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1 **Evaluation of halogen chain-end functionality in 2-bromo-**
2 **2-methylpropanoate esters of poly(oxyalkylene) polymers**
3 **by MALDI-TOF spectroscopy**

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10

11

12 **Keywords**

13 MALDI-TOF MS; end-functionalization; PEG-based macroinitiators

14 **Abstract**

15 Esters of 2-bromo-2-methylpropanoate of poly(oxyalkylene) polymers such as poly(ethylene glycol)
16 or α -methyl poly(ethylene glycol) were prepared in high yields and characterized by spectroscopic
17 and chromatographic methods (NMR, FT-IR, mass spectroscopy and SEC). The halogen chain-end
18 group in the poly(oxyalkylene) bromine-terminated esters were characterized by MALDI-TOF MS.
19 The effect of the solvents (methanol or tetrahydrofuran) and the cationic agents such as silver
20 trifluoroacetate (AgTFA), silver trifluoromethanesulfonate (AgTFS) and sodium trifluoroacetate
21 (NaTFA) on the mass spectra was studied. Analysis of the mass spectra demonstrated that the analyte
22 was transformed to unsaturated (elimination), alkoxy or hydroxyl end groups (substitution) molecules
23 when silver cationic agents were used, these results were also supported by ¹H NMR study. When
24 sodium salt was used as a cationic agent, well-defined bromine-terminated macromolecules were
25 successfully determined through MALDI-TOF MS. Well characterized esters of 2-bromo-2-

1 methylpropanoate of poly(oxyalkylene) polymers could be used as ATRP macroinitiators for the
2 synthesis of a variety of polymeric architectures of interest as drug delivery bioconjugates.

3

4 **Introduction**

5 Poly(oxyalkylene) polymers are known as hydrophilic polymers, and the most representative are
6 poly(ethylene glycol) (PEG) and α -methyl poly(ethylene glycol) (MPEG), these type of materials are
7 frequently used for the synthesis of new and complex materials with applications in several areas,
8 mainly due to their biocompatibility and biodegradability properties [1][2][3]. In addition, when these
9 polymers are end-modified with a suitable functional group, they can be used as macroinitiators in
10 the reversible-deactivated radical polymerization (RDRP) mechanisms, including nitroxide-mediated
11 radical polymerization (NMP), reversible addition-fragmentation chain transfer (RAFT)
12 polymerization, and atom transfer radical polymerization (ATRP), which are the most commonly
13 used polymerization methods to obtain hydrophilic or amphiphilic polymeric materials [4][5][6][7].

14 ATRP is a versatile and efficient RDRP technique for the preparation of macromolecules with
15 predetermined molar masses, narrow molar mass distributions, well-defined topologies, and high
16 degrees of chain-end functionality [8]. This is possible due to its specific catalytic process, where an
17 halide atom is required to react with the metal complex to generate a radical that can act as an initiator
18 in the ATRP process [9][10]. Thus, the quantification and identification of these halide groups are
19 critical when materials with specific characteristics are required [11].

20 Traditional techniques, such as nuclear magnetic resonance (NMR), Fourier Transform Infrared (FT-
21 IR) or size exclusion chromatography (SEC), could give inaccurate results in the characterization and
22 quantification of halogen end-groups, mainly due to the low intensity of the end-group signals
23 compared with the signal intensity of the main polymer chain. This drawback is magnified when the
24 molecular weight is increased and the end-group signals may be too small and indistinguishable when
25 compared with the noise, therefore it cannot be quantified correctly [12][13]. In addition, these
26 techniques, provide information related with the average of all macromolecules rather than a
27 distribution of the polymer size, an important issue in ATRP [14].

28 Mass spectroscopy was addressed to solve these challenges through the development of soft
29 ionization techniques, such as matrix-assisted laser desorption/ionization-time of flight mass
30 spectrometry (MALDI-TOF MS). With this technique, the polymer mass spectra are obtained without
31 fragmentation, and the exact molar mass of a single macromolecule can be accurately determined

1 [15]. In the MALDI process, the sample is ionized and transferred into the gas-phase, thus molecular
2 ions ($[M]^+$) can be analysed [16][17]. Through this technique, the number-average molar mass (M_n),
3 mass-average molar mass (M_w), degree of polymerization (DP) and dispersity (D) can be determined
4 with high precision [18][19]. However, MALDI data are accurate and precise only for polymers with
5 low dispersity ($D > 1.2$). Materials with higher than this value, discrete discrepancies between the
6 experimental and theoretical molar masses values could be registered [20].

7 In order to get an accurate MALDI analysis, the selection of the matrix is crucial, the right matrix
8 facilitating the transfer of energy to polymer chains during the ionization process. Commonly, metal
9 salts are added to improve the ionization [21]. To this purpose, the sample preparation is an overriding
10 step for collecting high-quality MALDI-TOF spectra. It is important to consider the solubility of all
11 components (polymer, matrix, and metal salt) in a suitable solvent. Once the solutions of these
12 materials are placed in the MALDI target plate, the solvent is evaporated, and a proper co-
13 crystallization is needed to assure the interaction between all components and promotes the optimum
14 ionization conditions.

15 However, there is controversy in the scientific community regarding the analysis of end-
16 functionalized polymers obtained by RDRP in the attempts of obtain telechelics materials, where it
17 could be misunderstanding in the assignation of the correct structures through MALDI analysis.
18 Different examples are found in the art, Lallana *et al.* [22], found in poly(propylene sulfides)
19 functionalized at the end with an ester groups analyzed by MALDI a decarboxyalkylation reaction
20 during the ionization process. Borman *et al.* [23] found in PMMA bromine end functionalized a loss
21 of methylbromide followed by cyclisation of the final two monomer repeat units to give a lactone end
22 group. Matyjaszewski *et al.* [24] reported the loss of HBr in poly(acrylates) obtained by ATRP. In
23 addition, PMMA obtained with ATRP it was found a loss of the chlorine atom as the end group during
24 the MALDI analysis with the use of silver as cation agent [25]. Couthouis *et al.* [26] reported on the
25 presence of the disproportionation products as the main structures found in MALDI spectra, in spite
26 of PMMA samples with low dispersity, first-order kinetics related to the monomer consumption, good
27 control in the molar masses, thus suggesting mistakes in the assigned polymer structures.

28 According to previous reports [27][28], it is accepted that the halogen atom (X) cannot be observed
29 due to the lability of C-X covalent bonds, resulting from a hydro-halo elimination reaction during the
30 sample preparation or in the MALDI-TOF MS process. These reactions provide unsaturated chain-
31 end groups, which can be confused with an unsaturated terminated polymer that can be obtained by

1 disproportionation during the synthesis of the macroinitiator by ATRP, leading in a doubtful quality
2 of the ATRP macroinitiators [29].

3 Some authors, like Ladavière *et al.* [30], employed MALDI-TOF MS for the analysis of bromine-
4 terminated polystyrene (PS-Br) and chlorine-terminated polystyrene (PS-Cl) prepared *via* ATRP
5 using AgTFA or sodium iodide (NaI) as cationizing agents. Poor ionization was obtained with NaI,
6 because the signal-to-noise ratio was not significant enough to assign any signal. In contrast, when
7 AgTFA was used, unsaturated macromolecules were observed, produced from elimination of
8 hydrochloric acid (HCl) or hydrobromic acid (HBr). This phenomenon was attributed to the MALDI-
9 TOF process, including the ionization step. In addition, other species of minor intensity were
10 observed, and not fully identified. Tintaru *et al.* [27] also analyzed by MALDI-TOF PS-Br samples
11 prepared by ATRP, which was previously characterized by NMR and electrospray ionization-mass
12 spectroscopy (ESI-MS). They concluded that when the silver cation (Ag^+) was mixed with the PS-Br
13 macromolecules, the elimination of the bromine atom occurred, thus generating macromolecules with
14 different end groups, depending on the solvent, solution composition, matrix, and metal salts used.
15 Nonetheless, in all the cases, the loss of the bromine functionality was observed. Similar results were
16 reported by Kim *et al.* [28] for PS-Br synthesized by ATRP and characterized with MALDI-TOF MS
17 using AgTFA, NaTFA, or silver pentafluoropropionate (AgPFP) as cationization agents and
18 tetrahydrofuran (THF), toluene, chloroform, acetone, methanol and ethanol as solvents. They found
19 some PS macromolecules with unsaturated terminations, hydroxyl (-OH) and other functionalities at
20 the chain end of the polymers, attributed to reactions between the PS macromolecules and the solvent
21 or the employed cations. As stated before, the most accepted postulate is the loss of the halogen atom
22 at the polymer chain-end during the sample preparation. Recently, Altintas *et al.* [31] analyzed PS-
23 Br synthesized *via* activators regenerated by electron transfer (ARGET) atom transfer radical
24 polymerization (ATRP). These authors reported that the removal of halide group occurred during the
25 ionization process and molecular species with unsaturated and hydroxyl chain-end groups were
26 mainly observed.

27 Here we report the characterization of chain end-functionalization of poly(oxyalkylene) bromine-
28 terminated esters by MALDI-TOF MS. Six poly(oxyalkylene) polymers with a molecular weight
29 range between 700-7,000 Da were esterified with 2-bromo-2-methylpropionyl bromide and the
30 correspondent esters were purified and characterized by spectroscopic techniques. The effect of the
31 analyte molecular weight, solvents (methanol or tetrahydrofuran) and the cationic agents such as
32 silver trifluoroacetate (AgTFA), silver trifluoromethanesulfonate (AgTFS) and sodium
33 trifluoroacetate (NaTFA) on the mass spectra was studied.

1

2 **Experimental**

3 **Materials.** Powders of poly(ethylene glycol) (2000, 3350 and 6000 Da) and poly(ethylene glycol)
4 monomethyl ether (750 (as wax), 2000 and 5000 Da) were purchased from Sigma-Aldrich and dried
5 in a vacuum oven (10 mmHg) at room temperature for 24 hours prior to use. Dichloromethane
6 (CH_2Cl_2 , JTBK) was distilled twice from phosphorus pentoxide (P_2O_5 , Aldrich, 99%). Triethylamine
7 (TEA, Aldrich, 99%) was dried by refluxing over calcium hydride (CaH_2) and distilled before use. 2-
8 Bromo-2-methylpropanoyl bromide (BIBB, Aldrich 98%), tetrahydrofuran (THF, JTBK, 99%),
9 methanol (CH_3OH , JTBK, 97%), methanol- d_4 99.8 atom % D (CD_3OD , Aldrich,), trans-2-[3-(4-tert-
10 butylphenyl)-2-methyl-2-propenylidene] malononitrile (DCTB, Aldrich,), silver
11 trifluoromethanesulfonate (AgTFS , Aldrich, 99%), sodium trifluoroacetate (NaTFA , Aldrich, 99%),
12 and chloroform- d 99.8 atom % D (CDCl_3 Aldrich,) were used as received. Silver trifluoroacetate
13 (AgTFA) was prepared from aqueous silver nitrate and trifluoroacetic acid, the product being
14 evaporated and washed with methanol and diethyl ether and finally vacuum dried (1 mmHg)
15 overnight at room temperature.

16 **Bromine end-functionalization in poly(ethylene glycol) and α -methyl poly(ethylene glycol).** In a
17 three-neck flask, 0.001 mmol $\text{OH}-(\text{PEG})_n-\text{OH}$ or $\text{CH}_3-(\text{PEG})_n-\text{OH}$ were dissolved in 80 mL dried
18 CH_2Cl_2 , then 0.006 (for PEG) or 0.003 mmol (for MPEG) of TEA were added, mixed, and cooled to
19 0 °C. After this step, 0.002 or 0.001 mmol of BIBB respectively were dissolved in 20 mL of dry
20 CH_2Cl_2 and added dropwise within a 1h-period under N_2 to the reaction for 7 h at 40 °C. The reaction
21 mixture was concentrated in a rotary evaporator and extracted twice, first with an aqueous HCl
22 solution 5% v/v, then with an aqueous NaHCO_3 solution (10 % w/v), and finally with CH_2Cl_2 . The
23 organic layers were collected and dried over MgSO_4 .

24 **Sample preparation for NMR Analysis.** Solution A was prepared in a 5 mL sample vial, 20 mg of
25 **2d** was accurate weighted in 2 mL of tetradeuteromethanol (CD_3OD) then, the vial was immersed in
26 an ice bath for five minutes. Solution B was obtained when 28 mg of AgTFA was accurate weighed
27 in a 5 mL sample vial and dissolved in 2mL of CD_3OD after, the sample vial was placed in an ice
28 bath for five minutes. The final solution was obtained when 0.5 mL of the solutions A and B were
29 mixed and placed in a 5mm NMR tube, this sample was analyzed by NMR.

30 **Analytical techniques.** The polymer samples were characterized by size exclusion chromatography
31 (SEC) using a Waters Alliance chromatograph model 2695 equipped with a refractive index detector

1 model 2414 and two columns Agilent PL gel 5 μm Mixed C. The samples were dissolved in
2 anhydrous THF (10 mg mL⁻¹), and the solutions were filtered through 0.2 μm nylon membranes. THF
3 was used as an eluent at a flow rate of 1 mL min⁻¹ at 30°C. The system was calibrated with a linear
4 calibration curve built from polystyrene standards (1,350 to 1,997,000 Da PS), and the correction for
5 the related to changes in the hydrodynamic volumes was carried out with the Kuhn-Mark-Houwink-
6 Sakurada constants for the PEG-THF system ($[\eta] = 3.39 \times 10^{-4} \text{M}^{0.66}$) [32].

7 Proton nuclear magnetic resonance (¹H NMR) spectra were generally recorded at room temperature
8 (298°K) in CDCl₃ with TMS as an internal standard on a Bruker AVANCE III spectrometer (500
9 MHz).

10 Fourier-transform infrared (FT-IR) spectra were performed on a Thermo-Nicolet iS10 spectrometer
11 in transmittance mode with 64 scans and a spectral resolution of 2 cm⁻¹ in the range from 4000 to 400
12 cm⁻¹. The samples were analyzed on KBr pellet.

13 **MALDI-TOF Mass Spectrometry.** Matrix-assisted laser desorption/ionization-time of flight mass
14 spectrometry (MALDI-TOF MS) were acquired on a Bruker autoflexTM speed mass spectrometer
15 (Bruker Daltonics, Billerica Ma.). The system uses a frequency-tripled Nd:YAG laser (355 nm) and
16 a 2 kHz repetition rate (Smartbeam-IITM). Measurements were carried out in reflectron mode (for
17 sample with the mass range from 0.7 to 5 kDa) or linear mode (for sample with molar masses up to 5
18 kDa). Positive-ion mode was used for all analyses with an acceleration voltage of 20.00 Kv and
19 delayed extraction. Ions in the mass range (m/z) of 700–7000 were detected with a sampling rate of
20 5.0 GS⁻¹ for reflectron mode and 0.63 GS⁻¹ for linear mode. The collected data were added with
21 over 500 shots at a frequency of a 2000 Hz; the laser probe was slowly moved to avoid poor signals.
22 The laser power energy was tuned to yield sufficiently intense signals (60% in linear mode and 80%
23 reflectron mode). Insulin (5734.52 Da), cytochrome c (6161.05 Da), myoglobin (8476.66), ubiquitin
24 I (8565.89 Da), cytochrome c (12360.97 Da), and myoglobin (16952.31 Da) were used as external
25 calibrants enabling a mass accuracy of about 50 ppm. The resolution of the MALDI spectra reaches
26 ranges between 2000 and 18000, depending on molar mass distribution, purity and cationic agent
27 used.

28 **Sample Preparation.** PEG, MPEG, and their corresponding esters were dissolved in CH₃OH or THF
29 at a concentration of 5 mg mL⁻¹. DCTB solution was prepared with a concentration of 20 mg mL⁻¹.
30 0.1 M solutions of cationization agents (AgTFS, AgTFA, NaTFA) were also prepared. Solutions of
31 10 μL of the polymer, 10 μl of DCTB, and 2.0 μl cationization agents were mixed and deposited on
32 a MALDI-TOF MS sample plate, and the spots were dried in air at room temperature before analysis.

1 **Data Analysis.** Data acquisition was performed using flexControl software 3.4 (Bruker Daltonics,
2 Billerica Ma.) and data analysis the mass of each selected monoisotopic peak was determined using
3 a centroid algorithm calculated with FlexAnalysis software 3.4 (Bruker Daltonics, Billerica Ma.)
4 assuming PEG elemental composition. MS data were processed using PolyTools 1.31 (Bruker
5 Daltonics).

6 **M_n , M_w , and D calculation with MALDI-TOF MS.** M_n , M_w , and D values for PEG, MPEG, and
7 their corresponding esters were calculated without software support. M_n was calculated as follows:
8 $M_n = \Sigma(n_i M_i) / \Sigma n_i$, n_i representing the intensity found in the MALDI spectra and M_i the m/z ratio. M_w
9 was calculated as follows: $M_w = \Sigma(n_i M_i^2) / \Sigma(n_i M_i)$. D was inferred from the resulting M_w/M_n ratio.

10

11 **Results and Discussion**

12 **PEG and MPEG Characterization.** The molar masses of the six samples of poly(oxyalkylene)
13 polymers (**1a-f**) were determined by MALDI-TOF MS and compared with those obtained by NMR
14 and SEC, the results being listed in **Table 1**. The experimental peak values of molar masses (M_p)
15 were obtained from MALDI-TOF analysis, and they had the largest intensity in the observed
16 distributions of the mass spectra. Theoretical molar masses were calculated for PEG or MPEG
17 considering the degree of polymerization (DP) and hydroxyl vs. methyl substituents at α and ω
18 positions. M_n , DP , and D values were calculated from the mass spectra. The experimental values M_p
19 were compared with the theoretical ones for the six poly(oxyalkylene) materials characterized by
20 MALDI-TOF MS, and an excellent agreement between these values ($\Delta M \approx 1$) was obtained.
21 Therefore, the molecular formula of these polymers can be established as $\text{HO}(\text{CH}_2\text{CH}_2\text{O})_n\text{H}$ for PEG
22 and $\text{CH}_3\text{O}(\text{CH}_2\text{CH}_2\text{O})_n\text{H}$ for MPEG. When the MALDI results were compared with the molecular
23 weight obtained with SEC, differences among them can be appreciated. In Table 1, higher molecular
24 weight values were determined with SEC, in spite of the correction to the changes in the
25 hydrodynamic volumes with the Kuhn-Mark-Houwink-Sakurada constants for the PEG-THF system
26 ($[\eta] = 3.39 \times 10^{-4} M^{0.66}$). In addition, the average molecular weight was calculated by NMR which
27 shown better agreement with those determined with MALDI-TOF, its behavior could lead to suppose
28 an overestimation of the molecular weight with SEC analysis. With these results, can be stated that
29 the ion suppression phenomena it is absent during the MALDI analysis, due to the observed narrow
30 dispersities ($D < 1.03$) for PEG and MPEG polymers [33].

31

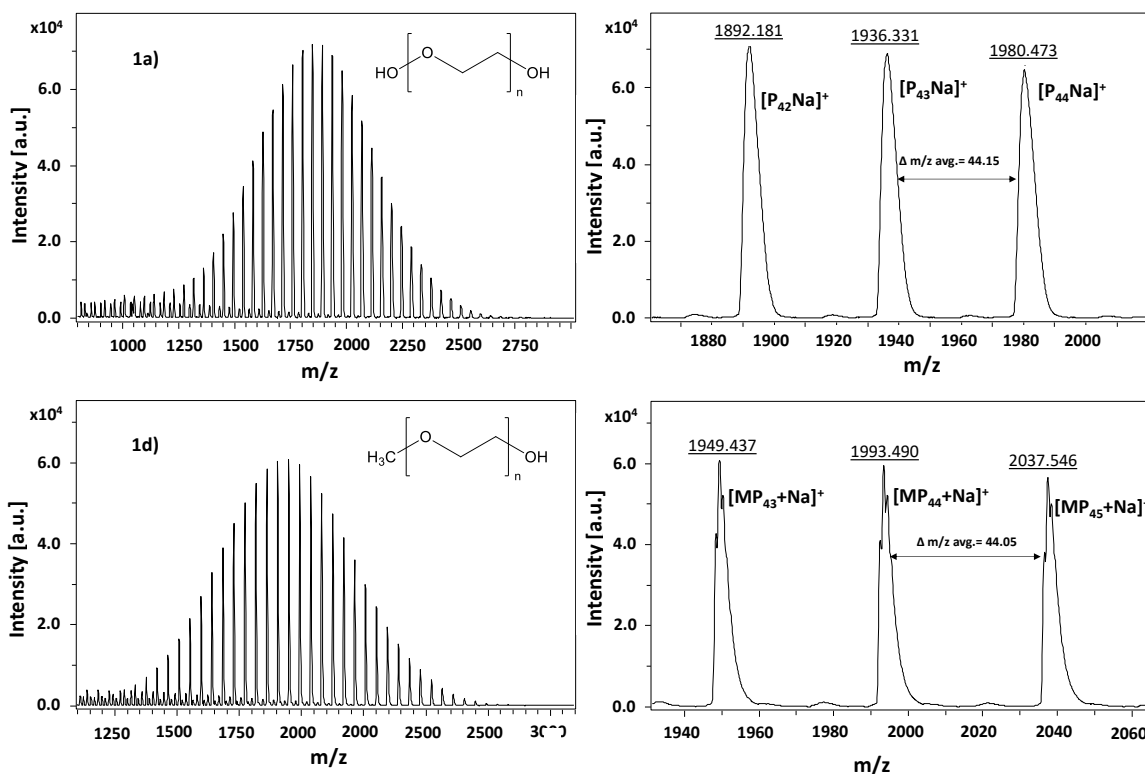
1 **Table 1.** Mass characterization of PEG and MPEG by MALDI-TOF MS, NMR and SEC in THF.

Entry	MALDI-TOF MS ^a					¹ H-NMR		SEC		
	M _p theoretical ([M _p +Na] ⁺) (Da)	M _p exp. ([M _p +Na] ⁺) (Da)	M _n MALDI (Da)	DP MALDI	Đ	M _n NMR (Da)	DP NMR	M _n (Da)	DP	Đ
1a	1935.303	1936.331	1845.792	41.49	1.03	1876.885	42.20	2472	56	1.1
1b	3300.96	3301.365	3387.09	76.477	1.00	3522.105	79.54	4916	112	1.1
1c	5812.006	5812.508	5894.964	133.41	1.00	5971.736	135.15	9508	216	1.1
1d	715.834	715.343	710.932	15.729	1.03	669.323	14.78	824	19	1.1
1e	1993.384	1993.338	1944.913	43.74	1.01	1965.605	44.21	2683	61	1.1
1f	5209.285	5210.323	5116.76	115.74	1.01	5555.810	125.71	7939	180	1.1

2 ^aDCTB as a matrix and NaTFA as an ionic agent were used.

3

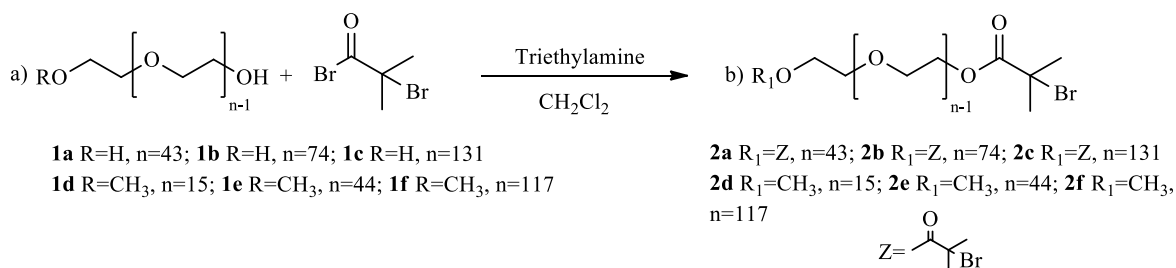
4 The PEG and MPEG samples (**1a-f**) were evaluated with the ionization system DCTB/NaTFA. Only
 5 one type of molecular ion for PEG ([P_n+Na]⁺) and MPEG ([MP_n+Na]⁺) was observed in the MALDI-
 6 TOF MS spectra, giving an idea of the absence of side reaction with any of the components under the
 7 analytical conditions. Supporting this statement, the mass spectra for PEG (**1a**) and MPEG (**1d**) with
 8 M_p around 2000 Da respectively are shown in **Figure 1**.



1

2 **Figure 1.** MALDI-TOF MS obtained in reflectron mode of PEG (**1a**) and MPEG (**1d**) in DCTB as a
 3 matrix and NaTFA as an ionic agent in THF.

4 **Synthesis of ATRP macroinitiators from PEG and MPEG.** Once the poly(glycol)s were
 5 characterized, and with the aim to obtain end-functionalized polymers as ATRP macroinitiators, the
 6 esterification of the poly(glycol)s were performed through their reaction with 2-bromo-2-
 7 methylpropanoyl bromide and triethylamine in dichloromethane for 7 h at 40°C (**Scheme 1**).

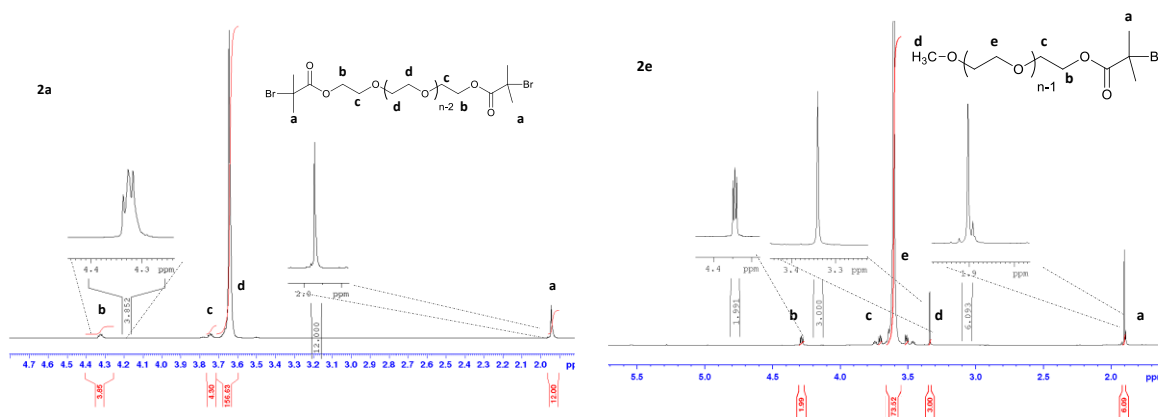


8

9 **Scheme 1.** PEG and MPEG esterification with 2-bromo-2-methylpropanoyl bromide.

10 The ester groups of poly(glycol)s (**2a-f**) were characterized *via* spectroscopic techniques and yields
 11 were gravimetrically calculated after the purification process. The spectroscopic characterization was
 12 focused on identifying the 2-bromo-2-methylpropanoate moiety in the esterified polymer samples.
 13 FT-IR analysis of the esters (**2a-f**) showed a stretching band at 1734 cm⁻¹, characteristic of the ester

1 group (C=O) (Figure S-1 in Supporting Information). In the ^1H NMR spectra of the esters **2a-f**, the
 2 2-bromo-2-methylpropanoate moiety was identified as a triplet at 4.29 ppm, as it was a signal
 3 characteristic of the methylene ($-\text{CH}_2$) adjacent to the oxygen atom in the ester group. In addition,
 4 the signal for the α -methyl groups of the ester moiety had a chemical shift of 1.85 ppm (Figure 2).



5

6 **Figure 2.** ^1H NMR (500 MHz) spectra of **2a** and **2e** macroinitiators in CDCl_3 .

7 Once the chemical structure was established, the ester functionalization degree was calculated from
 8 the integration ratio of the signals associated with characteristic protons. Indeed, the signal at 1.85
 9 ppm for the methyl of the ester group and the band at 3.37 ppm for the methoxy group were taken as
 10 reference for the MPEG samples, while the band at 1.85 ppm and the ethylene resonances at 3.63
 11 ppm were considered for the PEG polymers. The values demonstrated a near quantitative
 12 functionalization (Table 2). Theoretical molar weight of each functionalized polymer (**2a-2f**) was
 13 calculated considering the average degree of polymerization obtained in the previous MALDI-TOF
 14 MS analysis (see Table 1) and the 2-bromo-2-methylpropanoate moiety.

15 **Table 2.** Esterification of poly(glycol)s with 2-bromo-2-methylpropanoyl bromide in CH_2Cl_2

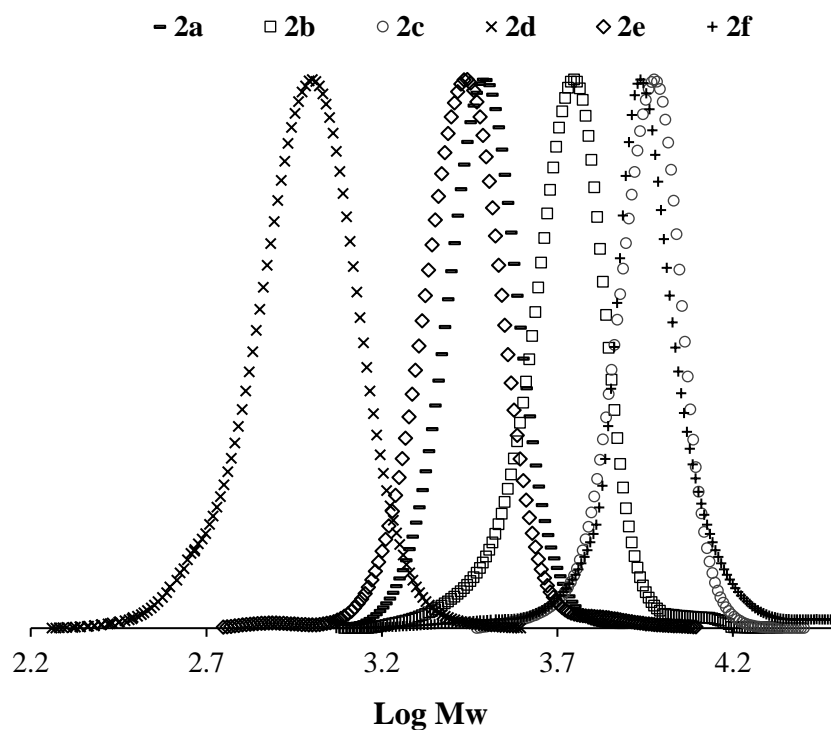
Entry	Yield (%)	Functionalization degree ^a (%)	M_n (Da) ^b	DP_{MALDI}
2a	93	97	2143.747	41.49
2b	94	94	3685.029	76.48
2c	92	93	6192.879	133.41
2d	97	98	873.938	15.73
2e	95	95	2107.907	43.74
2f	93	98	5279.723	115.74

16 ^a Functionalization degree calculated from ^1H NMR spectrum.

17 ^b Theoretical M_n as calculated from the average DP from MALDI-TOF MS analysis.

1

2 **Molar mass distribution analysis.** The main purpose for the estimation of the molar mass
 3 distributions of PEG or MPEG esters of 2-bromo-2-methylpropanoate (**2a-f**) was to ensure that
 4 esterification was the sole reaction that had taken place during the preparation of these materials. The
 5 chromatographic separations of all polymers were performed by SEC. The results obtained shown
 6 that dispersities remain in the same values ($D < 1.11$) and slight increments in their molecular weights
 7 (see Table S-1 in Supporting Information) typical chromatograms are depicted in **Figure 3**. These
 8 curves indicate monomodal molar mass distributions and low molar mass dispersities. Nevertheless,
 9 one could not exclude any dimerization or other side reaction under uncontrolled conditions. This
 10 concern was based upon the possible reaction between the bromine atom at the methylpropanoate
 11 group with trimethylamine, which was present in excess during the esterification reaction. This base
 12 might give a hydro-bromo elimination reaction leading to the formation of methacrylate functional
 13 group that could eventually undergo a dimerization reaction [29].



14

15 **Figure 3.** Molar mass distribution of esters of 2-bromo-2-methylpropanoate of poly(glycol)s (**2a-f**).

16 **MALDI-TOF MS investigation of bromine end-groups.** End-functionalized polymers with
 17 halogen groups can be used as macroinitiators for the preparation of complex macromolecular
 18 architectures. However, these halogenated end groups must be characterized by a proper technique.

1 Focusing on polymers obtained by ATRP, unsaturated groups at the chain end are commonly
2 observed in MALDI-TOF mass spectra. This apparently originates through the loss of the halogen
3 atom ($X = \text{Br}, \text{Cl}$) during the MALDI-TOF MS analysis [29]. Formation of the unsaturated
4 compounds may also occur as a result of lack of control during the ATRP polymerization process,
5 due to the free-radical disproportionation at the growing chain end [34]. Thus, the problem is to
6 discriminate between these two alternatives in order to establish an accurate structure of ATRP
7 macroinitiators. As previously discussed, end-functionalized esters of PEG or MPEG with 2-bromo-
8 2-methylpropanoate were prepared *via* esterification. With this strategy, the presence of unsaturated
9 polymers was avoided, because poly(glycol)s with narrow dispersities as starting reagent were used.

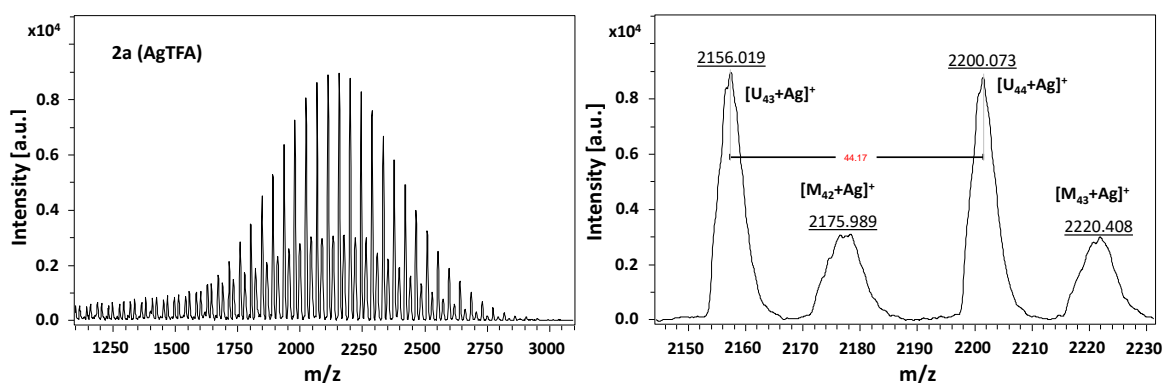
10 In the literature, in some protocols of analysis for PEG or MPEG by MALDI-TOF-MS avoid the use
11 of cationic agents, in spite of this species like $[\text{M}+\text{H}]^+$, $[\text{M}+\text{Na}]^+$ and $[\text{M}+\text{K}]^+$ have been found, this
12 fact could be explained considering that the protonated species came from the matrix and the alkaline
13 species from the residues of these alkaline metals present in the water or solvent used [35][36]. For
14 this reason, our first approach, was centered in the analysis of the polymers **2a** and **2e** by MALDI-
15 TOF MS with DCTB matrix without any cationic agent. Poor ion generation was found in this
16 analysis without the cationization agent and not sufficient for a precise analysis of the halogen end
17 functionalization of ATRP macroinitiators. These results were compared with the samples in which
18 AgTFA was used as the cationic agent and clear differences could be seen in the ion formation, these
19 spectra were included in the supplemental information (*Figures S-2 and S-3*).

20 Taking into account the previous results, it was evaluated the influence of the cationizing agents with
21 different acid strengths, like silver trifluoromethanesulfonate (AgTFS) or silver trifluoroacetate
22 (AgTFA), and with absolute hardness value like sodium trifluoroacetate (NaTFA). Their nature was
23 evaluated in the ionization process, as well as their effect in the occurrence of secondary peaks in the
24 MALDI-TOF MS spectra. Under these conditions, it was observed a higher signal intensity,
25 indicating good ionization in each case. In all the evaluated samples, ion sequences were separated
26 by a nominal value close to 44.053 Da, which was consistent with the molar mass of the repeating
27 unit (OCH_2CH_2) present in the glycol polymers. Different molecular species were observed
28 depending on the cationization salt or solvent employed. The detailed discussion of this results is
29 given in the following sections.

30 **Influence of ionic agents during MALDI-TOF MS analysis.** For this MALDI-TOF-MS study,
31 DCTB was employed as the matrix, silver trifluoroacetate as a cationic agent and methanol as the
32 solvent. As stated before, the mechanism for the interactions between the silver and the polymeric

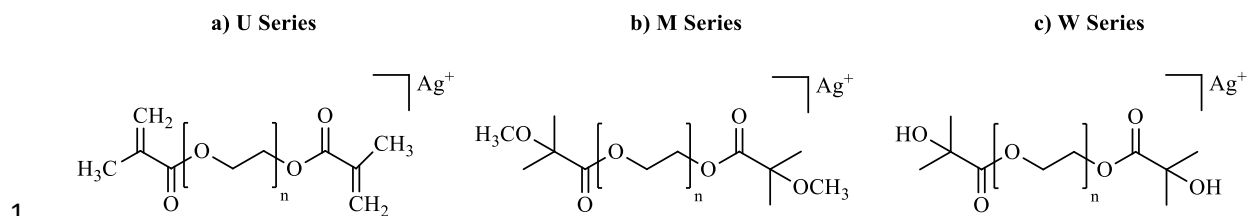
1 analyte remains unknown [37]. However, it was proposed that the reaction between silver salts with
 2 halogenated compounds occurred prior to the excitation, in other words, before the impact of the laser
 3 source into the matrix. For example, Tintaru *et al.* [27] concluded that the elimination of HBr had
 4 most likely occurred during sample preparation.

5 In this study, a molar ratio for DCTB/polymer/AgTFA of 310/1/18 was used. An efficient ionization
 6 was thus obtained for the six esters of 2-bromo-2-methylpropanoate of PEG or MPEG (**2a-f**). The
 7 analysis was focused on the peaks with the highest intensity, the experimental m/z ratio was compared
 8 to the calculated molar mass of the possible structures. The molar mass distribution of the ester **2a**
 9 ($DP = 41$) obtained in the MALDI analysis is shown in **Figure 4**. In this Figure, two patterns were
 10 clearly identified, that with the highest intensity was assigned to the unsaturated termination (structure
 11 as shown in **Figure 5a** and named as U Series).



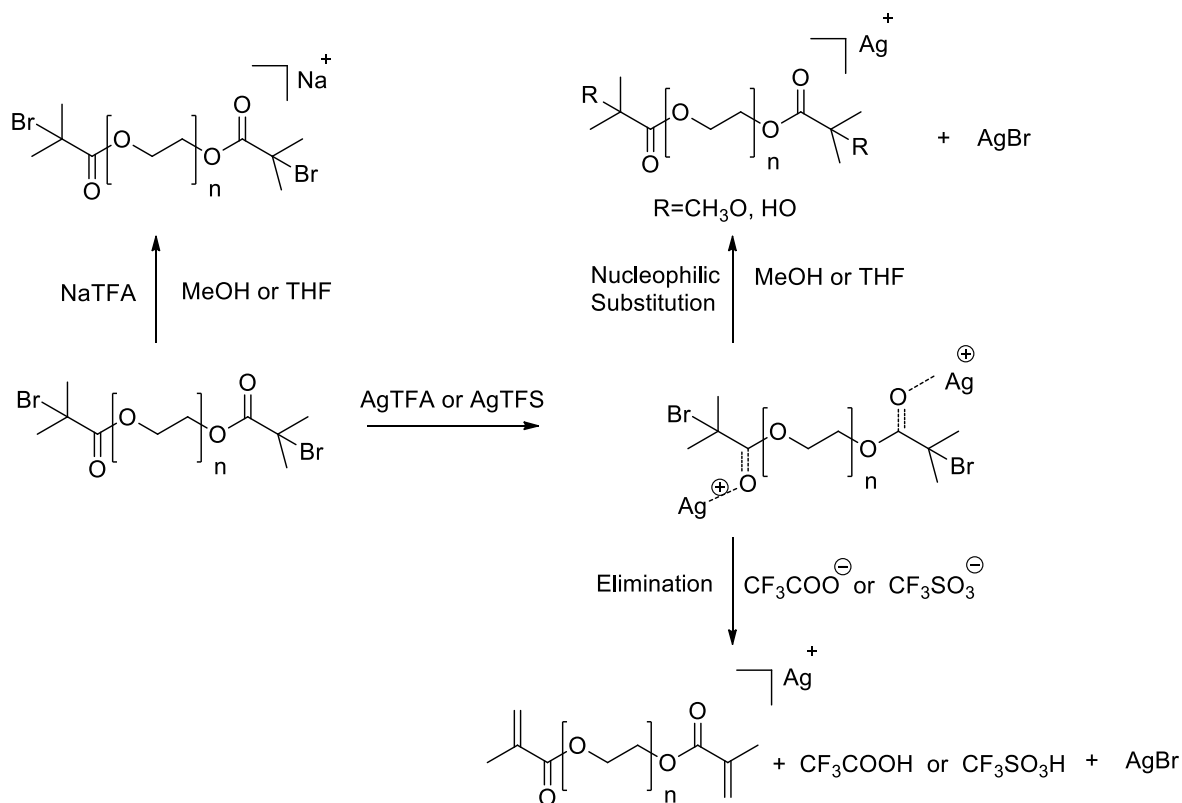
12
 13 **Figure 4.** Molar mass distribution of PEG bis(2-bromo-2-methylpropanoate) $DP = 41$ (**2a**) obtained
 14 by MALDI in reflectron mode with AgTFA as cationic agent.

15 The unsaturated compound was formed due to the elimination of bromine from the original ester **2a**.
 16 The explanation for this observation arises from the fact that silver (Ag^+) has a low cationic absolute
 17 hardness value ($\eta = 6.9$ eV), and this cation has the ability to react with halo-organic compounds with
 18 a softer character. However, it was reported that, as a result of this interaction, a nucleophilic
 19 substitution was promoted [36]. Through this reaction, the loss of the terminal bromine could be
 20 promoted by a silver cation giving a complex, this intermediate reacting with the conjugated acid of
 21 the cationic agent and thus giving an unsaturated compound, a silver bromide and the corresponding
 22 acid. The second ion sequence was assigned to methoxylated products formed during the interaction
 23 of the intermediate and methanol that was used as a solvent. These methoxylated derivatives can be
 24 observed in **Figure 4** as secondary peaks with the lowest intensity (structure as depicted in **Figure**
 25 **5b** and named as M Series). The proposed mechanism is displayed in **Scheme 2**.



2 **Figure 5.** Compounds identified in MALDI analysis of bis(2-bromo-2-methylpropanoate) of PEG.

3



5 **Scheme 2.** Proposed mechanisms for 2-bromo-2-methylpropanoate end-functionalized esters during
6 MALDI-TOF analysis with Ag^+ and Na^+ as cationic agents.

7

8 With an increase in molar mass of the esters derived from PEG, a reversal in the sequence intensities
9 was observed (entries **2b** and **2c** in **Table 3**). In these samples, the methoxylated esters had greater
10 intensities than those of the unsaturated compounds, when employing the same ionization system (see
11 *Figure S-4 and Figure S-5 in Supporting Information*). In the esterified MPEG a similar behavior was
12 found, unsaturated end groups were identified as the main products (entries **2d-e** in **Table 3**).

1 Nonetheless, a secondary ion sequence pattern with lower intensity was identified arising from
 2 hydroxyl substitution of the brominated esters (W Series in **Figure 5c**). In the case of a higher molar
 3 mass sample (**2f**), the W Series was higher in intensity than the U Series (entry **2f**, **Table 3**). It was
 4 clear that with the increase in molar mass, a decrease in the unsaturated products was observed. The
 5 MALDI-TOF mass spectra of MPEG esters are illustrated in Supporting Information (*Figures S-6 to*
 6 *S-8*). In all experiments with AgTFA/methanol, it was clear that with the increment of the molar mass
 7 in PEG or MPEG esters, a decrement in the unsaturated products was observed.

8

9 **Table 3.** Results for MALDI-TOF MS analysis of brominated esters **2a-f** with DCTB/AgCF₃COO
 10 and MeOH as the solvent.

MI	DP_p^a	M_p MI ^b ([M _p +Ag] ⁺) (Da)	Peaks with Highest Intensity			Peaks with Lowest Intensity		
			M_p found ([M _p +Ag] ⁺) (Da)	Assigned Structure	M_p Calculated ([M _p +Ag] ⁺) (Da)	M_p found ([M _p +Ag] ⁺) (Da)	Assigned Structure	M_p calculated ([M _p +Ag] ⁺) (Da)
2a	43	2341.125	2156.019	[U+Ag] ⁺	2156.332	2220.408	[M+Ag] ⁺	2220.396
2b	74	3706.768	3585.934	[M+Ag] ⁺	3586.039	3521.792	[U+Ag] ⁺	3521.989
2c	131	6217.789	5988.232	[M+Ag] ⁺	5989.192	5924.564	[U] ⁺	5925.167
2d	15	972.682	869.487	[U+Ag] ⁺	868.787	887.530	[W+Ag] ⁺	886.795
2e	44	2250.219	2146.178	[U+Ag] ⁺	2146.337	2164.480	[W+Ag] ⁺	2164.332
2f	117	5466.088	5380.624	[W+Ag] ⁺	5380.201	5362.534	[U+Ag] ⁺	5362.238

11 ^a DP_p value corresponding to M_p .

12 ^b Theoretical molar mass of macroinitiators (MI) related to corresponding DP_p value.

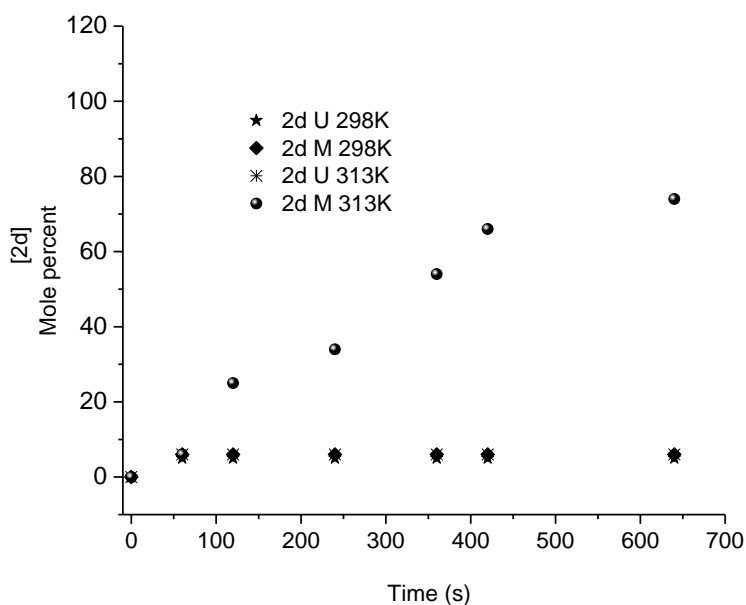
13 Tintaru *et al.* [27] also reported the presence of unsaturated and methoxylated species obtained from
 14 the loss of the halide end group in bromine end-functionalized ω -polystyrene samples analyzed by
 15 MALDI TOF MS with silver cationic agents. They concluded that the elimination reaction took place
 16 during the sample preparation, prior to the ionization; this assumption was based on NMR analysis
 17 of the samples.

18 Here, the reaction between MPEG 2-bromo-2-methylpropanoate ester (**2d**) with silver trifluoroacetate
 19 (AgTFA) at room temperature (298 K) was studied by NMR employing deuterated methanol as
 20 solvent. In this analysis, only the reaction of the ester with the silver salt was considered with molar
 21 ratio of 1:5 MPEG 2-methyl-2-bromopropionate (**2d**): AgTFA, without the use of DCTB. Bearing in
 22 mind that the main function of this matrix in the MALDI analysis was to transfer the energy from the

1 laser irradiation to the sample during the ionization process, it did not have any influence on the
2 bromine elimination reaction. In the ^1H NMR spectrum, the chemical shifts of the **2d** ester could be
3 appreciated (see *Figure S-9 in Supporting Information*). This ester was stable for at least 60 s; during
4 this time, there were no observable signals in the ^1H NMR spectrum for the unsaturated compound
5 (**2dU**). After this time lapse, a very low yield (< 6 %) of the unsaturated product (U Series) was
6 identified; its concentration was calculated by the integration values for the signals of the vinyl
7 protons at 6.13 and 5.66 ppm respectively and compared to the signals for the CH_2 protons from the
8 carbonyl ester at 4.27 ppm.

9 The methoxylated or hydroxylated added products (M or W Series) at the end of the polymer chains
10 were characterized indirectly by changes in the magnetic environment surrounding the 2-methyl
11 group of the 2-methylpropanoate moiety. The methyl group near the bromine atom had a chemical
12 shift of 1.95 ppm in the ester **2d**. It shifted to 2.06 ppm in the unsaturated product (U Series) and to
13 1.20 ppm in the hydroxylated or methoxylated ester (M Series). The evolution of these two products
14 was followed and quantified during 700 s at 298 K, the concentration of these two products remaining
15 constant with minimal variation during this time.

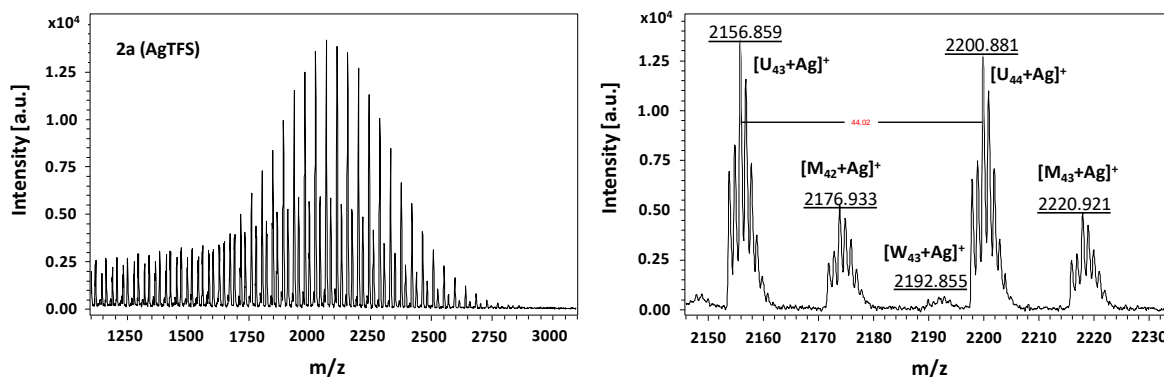
16 In order to emulate the ionization process, the temperature of the NMR probe was increased [38] from
17 room temperature (298K) to 313K, and changes in the mixture of **2d** and AgTFA in deuterated
18 methanol were monitored, the results are depicted in **Figure 6**. The concentration of the M Series
19 increased to 50% after 300 s, while the concentration of the unsaturated compound (U Series)
20 remained constant throughout the entire experiment. According to these observations, we could
21 conclude that the changes in the structure of the brominated esters would be promoted by an energy
22 source such as the ionization process and not during sample preparation. The increase in the
23 concentration of substitution products (M Series) at higher temperature instead of that of the
24 elimination products (U Series) suggested the presence of an intermediate promoted by the reaction
25 between silver ion and the bromine atom.



1

2 **Figure 6.** Influence of AgTFA on stability of the **2d** ester obtained by ^1H NMR spectroscopy in
 3 deuterated methanol.

4 In order to explain the previous results and how the end groups are formed during the MALDI
 5 ionization process, the possibility of γ -hydrogen abstraction of PEG or MPEG esters followed by the
 6 formation of an intermediate and a subsequent substitution or elimination reaction promoted by the
 7 interaction with the silver ion was considered. It was then proposed the use of silver
 8 trifluoromethanesulfonate (AgCF_3SO_3) as a cationic agent in which the conjugated acid of the
 9 counterion has a different acid strength and would influence the presence of the elimination
 10 compounds. MALDI conditions with an equal molar ratio of DCTB/**2a-f**/ AgCF_3SO_3 of 310/1/18 were
 11 selected for the new series of experiments. Excellent ionization of the six 2-bromo-2-
 12 methylpropanoate esters derived from PEG or MPEG was found. In **Figure 7**, the MALDI TOF MS
 13 spectra for the **2a** ester are shown. Two patterns were mainly observed, *i.e.* the U and M Series, which
 14 corresponded to the elimination or substitution products. The mass spectra of the other macroinitiators
 15 (**2b-f**) are shown in Supporting Information (*Figure S-9 to Figure S-13*).



1
2 **Figure 7.** MALDI-TOF spectra of the **2a** brominated ester using AgTFS/2a/DCTB with a molar ratio
3 of 310/1/18 employing methanol as the solvent, obtained in reflectron mode.

4 The m/z ratios obtained in each MALDI-TOF mass spectrum were compared with the theoretical
5 molar masses of the possible structures, and the results are listed in **Table 4**. When the six brominated
6 esters were compared with the esters characterized with AgTFA as the ionic agent, a similar behavior
7 was observed under the new ionization conditions. The loss of the bromine atom was also observed,
8 thus contributing to elimination or substitution reactions. The main products corresponded to U, M
9 or W Series, respectively. In the macroinitiators with molar masses lower than or equal to 2,000 Da,
10 the products from elimination were preponderant (U Series), and with the increment of the molar
11 mass, the formation of addition products was observed (M Series).

12

13 **Table 4.** Results for MALDI-TOF MS analysis of brominated esters **2a-f** with DCTB/AgCF₃SO₃ and
14 MeOH as the solvent.

M I	DP_p ^a	M_p PEG- Br ^b ([Mp+Ag] ⁺) (Da)	Peaks with Highest Intensity			Peaks with Lowest Intensity		
			M_p found ([Mp+Ag] ⁺) (Da)	Assigned Structur e	M_p Calculate d ([Mp+Ag] ⁺) (Da)	M_p found ([Mp+Ag] ⁺) (Da)	Assigned Structur e	M_p calculated ([Mp+Ag] ⁺) (Da)
2a	43	2341.125	2156.859	[U+Ag] ⁺	2156.332	2220.921	[M+Ag] ⁺	2220.396
2b	74	3706.768	3585.627	[M+Ag] ⁺	3586.039	3558.687	[W+Ag] ⁺	3557.985
2c	131	6217.789	6070.653	[W+Ag] ⁺	6069.006	6096.611	[U+Ag] ⁺	6097.060
2d	15	972.682	869.089	[U+Ag] ⁺	868.787	887.093	[W+Ag] ⁺	886.795
2e	44	2250.219	2147.411	[U+Ag] ⁺	2146.337	2165.427	[W+Ag] ⁺	2164.332
2f	117	5466.088	5380.217	[W+Ag] ⁺	5380.201	5362.621	[M+Ag] ⁺	5362.238

1 ^a DP value corresponding to M_p

2 ^b Theoretical molar mass related to corresponding DP_p value

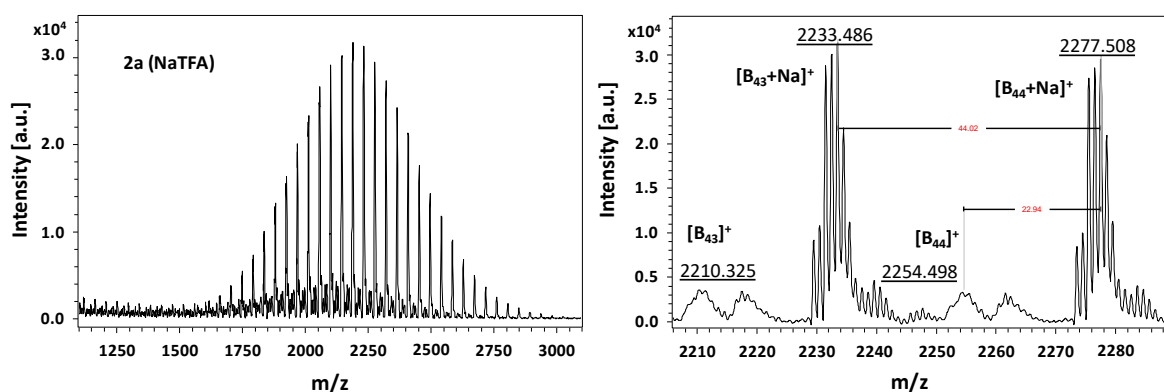
3 As it could be seen in **Table 3**, the ions with the highest intensity displayed the same tendency as the
4 previous results with the presence of unsaturated compounds in esters with molar masses lower than
5 or equal to 2,000 Da. Nevertheless, for the esters with molar masses higher than 2,000 Da (**2b**, **2c**,
6 and **2f** samples), no unsaturated end groups were detected. With these results, it could be mentioned
7 that the increment of the acidity of the counterion in the cationic agent would not have an influence
8 on the MALDI-TOF MS spectra. It is noteworthy that the esters, the matrix (DCTB), and the
9 cationization agent were dissolved in methanol, then a small aliquot of the mixture was deposited to
10 a sample plate and the matrix and polymer co-crystallized as the solvent evaporated. During this
11 process, methanol or water molecules might be trapped in the formed crystals, depending on the
12 environment conditions. At this stage, the polymers were arranged in the crystal according to their
13 polarities. Thus, functionalized polymers with lower molar masses had the 2-methyl-2-
14 bromopropionate end group available to interact with the cationic agent, followed by the proton
15 abstraction to produce unsaturated polymer. On the contrary, in polymers with molar masses higher
16 than 2,000 Da, the end group would be distant from the cationic agent, thus it was easier to react with
17 the rest of the solvent/water molecules, leading to the substitution products in the M or W Series
18 observed in the mass spectra.

19 Considering the previous results, when specific ionization conditions were employed, the bromine
20 atom was not present in the ATRP macroinitiators, due to its lability. This inaccurate analysis may
21 cause an uncertainty in the quality of the ATRP macroinitiators. In this study, the silver ion reacts
22 with the α -bromo carbonyl compound, due to their similar soft characteristic. Metals with higher
23 absolute hardness value, such as sodium ($\eta = 21.1$ eV), must have different reactivity with the halo-
24 carbonyl compound and will be more stable during the laser excitation in the ionization process on
25 the MALDI analysis.

26 With the purpose to prove the low reactivity of the α -halo-carbonyl compound with alkaline metals,
27 sodium trifluoroacetate (NaTFA) was selected as a cationic agent. All the samples were analyzed
28 with the same conditions and reagents as used before, DCTB as the matrix in methanol and a molar
29 ratio of DCTB/brominated esters **2a-f**/NaTFA of 310/1/18. The MALDI-TOF mass spectra of all the
30 esters revealed the presence of a single pattern of ions. Therefore, it may be deduced some stability
31 in the molecular ions during the ionization process. This result confirmed the fact that the sodium
32 cation had a low reactivity with the α -bromo esters, and no elimination or addition products (U, M

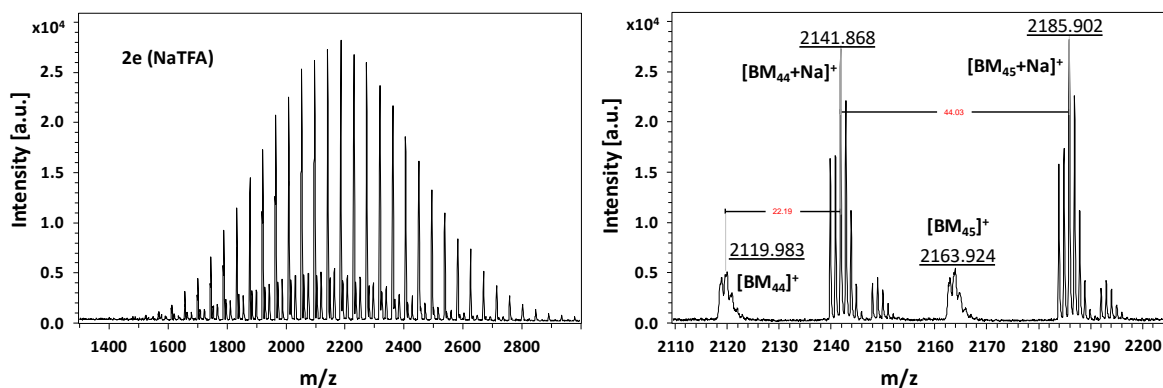
1 or W Series respectively) were identified in the mass spectra. In contrast, some secondary peaks with
 2 very low intensity were identified as molecular ions without the presence of cationic agent (Na^+).

3 As a typical example, **Figure 8** shows the molar mass distribution for the **2a** sample, in which two
 4 molecular species were identified as PEG molecules with 2-methyl-2-bromopropionate with and
 5 without counterion. These molecular structures (B Series in **Figure 10a**) were assigned based on the
 6 m/z ratio of ions observed in each mass spectrum and compared with the calculated molar mass for
 7 the brominated esters (**2a-f**). In all cases, the experimental isotopic pattern fitted well with the
 8 theoretical one, as it can be seen in **Table 5**. The mass spectra for **2b** and **2c** samples are shown in
 9 *Figure S-14* and *Figure S-15* in Supporting Information. It is important to mention that these samples
 10 (**2a-2c**) are dibromated esters, thus the resulting isotopic pattern in all mass spectra is due to natural
 11 bromine isotopes (^{79}Br and ^{81}Br).

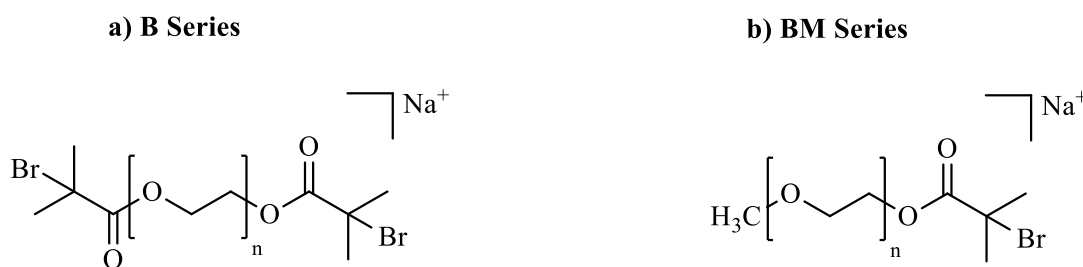


12
 13 **Figure 8.** MALDI-TOF spectra of the brominated ester **2a** using NaTFA/**2a**/DCTB with a molar ratio
 14 of 310/1/18 employing methanol as the solvent, obtained in reflectron mode.

15 The MALDI-TOF mass spectra of the MPEG 2-methyl-2-bromopropionate esters **2d-f** also displays
 16 the bromine isotopic peaks as the main ions in the molar mass distribution curve. The mass spectrum
 17 for the **2e** sample is shown in **Figure 9**. The MPEG molecules with bromine end-functionalization
 18 were identified as BM Series (see structure in **Figure 10b**). These MALDI-TOF results confirmed
 19 that the stabilization of the macroinitiators was achieved in the presence of the sodium cation. This
 20 high stability was sufficient to detect the molecular ions of the esters **2d-f**, where the cationic agent
 21 is absent (BM^+ Series in **Figure 9**). The results for **2d** and **2f** samples are shown in *Figure S-16* and
 22 *Figure S-17* in Supporting Information.



1
2 **Figure 9.** MALDI-TOF spectra of the brominated ester **2e** using NaTFA/**2e**/DCTB with a molar ratio
3 of 310/1/18 employing methanol as the solvent, obtained in reflectron mode.



5 **Figure 10.** Compounds identified in MALDI analysis of bis(2-bromo-2-methylpropanoate) of PEG
6 and MPEG with NaTFA/DCTB in methanol.

7 Further, the results listed in **Table 5** showed that the molar mass of the PEG 2-methyl-2-
8 bromopropionate esters **2a-c** or MPEG 2-methyl-2-bromopropionate esters **2d-f** had no influence on
9 the ionization and detection process in MALDI-TOF analysis. In all cases, the molar mass of the
10 brominated or dibrominated esters were accurately determined and the high quality of the ATRP-
11 macroinitiators was established.

12 **Table 5.** Results for MALDI-TOF-MS analysis of brominated esters **2a-f** in DCTB/NaTFA and
13 MeOH as the solvent.

M I	DP_p ^a	M_p PEG- Br ^b ([Mp+Na] + (Da))	Peaks with Highest Intensity			Peaks with Lowest Intensity		
			M_p found ([Mp+Na] + (Da))	Assigned Structur e	M_p calculated ([Mp+Na]+) (Da)	M_p found ([Mp+Na] + (Da))	Assigned Structur e	M_p calculated ([Mp+Na] + (Da))
2a	43	2233.257	2233.486	[B+Na] ⁺	2233.257	2210.325	[B] ⁺	2210.267
2b	74	3598.900	3597.883	[B+Na] ⁺	3598.900	3582.040	[W] ⁺	3582.276
2c	131	6109.921	6108.93	[B+Na] ⁺	6109.921	6085.570	[B] ⁺	6086.931

2d	15	864.814	865.128	[B+Na] ⁺	864.814	843.555	[B] ⁺	843.555
2e	44	2142.351	2141.868	[B+Na] ⁺	2142.351	2119.983	[B] ⁺	2119.361
2f	117	5358.220	5295.739	[W+Na] ⁺	5295.323	5358.219	[B+Na] ⁺	5358.220

^a DP value corresponding to M_p

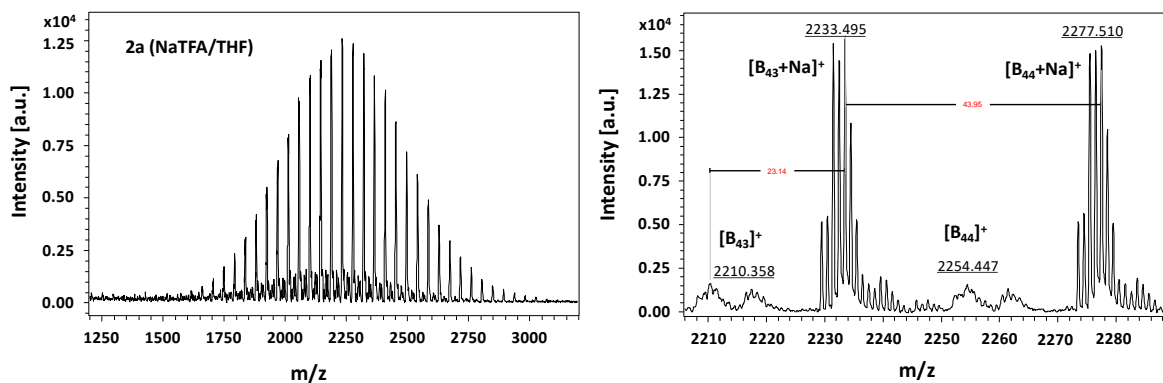
^b Theoretical molar mass related to corresponding DP_p value

3

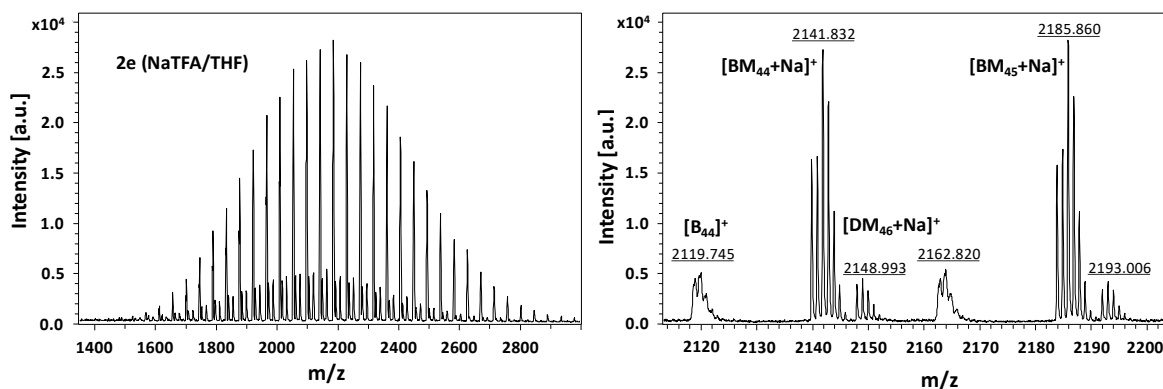
4 **Influence of solvent during MALDI-TOF MS analysis.** It is important to consider that in MALDI
5 TOF MS analysis, the sample preparation has a strong influence on the ionization process, and
6 definitely it does on the final chemical structure obtained. In this process, the sample will interact
7 with all components, *i.e.* matrix, cationic agent, and solvent, and depending on its compatibility with
8 the cationic agent, it will produce different compounds rather than the original molecules.

9 The solvent has an important role as it will promote solvation of the metal ion and make it available
10 for any chemical reaction. In addition, the solvent is also used as a vehicle to apply a homogeneous
11 mixture into the target. The solvent is evaporated and the mixture starts to crystallize, and depending
12 on the polarity and the solvent volatility, the sample and cationic agent are available to interact with
13 the energy source. For this instance, the effect of THF as a common solvent on the characterization
14 of PEG or MPEG 2-methyl-2-bromopropionate esters in the MALDI-TOF MS analysis was
15 evaluated. The six brominated esters **2a-f** were analyzed using the same reagents and molar ratios
16 (see *Table S-2 to S-4 in Supporting Information*).

17 According to the collected results, the use of THF had no influence on the ionization process of the
18 ATRP initiators. Indeed, the same molar mass distribution patterns were obtained when compared to
19 the results with methanol as a solvent. In the latter case, the main structures obtained with the sodium
20 cation were dibrominated molecular ions of the esters **2a-f** and a second pattern was identified for the
21 molecular ions without the sodium metal, as **is** evidenced in **Figure 11** and **Figure 12** for the esters
22 **2a** and **2e**. This study also demonstrated that the cationic metal agent was the main responsible of the
23 formation of unsaturated, methoxylated or hydroxylated esters.



1
2 **Figure 11.** MALDI-TOF spectra of the dibrominated ester **2a** using NaTFA/**2a**/DCTB with a molar
3 ratio of 310/1/18 and THF as the solvent, obtained in reflectron mode.



4
5 **Figure 12.** MALDI-TOF spectra of the brominated ester **2e** using NaTFA/**2e**/DCTB with a molar
6 ratio of 310/1/18 and THF as the solvent, obtained in reflectron mode.

7

8 Conclusions

9 The effect of the cationic agents on the determination of the molar mass by MALDI-TOF MS for
10 PEG or MPEG with 2-bromo-2-methylpropanoate end groups was thoroughly investigated. Two
11 silver salts (trifluoroacetate or trifluoromethanesulfonate) and one sodium salt (trifluoroacetate) in
12 methanol or tetrahydrofuran were chosen as promoters of cationic species and trans-2-[3-(4-tert-
13 butylphenyl)-2-methyl-2-propenylidene] malononitrile (DCTB) as the matrix. It was established that
14 the silver ions reacted with the α -bromo carbonyl compound, due to their similar soft characteristic,
15 enhancing the loss of the bromine atom, thus contributing to elimination or substitution products.
16 This reaction was confirmed by ^1H NMR experiments, from which it was found that it was triggered
17 when the source of energy was applied. No reaction with the halo-carbonyl compounds was observed

1 with the use of sodium as cationic agent, thus resulting in more stable molecular ions during the laser
2 excitation in the MALDI analysis. Poly(glycol)s with 2-bromo-2-methylpropanoate end-
3 functionalization could be efficiently used as hydrophilic macroinitiators in ATRP polymerizations,
4 because their structure is accurately characterized by MALDI-TOF analysis with the use of sodium
5 cationic agents.

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11 support during MALDI-TOF measurements.

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