



## Fragmentation pathways of methacrylic homopolymers with labile trialkylsilyl ester side-groups—A mass spectrometric investigation of the RAFT process

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### ARTICLE INFO

#### Article history:

Received 27 October 2011

Received in revised form

25 November 2011

Accepted 26 November 2011

Available online 6 December 2011

#### Keywords:

Synthetic polymer

Poly(methacrylate)

Dissociation rule

Structural characterization

RAFT process

### ABSTRACT

Fragmentation pathways of methacrylic polymers containing labile silyl ester pendant groups were characterized upon collisional activation of electrosprayed oligomer adducts. Dissociation of lithiated oligomers mainly generated low mass product ions containing the  $\alpha$  end-group and arising from backbone bond homolytic cleavages, as typically observed for poly(alkylmethacrylate)s. Combined with the sum of the end-group masses as determined from MS data, this main reaction allowed both end-groups to be validated. In contrast, loss of HCOOR (with R = triisopropylsilyl) or elimination of alkene species from alkylsilyl groups, such as reported from poly(butylmethacrylate), was not observed here, probably due to steric hindrance of the pendant moieties. Activation of ammonium oligomer adducts was found to provide highly complementary information, since they exhibited a similar behavior as compared to poly(methacrylic acid), with serial eliminations of a triisopropylsilanol neutral conducting to the determination of the polymerization degree of the dissociating precursor ion. It should be noted however that this useful pathway was not always observed to efficiently compete with dissociation of reactive  $\omega$  end-groups. Based on these fragmentation rules, five poly(triisopropylsilyl methacrylate)s were identified in a sample obtained *via* reversible addition-fragmentation chain transfer (RAFT) polymerization using cyanoisopropyl dithiobenzoate as the chain transfer agent. Their structure could be rationalized with regards to RAFT processes: (i) dormant chains initiated by a cyanoisopropyl group and terminated by a dithiobenzoate group, as the main species; (ii) proton- and (iii) vinyl-terminated dead chains produced by disproportionation termination events; (iv)  $\alpha,\omega$ -cyanoisopropyl-terminated polymer chains arising from a combination termination between two macromolecular propagating radicals, and (v) dormant chains containing methacrylic acid monomer units within the chain.

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### 1. Introduction

Synthesis and design of polymer materials containing hydrolytically labile bonds have been a subject of scientific and commercial interest over the past 40 years in marine antifouling applications [1]. Bioactive polymer materials are specifically formed by direct incorporation of bioactive agents into a seawater hydrolyzable polymer matrix. In this context, the initially water-insoluble polymer matrix is solubilized in water through hydrolysis of labile ester bonds. This polymer hydrolysis reaction leads to a mass loss of the material with time and this resulting erosion mechanism contributes to the bioactive agent elution response. Use of trialkylsilyl (meth)acrylate based-polymers as potential delivery systems has been rarely reported in the literature [2]. It is worth noting that trialkylsilyl ester groups are well known as

conventional protecting groups of carboxylic acid functions and are readily deprotected under basic and/or acidic hydrolysis reaction [3]. In addition, the reactivity of a silyl ester linkage was reported to be highly dependent upon the steric and electronic properties of the alkyl groups attached to the silicon atom [4]. In this work, reversible addition-fragmentation chain transfer (RAFT) polymerization was selected to synthesize triisopropylsilyl methacrylate-based polymers (poly(TIPSiMA)) with a well-defined chain architecture and a narrow molecular weight distribution. The RAFT process is based on the main principle that consists of the introduction of thio compound derivatives acting as chain-transfer agents (Supplementary Scheme S1). In this procedure, control is achieved through a rapid equilibration between a low concentration of active propagating radicals ( $P_n^\bullet$ ) and a predominant fraction of dormant species end-capped by a thiocarbonylthio group [5]. A too high concentration of propagating radicals  $P_n^\bullet$  affects the control of the polymer chain growth with the formation of dead polymer chains through combination and disproportionation termination reactions [6]. The preservation of thiocarbonylthio chain end functionality is

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therefore the most important criterion of the “livingness” for this controlled/living radical polymerization (CRP) system. It opens new synthetic pathways to precisely design polymers with complex architectures [7].

Determination of terminal moieties in synthetic polymers is an analytical issue efficiently addressed by mass spectrometry, providing intact oligomer adducts are produced in the gas phase *via* electrospray ionization (ESI) or matrix-assisted laser desorption/ionization (MALDI). Although a single-stage mass spectrum can readily confirm the expected sum of the end-group masses, tandem mass spectrometry (MS/MS) is mandatory for each end-group to be individually mass-characterized and MS/MS data should be analyzed with regards to fragmentation rules established for the targeted polymer family. Dissociation behavior of poly(TIPSiMA) studied here has never been reported before and would hence have to be defined. However, Wesdemiotis et al. have recently reviewed fragmentation pathways of diverse polymer ions, including poly(methyl)- or (butyl)-methacrylate and poly(methyl)- or (butyl)-acrylate [8], which might be relevant references since they exhibit the same kind of polymeric backbone.

## 2. Experimental

### 2.1. Chemicals

Methanol was purchased from SDS (Peypin, France) while tetrahydrofuran (THF) was from Riëdel-de Haen (Seelze, Germany). Lithium fluoride, sodium iodide, potassium iodide and ammonium acetate used as cationizing agents in electrospray experiments were from Sigma Aldrich (St. Louis, MO) and used as received. Triisopropylsilyl methacrylate (TIPSiMA) was kindly supplied from Yuki Gosei Kogyo Co., Ltd., distilled under reduced pressure and stored under argon before use. 2-Cyanoprop-2-yl dithiobenzoate (CPDB) was purchased from Strem Chemicals (Bischeim, France) and used without further purification. 2,2'-Azobisisobutyronitrile (AIBN) was purchased from Aldrich and purified by recrystallization from methanol. Xylene was purchased from Acros (Illkirch, France) and distilled under reduced pressure with  $\text{CaH}_2$  before use.

### 2.2. Polymer synthesis

Synthesis of poly(TIPSiMA) shown in [Supplementary Scheme S1](#) is detailed elsewhere [9] and will only be briefly described here. Polymerization of TIPSiMA was performed in xylene using AIBN as initiator and CPDB as RAFT chain transfer agent with a molar ratio of 5/1. A solution of TIPSiMA ( $1.50 \text{ mol L}^{-1}$ ), CPDB ( $0.204 \text{ mol L}^{-1}$ ) and AIBN ( $0.041 \text{ mol L}^{-1}$ ) in xylene was prepared in a tube equipped with a magnetic stirrer and argon supply. The solution was degassed through bubbling with argon, sealed, and then placed for 24 h in an oil bath previously heated at  $70^\circ\text{C}$ . A poly(TIPSiMA) sample of low number-average molecular weight ( $M_n = 2800 \text{ g mol}^{-1}$ ) and low polydispersity index (PDI=1.3) was obtained at 83% of monomer conversion. The CPDB efficiency was estimated of around 60%. For mass analysis, the polymer sample ( $20 \mu\text{L}$ ) was first dissolved in 1 mL of THF, diluted a first time (1:10, v/v) in THF and a second time (1:10, v/v) using methanolic salt ( $1 \text{ mM}$ ) solution.

### 2.3. Mass spectrometry

High resolution MS and MS/MS experiments were performed using a QStar Elite mass spectrometer (Applied Biosystems SCIEX, Concord, ON, Canada) equipped with an electrospray ionization source. In the positive ion mode, the capillary voltage was set at  $+5500 \text{ V}$  and the cone voltage at  $+70 \text{ V}$ , while in the negative ion mode, these two parameters were respectively  $-4200 \text{ V}$  and  $-70 \text{ V}$ .

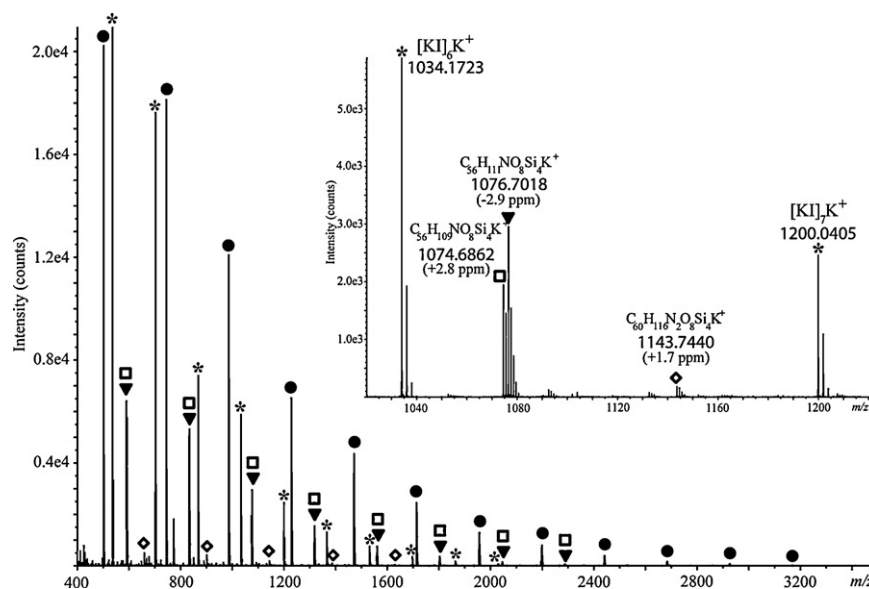
In this hybrid instrument, ions were measured using an orthogonal acceleration time-of-flight (oa-TOF) mass analyzer. A quadrupole was used for selection of precursor ions to be further submitted to collision-induced dissociation (CID) in MS/MS experiments. In MS, accurate mass measurements were performed using two reference ions consisting of alkali salt clusters as internal standards (see Section 3.1). The precursor ion was used as the reference for accurate measurements of product ions in MS/MS spectra. To support all proposed MS/MS filiations, MS<sup>3</sup> experiments were performed using a 3200 Q-TRAP mass spectrometer (Applied Biosystems SCIEX), equipped with an electrospray ionization source operated in the positive mode (capillary voltage:  $+5500 \text{ V}$ , cone voltage:  $+70 \text{ V}$ ). Primary precursor ions generated in the ion source were selected in the quadrupole analyzer and submitted to CID in a collision cell. Secondary precursor ions produced during collisions were selected and then fragmented in a linear ion trap. In both instruments, air was used as the nebulizing gas ( $10 \text{ psi}$ ) while nitrogen was used as the curtain gas ( $20 \text{ psi}$ ) as well as the collision gas. Collision energy was set according to the experiments. Instrument control, data acquisition and data processing of all experiments were achieved using Analyst software (QS 2.0 and 1.4.1 for the QqTOF and the QqTrap instruments, respectively) provided by Applied Biosystems. Sample solutions were introduced in the ionization source at a  $5 \mu\text{L min}^{-1}$  flow rate using a syringe pump.

## 3. Results and discussion

### 3.1. ESI-MS analysis

Mass spectra obtained after electrospray ionization of the polymer sample clearly showed four poly(TIPSiMA) oligomeric distributions with a  $242 \text{ Da}$  repeating unit ([Fig. 1](#)). In contrast to data obtained in MALDI-MS (not shown), where Gaussian-like distributions were consistent with the low polydispersity index of 1.3 determined by gel permeation chromatography experiments implemented with a triple detection, the shape of distributions observed in [Fig. 1](#) suggests a strong discrimination for lower mass against higher mass oligomers in ESI.

Different solutions of the sample with various cationizing agents were electrosprayed to unambiguously determine the sum of the end-group masses from mass shifts experienced by adducts produced in the gas phase. The expected  $\mathbf{I}_n$  molecules with  $m_\alpha + m_\omega = 221 \text{ Da}$  gave rise to the most abundant ions throughout the mass range, as annotated by filled circles in [Fig. 1](#). Structural assumptions could be proposed for each of the three other detected polymers ([Scheme 1](#)) based on the chemistry of the synthesis. As shown in [Supplementary Scheme S1](#), concomitant and successive reactions occur in the RAFT process. In contrast to conventional free radical polymerizations, the polymerization rate of monomer is affected by the presence of the RAFT agent. The chain transfer constant is the key parameter that determines the extent to which the RAFT polymerization exhibits the characteristics of a living process, *i.e.*, an equal probability for all chains to grow with monomer conversion and a narrow dispersity polymer (low PDI value). This result comes from maintaining a constant number of chains throughout the polymerization initiated by  $\text{R}^\bullet$  and terminating by a dithioester moiety ( $\mathbf{I}_n$  structure). Both AIBN-initiating or CPDB-initiating polymer chain propagations give rise to the formation of a similar cyanopropyl  $\alpha$  moiety. The relative intensity of chains initiating by the RAFT agent could not be differentiated by this way while the dithioester  $\omega$  terminating moiety ( $\mathbf{I}_n$  structure) gives us more information about the living character of the polymer chains. Earlier results for CPDB-mediated polymerizations of *tert*-butyldimethylsilyl methacrylate demonstrated the appearance of an uncontrolled period in the early stage of the polymerization [9].

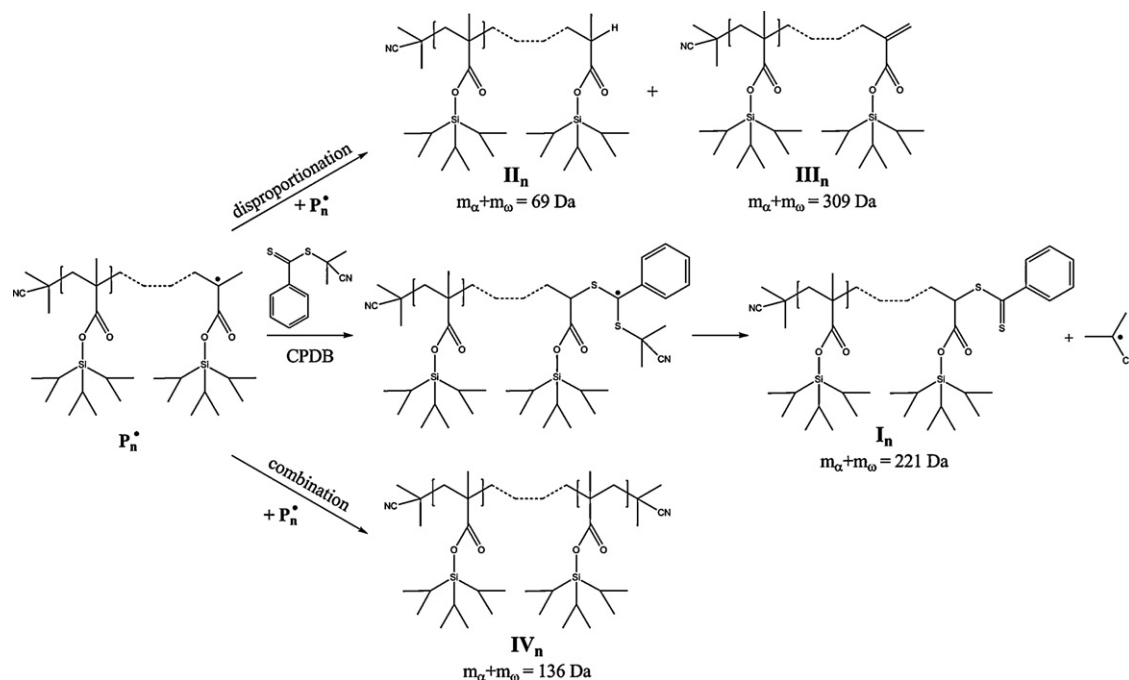


**Fig. 1.** ESI mass spectrum of the polymer sample in a methanolic solution containing KI, indicating four main oligomeric distributions:  $I_n$  (filled circles),  $II_n$  (filled triangles),  $III_n$  (open squares) and  $IV_n$  (open diamonds). Inset: zoom on the  $m/z$  1020–1240 range showing the use of potassium iodide clusters (annotated with stars) as internal standards for accurate mass measurement of cationized oligomers.

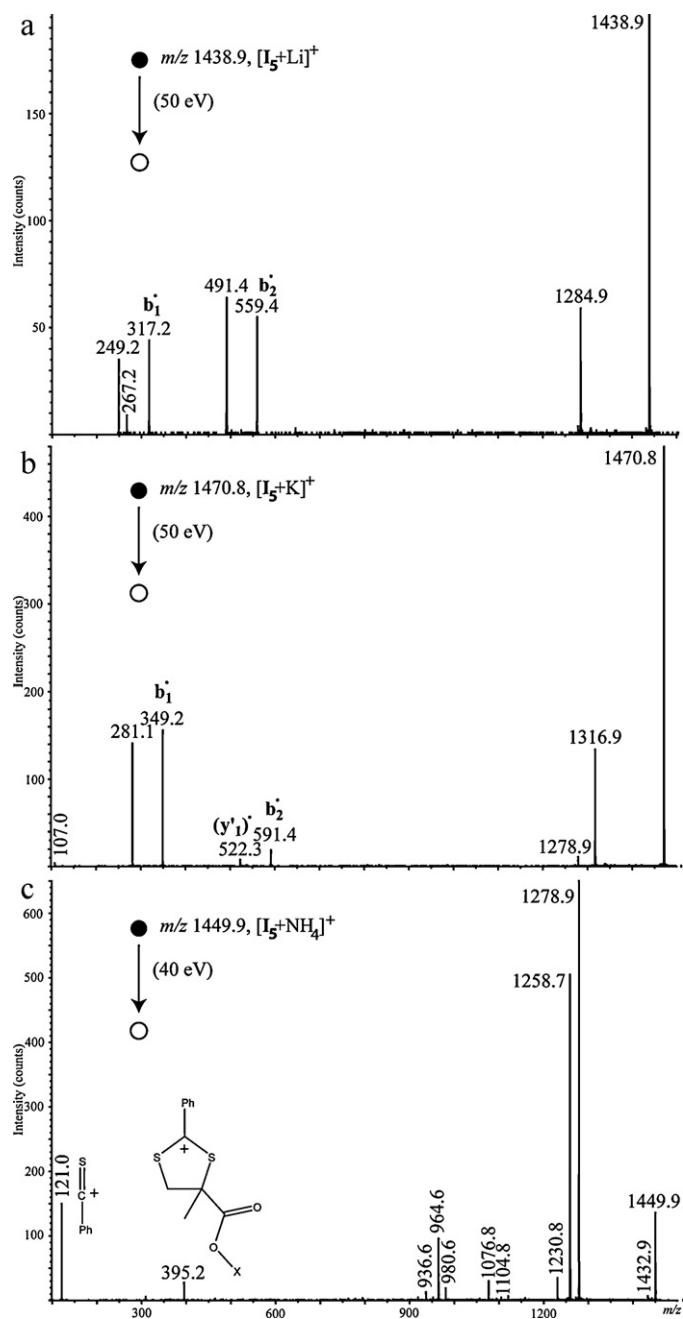
A similar behavior was encountered for TIPSiMA polymerization by RAFT, suggesting that the chain transfer and equilibrium steps are not fast enough to diminish the termination events. Termination refers to the bimolecular reaction of propagating radicals by combination or disproportionation that leads to the deactivation of propagating radical chain ends (Scheme 1). As a result, two termination reactions could occur in an AIBN-initiating conventional free radical polymerization of vinylic monomers. A disproportionation termination between two macromolecular radicals  $P_m^\bullet$  and  $P_n^\bullet$  would imply the formation of a vinylidene end group ( $III_n$  structure) as a consequence of  $\beta$ -hydrogen abstraction from a terminal radical ( $II_n$  structure), while a combination termination between the macromolecular radical  $P_m^\bullet$  and primary radical  $I^\bullet$  or  $P_n^\bullet$  and

$R^\bullet$  would lead to the  $IV_n$  structure. The sum of the end-group masses calculated from MS data of Fig. 1 strongly suggests that  $II_n$ ,  $III_n$  and  $IV_n$  were indeed formed as side-products of the targeted poly(TIPSiMA)  $I_n$  in the polymer sample. This result confirmed the significant contribution of disproportionation when the propagating radical possesses easily abstractable  $\beta$ -hydrogens such as for  $\alpha$ -methylvinyl monomers like methyl methacrylate [10,11].

From solutions containing alkali, cationized salt clusters were also generated on the whole scrutinized  $m/z$  range. Peaks of this distribution were used as internal standards to bracket cationized oligomers for their accurate mass measurement [12] as exemplified with  $[KI]_x K^+$  ions in the inset of Fig. 1, further supporting elemental composition of oligomer adducts (Supplementary Tables S1–S4).



**Scheme 1.** Mechanisms occurring in the RAFT process and structure proposed for the poly(TIPSiMA)s  $I_n$  to  $IV_n$ .



**Fig. 2.** MS/MS spectra of the 5-mer in distribution  $I_n$  adducted with (a) lithium, (b) potassium and (c) ammonium. Collision energies are reported in laboratory frame.

Validation of these structural assumptions was carried out by performing MS/MS experiments.

### 3.2. MS/MS study of $I_n$

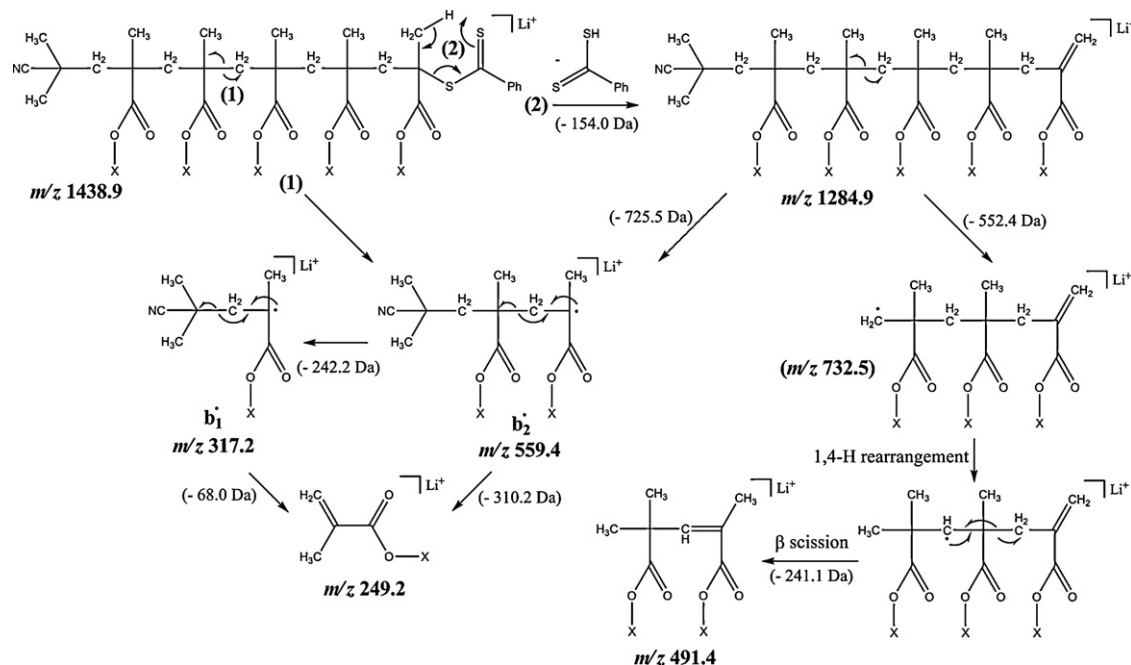
Based on their structure, the studied polymers were expected to behave like poly(alkylmethacrylate)s in MS/MS, which dissociation reactions have been thoroughly described in the literature [8,13–17]. Therefore, lithiated adducts were selected for CID experiments, since the higher binding of  $Li^+$  versus larger alkali toward oxygen atoms [18] was shown to minimize the extent of metal ion detachment upon activation [8]. As expected, product ions of  $[I_n+Li]^+$  were mostly observed in the low  $m/z$  range of the MS/MS spectrum, as exemplified for the 5-mer in Fig. 2a. According to dissociation rules established for PMA-like oligomers, ions detected

at  $m/z$  317.2 and  $m/z$  559.4 could respectively be assigned to  $b_1^*$  and  $b_2^*$ , two radical cations containing the  $\alpha$  end-group and arising from homolytic cleavage of the second type of bonds found in  $I_n$  oligomers [8]. Their formation could be illustrated by pathway (1) in Scheme 2, although these ions most probably arose from random homolytic bond scission followed by a fast depolymerization process, as usually reported for poly(methylmethacrylate) (PMMA) [8] and as supported by the detection of the  $m/z$  249.2 product ion, assigned to a lithiated monomer based on accurate mass data (Supplementary Table S5). Further  $\beta$ -H $\cdot$  loss from these  $b_i^*$  to form the corresponding  $b_i$  products with unsaturated chain ends [8] was observed to occur to an extremely low extent.

Elimination of the  $\omega$  end-group from the precursor ion is proposed to account for the formation of the  $m/z$  1284.9 product ion. As described in Scheme 2 (pathway (2)), it would proceed via a 1,5-proton transfer from the methyl group of the last monomer to one of the sulfur atom in the terminal group, according to McLafferty-like rearrangement, leading to the release of  $Ph-C(SH)=S$  (154 Da). The quite high abundance of this product ion indicates that release of the  $\omega$  end-group efficiently competes with backbone bond homolysis. Dissociation of the so-formed  $m/z$  1284.9 could also generate  $b_i^*$  ions. Complementary lithiated radicals were not detected, presumably because they further dissociate via a fast backbiting rearrangement and subsequent  $\beta$  scission, as reported for other polymer adducts [8,19]. As illustrated in the right-hand side of Scheme 2, this mechanism would account for the formation of the  $m/z$  491.4 product ion. Finally,  $m/z$  267.2 was proposed to arise from consecutive rearrangement of  $m/z$  491.4 (Supplementary Scheme S2) and was thus not found to be structurally informative.

It should be noted that activated precursor ions were not observed to lose  $H-COOX$  (with  $X = Si(CH_3)_2$ ) via a 1,5-proton transfer with six-membered ring intermediates formed from the backbone atoms, as described for poly(alkyl methacrylate) with methyl, ethyl or *n*-butyl as the alkyl group [13]. In addition, studied lithiated oligomers did not eliminate alkene species from the alkyl silyl group, as reported in the case of poly(*t*-butyl methacrylate) or poly(*n*-butyl methacrylate) [17]. The absence of these channels is presumably caused by the steric hindrance imposed by the bulky triisopropylsilyl group.

In contrast to the three other polymers of the sample (*vide infra*), informative product ions could also be obtained for sodium and potassium adducts of  $I_n$ , suggesting the unique  $\omega$  end-group of this polymer is involved in these alkali binding. Elimination of  $Ph-C(SK)=S$  (192 Da) from the  $[I_5+K]^+$  precursor ion at  $m/z$  1470.8 to generate  $m/z$  1278.9 (in addition to the loss of  $Ph-C(SH)=S$  to form  $m/z$  1316.9) further supports this assumption (Fig. 2b). A similar result was observed starting from  $[I_n+Na]^+$  (data not shown). Such an elimination of the metal in a salt species from the binding sites of the polymer chain was previously reported to generate a carbocation in the case of poly(vinyl acetate) [20]. This  $m/z$  1278.9 carbocation was not observed to further dissociate since all product ions detected at lower  $m/z$  values all contain potassium according to accurate mass measurements (Supplementary Table S6). Location of  $K^+$  near the end-side of the oligomer is further supported by detection of a  $y^*$  product ion, formed after  $[I_5+K]^+$  has eliminated  $Ph-C(SH)=S$ . This  $m/z$  522.3 was named  $(y'_1)^*$  since it does no longer contain the original  $\omega$  end-group. A homologous fragment was also observed in the case of sodiated oligomers. The  $[I_5+K]^+$  precursor ion would also experience PMMA-like dissociation reactions, as indicated by the peaks observed at  $m/z$  349.2 and  $m/z$  591.4 respectively assigned to  $b_1^*$  and  $b_2^*$  in Fig. 2b. A small peak at  $m/z$  107.0 revealed the formation of  $\alpha^*$ . Detection of radical product ions containing the  $\alpha$  end-group shows that many isomeric structure of  $[I_5+K]^+$  should exist, with the alkali interacting with different binding sites such as the cyano group at the  $\alpha$ -chain end and the thioester moiety of the  $\omega$  end-group, leading to the formation of



Scheme 2. Proposed fragmentation pathways of  $[I_5+Li]^+$ , with  $X = Si(CH_2CH_3)_3$ .

potassiated fragments containing one or the other original termination as the precursor ion undergoes charge-remote dissociation. Finally, the  $m/z$  281.1 was assigned to a monomer potassium adduct  $[monomer+K]^+$ , i.e., the homologue of  $m/z$  249.2 generated during MS/MS of lithiated oligomers.

Complementary structural information could be obtained from the dissociation of  $[I_n+NH_4]^+$ . A molecule of  $NH_3$  was readily eliminated from the ammonium adduct, as shown in Fig. 2c with the production of  $m/z$  1432.9 from the  $[I_5+NH_4]^+$  precursor ion at  $m/z$  1449.9. The product ion at  $m/z$  1278.9 would be formed upon release of the  $\omega$  end-group as a 154 Da neutral from  $[I_5+H]^+$  (as previously depicted to occur from  $[I_5+Li]^+$  in Scheme 2, pathway (2)). However, its high abundance strongly suggests here a charge-assisted process. A unique dissociation reaction observed from  $[I_n+H]^+$  was the elimination of triisopropylsilanol (174 Da), as revealed by an abundant  $m/z$  1258.7 product ion in the case of  $I_5$  (Fig. 2c). This reaction would most probably proceed via a charge-assisted mechanism since this 174 Da neutral loss was not observed from alkali adducts. As depicted in Supplementary Scheme S3 (pathway with plain arrows), this mechanism would be assisted by a neighboring carbonyl to form an anhydride moiety, accounting for the low abundance of the  $m/z$  1230.8 product ion expected to be formed when elimination of triisopropylsilanol is accompanied by release of carbon monoxide (Supplementary Scheme S3, dotted arrow). Such a dissociation pathway was typically observed to occur from poly(methacrylic acid) (PMAA) oligomers, either in the negative [21] or positive [22] ion mode, giving rise to successive dehydration steps, as well as from electrosprayed poly(methacrylic acid)/poly(methyl methacrylate) copolymers which random nature could be evidenced based on elimination of water and methanol molecules [23].

Both  $m/z$  1258.7 and  $m/z$  1230.8 would lose the  $\omega$  end-group as a 154 Da neutral in secondary dissociation reaction to generate  $m/z$  1104.8 and  $m/z$  1076.8, respectively. Two product ions in the low  $m/z$  range of the MS/MS spectrum were found to contain either part of or the entire  $\omega$  end-group. The structure proposed in Fig. 2c for  $m/z$  395.2 would be produced upon a backbiting process of the C=S group in the terminal moiety onto the methylene group of the last monomer, thereby assisting protonation of the carbonyl

group in the preceding unit via the formation of a double bond between the quaternary and the carbonyl carbons. Charge-assisted protonation of a sulfur atom in  $\omega$  end-group would account for the peak observed at  $m/z$  121.0. Finally, product ions detected at  $m/z$  980.6,  $m/z$  964.6 and  $m/z$  936.6 were proposed to be formed upon rearrangement processes (Supplementary Schemes S4–S6) and were hence less structurally useful. All these pathways were supported by both MS<sup>3</sup> experiments and accurate mass measurements (Supplementary Table S7).

In summary, dissociation of alkali adducts of  $I_n$  mainly allowed  $\alpha$ -containing products to be generated, either from backbone bond homolytic cleavages or after specific elimination of the  $\omega$  end-group. Loss of a single triisopropylsilanol molecule from  $I_n$  ammonium adducts confirmed the nature of the monomer pendant group. Combining these results with the sum of the end-group masses as determined from MS data allowed both terminations to be structurally validated in the expected  $I_n$  polymer. MS/MS data obtained for secondary oligomeric distributions were then analyzed based on dissociation rules established for  $I_n$ .

### 3.3. MS/MS study of $II_n$

According to the structure proposed from MS data, polymer  $II_n$  would have the same  $\alpha$  initiating group as compared to  $I_n$  but a H atom as the  $\omega$  end-group. A first evidence for the absence of a dithiobenzoate terminal moiety in  $II_n$  was provided by CID of  $[II_n+Li]^+$ , which did not experience a 154 Da loss (data not shown). Moreover, activation of potassium or sodium adducts mainly produced the naked alkali cation, further supporting the assumption of a strong alkali binding to the  $\omega$  termination in  $I_n$  (vide supra). Three ions of low abundance were mainly generated upon dissociation of lithiated adducts of  $II_n$ . As previously described in the case of  $I_n$ , a lithiated monomer at  $m/z$  249.2 and  $b_1^+$  at  $m/z$  317.2 were produced from  $[II_n+Li]^+$ , supporting the structure proposed for  $\alpha$ . A third peak was systematically observed at an  $m/z$  value corresponding to the loss of one monomer from the precursor ion. A 1,5 transfer of the terminal H to the oxygen of the carbonyl group in the  $(n-1)$ th unit, proceeding via a six-membered ring intermediate, would account

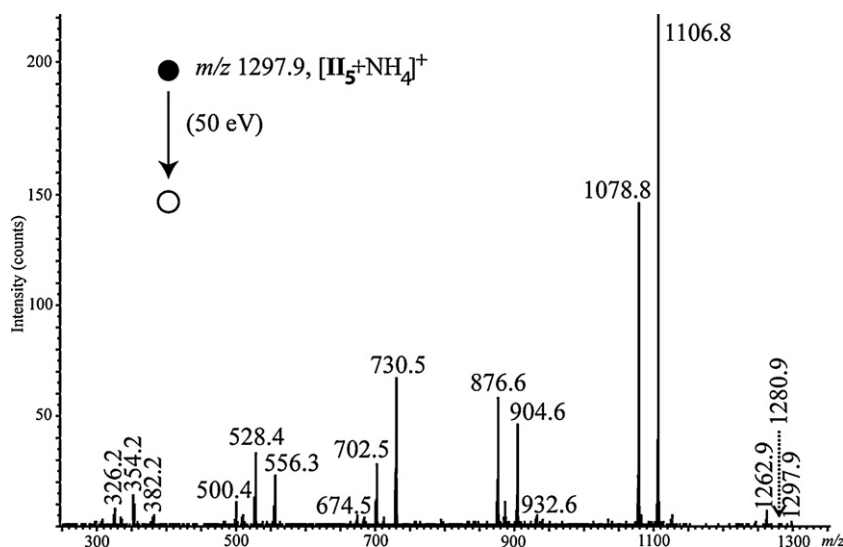


Fig. 3. MS/MS spectrum of  $[\text{II}_5+\text{NH}_4]^+$  at  $m/z$  1297.9, obtained at a 50 eV collision energy (laboratory frame).

for the formation of this product ion, further supporting the nature of the  $\omega$  end-group in  $\text{II}_n$  molecules.

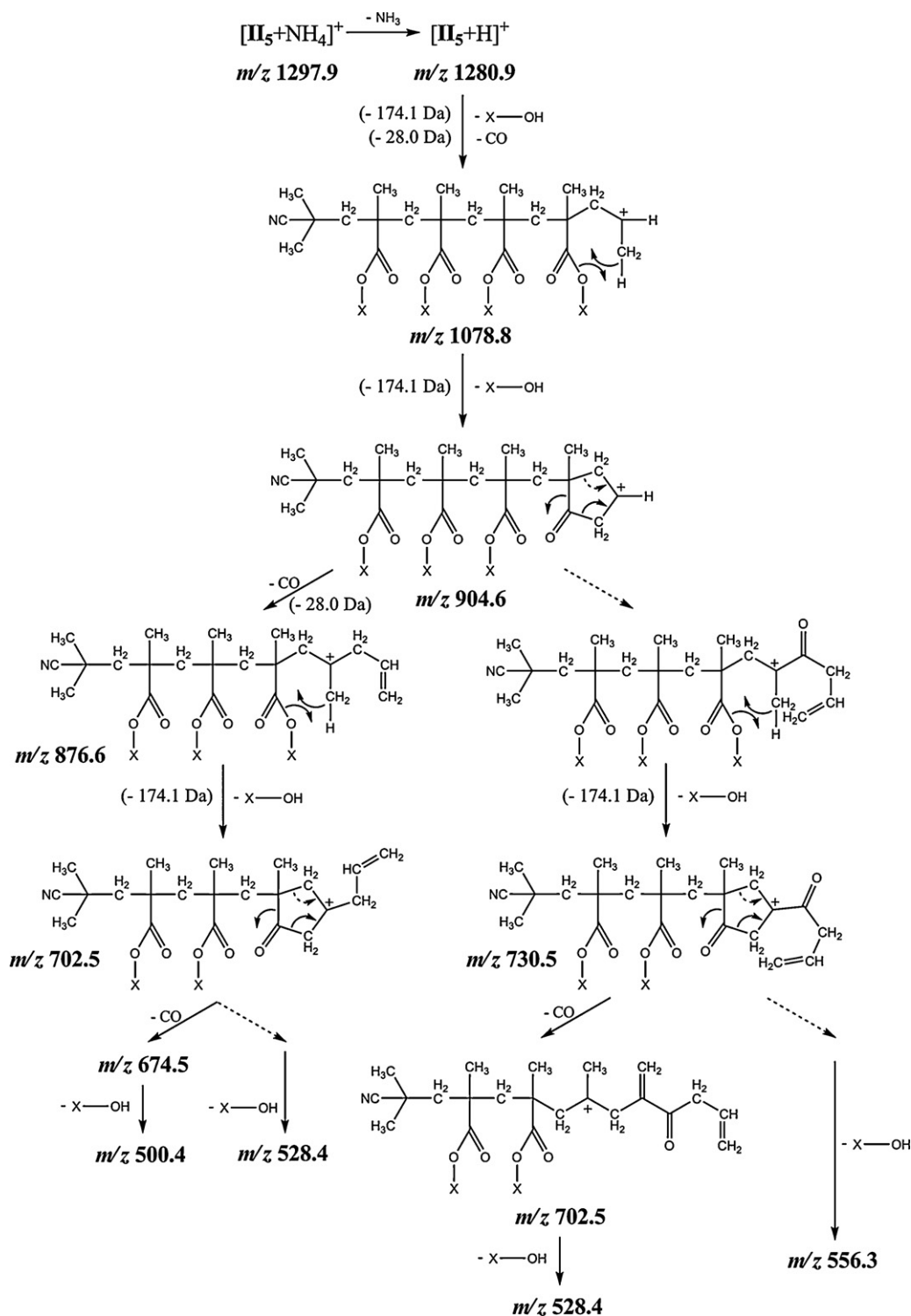
Additional information could be obtained from MS/MS data of  $\text{II}_n$  ammonium adducts. In contrast to the case of  $\text{I}_n$ , serial elimination of the 174 Da neutral could be observed from protonated oligomers formed upon release of ammonia from  $[\text{II}_n+\text{NH}_4]^+$ . As illustrated in Fig. 3 for the 5-mer, loss of  $\text{NH}_3$  from the precursor ion at  $m/z$  1297.9 would first generate  $m/z$  1280.9. This so-formed  $[\text{II}_5+\text{H}]^+$  would then eliminate triisopropylsilanol (174 Da) to form  $m/z$  1106.8, according to the same mechanism as proposed in Scheme S3 for  $\text{I}_n$ . Release of a second 174 Da neutral from  $m/z$  1106.8 is clearly less favored than loss of a CO molecule, according to intensities respectively measured for  $m/z$  932.6 and  $m/z$  1078.8. Elimination of triisopropylsilanol from this  $m/z$  1078.8 product ion would account for the formation of the  $m/z$  904.6 product ion, consistently with accurate mass measurements (Supplementary Table S8). This reaction would occur via a 1,6-transfer of a proton from a methyl group, as depicted in Scheme 3. Further opening of the so-formed five-membered ring in  $m/z$  904.6 could proceed according to two different pathways. One route would consist of the loss of a CO molecule (Scheme 3, plain arrows), yielding  $m/z$  876.6 which would further release a 174 Da neutral to generate  $m/z$  702.5. An alternative rearrangement of the  $m/z$  904.6 structure (Scheme 3, dotted arrows) would allow triisopropylsilanol to be released, giving rise to  $m/z$  730.5. Further iteration of these two pathways would account for all peaks observed at lower  $m/z$  values in the MS/MS spectrum of Fig. 3.

It should however be noted that product ions with the same elemental composition but different structure would be formed, dependent upon the pathway invoked, e.g.,  $m/z$  702.5 formed from  $m/z$  876.6 (left-hand part of Scheme 3) or from  $m/z$  730.5 (right-hand part of Scheme 3). As a result, the number of successive 174 Da release steps within an MS/MS filiation allows the polymerization degree to be determined for each polymeric chain, similarly to the case of PMAA [21,22]. This is in great contrast with results obtained for polymer  $\text{I}_n$  for which CID of the ammonium adduct indicating elimination of only one triisopropylsilanol (174 Da), presumably because this reaction did not efficiently compete with the release of the more reactive  $\omega$  end-group of  $\text{I}_n$ . Finally, minor other peaks observed for example at  $m/z$  1262.9,  $m/z$  886.6,  $m/z$  712.5 and  $m/z$  510.3 would indicate that a dehydration reaction would occur to a low extent from  $m/z$  1280.9,  $m/z$  904.6,  $m/z$  730.5 and  $m/z$  528.4, respectively.

In summary, combining the sum of the end-group masses calculated from MS data with the number of monomers in the precursor ion as determined from MS/MS of  $[\text{II}_n+\text{NH}_4]^+$  and with CID data from  $[\text{II}_n+\text{Li}]^+$  (in which some product ions contain only the  $\alpha$  end-group) allowed an unambiguous structural characterization of polymer  $\text{II}_n$ . Lack of a reactive end-group in  $\text{II}_n$ , such as the dithiobenzoate  $\omega$  end-group found in  $\text{I}_n$ , allowed more general dissociation rules to be established for poly(TIPSiMA) polymers, which could usefully be applied to structurally characterize both  $\text{III}_n$  and  $\text{IV}_n$  from their MS/MS data.

#### 3.4. MS/MS study of $\text{III}_n$ and $\text{IV}_n$

While CID of  $[\text{III}_n+\text{Na}]^+$  or  $[\text{III}_n+\text{K}]^+$  mainly produced a bare alkali, MS/MS spectra obtained for the lithiated adduct exhibited a low abundance peak at  $m/z$  249.2 (a lithiated monomer) as well as  $b_1^*$  at  $m/z$  317.2, supporting the nature of the  $\alpha$  end-group assigned to  $\text{III}_n$  (Scheme 1). Absence of a peak corresponding to the loss of one monomer from the precursor ion would be consistent with the structure proposed for the  $\omega$  end-group, lacking a hydrogen atom in position 5 toward the carbonyl group in the last monomer. Detection of additional small signals (at an  $m/z$  value corresponding to release of a 154 Da neutral from the precursor ion as well as at  $m/z$  491) would, in contrast, be in favor of a dithiobenzoate  $\omega$  end-group such as that found in  $\text{I}_n$ . However, as better emphasized with the study of  $[\text{III}_n+\text{NH}_4]^+$ , presence of these two last signals could be explained by isotopic interference of a low abundance fifth polymeric distribution. Dissociation of  $\text{III}_n$  ammonium adducts is indeed consistent with the structure proposed for the end-groups of this polymer, as exemplified by the case of the 4-mer at  $m/z$  1295.5 in Fig. 4. The protonated oligomer at  $m/z$  1277.5 was detected upon elimination of ammonia from the precursor ion (not seen in Fig. 4 but clearly observed at low collision energy). Then, a dissociation behavior similar to that described for  $\text{II}_n$  polymer could be applied. Elimination of triisopropylsilanol (174 Da) from  $[\text{III}_4+\text{H}]^+$  is revealed by an abundant product ion at  $m/z$  1104.8, which further eliminates CO to yield  $m/z$  1076.8. The latter product ion would then release a 174 Da neutral, giving rise to  $m/z$  902.6. Consecutive dissociation of  $m/z$  902.6 would then proceed according to pathways described from  $m/z$  904.6 in Scheme 3, consisting of either loss of CO followed by release of triisopropylsilanol (i.e., the MS/MS filiation  $m/z$  902.6  $\rightarrow$   $m/z$  874.6  $\rightarrow$   $m/z$  700.5), or elimination of a 174 Da molecule to generate  $m/z$  728.5. Further



**Scheme 3.** Proposed pathways to account for the formation of main product ions observed during CID of  $[\text{III}_5+\text{NH}_4]^+$  at  $m/z \ 1297.9$ .

implementation of these two dissociation routes, together with dehydration of some of the product ions as previously reported in the case of  $\text{II}_n$ , allowed most peaks observed in the CID spectrum to be accounted for. A total of five 174 Da losses were observed to occur from  $[\text{III}_4+\text{H}]^+$ , which is consistent with the presence of a triisopropylsilyl ester pendant moiety in the proposed  $\omega$  end-group and four monomers in the precursor ion.

At first glance, three additional signals (annotated with a star in Fig. 4) were however found to contradict the above mentioned

conclusion. Dehydration of  $[\text{III}_4+\text{H}]^+$  would explain the peak at  $m/z \ 1260.8$ , but in contrast to the case of  $\text{II}_n$ , this reaction was observed to proceed at a quite high yield for  $\text{III}_n$ . More importantly, detection of product ions at  $m/z \ 1124.8$  (arising from the loss of a 154 Da neutral from  $m/z \ 1278.8$ ) and at  $m/z \ 121.0$  (assigned to  $\text{Ph}-\text{C}(=\text{S})^+$  as in Fig. 2c) was clearly in favor of a dithiobenzoate  $\omega$  end-group. However, a careful inspection of the ESI-MS spectrum obtained from the polymer solution supplemented with ammonium acetate showed that an additional oligomeric distribution

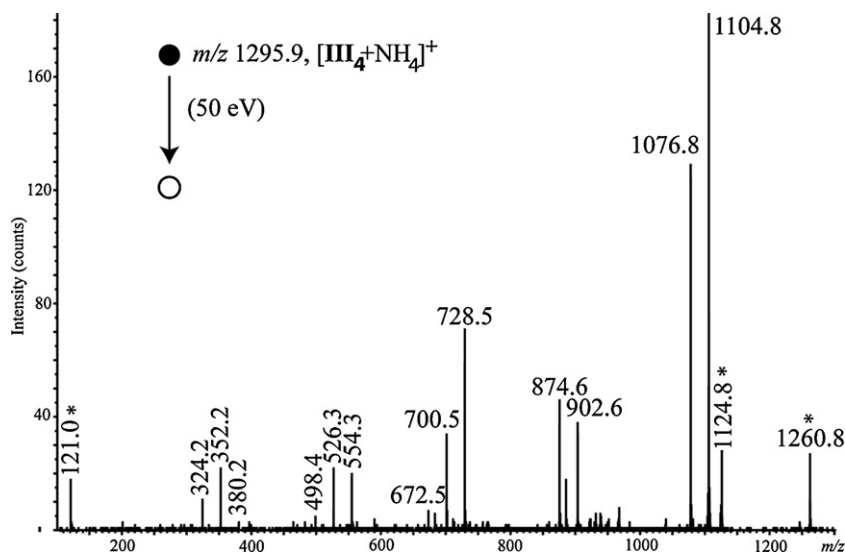


Fig. 4. MS/MS spectrum, on the 1200–1270  $m/z$  range, of  $[\text{III}_4+\text{NH}_4]^+$  at  $m/z$  1295.9, obtained at a 50 eV collision energy (laboratory frame).

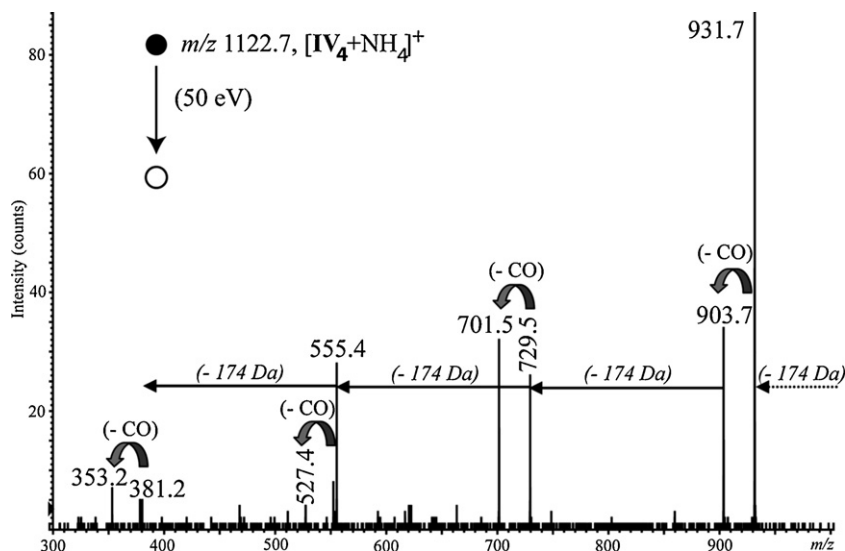


Fig. 5. MS/MS spectrum, on the 300–1000  $m/z$  range, of  $[\text{IV}_4+\text{NH}_4]^+$  at  $m/z$  1122.7, obtained at a 50 eV collision energy (laboratory frame).

(polymer  $\text{V}_n$ ) was present with a 2 Da down shift as compared to  $\text{III}_n$  (Supplementary Fig. S1). As a result, in addition to the monoisotopic form of  $[\text{III}_4+\text{NH}_4]^+$ , the  $m/z$  1295.5 precursor ion selected by the quadrupole analyzer in the MS/MS experiment of Fig. 4 would also be the ammonium adduct of a  $\text{V}_n$  oligomer containing either two  $^{13}\text{C}$  or one  $^{34}\text{S}$ . This would explain the presence of isotopic peaks in some product ions, for example at  $m/z$  122.0 and  $m/z$  123.0. This assumption was unambiguously validated by CID data obtained for  $m/z$  1293.5, the monoisotopic form of these interfering ions (Supplementary Fig. S2), which indeed clearly showed  $\text{V}_n$  contained a dithiobenzoate  $\omega$  end-group. Moreover,  $[\text{V}_n+\text{H}]^+$  were observed to dehydrate to a large extent, accounting for the high abundance of  $m/z$  1260.8 in Fig. 4. Polymer  $\text{V}_n$  could be structurally characterized from CID spectra of its ammonium and lithium adducts (see detailed analysis in Supplementary Information) and was found to be a poly(TIPSiMA) polymer containing a methacrylic acid (MAA) unit and bearing the same end-groups as  $\text{I}_n$ . This result was confirmed by measuring a mass spectrum in the negative ion mode, which clearly displays a main distribution of  $[\text{V}_n-\text{H}]^-$  ions,  $n$  ranging from 1 to 7 (Supplementary Fig. S4 and Table S11). The presence of methacrylic acid monomer units within the polymer chain could

be easily explained by the hydrolysis of the silyl ester bond of tri-alkylsilyl methacrylate monomer units during polymerization or storage in atmospheric conditions [24].

Similarly to the case of  $\text{III}_n$ , structure proposed from MS data for the end-groups in polymer  $\text{IV}_n$  (Scheme 1) could be validated by combining MS/MS results obtained for oligomer with lithium and ammonium adducts. While the nature of  $\alpha$  could be confirmed from the detection of  $b_1^*$  at  $m/z$  317.2 during CID of  $[\text{IV}_n+\text{Li}]^+$ , polymerization degree of the precursor ion could be determined from the dissociation spectrum of  $[\text{IV}_n+\text{NH}_4]^+$ , thus validating the mass assigned to  $\omega$ . As illustrated for the 4-mer in Fig. 5, once the precursor ion at  $m/z$  1122.7 has eliminated ammonia (data not shown), release of up to four triisopropylsilanol molecules was observed to occur, in competition with loss of CO, as indicated in Fig. 5 for most abundant product ions.

#### 4. Conclusion

Based on the dissociation behavior of cationized poly(alkylmethacrylate)s used as models, some fragmentation



pathways of electrosprayed poly(TIPSiMA)s could be rationalized. However, while some reactions reported for the reference polymers were not observed here, the nature of some end-groups arising from the polymerization procedure as well the peculiar chemistry and steric hindrance of TIPSiMA monomers allowed alternative dissociation routes to proceed. In particular, similarly to the case of PMAA, sequential elimination of triisopropylsilanol (174 Da) molecules observed to occur from oligomer ammonium adducts provided a direct determination of the number of monomers in the precursor ion. Combination of MS data together with these highly complementary MS/MS results and accurate mass measurements enabled us to reliably investigate different poly(TIPSiMA)s generated as side-products in the RAFT process, allowing a deeper insight into the reaction mechanisms involved during polymerization. Results clearly showed that disproportionation termination events occurred between propagating radicals during the RAFT process, proving a non-ideal RAFT polymerization. More importantly, data indicated that most of the polymer chains were terminated by the active dithiobenzoate group derived from the RAFT agent.

### Acknowledgments

L. Charles acknowledges support from Spectropole, the Analytical Facility of Aix-Marseille University, by allowing a special access to the instruments purchased with European Funding (FEDER OBJ2142-3341). M. Lejars and C. Bressy acknowledge the Direction Générale de l'Armement (DGA) for financial support.

### Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.ijms.2011.11.015.

### References

- [1] I. Omae, General aspects of tin-free antifouling paints, *Chem. Rev.* 103 (2003) 3431–3448.
- [2] C. Bressy, A. Margailan, F. Fay, I. Linossier, K. Rehel, Tin-free self-polishing marine antifouling coatings, in: C. Hellio, D.M. Yebra (Eds.), *Advances in Marine Antifouling Coatings and Technologies*, Woodhead Publishing, Cambridge, UK, 2009, pp. 445–491.
- [3] M. Schelhaas, H. Waldmann, Protecting group strategies in organic synthesis, *Angew. Chem. Int. Ed.* 35 (1996) 2056–2083.
- [4] J.M. Weinberg, S.P. Gitto, K.L. Wooley, Synthesis and characterization of degradable poly(silyl ester)s, *Macromolecules* 31 (1998) 15–21.
- [5] W.A. Braunecker, K. Matyjaszewski, Controlled/living radical polymerization: features, developments, and perspectives, *Prog. Polym. Sci.* 32 (2007) 93–146.
- [6] G. Moad, E. Rizzardo, S.H. Thang, Living radical polymerization by the RAFT process—a second update, *Aust. J. Chem.* 62 (2009) 1402–1472.
- [7] A. Gregory, M.H. Stenzel, Complex polymer architectures via RAFT polymerization: from fundamental process to extending the scope using click chemistry and nature's building block, *Prog. Polym. Sci.* 37 (2011) 38–105.
- [8] C. Wesdemiotis, N. Solak, M.J. Polce, D.E. Dabney, K. Chaicharoen, B.C. Katzenmeyer, Fragmentation pathways of polymer ions, *Mass Spectrom. Rev.* 30 (2011) 523–559.
- [9] M.N. Nguyen, C. Bressy, A. Margailan, Controlled radical polymerization of a trialkylsilyl methacrylate by reversible addition-fragmentation chain transfer polymerization, *J. Polym. Sci. Part A: Polym. Chem.* 43 (2005) 5680–5689.
- [10] B. Yamada, P.B. Zetterlund, General chemistry of radical polymerization, in: K. Matyjaszewski, T.P. Davis (Eds.), *Handbook of Radical Polymerization*, John Wiley & Sons, Inc., 2002, pp. 117–185.
- [11] F.J. Wyzgoski, M.J. Polce, C. Wesdemiotis, M.A. Arnould, Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry investigations of polystyrene and poly(methyl methacrylate) produced by monoacylphosphine oxide photoinitiation, *J. Polym. Sci. Part A: Polym. Chem.* 45 (2007) 2161–2171.
- [12] L. Charles, Influence of internal standard charge state on the accuracy of mass measurements in orthogonal acceleration time-of-flight mass spectrometers, *Rapid Commun. Mass Spectrom.* 22 (2008) 151–155.
- [13] A.T. Jackson, H.T. Yates, J.H. Scrivens, M.R. Green, R.H. Bateman, Utilizing matrix-assisted laser desorption/ionization-collision induced dissociation for the generation of structural information from poly(alkyl methacrylate)s, *J. Am. Soc. Mass Spectrom.* 8 (1997) 1206–1213.
- [14] C.D. Borman, A.T. Jackson, A. Bunn, A.L. Cutter, D.J. Irvine, Evidence for the low thermal stability of poly(methyl methacrylate) polymer produced by atom transfer radical polymerisation, *Polymer* 41 (2000) 6015–6020.
- [15] A.T. Jackson, A. Bunn, M.S. Chisholm, Utilising matrix-assisted laser desorption/ionisation techniques for the generation of structural information from different end-group functionalised poly(methyl methacrylate)s, *Polymer* 49 (2008) 5254–5261.
- [16] A. Baumgaertel, C.R. Becer, M. Gottschaldt, U.S. Schubert, MALDI-TOF MS coupled with collision-induced dissociation (CID) measurements of poly(methyl methacrylate), *Macromol. Rapid Commun.* 29 (2008) 1309–1315.
- [17] K. Chaicharoen, M.J. Polce, A. Singh, C. Pugh, C. Wesdemiotis, Characterization of linear and branched polyacrylates by tandem mass spectrometry, *Anal. Bioanal. Chem.* 392 (2008) 595–607.
- [18] M.C. Bordeje, O. Mo, M. Yanez, Binding energies of metal monocations to beta-lactones and beta-lactams. A theoretical study of cyclization effects, *Struct. Chem.* 7 (1996) 309–319.
- [19] M.J. Polce, M. Ocampo, R.P. Quirk, A.M. Leigh, C. Wesdemiotis, Tandem mass spectrometry characteristics of silver-cationized polystyrenes: internal energy, size, and chain end versus backbone substituent effects, *Anal. Chem.* 80 (2008) 355–362.
- [20] M.S. Giguere, P.M. Mayer, Climbing the internal energy ladder: the unimolecular decomposition of ionized poly(vinyl acetate), *Int. J. Mass Spectrom.* 231 (2004) 59–68.
- [21] R. Giordanengo, S. Viel, B. Allard-Breton, A. Thevand, L. Charles, Tandem mass spectrometry of poly(methacrylic acid) oligomers produced by negative mode electrospray ionization, *J. Am. Soc. Mass Spectrom.* 20 (2009) 25–33.
- [22] R. Giordanengo, S. Viel, B. Allard-Breton, A. Thevand, L. Charles, Positive mode electrospray tandem mass spectrometry of poly(methacrylic acid) oligomers, *Rapid Commun. Mass Spectrom.* 23 (2009) 1557–1562.
- [23] R. Giordanengo, S. Viel, M. Hidalgo, B. Allard-Breton, A. Thevand, L. Charles, Analytical strategy for the molecular weight determination of random copolymers of poly(methyl methacrylate) and poly(methacrylic acid), *J. Am. Soc. Mass Spectrom.* 21 (2010) 1075–1085.
- [24] C. Bressy, M.N. Nguyen, B. Tanguy, V.G. Ngo, A. Margailan, Poly(trialkylsilyl methacrylate)s: a family of hydrolysable polymers with tuneable erosion profiles, *Polym. Degrad. Stab.* 95 (2010) 1260–1268.