmentation spectra, we believe that the gas phase depolymerization for these polymeric radicals is faster than a 1,5-H-shift.

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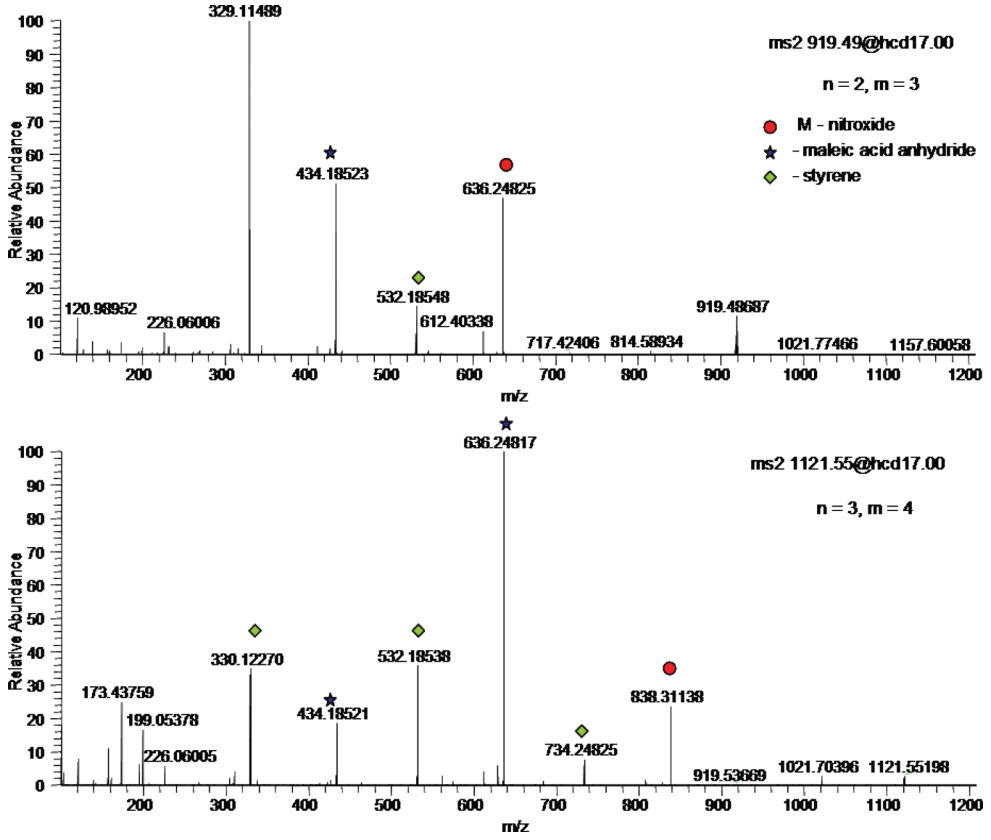
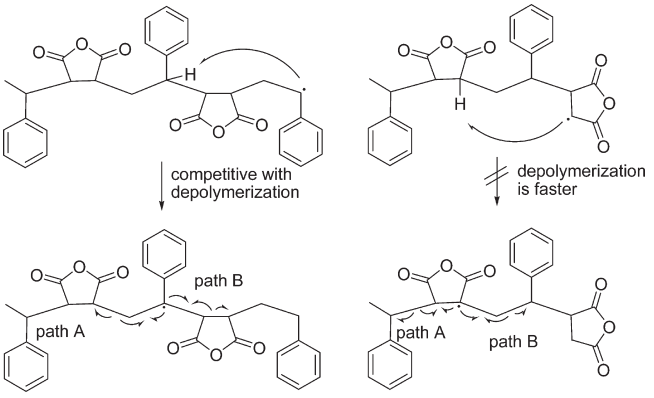


Figure 18. ESI spectra: HCD fragmentation of alternating co-oligomer with $n = 2$, $m = 3$, and $n = 3$, $m = 4$ ($m/z = 919$ and 1122, Na^+ addition) regulated by initiator **2**.

Scheme 7. 1,5-H-Shift Followed by Possible Fragmentation Pathways for Alternating Co-oligomers of Maleic Acid Anhydride and Styrene



CONCLUSIONS

We presented the controlled and living copolymerization of MMA with 10 mol % styrene by using initiator **2**. The mass spectrometric sequential analysis of oligomers was applied to systems consisting of styrene, *n*-butyl acrylate, and NIPAM and successfully allowed to identify general and specific mechanisms for fragmentations under MS conditions. The structure of the co-oligomers of MMA and styrene could be determined by MS. We proved experimentally that the last monomer embedded in such polymers prepared by NMP is a styrene monomer. Termination by hydroxylamine fragmentation is suppressed. The sequential analysis by MS of maleic acid anhydride/styrene co-oligomers prepared by NMP clearly showed an alternating monomer composition of the polymer chain. This article shows that mass spectrometry allows to accurately characterize the sequence of various oligomers, especially for co-oligomers.

ASSOCIATED CONTENT

Supporting Information. Figures S1−S9. This material is available free of charge via Internet at http://pubs.acs.org.

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