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Reversible Addition Fragmentation Chain Transfer (RAFT) Polymerization of Methyl Acrylate: Detailed Structural Investigation via Coupled Size Exclusion Chromatography−Electrospray Ionization Mass Spectrometry (SEC−ESI-MS)

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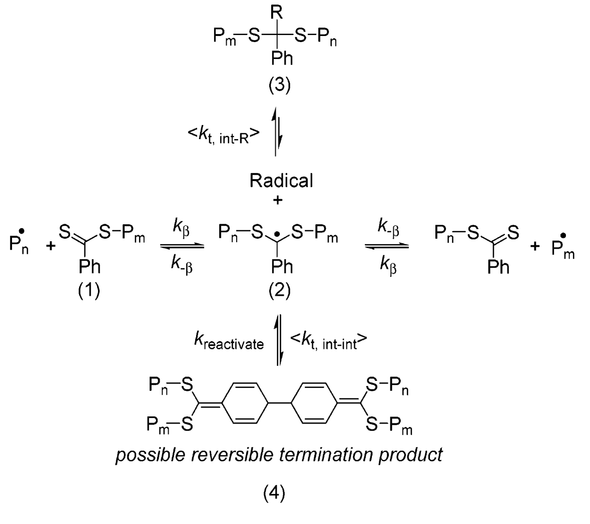
ABSTRACT: The on-line coupling of size exclusion chromatography (SEC) with electrospray ionization mass spectrometry (ESI-MS) was applied to study the polymeric product spectrum generated by the (strongly rate retarded) 2,2′-azobisisobutyronitrile (AIBN) and 1,1′-azobis(cyclohexanecarbonitrile) (ACHCN) initiated, cumyl dithiobenzoate (CDB) mediated methyl acrylate (MA) polymerization in detail. Products corresponding to the polymeric reversible addition fragmentation chain transfer (RAFT) agent and the combination and disproportionation termination products (with both cumyl, cyanocyclohexyl, and cyanoisopropyl end groups) along with a product stream arising from an oxidation process of the polymeric RAFT agent yielding sulfines and thioesters could be clearly identified. Termination products associated with the intermediate radical, that is, three- or four-armed star polymers, were not present. There is a degree of ambiguity over the disproportionation product of the macroRAFT radical. The experiments suggest that either the RAFT intermediate disproportionation product or the actual RAFT intermediate radical is present in the ESI-MS spectrum.

Introduction

Reversible addition fragmentation chain transfer (RAFT) polymerization[1−3] has—along with other equally important living free radical techniques[4,5]—revolutionized free radical polymerization, as it allows for the generation of complex macromolecular architectures such as comb, star, and block copolymers with narrow polydispersities. Since the invention of the RAFT process, various research groups have attempted to obtain information on the mechanism and kinetics of the process, either through the interpretation of dynamic kinetic and molecular weight data employing computer-based modeling strategies[6−10] or the direct observation of intermediate species[11,12] or through high-level ab initio molecular orbital calculations.[13] The scientific debate has focused particular attention on the fate of the so-called intermediate macroRAFT radicals (species **2**, Scheme 1) that are formed in the pre-equilibrium and main equilibrium of the RAFT process.[14] Evidence has been put forward for a relatively long lifetime, τ, of the intermediate radicals in cases where high stabilization of such radicals is possible (i.e. τ on the order of seconds),[3,6−9,13,15] as well as for a cross-termination reaction (either reversible[15,16] or irreversible[11,12]) of the intermediate radicals with themselves or with propagating chains. Possible reaction pathways of the intermediate macroRAFT radicals are given in Scheme 1 for the example of a dithioester-type RAFT agent carrying a phenyl group as the "so-called" stabilizing Z-group.

Scheme 1. Possible Reaction Pathways of the Intermediate MacroRAFT Radical during a RAFT Agent Mediated Polymerization



Efforts to obtain information about the fate of the intermediate macroRAFT radical have mostly been based on information regarding the intermediate radical (species **2**),[11−13] while little effort has been put into finding the possible reversible or irreversible termination side products (i.e. species **3** and **4** in Scheme 1) within the polymeric material after the completion of the polymerization process. It has been pointed out by Fukuda and co-workers[12] that (possibly) the concentration of such species—should they exist—would be rather low, and they may thus not be clearly identified via standard molecular weight analysis techniques such as size exclusion chromatography (SEC). Monteiro et al.

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claimed to have observed a peak in the SEC experiment corresponding to a three-armed star.[17] Unfortunately, this result could not be reproduced.[15] In addition, SEC does not provide a structural analysis and is therefore quite a limited technique for the identification of intermediates. Mass spectrometry techniques, however, provide the sensitivity and resolution together with structural information to determine even the smallest traces of products. In the past, a series of reviews has highlighted the strength of mass spectrometric analysis for synthetic polymers,[18−21] and especially hyphenated techniques, such as size exclusion chromatography (SEC)−electrospray ionization mass spectrometry (ESI-MS), have proven to be useful tools in minimizing the complexity of polymer molecular weight distributions via the analysis of close to monodisperse chromatographic fractions.[22,23] It therefore seems appropriate to address the analytical problem by carefully mapping the product spectrum generated by the RAFT process and to study the generated polymeric material via highly sensitive mass analysis techniques. In the past, matrix assisted laser desorption ionization (MALDI)−time-of-flight (TOF) mass spectrometry has been employed to study RAFT generated polymers.[24−29] We have chosen an alternative soft ionizing mass spectrometry technique and reported in an earlier paper on the successful observation of various RAFT made polymers via electrospray ionization−mass spectrometry (ESI-MS).[30] ESI-MS is a highly sensitive technique and is able to register very low concentrations of polymer chains, provided they are readily ionizable. It is for this reason that we employed methyl acrylate (MA) as monomer in our previous study. In the present communication we wish to extend our previous work by obtaining very low concentration sensitive molecular weight data via coupled size exclusion chromatography−mass spectrometry (SEC−ESI-MS). In this technique, the polymer is preseparated in a low molecular weight SEC system before entering the mass spectrometer. Thus, a “slice-by-slice” analysis of the molecular weight distribution is achieved. Such a preseparation has the advantage of removing potentially interfering substances (such as nonused initiator and traces of monomer) from the sample before it enters the ESI-MS instrument. It additionally effects very low ion concentrations, reducing the extent of possible ion suppression and/or shielding effects and thus resulting in a more quantitative detection. Further, in direct mass spectrometry, fragmentation may be a concern, especially for less stable polymers. In some circumstances, it may be unclear whether a registered peak is a molecular or fragment ion. SEC separation prior to mass spectrometry addresses these issues, as true low mass components will appear at larger retention times than low mass fragments resulting from fragmentation of higher molecular weight polymers.

The debate regarding the occurrence of intermediate termination products such as species **3** and **4** is centered on systems that display RAFT agent concentration dependent polymerization rate retardation phenomena.[3] Such rate retardation occurs almost exclusively with RAFT agents that carry a radical-stabilizing Z-group, such as phenyl (see Scheme 1). A typical RAFT agent that falls into this category is cumyl dithiobenzoate (CDB), which effects living free radical polymerizations of a wide range of monomers including methyl acrylate and styrene. Strong rate retardation effects are observed for both styrene and methyl acrylate; however, polystyryl dithiobenzoate is difficult to ionize via the ESI technique, whereas polymeric material having a methyl acrylate backbone undergoes facile ionization under the same conditions. In addition, some of the strongest rate retardation effects are observed for the MA/CDB system.[31] In an attempt to clarify the reaction mechanism and detect even trace amounts of species **3** and **4**—along with the potential product stream due to disproportionation reactions of **2**—in the final polymeric material, we subjected polymeric material of varying molecular weight generated via the CDB mediated free radical polymerization of methyl acrylate to SEC−ESI-MS. While the finding of intermediate termination products would confirm the existence of intermediate termination pathways, the inability to find such products does not prove their absence. However, if such products cannot be detected with state of the art analytical techniques, their concentration may be extremely low, which in turn indicates that such pathways are unlikely to be an essential part of the reaction mechanism. Alternatively, if fragmentation during the ESI process occurs, then the fragmented products will still appear in the ESI spectrum as a “smoking gun”.

In summary, SEC−ESI-MS analysis on an actual RAFT generated polymer provides an excellent analytical tool for deducing the actual mechanistic events that occur in the course of a RAFT polymerization that displays retardation effects.

Experimental Section

Polymer Synthesis. Methyl acrylate (MA, Aldrich 99%) was purified by passing over basic alumina and thoroughly deoxygenated by purging with nitrogen gas. Cumyl dithiobenzoate (CDB) was prepared using the method of Oae et al.[32] using *n*-hexane as the solvent. The purity of the cumyl dithiobenzoate was close to 99%, as confirmed via ^{1}H NMR and elemental analysis. Mixtures of 60 mg of RAFT agent ($c^\circ_{\mathrm{RAFT}} = 2.2 \times 10^{-2}$ mol L^{-1}), 10 mL of MA ($c^\circ_{\mathrm{MA}} = 11.1$ mol L^{-1}), and 10 mg of 2,2′-azobisisobutyronitrile (AIBN, Aldrich, 99%, recrystallized twice from ethanol, $c^\circ_{\mathrm{AIBN}} = 6.1 \times 10^{-3}$ mol L^{-1}) or 10 mg of 1,1′-azobis(cyclohexanecarbonitrile) (ACHCN, Aldrich, 98%, $c^\circ_{\mathrm{ACHCN}} = 4.1 \times 10^{-3}$ mol L^{-1}) as the initiator were heated at 80 or 88 °C, respectively. Polymerizations were carried out for 10 (sample A), 15 (B), and 20 min (C). The reaction time can be rather short due to the extremely high propagation rate coefficient of MA ($k_p \cong 32\,000$ L mol^{-1} s^{-1} at 80 °C).[33] The resulting polymers were isolated by evaporating the residual monomer.

Coupled Size Exclusion Chromatography−Mass Spectrometry. SEC−ESI-MS experiments were carried out using a Thermo Finnigan LCQ Deca ion trap mass spectrometer (Thermo Finnigan, San Jose, CA) coupled with an HPLC pump including a solvent mixing unit and an autosampler (Thermo Finnigan SCM1000, P4000, and AS3000), two low molecular weight high-resolution size exclusion chromatography columns (Phenomenex Phenogel 50 and 100 Å, bead size 5 μm, column temperature 25 °C), and a UV/VIS detector set to the absorption maximum of the dithiobenzoate end groups in the polymeric material at 500 nm (Thermo Finnigan UV2000). The flow rate of the system was 0.35 mL min^{-1}, the injection sample concentration was close to 1×10^{-3} mol L^{-1}, and the injection volume into the SEC system was 5.0 μL. Thus, prior to mass spectrometric analysis, the polymer is fractionated via the SEC system. The ESI-MS spectrometer is equipped with an atmospheric pressure ionization source operated in nebulizer assisted electrospray mode. The instrument was calibrated with caffeine, MRFA, and Ultramark 1621 (all from Aldrich) in the mass range 195−1822 amu. All spectra were acquired in positive ion mode over the range m/z 100−2000 with a spray voltage of 5 kV, a capillary voltage of 26 V, and

Table 1. Theoretical *m*/*z* Values for the Single Charged Ions Depicted in Chart 1 and the Expected Peaks at Various Chain Lengths for Each of the Products Using CDB as the RAFT Agent and 2,2′-Azobisisobutyronitrile (AIBN) as the Initiator[a]

ion	**1a**	**1b**	**1c**	**1d**	**3a**	**3b**	**4**	**5a**	**5b**	**5c**	**6a, 6b**[b]
end groups + Na^+	295.1	279.1	311.1	244.0	533.3	415.2	805.3	261.2	210.1	159.1	142.1
1 MA unit	381.1	365.1	397.1	330.1	619.3	501.2	891.4	347.2	296.2	245.1	228.1
2 MA units	467.2	451.2	483.1	416.1	705.3	587.2	977.4	433.3	382.2	331.2	314.2
3 MA units	553.2	537.2	569.2	502.2	791.4	673.3	1063.4	519.3	468.3	417.2	400.2
4 MA units	639.2	623.3	655.2	588.2	877.4	759.3	(1149.5)	605.3	554.3	503.3	486.3
5 MA units	725.3	709.3	741.3	674.2	963.5	845.4	1235.5	691.4	640.3	589.3	572.3
6 MA units	811.3	795.3	827.3	760.3	1049.5	931.4	1321.6	777.4	726.4	675.3	658.3
7 MA units	897.4	881.4	913.3	846.3	(1135.5)	1017.4	1407.6	863.5	812.4	761.4	744.4
8 MA units	983.4	967.4	999.4	932.4	1221.6	***1103.5***	1493.6	949.5	898.5	847.4	830.4
9 MA units	***1069.4***	1053.5	***1085.4***	1018.4	1307.6	1189.5	1579.7	1035.5	984.5	933.5	916.5
10 MA units	1155.5	***1139.5***	1171.5	***1104.4***	1393.7	1275.6	1665.7	***1121.6***	***1070.5***	1019.5	1002.5
11 MA units	1241.5	1225.5	1257.5	1190.5	1479.7	1361.6	1751.8	1207.6	1156.6	***1105.5***	***1088.5***
12 MA units	1327.6	1311.6	1343.5	1276.5	1565.7	1447.6	1837.8	1293.7	1242.6	1191.6	1174.6
13 MA units	1413.6	1397.6	1429.6	1362.6	1651.8	1533.7	1923.8	1379.7	1328.7	1277.6	1260.6
14 MA units	1499.6	1483.7	1515.6	1448.6	1737.8	1619.7	2009.9	1465.7	1414.7	1363.7	1346.7

[a] All masses given are monoisotopic. The bold/italicized numbers correspond to the peak assignments in Figure 3. The potential additional presence of the italicized ion masses (i.e. **3b**, **5b**, and **5c**) is not visible in Figure 3 due to peak overlap. Parentheses denote peaks that are not present in the spectrum/product stream. [b] The mean value of the two occurring peaks is reported.

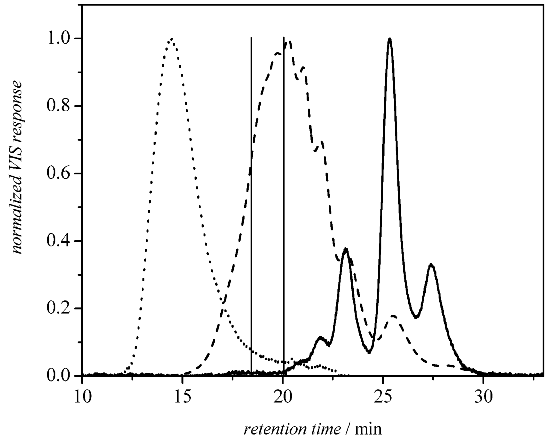


Figure 1. Distribution of the polymeric material generated via the CDB mediated free radical polymerization of methyl acrylate (MA) at 80 °C after varying reaction times: 10 min (full line, sample A), 15 min (dashed line, sample B), 20 min (dotted line, sample C). The CDB concentration was close to 2.2×10^{-2} mol L^{-1} in each case. The initiator was AIBN at a concentration of 6.1×10^{-3} mol L^{-1}. The full vertical lines indicate the positions in the MWD of the ESI-MS spectra displayed in Figures 2 and 3.

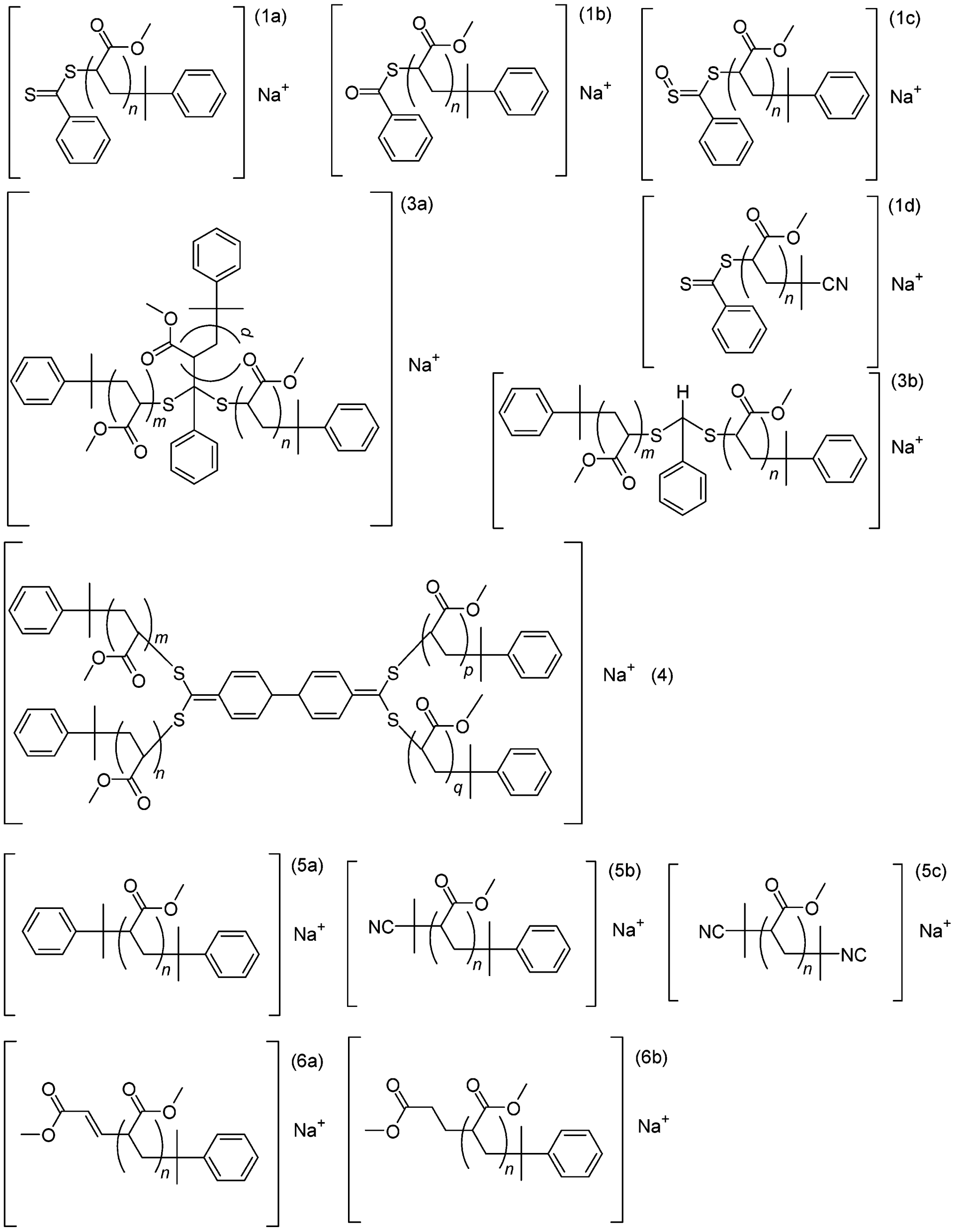
a capillary temperature of 275 °C. Nitrogen was used as sheath gas (flow: 50% of maximum) while helium was used as auxiliary gas (flow: 10% of maximum). The eluent was a 4:6 v/v mixture of THF/0.25 mM sodium acetate in methanol solution at a concentration of 60 mg mL^{-1}. After chromatographic analysis the sample was pumped into the electrospray interface. The ESI-MS spectra were recorded in centroid mode with an instrumental resolution of 0.1 amu. All reported molecular weights were calculated via the program package CS ChemDraw 6.0 and are monoisotopic. The use of monoisotopic masses is correct for molecular weights below ~1500 amu in the case of poly(methyl acrylate), as the first and most abundant peak in any given isotopic pattern corresponds to the main isotopes of the constituent atoms.

Results and Discussion

The full molecular weight distributions of the polymeric material prepared via CDB mediated, AIBN initiated MA polymerization at 80 °C are given in Figure 1. Although multiple charging is often observed in ESI-MS, no such effect was observed in our experiments. The ESI-MS unit only allows for mass analysis in the *m*/*z* range below 2000; thus, for the solutions prepared, short polymerization times of 10−20 min are required. Using a higher initial RAFT agent concentration in conjunction with extended reaction times will also result in low molecular weight polymers; however, this moves the system away from typical initial RAFT agent concentrations used in synthetic applications (i.e. $c^{\circ}_{\mathrm{RAFT}} \ll 10^{-1}$ mol L^{-1}). However, it should be noted that the pre-equilibrium of the RAFT process only lasts up to 5 min under the current reaction conditions, indicated by a distinct color change from purple to red of the initial reaction mixture.[34] It seems thus justified to assume that the polymeric material analyzed is formed after the pre-equilibrium has passed. With increasing molecular weight (i.e. going from the full to the dotted distribution in Figure 1), the resolution of individual chains in the size exclusion chromatograms becomes less pronounced, and it disappears for chains heavier than approximately 1000 g mol^{-1} (corresponding to 3−9 MA repeat units, depending on the molecular architecture; see Table 1).

Figure 2 shows the MS spectrum between ~800 and 1100 amu of a typical slice of the molecular weight distribution recorded at a retention time of 20.04 min from polymer sample B (dashed line). Clearly, the spectrum is very simply structured, having just one peak per repeat unit corresponding to the pure polyRAFT agent (species **1a**, Chart 1). The agreement between experimental and theoretical molecular weight (assuming a single charged species with one sodium cation attached) is excellent (e.g. m/z^{exp} 897.2 and m/z^{theo} 897.4 for the heptamer corresponding to $[C_{44}H_{58}O_{14}S_2]Na$). The spectrum does not indicate any noticeable additional peaks at this scaling, with maybe a hint of another peak present just before the main peak. When going to higher molecular weights in conjunction with an enlargement of the baseline area, the presence of at least four additional repetitive peaks becomes clearly evident. The ratio of the relative abundance of the additional peaks to the main peak (**1a**) is close to 1:100 over the entire measured mass range. Figure 3 shows the MS spectrum of a slice of the same molecular weight distribution at a retention time of 18.40 min (corresponding to higher molecular weights). Enlargement of the baseline now clearly indicates the repetitive pattern of four additional peaks markedly different from those of species **1a**. It should be mentioned that the part of the spectrum shown in Figure 3 is similar to that

Chart 1. Overview of the Possible Ions Generated by Electrospray Ionization of the Polymeric Material Generated via the CDB Mediated Methyl Acrylate Polymerization (for Details See Text)



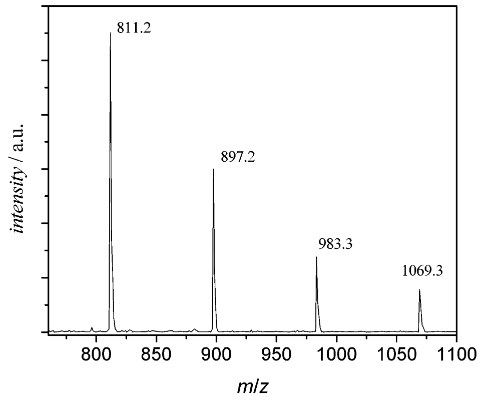


Figure 2. Electrospray ionization mass spectrum of a slice (retention time 20.04 min) of the molecular weight distribution corresponding to the dashed line in Figure 1 (i.e. total reaction time of 15 min.). The *m/z* ratios of the peaks are also given.

observed at other molecular weight ranges, including higher molecular weights obtained at longer reaction times (i.e. the molecular weight distribution associated with 20 min reaction time in Figure 1).

Chart 1 gives an overview of the product spectrum that may be expected from a CDB mediated, AIBN initiated methyl acrylate polymerization. While the bulk of the chains have been initiated by cumyl groups—the reinitiating leaving group moiety of the RAFT agent—leading to the formation of the main product (**1a**), a few chains also carry a cyanoisopropyl end group from the AIBN initiator molecule and yield **1d**. The presence of this species is consistent with previous studies.[24,26] The agreement between experimental and theoretical molecular weights for this species (**1d**) is excellent (i.e. m/z^{exp} 1104.3 and m/z^{theo} 1104.4). In an earlier communication we reported on the exchange of the double bonded sulfur atom in species **1a** by oxygen to give species **1b** in the presence of organic hydroperoxides in a quantitative fashion.[30] Since the eluent of the SEC system carries a THF content of 60 vol %, it is not surprising that a fraction of the main product is

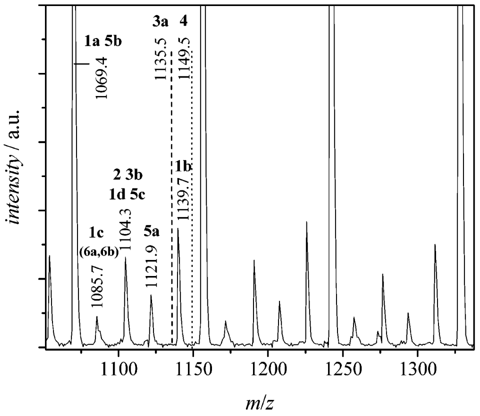


Figure 3. Enlarged part of the electrospray ionization mass spectrum of a slice (retention time 18.40 min) of the molecular weight distribution corresponding to the dashed line in Figure 1 (i.e. total reaction time of 15 min., sample C). The *m/z* ratios of the peaks are indicated. In addition, the dashed line and dotted vertical line give the potential *m/z* values for species **3a** and **4**, respectively.

converted to **1b** by the peroxides, which are present in small amounts even in stabilized THF. Again, the agreement between experimental and theoretical masses is very good (m/z^{exp} 1139.7 and m/z^{theo} 1139.5). Even in a living polymerization, termination events occur to some extent, which can be clearly seen by the presence of species **5a**, which corresponds to a methyl acrylate chain terminated by cumyl groups on either end (m/z^{exp} 1121.9 and m/z^{theo} 1121.6), originating from termination via combination events. Dead polymer chains carrying a cumyl and cyanoisopropyl group or two cyanoisopropyl groups on either end should be proportionally less present, due to the fact that the bulk of the chains have been initiated by cumyl groups. The ion peaks associated with these compounds, however, overlap with more intense peaks in the spectrum. For example, the peak associated with species **5b** overlaps with the peak from **1a** (m/z^{theo}(**1a**) 1069.4 and m/z^{theo}(**5b**) 1070.5), and the peak associated with **5c** partially overlaps with that from species **1d** (m/z^{theo}(**5c**) 1105.5 and m/z^{theo}(**1d**) 1104.4). It should be pointed out that the occurrence of **5c** is relatively unlikely due to the very low concentration of AIBN initiated chains. The last remaining peak in the spectrum lies at *m/z* 1085.7 (plus or minus multiples of methyl acrylate repeat units). The peak is slightly broader than the others, indicating contributions from a series of individual ions. The main peak at *m/z* 1085.7 originates from a precursor molecule in the formation of the thioester (**1b**).[30] This precursor is a sulfine (**1c**), which is readily obtained by reacting dithioester compounds with peroxides.[35-37] The subsequent rearrangement of the sulfine effects the sulfur oxygen exchange described above leading to the thioester (**1b**) and elemental sulfur. These reactions are well documented in the literature, and it comes as no surprise that they occur in solutions of THF to some extent. The broadening of the peak with its maximum intensity at *m/z* 1085.7 in Figure 3 may be due to the presence of dead polymer chains formed via termination by disproportionation events (species **6a** and **6b** in Chart 1). It has been shown in an earlier communication that disproportionation does occur in the free radical polymerization of methyl acrylate to a significant extent.[38] A full assignment of all (potential) species in the product stream is given in Table 1.

The product stream arising from termination processes of reversible and/or irreversible nature involving the intermediate macroRAFT radical (i.e. yielding species **3a**, **3b**, and **4** and their respective structural isomers, i.e., termination occurring at other positions where radical delocalization is possible) cannot be identified within the spectra resulting from AIBN initiated polymerizations. The potential locations of the two termination products generated by combination events within the spectra are indicated in Figure 3 by the dashed (**3a**) and dotted (**4**) lines. Clearly, no indication of the presence of such products can be seen, also at multiples of the methyl acrylate repeat unit. To further confirm the absence of **3a** and **4**, RAFT polymerizations were conducted with high concentrations of CDB and AIBN ($c_{\text{CDB}} = 0.2$ mol L^{-1}, $c_{\text{AIBN}} = 0.07$ mol L^{-1}). Using the termination rate coefficients for cross termination estimated by Kwak et al.,[12] species **3a** would contribute a significant proportion to the termination products. Again, no evidence of species **3a** or **4** was observed. However, the termination process may also proceed via a disproportionation pathway to yield **3b** and **6a**. Considering the sterically hindered nature of the intermediate radical, termination by disproportionation seems more likely than termination by combination. Theoretically, the arising product stream (**3b**) has a *m/z* ratio of 1103.5 (plus or minus multiples of MA repeat units). This number is very close to that of an already existing peak with *m/z* 1104.3, and **3b** may thus overlap with **1d**. Hence, a second set of polymerizations were undertaken to isolate **3b** from other compounds in the polymerization product stream.

Changing the initiator from AIBN to 1,1-azobis(cyclohexanecarbonitrile) in the polymerization system results in a mass change of **1d** by the substitution of the cyanoisopropyl end group with a cyanocyclohexyl end group. The same principal product stream as depicted in Chart 1 can be envisaged, when replacing all cyanoisopropyl end groups by cyanocyclohexyl moieties. The initiator change also leads to a shift in mass of species **5b** and **5c**, with masses of all (potential) products outlined in Table 2. Figure 4 represents an enlarged section of an ESI-MS spectrum of an 1,1-azobis(cyclohexanecarbonitrile) initiated and cumyl dithiobenzoate (CDB) mediated methyl acrylate polymerization. Again, there is no evidence of multiple charging of polymer chains and the correlation between theoretical and experimental masses for most species was excellent (see below). The spectrum depicted in Figure 4 confirms observations from the AIBN initiated system. That is, there is an absence of species **3a** and **4**, as highlighted by the dashed and dotted lines, respectively, the oxidation products (**1b** and **1c**) are present in small concentrations, and the combination product (**5a**) again appears to a significant amount in the product stream. Inspection of Figure 4 shows a very small peak on the high molecular weight side of the dotted line (**4**). However, this small peak is nonrepetitive; that is, it is not present in corresponding sections of the spectrum at other multiples of the repeat unit, underpinning the results obtained from the AIBN initiated system. The mass shifts of **1d** and **5c**, rendered possible by the initiator change, exposed a peak at m/z^{exp} 1101.8. Surprisingly, this residual peak corresponds to a compound with a significant concentration in the product stream while the initiator derived chains (**1d**)—although resulting in a distinct peak—give a smaller

Table 2. Theoretical *m/z* Values for the Single Charged Ions Derived from Chart 1, When Replacing All Cyanoisopropyl with Cyanocyclohexyl End Groups, and the Expected Peaks at Various Chain Lengths for Each of the Possible Products using CDB as the RAFT Agent and 1,1′-Azobis(cyclohexanecarbonitrile) (ACHCN) as the Initiator[a]

ion	**1a**	**1b**	**1c**	**1d**[c]	**3a**	**3b**	**4**	**5a**	**5b**[c]	**5c**[c]	**6a, 6b**[b]
end groups + Na^+	295.1	279.1	311.1	284.1	533.3	415.2	805.3	261.2	250.2	239.2	142.1
1 MA unit	381.1	365.1	397.1	370.1	619.3	501.2	891.4	347.2	336.2	325.2	228.1
2 MA units	467.2	451.2	483.1	456.1	705.3	587.2	977.4	433.3	422.3	411.2	314.2
3 MA units	553.2	537.2	569.2	542.2	791.4	673.3	1063.4	519.3	508.3	497.3	400.2
4 MA units	639.2	623.3	655.2	628.2	877.4	759.3	(1149.5)	605.33	594.3	583.3	486.3
5 MA units	725.3	709.3	741.3	714.3	963.5	845.4	1235.5	691.4	680.4	669.4	572.3
6 MA units	811.3	795.3	827.3	800.3	1049.5	931.4	1321.6	777.4	766.4	755.4	658.3
7 MA units	897.4	881.4	913.3	886.3	(1135.5)	1017.4	1407.6	863.5	852.5	841.4	744.4
8 MA units	983.4	967.4	999.4	972.4	1221.6	***1103.5***	1493.6	949.5	938.5	927.5	830.4
9 MA units	***1069.4***	1053.5	***1085.4***	1058.4	1307.6	1189.5	1579.7	1035.5	1024.5	1013.5	916.5
10 MA units	1155.5	***1139.5***	1171.5	***1144.5***	1393.7	1275.6	1665.7	***1121.6***	(1110.6)	(1099.6)	1002.5
11 MA units	1241.5	1225.5	1257.5	1230.5	1479.7	1361.6	1751.8	1207.6	1196.6	1185.6	***1088.5***
12 MA units	1327.6	1311.6	1343.5	1316.5	1565.7	1447.6	1837.8	1293.7	1282.7	1271.6	1174.6
13 MA units	1413.6	1397.6	1429.6	1402.6	1651.8	1533.7	1923.8	1379.7	1368.7	1357.7	1260.6
14 MA units	1499.6	1483.7	1515.6	1488.6	1737.8	1619.7	2009.9	1465.7	1454.7	1443.7	1346.7

[a] All masses given are monoisotopic. The bold/italicized numbers correspond to the peak assignments in Figure 4. Parentheses denote peaks that are not present in the spectrum/product stream. [b] The mean value of the two occurring peaks is reported. [c] Highlights the species whose mass is altered from those in Table 1 due to the initiator change.

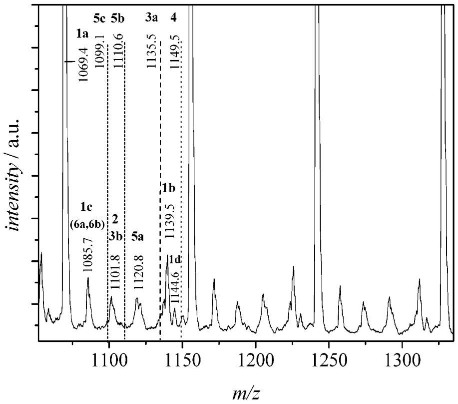


Figure 4. Enlarged part of the electrospray ionization mass spectrum for the polymerization system with 1,1-azobis(cyclohexanecarbonitrile) as the initiator. The *m/z* values of the peaks are indicated. The assignments of species are taken from Table 2. In addition, the dashed line and dotted vertical lines give the potential *m/z* values for species **5a**, **5b**, **3a**, and **4**.

contribution to the overall products of this RAFT system. Masses corresponding to species **5b** and **5c** are highlighted by dashed lines in Figure 4. The spectrum suggests that these products are not present to a significant amount in the polymerization mixture. The newly exposed peak is in the general region of species **3b**. However, although the theoretical/experimental mass correlation was excellent for all other species, the deviation between the uncovered peak and the theoretical mass of **3b** was close to 2 Da (m/z^{theo} 1103.5 vs m/z^{exp} 1101.8). In mass spectrometry such a mass deviation is quite substantial, suggesting that the peak cannot be assigned to **3b** but the signal belongs to a different species. One alternative is that the peak corresponds to species **2**, the RAFT intermediate radical (see Scheme 1). Compound **2** has an exact mass closer to the observed experimental result, almost within the experimental accuracy of ESI-MS of 0.5 Da (m/z^{theo} 1102.5, deviation of 0.7 Da from the unidentified peak).

In an attempt to identify whether the species is the disproportionation product (**3b**) or the intermediate macroRAFT radical (**2**), a series of radical trapping experiments were conducted. Solutions of 20 mg of 2,2,6,6-tetramethylpiperidinoxyl (TEMPO) in 2 mL of tetrahydrofuran were injected into CDB mediated and ACHCN initiated methyl acrylate polymerization mixtures at both 25 and 88 °C in an attempt to trap any radicals present. It was hypothesized that if **2** is truly present and undergoes termination reactions readily, a shift in mass to *m/z*(TEMPO−**2**) 1087.5 would be seen corresponding to the combination of a TEMPO radical with the intermediate macroRAFT radical. However, no signal corresponding to TEMPO−**2** or variance in the original peak intensity was observed. If the peak corresponds to species **2**, then this radical may not readily undergo termination. Additional evidence that may help to differentiate the possible species (i.e. **3b** or **2**) is the abundance of the disproportionation product generated by the hydrogen abstraction of the RAFT intermediate radical. If the peak corresponds to moiety **3b**, then there should be an equally intense peak for the second disproportionation product (**6a**). However, as mentioned earlier, **6a** is overlapped by species **1c** (m/z^{theo} 1088.5 and 1085.4, respectively), and differentiating these two products is very difficult. There is also the possibility that the signal corresponds to a species not included in the possible products in Chart 1. In this case, the product lies outside the framework of the currently debated RAFT mechanism, which we believe to be unlikely. What is clear is that there is a significant signal in the ESI-MS spectrum close to the **3b**/**2** region. Identification of the species corresponding to this peak is subject to further experimentation.

If irreversible termination processes are truly operational and proceed with termination rate coefficients typical for combination and disproportionation events ($\langle k_t \rangle \approx 10^8$ L mol^{-1} s^{-1}),[12] it is reasonable to assume that the resulting products register as peaks in the ESI-MS spectrum. The experimentally measured concentrations of the intermediate species[12] are within the same order of magnitude as those reported for propagating radical chains. The finding that the three- and four-armed star polymer products **3a** and **4**, respectively, cannot be identified by state of the art analytical tools—while other (similar) termination products can be found—indicates that they may not form at all or with such small termination rate coefficients as to lower their concentration below the detection limit of SEC−ESI-MS. The absence of **3a** and **4** in highly sensitive analytical tests combined with the fact that quantum mechanical ab initio calculations predict (relatively) stable intermediate radicals for phenyl Z-group stabilized RAFT agents[13] suggests that the fragmentation process for such stabilized macroRAFT radicals is slow (i.e. fragmentation rate coefficients on the order of 10^{-1} s^{-1}). This evidence is further underpinned by the ability of the CDB/MA and CDB/styrene system to effectively store free radicals over a substantial (hours) period of time.[31,39] However, ambiguity remains about the presence of termination events of the intermediate macroRAFT radicals that proceed via disproportionation to give species **3b** or the presence of the intermediate RAFT radical (**2**). In addition, it is mandatory to mention within the context of this SEC–ESI-MS study that the absence of proof of the existence of the intermediate termination products **3a** and **4** is not necessarily proof of their absence. Species **4**, which may be formed reversibly within the RAFT polymerization, is believed to be relatively unstable and may easily decompose within the ionization process with its elevated temperature. The three-armed star **3a**, on the other hand, was reported to be thermally stable.[12,40] The ionization process should not affect its integrity, and it should hence register in the product stream. Although very unlikely, it may still be that the ionization potentials of **3a** and **4** are vastly different from those of all other chains in the sample. Furthermore, some process may prevent these species from undergoing ionization at all, thus suppressing their signal in the mass spectrum. Additionally—but equally speculative—the termination rate coefficient for such termination processes may be very low, making the process an unfrequented reaction pathway. In this case, however, the intermediate termination mechanism cannot be held responsible for rate retardation processes but would rather be an additional reaction pathway due to the relatively high stability of the intermediate macroRAFT radicals.

Conclusions

The coupling of SEC with ESI-MS technology was applied to study the polymeric product spectrum generated by the AIBN/ACHCN initiated, cumyl dithiobenzoate (CDB) mediated methyl acrylate (MA) polymerizations in detail. While the products corresponding to the polymeric RAFT agent and the combination and disproportionation termination products (with cumyl, cyanocyclohexyl, and cyanoisopropyl end groups) could be identified, no evidence of termination products yielding three- or four-armed star polymers associated with the intermediate radical was identified. Using rate coefficients predicted by other researchers,[12] the reaction conditions were adjusted to maximize the yield of three- or four-armed stars. Even under such conditions, no evidence of termination products was observed. Such a finding—in conjunction with additional evidence (including ab initio calculations) for the relative stability of the intermediate RAFT radicals in this particular case—considerably lowers the possibility of such a reaction being an essential part of the RAFT mechanism with consequences for the rate of polymerization as manifested in rate retardation and inhibition phenomena. However, there is a certain degree of ambiguity surrounding the disproportionation product of the RAFT intermediate. A second set of experiments utilizing 1,1-azobis(cyclohexanecarbonitrile) as the initiator shows a significant peak in close vicinity to the theoretical expected mass of the disproportionation product. However, the observed peak corresponds more closely to the intermediate macroRAFT radical itself.

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