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RAFT polymerization of Bromotyramine-based 4 -acryloyl-1,2,3-triazole: A Functional Monomers and Polymers Family through Click Chemistry.

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Four new functional acryloyl-triazole monomers derived from bromotyramine were successfully synthesized. These monomers were prepared in an efficient way from organic azides and propargyl acrylate via a copper catalyzed 1,3-dipolar cycloaddition. Polymers containing bromotyramine as a pendant group were obtained via the reversible addition-fragmentation chain transfer (RAFT) polymerization. The influence of the chain transfer agent (CTA), solvent, temperature and the length of the linker between the triazole and bromotyramine groups on polymerization kinetics was studied. It was found that triazole containing acrylate monomers are characterized by fast polymerization and polymers with controlled molar masses (20 000 g.mol^{-1}) and low dispersities ($Đ_M$<1.5) can be prepared. Glass transition temperatures of these acrylic polymers ranged from 48°C to 20°C by controlling the length of the linker between the bromotyramine side groups and the backbone.

1. Introduction

The prevention of biofilm development and the reduction of surface contamination are important issues in medical devices [1,2], food packaging [3,4], shipping [5], aquaculture [6], offshore petroleum industry [7]... In the literature, antimicrobial and antibiofilm agents are numerous and large-scale used to prevent the adhesion of biofilm or to kill microorganisms. The incorporation of these biocides into coatings was the most efficient way to protect materials against microorganisms and inhibit the spread of microbial colonization. [8-11] Any release of biocidal products from coatings into the surrounding environment lead to a decrease in efficacy with time. They were often found to be toxic against non-target species. [12-23]

An alternative approach is the design of polymers that can inhibit biofilm formation thanks to covalently linked biocidal side groups. This approach avoids any release of biocidal products and maintains a continious activity. [24] One method of achieving these polymers is to initially synthesize monomers containing biocidal moieties and then polymerize them subsequently or copolymerize them with other co-monomers.[24-29] An alternative method is to chimically modify existing polymers. [24,30,31] Then, biocidal polymers can be used as non-releasing coatings active by contact. [32,33] The advantage of biocidal polymers is justified by the minimization of environmental impacts. Recently, the demand of eco-friendly antifouling materials has substantially increased and non-toxic strategies including the incorporation of natural antifouling compounds from marine organisms into coatings has been extensively investigated. [10,34-38]

Bromotyramine-based compounds e.g. Moloka'iamine (**A**) [39,40], 3,5-dibromo-4-methoxy-b-phenethylamine (**B**) [41] and N-methyl-3-bromotyramine (C) [42] have been reported into the literature to be efficient antifoulants against several marine organisms [37,39,42 ,43] (Figure 1). Synthetic analogues of this series of marine compounds were studied in our laboratory and were shown to display an anti-bacterial activity. Therefore, polymers containing bromotyramine side groups could be an alternative approach to develop surfaces which could inhibit any marine biofilm formation.

The Cu-catalyzed Huisgen 1,3-cycloaddition is one of the most powerful post functionalization strategy. It has been combined with great success with controlled polymerization methods to synthesize a wide range of functional materials. [31,44,45] There are a plethora of examples using the click chemistry in polymer science. [45-46,47] The development of this reaction has also contributed to the design of a broad library of C-vinyl and N-vinyl-1,2,3-triazole based monomers and their resulting polymers. [48-55] For example, a series of vinyl-1,2,3-triazole having various substituent groups has been reported to be successfully employed for the synthesis of functional polymers and block copolymers using conventional radical polymerization [55], reversible addition-fragmentation chain transfer (RAFT) [48,51,52] and nitroxide-mediated polymerizations. [49,50] Most of triazole containing polymers are prepared from conventional vinylic monomers. To our

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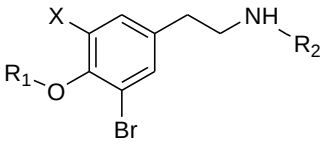
knowledge, no polymers have been prepared directly from acryloyl-1,2,3-triazole monomers via the RAFT process. The present study aims at preparing a series of 4-acryloyl-1,2,3-triazole (**4-ATri**) monomers and their resulting bromotyramine-containing homopolymers using the RAFT process. These polymers will combine the inherent properties of the 1,2,3-triazole linker group and the active bromotyramine group for further developing anti-adhesive surfaces for marine bacteria. The general structure of these novel monomers, as well as the synthetic pathway, are reported in Scheme 1. These monomers have been prepared in an efficient way from organic azides and propargyl acrylic via copper catalyzed 1,3-dipolar cycloaddition. The polymerization ability of these triazole acrylic monomers has been investigated and kinetics has been carried out to point out the controlled character of the polymerization process. Then, the thermal properties of the polymers were studied using differential scanning calorimetry (DSC) and thermogravimetric analysis (TGA).



A : $R_1 = (CH_2)_3NH_2$, R_2=H , X=Br
B : $R_1 = CH_3$, R_2=H, X=Br
C : R1 = H , $R_2 = CH_3$, X=H

Figure 1. Bromotyramine derivatives

2. Experimental section

Materials. Anhydrous acetonitrile (CH_3-CN), N-Bromosuccinimide (NBS), sodium carbonate (Na_2CO_3), sodium sulfate (Na_2SO_4), sodium azide (NaN_3) , *N,N*-dimethylformamide (DMF), dimethyl sulfoxide (DMSO), dimethyl sulfoxide-d_6 (DMSO-d_6), *N,N*-dimethylformamide-d_7 (DMF-d_7), chloroform-d ($CDCl_3$), methanol, ethyl acetate (EtOAc), cyclohexane, diethyl ether (Et_2O), propargyl acrylate, Copper(II) sulfate pentahydrate ($CuSO_4.5H_2O$), sodium ascorbate, 1-(chloromethyl)-4-methoxybenzene, 1-(3-bromopropyl)-4-methoxybenzene and 4-methoxybenzyl chloride were purchased from Aldrich and used as received. 1-(2-Chloroethyl)-4-methoxybenzene was purchased from ACROS. Cyanomethyl dodecyl trithiocarbonate (CMDT) and 2-(dodecylthiocarbonothioylthio)-2-methylpropionic acid (DDMAT) were used as chain transfer agents (Aldrich). Azobis(isobutyronitrile) (AIBN, Aldrich) was recrystallized from methanol prior to be used.

Characterizations. ^{1}H- (400 MHz) and ^{13}C- (100 MHz) NMR spectra were recorded on a Brucker Advance NMR spectrometer. Mass spectra were measured on an ion trap mass spectrometer fitted with an ESI interface (Esquire 6000, Bruker Daltonics).The number-average molar mass (M_n) and dispersity ($Đ_M$) of polymers were determined by triple detection size exclusion chromatography (TD-SEC). Analyses were performed on a Viscotek apparatus, composed of a GPC Max (comprising a degasser, a pump and an autosampler) with a TDA-302 (refractive index detector, right and low angle light scattering detector at 670 nm and viscometer) and a UV detector (λ = 303 nm). The following columns were used: a Viscotek HHR-H precolumn and two Viscotek ViscoGel GMHHR-H columns. THF was used as the eluent with a flow rate of 1 mL.min^{-1} at 30°C. For each precipitated polymer, the refractive index increment (dn/dc) was determined using the OmniSec software, from a solution of known concentration (ca. 10 mg.mL^{-1}) filtered through a 0.2 µm PTFE filter.

The glass transition temperatures (T_g) of the homopolymers were measured with a Q10 differential scanning calorimeter (TA Instruments). The samples were cooled down to -10°C or 0°C and then scanned at a heating rate of 20°C min^{-1} from -10°C or 0°C to 140°C. The T_g values were determined as the midpoint between the onset and the end of a step transition on the second heating run using the TA Instruments Universal Analysis 2000 software.

Thermalgravimetric analysis (TGA) was conducted on a TA Instruments Q600 using a heating rate of 10°C/min from 300 to 800°C under constant nitrogen flow.

Typical experimental procedure for the bromination of methoxybenzene: General procedure for the synthesis of **2a**-**c**. To a solution of appropriate aromatic halide (**1a, 1b, 1c**) (1 eq.) in anhydrous acetonitrile at 0 °C, was added portion wise *N*-bromosuccinimide (NBS) (1.5 eq.) under argon atmosphere. The mixture was stirred at room temperature for 4 h in which time TLC indicated complete conversion. Solvent was evaporated under vacuum and the residue was dissolved in Et_2O. The organic layer was washed successively with sat. Na_2CO_3, sat. NaCl and H_2O. The solvent was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was used in the next step without further purification.

1. 2-bromo-4-(chloromethyl)-1-methoxybenzene (**2a**). **2a** was prepared using 1-(chloromethyl)-4-methoxybenzene (**1a**) (4.7 g, 30 mmol) and NBS (8 g, 45 mmol) in acetonitrile (60 mL). **2a** was obtained as a yellow oily substance (6.68 g, 94.5%).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, ^4J = 2.2 Hz, 1H, C-H_{Ar}), 7.30 (dd, ^3J = 8.4, ^4J =2.2 Hz, 1H, C-H_{Ar}), 6.87 (d, ^3J = 8.4 Hz, 1H, C-H_{Ar}), 4.52 (s, 2H, $\underline{CH_2}$-Cl), 3.90 (s, 3H, $\underline{CH_3}$-O).
^{13}C NMR (100 MHz, $CDCl_3$) δ 155.5($\underline{C_{Ar}}$-OCH_3), 133.2 ($\underline{CH_{Ar}}$), 130.6($\underline{C_{Ar}}$), 128.7($\underline{CH_{Ar}}$), 111.5($\underline{CH_{Ar}}$), 111.2($\underline{CBr_{Ar}}$-OCH_3), 55.9($\underline{CH_3}$-O), 45.0 ($\underline{CH_2}$-Cl).

2. 2-bromo-4-(2-chloroethyl)-1-methoxybenzene (**2b**). **2b** was prepared using 1-(2-chloroethyl)-4-methoxybenzene (**1b**) (6.82 g, 40 mmol) and NBS (10.68 g, 60 mmol) in acetonitrile (80 mL). **2b** was obtained as a yellow oily substance (9.9 g, 99%).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, ^4J = 2.2 Hz, 1H, C-H_{Ar}), 7.13 (dd, ^3J = 8.4, ^4J =2.2 Hz, 1H, C-H_{Ar}), 6.85 (d, ^3J = 8.4 Hz, 1H, C-H_{Ar}), 3.88 (s, 3H, $\underline{CH_3}$-O), 3.67 (t, ^3J = 7.3 Hz, 2H, CH_2-$\underline{CH_2}$-Cl), 2.98 (t, ^3J = 7.3 Hz, 2H, $\underline{CH_2}$-CH_2-Cl).

^{13}C NMR (100 MHz, $CDCl_3$) δ 154.1($\underline{C}_{Ar}$-OCH_3), 132.8($\underline{CH}_{Ar}$), 131.0($\underline{C}_{Ar}$), 128.4($\underline{CH}_{Ar}$), 111.3($\underline{CH}_{Ar}$), 110.8 ($\underline{C}$-Br_{Ar}), 55.6($\underline{CH_3}$-O), 44.5(CH_2-$\underline{CH_2}$-Cl), 37.1($\underline{CH_2}$-CH_2-Cl).

3. 2-bromo-4-(3-bromopropyl)-1-methoxybenzene (**2c**). **2c** was prepared using 1-(chloromethyl)-4-methoxybenzene (**1c**) (3.44 g, 15 mmol) and NBS (4 g, 22.5 mmol) in acetonitrile (30 mL). **2c** was obtained as a dark brown oily substance (4.58 g, 99%).
1H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, ^4J = 2.2 Hz, 1H, C-H_{Ar}), 7.11 (dd, ^3J = 8.4, ^4J =2.2 Hz, 1H, C-H_{Ar}), 6.84 (d, ^3J = 8.4 Hz, 1H, C-H_{Ar}), 3.88 (s, 3H, $\underline{CH_3}$-O), 3.38 (t, ^3J = 6.5 Hz, 2H, $\underline{CH_2}$-Br), 2.71 (t, J = 7.3 Hz, 2H, $\underline{CH_2}$-CH_2-CH_2-Br), 2.13 (m, 2H, CH_2-$\underline{CH_2}$-CH_2-Br).
^{13}C NMR (100 MHz, $CDCl_3$) δ 154.0($\underline{C}_{Ar}$-OCH_3), 133.8 ($\underline{C}_{Ar}$), 132.9($\underline{CH}_{Ar}$), 128.3($\underline{CH}_{Ar}$), 111.7($\underline{CH}_{Ar}$), 111.2($\underline{C}$-Br_{Ar}), 56.0($\underline{CH_3}$-O), 33.8(CH_2-CH_2-$\underline{CH_2}$-Br), 32.8($\underline{CH_2}$-CH_2-CH_2-Br), 32.4($\underline{CH_2}$-CH_2-CH_2-Br).

General Procedure for the synthesis of azides 3a-d.
A mixture of appropriate halide (1 equiv) and sodium azide (NaN_3) (2.6 equiv) in *N,N*-dimethylformamide (DMF) was stirred for 5 h at 90 °C. The reaction temperature was allowed to warm to room temperature and the reaction mixture was diluted with Et_2O. The organic phase was washed with brine and water, dried over Na_2SO_4, and concentrated under vacuum. The azide products were directly used for the next reaction without further purification.

4. 4-(azidomethyl)-2-bromo-1-methoxybenzene (**3a**). **3a** was prepared using **2a** (5.89 g, 25 mmol) and sodium azide (NaN_3) (4.22 g, 65 mmol) in *N,N*-dimethylformamide (50 mL). **3a** was obtained as dark brown oil (5.99 g, 99%).
1H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, ^4J = 2.2 Hz, 1H, C-H_{Ar}), 7.23 (dd, ^3J = 8.4, ^4J =2.2 Hz, 1H, C-H_{Ar}), 6.90 (d, ^3J = 8.4 Hz, 1H, C-H_{Ar}), 4.26 (s, 2H, $\underline{CH_2}$-N_3), 3.90 (s, 3H, $\underline{CH_3}$-O).
^{13}C NMR (100 MHz, $CDCl_3$) δ 155.2($\underline{C}_{Ar}$-OCH_3), 132.5($\underline{CH}_{Ar}$), 128.4($\underline{C}_{Ar}$), 128.0($\underline{CH}_{Ar}$), 111.4($\underline{CH}_{Ar}$), 111.1($\underline{C}$-Br_{Ar}), 55.5($\underline{CH_3}$-O), 52.9($\underline{CH_2}$-N_3).
IR (thin film) ν_{N3} 2092 cm^{-1}.

5. 4-(2-azidoethyl)-2-bromo-1-methoxybenzene (**3b**). **3b** was prepared using **2b** (8.98 g, 36 mmol) and sodium azide (NaN_3) (6.09 g, 93.6 mmol) in *N,N*-dimethylformamide (70 mL). **3b** was obtained as dark brown oil (8.8 g, 95.5%).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, ^4J = 2.2 Hz, 1H, C-H_{Ar}), 7.12 (dd, ^3J = 8.4, ^4J =2.2 Hz, 1H, C-H_{Ar}), 6.85 (d, ^3J = 8.4 Hz, 1H, C-H_{Ar}), 3.88 (s, 3H, $\underline{CH_3}$-O), 3.47 (t, ^3J = 7.1 Hz, 2H, $\underline{CH_2}$-$\underline{CH_2}$-N_3), 2.80 (t, ^3J = 7.1 Hz, 2H, $\underline{CH_2}$-CH_2-N_3).
^{13}C NMR (100 MHz, $CDCl_3$) δ 154.7($\underline{C}_{Ar}$-OCH_3), 133.4($\underline{CH}_{Ar}$), 131.6($\underline{C}_{Ar}$), 128.8($\underline{CH}_{Ar}$), 111.9($\underline{CH}_{Ar}$), 111.5($\underline{C}$-Br_{Ar}), 56.2($\underline{CH_3}$-O), 52.33(CH_2-$\underline{CH_2}$-N_3), 34.04($\underline{CH_2}$-CH_2-N_3).
IR (thin film) ν_{N3} 2090 cm^{-1}.

6. 1-(2-azidoethyl)-4-methoxybenzene (3c). **3c** was prepared using **1b** (5.1 g, 30 mmol) and sodium azide (NaN_3) (5.07 g, 78 mmol) in N,N-Dimethylformamide (60 ml). **3c** was obtained as yellow oil (5.06 g, 95%).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (m, 2H, 2 C-H_{Ar}), 6.89 (m, 2H, 2 C-H_{Ar}), 3.81 (s, 3H, $\underline{CH_3}$-O), 3.48 (t, J = 7.2 Hz, 2H, CH_2-$\underline{CH_2}$-N_3), 2.86 (t, J = 7.2 Hz, 2H, $\underline{CH_2}$-CH_2- N_3).
^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5($\underline{C}_{Ar}$-OCH_3), 130.0($\underline{C}_{Ar}$), 129.7 (2 $\underline{CH}_{Ar}$), 114.1 (2 $\underline{CH}_{Ar}$), 55.2($\underline{CH_3}$-O), 52.7(CH_2-$\underline{CH_2}$-N_3), 34.5($\underline{CH_2}$-CH_2-N_3).
IR (thin film) ν_{N3} 2090 cm^{-1}.

7. 4-(3-azidopropyl)-2-bromo-1-methoxybenzene (**3d**). **3d** was prepared using **2c** (4 g, 13 mmol) and sodium azide (NaN_3) (2.2 g, 33.8 mmol) in *N,N*-dimethylformamide (30 mL). **3d** was obtained as dark brown oil (3.32 g, 94.5%).
1H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, ^4J = 2.2 Hz, 1H, C-H_{Ar}), 7.08 (dd, ^3J = 8.4, ^4J =2.2 Hz, 1H, C-H_{Ar}), 6.83 (d, ^3J = 8.4 Hz, 1H, C-H_{Ar}), 3.87 (s, 3H, $\underline{CH_3}$-O), 3.28 (t, J = 6.7 Hz, 2H, CH_2-CH_2-$\underline{CH_2}$-N_3), 2.62 (t, J = 7.7 Hz, 2H, $\underline{CH_2}$-CH_2-CH_2-N_3), 1.87 (m, 2H, CH_2-$\underline{CH_2}$-CH_2-N_3).
^{13}C NMR (100 MHz, $CDCl_3$) δ 154.0($\underline{C}_{Ar}$-OCH_3), 134.2($\underline{C}_{Ar}$), 132.8($\underline{CH}_{Ar}$), 128.2($\underline{CH}_{Ar}$), 111.8($\underline{CH}_{Ar}$), 111.3($\underline{CBr}_{Ar}$), 55.9($\underline{CH_3}$-O), 50.2(CH_2-CH_2-$\underline{CH_2}$-N_3), 31.2($\underline{CH_2}$-CH_2-CH_2-N_3), 30.2(CH_2-$\underline{CH_2}$-CH_2-N_3).
IR (thin film) ν_{N3} 2090 cm^{-1}.

Typical method for preparation of monomers
An appropriate azide (1 equiv.) and propargyl acrylate (1.5 equiv.) were dissolved in a 1:2 mixture of water and ethanol. To the solution was added $CuSO_4.5H_2O$ (0.04 equiv) and sodium ascorbate (0.08 equiv). The resultant mixture was stirred at room temperature for 12 h at which time TLC revealed complete conversion. The reaction solution was diluted with brine and extracted three times with EtOAc. The organic layers were washed with water, dried over Na_2SO_4 and evaporated under vacuum. Crude triazoles were purified by silica gel column chromatography using a mixture of EtOAc/cyclohexane (70/30) as mobile phase.

8. (1-(3-bromo-4-methoxybenzyl)-1H-1,2,3-triazol-4-yl)methyl acrylate (**4-ATri4a**). **4-ATri4a** was obtained from azide **3a** (4.84 g, 20 mmol) and methyl propiolate (3.3 g, 30 mmol) as white solid (6.78 g, 96%).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (s, 1H, C-$H_{tr.}$), 7.41 (d, ^4J = 2.2 Hz, 1H, C-H_{Ar}), 7.14 (dd, ^3J = 8.4, ^4J =2.2 Hz, 1H, C-H_{Ar}), 6.79 (d, ^3J = 8.4 Hz, 1H, C-H_{Ar}), 6.30 (dd, ^3J = 17.3, ^2J =1.4 Hz, 1H, CH=CHH_E), 6.00 (dd, ^3J = 17.3, ^3J =10.4 Hz, 1H, CH=CH_2), 5.73 (dd, ^3J = 10.4, ^2J 1.4 Hz, 1H, CH=CHH_Z), 5.35 (s, 2H, CH_2-N), 5.17 (s, 2H CH_2-O-C=O), 3.77 (s, 3H, CH_3-O).
^{13}C NMR (101 MHz, $CDCl_3$) δ 165.7(C=O), 156.0(C_{Ar}-OMe), 143.0(C_{tr}), 133.0 ($\underline{CH}_{Ar}$), 131.4(CH=$\underline{CH_2}$), 128.5($\underline{CH}_{Ar}$), 127.8 (C_{Ar}), 127.8($\underline{CH}$=CH_2), 123.6 (CH_{tr}), 112.1($\underline{CH}_{Ar}$), 111.9($\underline{CBr}_{Ar}$), 57.5 ($\underline{CH_3}$-O), 56.2($\underline{CH_2}$-O-C=O), 52.8($\underline{CH_2}$-N).
M.p. = 99-100°C. (ESI, m/z) 352.05 ($[M+H,]^+$, ^{79}Br) 354.02 ($[M+H+2]^+$, ^{81}Br).

9. (1-(3-bromo-4-methoxyphenethyl)-1H-1,2,3-triazol-4-yl)methyl acrylate (**4-ATri4b**). **4-ATri 4b** was obtained from

azide **3b** (8.45 g, 33 mmol) and propargyl acrylate (5.45 g, 49.5 mmol) as white solid (11.7 g, 97%).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (s, 1H, C-H_{tr}), 7.14 (d, ^4J = 2.1 Hz, 1H, C-H_{Ar}), 6.83 (dd, ^3J = 8.4, ^4J =2.1 Hz, 1H, C-H_{Ar}), 6.66 (d, ^3J = 8.4 Hz, 1H, C-H_{Ar}), 6.26 (dd, ^3J = 17.3, ^2J =1.4 Hz, 1H, CH=CHH_E), 5.97 (dd, ^3J = 17.3, 10.4 Hz, 1H, C*H*=CH_2), 5.70 (dd, ^3J = 10.4, ^2J =1.4 Hz, 1H, CH=CHH_Z), 5.12 (s, 2H, CH_2-O-C=O), 4.42 (t, *J* = 7.2 Hz, 2H, CH_2-CH_2-N), 3.69 (s, 3H, CH_3-O), 2.99 (t, *J* = 7.2 Hz, 2H, CH_2-CH_2-N).
^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5(C=O), 154.6(C_{Ar}-OMe), 142.1(C_{tr}), 133.0(CH_{Ar}), 131.2(CH=CH_2), 130.2(CH_{Ar}), 128.5(C_{Ar}), 127.7(CH=CH_2), 124.0(CH_{tr}), 111.8(CH_{Ar}), 111.3(CBr_{Ar}), 57.3(CH_3-O), 55.9(CH_2-O-C=O), 51.2(CH_2-CH_2-N), 35.0(CH_2-CH_2-N).
M.p. = 69-70°C. (ESI, m/z) 366.05 ([M+H]$^+$, ^{79}Br) 368.06 ([M+H+2]$^+$, ^{81}Br).

10. (1-(4-methoxyphenethyl)-1H-1,2,3-triazol-4-yl)methyl acrylate (**4-ATri 4c**). **4-ATri 4c** was obtained from azide **3c** (4.78 g, 27 mmol) and propargyl acrylate (4.46 g, 40.5 mmol) as white solid (7.39 g, 95%).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (s, 1H, C-H_{tr}), 6.97 – 6.87 (m, 2H, 2C-H_{Ar}), 6.78 – 6.68 (m, 2H, 2C-H_{Ar}), 6.33 (dd, ^3J = 17.3, ^2J = 1.4 Hz, 1H, CH=CHH_E), 6.03 (dd, ^3J = 17.3, 10.4 Hz, 1H, C*H*=CH_2), 5.76 (dd, ^3J = 10.4, ^2J = 1.4 Hz, 1H CH=CHH_Z), 5.18 (s, 2H, CH_2-O-C=O), 4.46 (t, *J* = 7.3 Hz, 2H, CH_2-CH_2-N), 3.69 (s, 3H, CH_3-O), 3.06 (t, *J* = 7.3 Hz, 2H, CH_2-CH_2-N).
^{13}C NMR (101 MHz, $CDCl_3$) δ 165.7(C=O), 158.5(C_{Ar}-OMe), 142.2(C_{tr}), 131.2(CH=CH_2), 129.5 (2 CH_{Ar}), 128.7(C_{Ar}), 127.8(CH=CH_2), 124.1(CH_{tr}), 114.0 (2 CH_{Ar}), 57.5(CH_3-O), 55.0(CH_2-O-C=O), 51.7(CH_2-CH_2-N), 35.7(CH_2-CH_2-N).
M.p. = 42-43°C. (ESI, m/z) 288.11 [M+H]$^+$.

11. (1-(3-(3-bromo-4-methoxyphenyl)propyl)-1H-1,2,3-triazol-4-yl)methyl acrylate (**4-ATri 4d**). **4-ATri 4d** was obtained from azide **3d** (3.24 g, 12 mmol) and propargyl acrylate (1.98 g, 18 mmol) as yellow oil (4.38 g, 96%).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (s, 1H, C-H_{tr}), 7.28 (d, ^4J = 2.2 Hz, 1H, C-H_{Ar}), 7.00 (dd, *J* = 8.4, ^4J = 2.2 Hz, 1H, C-H_{Ar}), 6.77 (d, ^3J = 8.4 Hz, 1H, C-H_{Ar}), 6.36 (dd, ^3J = 17.3, ^2J = 1.4 Hz, 1H, CH=CHH_E), 6.06 (dd, ^3J = 17.3, 10.4 Hz, 1H, C*H*=CH_2), 5.79 (dd, ^3J = 10.4, ^2J = 1.4 Hz, 1H, CH=CHH_Z), 5.24 (s, 2H, CH_2-O-C=O), 4.28 (t, *J* = 7.1 Hz, 2H, CH_2-CH_2-CH_2-N), 3.79 (s, 3H, CH_3-O), 2.51 (t, *J* = 7.5 Hz, 2H, CH_2-CH_2-CH_2-N), 2.22 – 2.07 (m, 2H, CH_2-CH_2-CH_2-N).
^{13}C NMR (101 MHz, $CDCl_3$) δ 165.9(C=O), 154.3(C_{Ar}-OMe), 142.7(C_{tr}), 133.6(CH_{Ar}), 133.0(CH=CH_2), 131.5(CH_{Ar}), 128.4(C_{Ar}), 127.9(CH=CH_2), 123.8(CH_{tr}), 112.0(CH_{Ar}), 111.5(CBr_{Ar}), 57.6(CH_3-O), 56.2(CH_2-O-C=O), 49.3(CH_2-CH_2-CH_2-N), 31.5(CH_2-CH_2-CH_2-N), 31.1(CH_2-CH_2-CH_2-N). (ESI, m/z) 380.06 ([M+H]$^+$, ^{79}Br) 382.06 ([M+H+2]$^+$, ^{79}Br).

General Procedure for RAFT Polymerization

In situ ^{1}H NMR RAFT polymerizations were carried out using CMDT or DDMAT as CTAs and AIBN as initiator at a molar ratio [CTA]/[AIBN]=10. The concentration of CTA was adjusted to the targeted number-average molar mass (M_n^{target}), taking into account a full conversion of monomers and M_n^{th}, calculated as follows (Eqn.1):

$$M_n^{th} = \frac{[M]_0}{[CTA]_0} \times M_{monomer} \times conv. + M_{CTA} \qquad (1)$$

Where $[M]_0$ and $[CTA]_0$ are the initial concentrations of monomer and CTA respectively, $M_{monomer}$ and M_{CTA} are the molar mass of monomer and CTA respectively, and *conv*. is the monomer conversion.

All polymerizations were carried out in a high pressure/vacuum Wilmad NMR tube. A representative example is as follows: **4-ATri 4b** (137 mg, 0,375 mmol), cyanomethyl dodecyl trithiocarbonate (CMDT) (2.2 mg, 0.007 mmol), AIBN (0.114 mg, 0.0007 mmol), and DMSO-d_6 (0.25 mL) were placed in a dry high pressure/vacuum Wilmad NMR tube and then the solution was degassed by three freeze-evacuate-thaw cycles. The polymerization occurred into the NMR apparatus, heated at 60°C during 15h, and followed by ^{1}H NMR analysis at regular times. After cooling down to room temperature, the crude sample was dissolved in a small amount of DMSO, purified by reprecipitation into a large excess of methanol, and the resulting product was dried under vacuum at room temperature (84 mg, yield 62 %).

The conversion of **4-ATri 4b** is determined from *in situ* ^{1}H NMR analysis of the reaction mixture by comparing the integration (I_H) area of peaks at 6.10-6.20 ppm (one vinylic proton of monomer) and the peak at 7.90-8.06 ppm corresponding to the triazole proton of both monomer and polymer. The conversion of **4-ATri 4b** and M_n^{NMR} were determined with time as follows (Eqn.2 and 3):

$$Conv.(\%)(t) = \frac{I_{H,polymer}(t)}{I_{H,(monomer+polymer)(t)}} \times 100 \qquad (2)$$

with,
$I_{H,\ polymer} = I_{H,\ 7.90\text{-}8.06\ ppm} - I_{H,\ 6.10\text{-}6.20\ ppm}$
$I_{H(monomer\ +\ polymer)} = I_{H,\ 7.90\text{-}8.06\ ppm}$

$$M_n^{NMR}(t) = \frac{[M]_0}{[CTA]_{chain\ end}(t)} \times conv.(t) \times M_{monomer} + M_{CTA} \qquad (3)$$

where $M_{monomer}$ and M_{CTA} are the molar mass of monomer and CTA respectively, and $[CTA]_{\text{chain end }(t)}$ is the concentration of CTA converted into macro-CTA with time.

The conversion of macro-CTA ($[CTA]_{\text{chain end (t)}}$) is determined from *in situ* ^{1}H NMR analysis of the reaction mixture by comparing the integration (I_H) area of peaks at 4.4 ppm corresponding to two protons of unconsumed CTA (CH_3-$(CH_2)_{11}$-S-(C=S)-S-CH_2-CN) and the peak at 0.85 ppm corresponding to the three protons (CH_3-$(CH_2)_{11}$-S-(C=S)-S-CH_2-CN) of both unconsumed CTA and consumed CTA, as follows (Eqn.4):

$$[CTA]_{\text{chain end}}(t) = \left(1 - \frac{\frac{I_{2H,4.4\ ppm}(t)}{2}}{\frac{I_{3H,0.85\ ppm}(t)}{3}}\right) \times [CTA]_0 \ (4)$$

The final molar mass (M_n^{NMR}) of the polymer is also determined after precipitation in methanol as follows (Eqn.5):

$$M_n^{NMR} = X_n \times M_{monomer} + M_{CTA} \quad (5)$$

where X_n is the number of repeating unit. X_n is determined from ^{1}H NMR spectra of the purified polymer (Figures 1-3 in electronic supplementary information†) by comparing the integration (I_H) area of peaks at 3.80 ppm (methoxy protons (3H) of polymer) and the peak at 0.85 ppm corresponding to three protons of CTA inserted at the end of the polymer chains (Eqn.6).

$$X_n = \frac{I_{3H,polymer}}{I_{3H(CTA\ chain\ end)}} \quad (6)$$

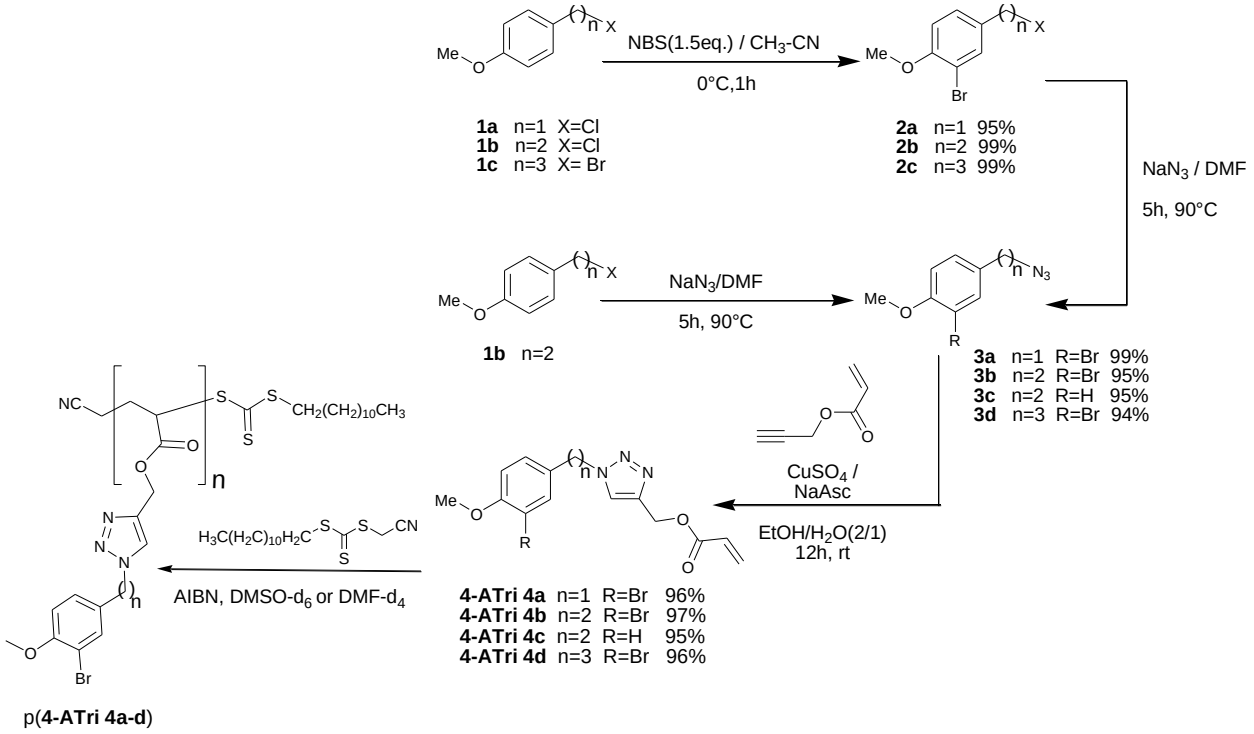
3. Results and Discussion

Synthesis of monomers

The synthesis of monomers **4a-d** is outlined in Scheme 1.

The aryl azide intermediates were synthesized from commercially available benzyl halides (**1a-c**) as shown in Scheme 1. Briefly, each derivative (**1a-c**) was first brominated with *N*-bromosuccinimide (NBS) in anhydrous acetonitrile affording brominated derivatives **2a-c** in excellent yields (>90%). Then, compounds **1b** and **2a-c** were treated with sodium azide in dimethylformamide leading to the corresponding azides **3a-d**. Theses azides with different length of the methylene spacer between the aromatic ring and azide group were obtained with excellent yields (>90%) and did not require any purification.

The synthesis of the targeted acrylic monomers (**4a-d**) was then achieved by performing the copper-catalyzed 1,3-dipolar cycloaddition of the organic azides with propargyl acrylate. In general, this reaction usually proceeds to completion in 6–36 h at room temperature in water with a variety of organic co-solvents, such as tert-butanol, ethanol, DMF, DMSO, THF, or CH_3CN. This reaction is used for a wide class of azides and alkynes.[56] Ethanol was chosen rather than DMF to allow an easier workup and a better purity of products as reported in our previous work.[57] In practice, propargyl acrylate was added to a solution of the appropriate azide (**3a-d**) with $CuSO_4$/sodium ascorbate in water/ethanol mixture (50/50). A reaction time of 12h was optimized at room temperature.



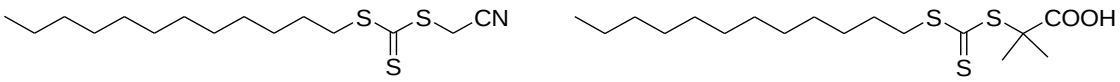
Scheme 1. Synthetic pathways for triazole acrylate monomers and polymers.

RAFT polymerization of monomers (4-ATri 4a-d)

The aim of this study was to demonstrate that the RAFT polymerization of these triazole containing monomers follows a controlled process. Herein, we first demonstrate the controlled character of the RAFT polymerization of 4-acryloyl-1-bromotyramine-1,2,3-triazole monomer (**4-ATri 4b**) which is the direct analogue of natural bromotyramines (Scheme 1). The RAFT polymerization was selected because it can be used with a wide range of monomers and reaction conditions, and in each case it provides polymers with controlled molar masses with narrow molar mass distributions.[58] Furthermore, the atom transfer radical polymerization (ATRP) of a 4-acryloyl 1,2,3-triazole monomer (ferrocenylmethyl triazole methyl acrylate) has initially failed.[59]

First, kinetics was investigated by using conventional free radical polymerization (Table 1, Entry Nr. 1). The monomer **4-ATri 4b** was successfully polymerized reaching 96 % of conversion and leading to a polymer with a high molar mass ($M_n^{TD\text{-}SEC}$ = 269 600 g.mol^{-1}) and a high dispersity ($Đ_M$ = 3.8). **4-ATri 4b** was further homopolymerized via the RAFT process to control the growth of polymer chains using two different CTAs. [60-62] The reactivity of the RAFT agent has to be adjusted to the reactivity of the monomer to obtain good control over time while retaining an ideally unaltered rate of polymerization. The reactivity of a RAFT agent is governed by its R and Z groups. Scheme 2 shows the RAFT agents selected in our study.

The homopolymerizations were first carried out with CMDT in DMSO-d_6 or DMF-d_7 at a molar ratio [CTA]/[AIBN] of 10/1 at different temperatures. Whatever the conditions used, the targeted molar mass was 20 000 g.mol^{-1}. The results are summarized in Table 1 (Entries Nr. 2 to 8). Polymerizations carried out at low temperatures (40 and 50°C) failed because few amounts of radicals were generated at these lower temperatures. In addition, any impurities in monomer, RAFT agent or solvent could inhibit the polymerization (Entries 2 and 3, respectively). At 60°C, the disappearance of the vinyl protons from the acrylate group, around 5.6-6.4 ppm, and the appearance of broad peaks assigned to the main chain around 1.2-2.5 ppm (-CH_2-) suggested the successful polymerization for **4-ATri 4b** monomers (Figure 2).



Cyanomethyl dodecyl trithiocarbonate (CMDT) 2-(Dodecylthiocarbonothioylthio)-2-methylpropionic acid (DDMAT)

Scheme 2. RAFT agents employed in the controlled radical polymerization of 4-ATri 4b.

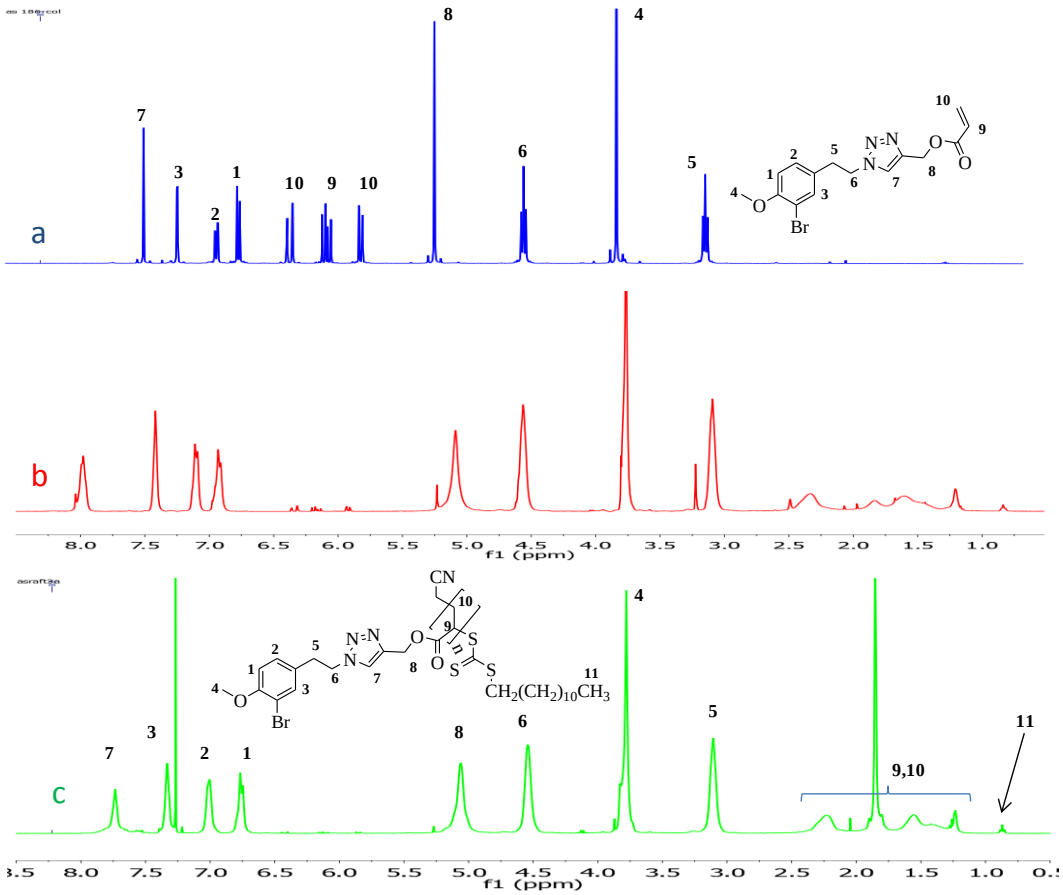


Figure 2. 1H-NMR spectra of (a) **4-ATri 4b** in $CDCl_3$, (b) its homopolymer poly(**4-ATri 4b**) after 15h of reaction in DMSO-d_6 at 60°C, and (c) the purified polymer in $CDCl_3$

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High monomer conversion values were obtained at 60 °C. The resulting poly(**4-ATri 4b**) exhibited a low dispersity value and the awaited M_n value (Entry 4, Table 1). An increase of the reaction temperature to 70°C led to faster kinetics with 86 % of conversion after 1h30mn while the polymerization reached 83 % of conversion after 5h at 60°C (electronic supplementary information†, Figure 4). Nevertheless, polymers with lower M_n values ($M_n^{TD\text{-}SEC}$ = 8 600 g.mol-1) than the targeted ones were obtained at 70°C. In addition, the resulting poly(**4-ATri 4b**) showed a TD-SEC peak with a broad molar mass distribution ($Đ_M$ = 2.9). This result suggests that side reactions or termination steps could occur resulting in low molar mass and high dispersity values at 70°C.

Similar kinetics was obtained in DMSO-d_6 and in DMF-d_7, whatever the reaction temperature (Figure 4 in electronic supplementary information†). Polymers with lower dispersities were prepared at 60°C in both solvents (Table 1, Entries 4 and 6). The substitution of CMDT by DDMAT led to a slight increase of the dispersity value from 1.3 to 1.5 (Table 1, entries 6 and 8, Figure 5 in electronic supplementary information†).

The linear semilogarithmic plots shown in Figure 3 demonstrate a control of the growth of the polymer chains with time. The non-brominated monomer (**4-ATri 4c**) showed a higher reactivity than the brominated one (**4-ATri 4b**). The lower reactivity of **4-Tri-4b** might result from a poorer solubility of this monomer relative to **4Tri-4c** and from the steric effect of the bromine atom. Figure 3 also shows that the length of the linker between the triazole function and the aromatic ring affects the polymerization rate of monomers. Increasing the methylene spacer from one carbon (**4-ATri 4a**) to two carbon atoms (**4-ATri 4b**) led to a decrease in polymerization rate. The increase of the length of the alkyl spacer should pull away the aromatic ring from the polymer backbone reducing any steric effect or electronic effect of the bromotyramine moiety on the polymerization rate. Surprisingly, the polymerisation rate of **4-ATri 4d** (with three methylene groups) is higher than the one for **4-ATri 4b** (with two methylene groups) which is slightly lower than the one found for **4-ATri 4a** (with one methylene group). The origin of the slow polymerization kinetics of **4-ATri 4b** comparing to the two other monomers was not investigated herein.

In a representative plot of RAFT polymerization of **4-ATri 4b**, M_n^{NMR} (t) increased linearly with monomer conversion, further confirming the controlled behavior of the polymerization process (Figure 4). All other polymers showed similar linear relationship of M_n^{NMR} (t) with monomer conversion (electronic supplementary information†, Figure 7-9). The final values of M_n were consistent with the expected ones with narrow molar mass distribution excepting for the one-carbon linker monomer (**4-ATri 4a**) where a higher $M_n^{TD\text{-}SEC}$ was obtained (Table 2).

Table 1. Experimental conditions for the RAFT polymerization of **4-ATri 4b** using AIBN as initiator. M_n, and $Đ_M$ values obtained after 15 h of reaction.

Entry	CTA	T (°C)	solvent	Conv[a] (%)	Yield[b] (%)	M_n^{th}[c] ($g.mol^{-1}$)	$M_n^{TD\text{-}SEC}$[d] ($g.mol^{-1}$)	$Đ_M$[e]	dn/dc[f]
1	-	70	DMSO	96	69	-	269 600	3.8	0.069
2	CMDT	40	DMSO	-[g]	-[g]	-[g]	-[g]	-[g]	-[g]
3	CMDT	50	DMSO	-[g]	-[g]	-[g]	-[g]	-[g]	-[g]
4	CMDT	60	DMSO	97	62	19 503	22 100	1.3	0.111
5	CMDT	70	DMSO	99	53	19 834	8 600	2.9	0.112
6	CMDT	60	DMF	95	48	19 000	23 700	1.5	0.099
7	CMDT	70	DMF	97	42	19 474	7 170	2.7	0.118
8	DDMAT	60	DMSO	98	45	19 495	18 900	1.5	0.104

[a] Monomer conversion determined by ^{1}H NMR (calculated from Eqn. 2) at 15 h of reaction.
[b] Yield determined gravimetrically.
[c] Calculated from Eqn. 1.
[d] Number-average molar mass obtained from TD-SEC.
[e] $Đ_M$ = M_w/M_n obtained from TD-SEC.
[f] Assessed by TD-SEC.
[g] No polymer obtained.

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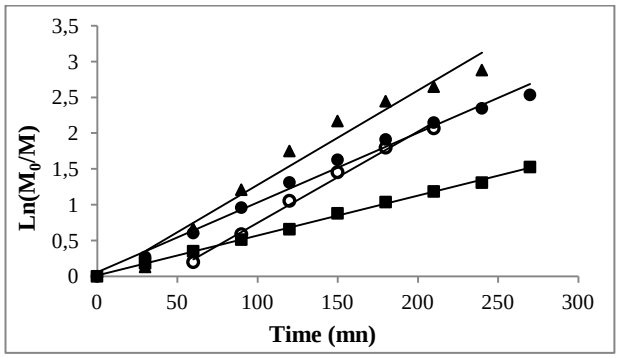

Figure 3. Ln([M]$_0$/[M]) *vs* time. Homopolymerizations of triazole acrylates in DMSO-d$_6$ at 60°C. CMDT/AIBN molar ratio of 10/1. **4-ATri 4a** (▲), **4-ATri 4b** (■), **4-ATri 4c** (o) and **4-ATri 4d** (●).

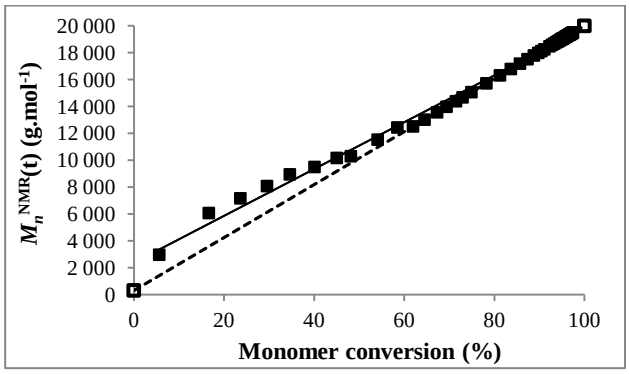

Figure 4. Evolution of M_n^{NMR} (t) *vs* monomer conversion during the RAFT polymerization of a representative monomer **4-ATri 4b** (■) in DMSO-d$_6$ at 60°C. Monomer/CDMT/AIBN molar ratio of 1.5/10/1. M_n^{th}=20 000 g.mol^{-1}. The solid line is the linear fit to the data. The dashed line is corresponding to the theoretical line.

Thermal properties

The thermal properties of the homopolymers were characterized by DSC. Thermal properties of homopolymers exhibited a strong relationship with length of the linker.

As shown in electronic supplementary information†(Figure 10), **4-ATri-4d**, which contains the longest linker, showed the lowest T_g around 20°C, whereas **4-ATri 4b** and **4-ATri 4a** with shorter linkers exhibited T_g at 42 and 48°C, respectively.

Clearly, the T_g value of homopolymers decreases with increasing the length of the linker between the bulky aromatic ring and the polymer backbone. The non-brominated monomer (**4-ATri 4c**) showed lower T_g (Tg = 34°C) than the brominated one (**4-ATri 4b**). This result demonstrates the significant influence of the sterically hindered bromine atom on the mobility of the polymer main chain. This is in agreement with the previous behavior shown during the polymerization. The thermal degradation of the homopolymers was studied by TGA (electronic supplementary information†, Figures 11 and 12). It was found that in inert atmosphere they all decompose in one major step, excepting the non-brominated one, with a maximum temperature around 320-330°C leaving a residue (char) which is thermally quite stable, decomposing at a low rate at higher temperature. The first degradation step (100-200°C) is assigned to the thermal decomposition of trithiocarbonate moieties, as previously reported.[63]

Table 2. Results for the RAFT polymerization of **4-ATri 4 a-d** at T = 60°C, in DMSO-d$_6$ after 15h of reaction. Monomer/CDMT/AIBN molar ratio: 1.5/10/1.

Monomer	Conv[a] (%)	Yield[b] (%)	M_n^{th}[c] (g.mol^{-1})	M_n^{NMR}[d] (g.mol^{-1})	$M_n^{TD\text{-}SEC}$[e] (g.mol^{-1})	$Đ_M$[f]	dn/dc[g]
4-ATri 4a	97	38	19 482	34 110	38 500	1.19	0.124
4-ATri 4b	97	62	19 503	22 290	22 100	1.28	0.111
4-ATri 4c	97	36	19 513	19 890	21 700	1.37	0.111
4-ATri 4d	98	47	19 598	19 970	23 500	1.28	0.109

[a] Monomer conversion determined by ^{1}H NMR (calculated from Eqn. 2).
[b] Yield determined gravimetrically.
[c] calculated from Eqn. 1.
[d] Number-average molar mass obtained from ^{1}H NMR using conversion of monomer (calculated from Eqn. 5).
[e] Number-average molar mass obtained from TD-SEC.
[f] $Đ_M = M_w/M_n$ obtained from TD-SEC.
[g] obtained from TD-SEC

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4. Conclusion

In this paper, new bromotyramine-based acryloyl-triazole monomers were synthesized with various lengths of methylene linkers between the triazole and the aromatic groups. Four monomers have been successfully prepared in high yields by taking advantage of the recently developed copper-catalyzed 1,3-dipolar cycloaddition reaction. The RAFT process enabled access to bromotyramine-containing homopolymers with narrow molar mass distributions and high conversions. The length of the linker and the bromination of the aromatic ring were shown to affect the kinetics of the RAFT polymerization. In addition, DSC analyses demonstrated that Tg values of homopolymers decreased with increasing the length of the linker. The bromine atom linked to the aromatic ring was shown to sterically affect the mobility of the polymer backbone leading to an increase of the Tg. No significant effect of the length of the linker on the thermal stability was demonstrated. Further investigations will be pursued to demonstrate that the RAFT polymerization is an effective way to prepare bromotyramine-based diblock copolymers. In addition, the marine bacterial anti-adhesion activity of bromotyramine-based polymers will be investigated. Triazolium-containing polymers could be also suitable as matrixes to promote the antibiofouling properties of coatings. Polytriazoliums prepared by a quaternization of the triazole groups will be a subsequent alternative to these materials.

Acknowledgements

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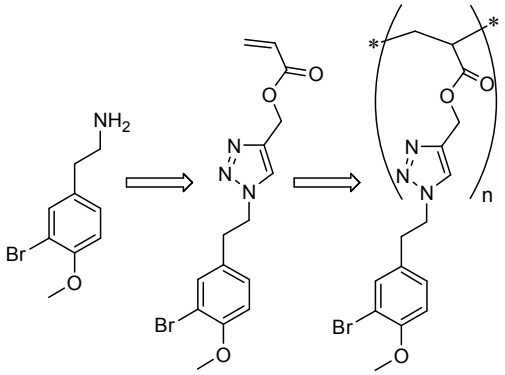
References

1 D. Lindsay and A. von Holy, *J. Hosp. Infect.*, 2006, **64**, 313.
2 A. Deshpande, G. W. G. Smith and A. J. Smith, *J. Hosp. Infect.*, 2015, **90**, 179.
3 S. Srey, I. K. Jahid and S.-D. Ha, *Food Control*, 2013, **31**, 572.
4 C. G. Kumar and S. K. Anand, *Int. J. Food Microbiol.*, 1998, **42**, 9.
5 D. M. Yebra, S. Kiil and K. Dam-Johansen, *Prog. Org. Coat.*, 2004, **50**, 75.
6 I. Fitridge, T. Dempster, J. Guenther and R. de Nys, *Biofouling*, 2012, **28**, 649.
7 T. Yan and W. X. Yan, *Biofouling*, 2003, **19**, 133.
8 A. A. Al-Juhni and B.-m. Z. Newby, *Prog. Org. Coat.*, 2006, **56**, 135.
9 E. Almeida, T. C. Diamantino and O. de Sousa, *Prog. Org. Coat.*, 2007, **59**, 2.
10 M. S. Acevedo, C. Puentes, K. Carreño, J. G. León, M. Stupak, M. García, M. Pérez and G. Blustein, *Int. Biodeterior. Biodegradation*, 2013, **83**, 97.
11 M. Pérez, M. García, M. Sánchez, M. Stupak, M. Mazzuca, J. A. Palermo and G. Blustein, *Int. Biodeterior. Biodegradation*, 2014, **89**, 37.
12 C. L. Alzieu, J. Sanjuan, J. P. Deltreil and M. Borel, *Mar. Poll. Bull.*, 1986, **17**, 494.
13 C. Alzieu, J. Sanjuan, P. Michel, M. Borel and J. P. Dreno, *Mar. Poll. Bull.*, 1989, **20**, 22.
14 D. V. Ellis and L. Agan Pattisina, *Mar. Poll. Bull.*, 1990, **21**, 248.
15 M. M. Saavedra Alvarez and D. V. Ellis, *Mar. Poll. Bull.*, 1990, **21**, 244.
16 T. Nakanishi, *J. Toxicol. Sci*, 2008, **33**, 269.
17 H. K. Okoro, O. S. Fatoki, F. A. Adekola, B. J. Ximba and R. G. Snyman, *Asian J. Chem.*, 2011, **23**, 473.
18 Y. Kotake, *Biol. Pharm. Bull.*, 2012, **35**, 1876.
19 R. A. Braithwaite and R. L. Fletcher, *J. Exp. Mar. Biol. Ecol.*, 2005, **322**, 111.
20 F. Cima, M. Bragadin and L. Ballarin, *Aquat. Toxicol.*, 2008, **86**, 299.
21 F. Gallucci, I. B. de Castro, F. C. Perina, D. M. de Souza Abessa and A. de Paula Teixeira, *Ecol. Indic.*, 2015, **58**, 21.
22 F. Cima and L. Ballarin, *Comp. Biochem. Physiol. C Toxicol. Pharmacol.*, 2015, **169**, 16.
23 E. Ytreberg, J. Karlsson and B. Eklund, *Sci. Total Environ.*, 2010, **408**, 2459.
24 E.-R. Kenawy, S. D. Worley and R. Broughton, *Biomacromolecules*, 2007, **8**, 1359.
25 B. Dizman, M. O. Elasri and L. J. Mathias, *Biomacromolecules*, 2005, **6**, 514.
26 H. Liu, B. Lepoittevin, C. Roddier, V. Guerineau, L. Bech, J.-M. Herry, M.-N. Bellon-Fontaine and P. Roger, *Polymer*, 2011, **52**, 1908.
27 R. Adelmann, M. Mennicken, D. Popescu, E. Heine, H. Keul and M. Moeller, *Eur. Polym. J.*, 2009, **45**, 3093.
28 R. Jellali, I. Campistron, P. Pasetto, A. Laguerre, F. Gohier, C. Hellio, J.-F. Pilard and J.-L. Mouget, *Prog. Org. Coat.*, 2013, **76**, 1203.
29 A. Jain, L. S. Duvvuri, S. Farah, N. Beyth, A. J. Domb and W. Khan, *Adv. Healthc. Mater.*, 2014, **3**, 1969.
30 M. A. Gauthier, M. I. Gibson and H.-A. Klok, *Angew. Chem., Int. Ed.*, 2009, **48**, 48.

31 M. Semsarilar, V. Ladmiral and S. Perrier, *Macromolecules*, 2010, **43**, 1438.
32 J. C. Tiller, C.-J. Liao, K. Lewis and A. M. Klibanov, *Proc. Natl. Acad. Sci.*, 2001, **98**, 5981.
33 S. B. Lee, R. R. Koepsel, S. W. Morley, K. Matyjaszewski, Y. Sun and A. J. Russell, *Biomacromolecules*, 2004, **5**, 877.
34 J.-P. Maréchal and C. Hellio, *Int. J. Mol. Sci.*, 2009, **10**, 4623.
35 R. de Nys, P. D. Steinberg, P. Willemsen, S. A. Dworjanyn, C. L. Gabelish and R. J. King, *Biofouling*, 1995, **8**, 259.
36 C. Hellio, D. De La Broise, L. Dufossé, Y. Le Gal and N. Bourgougnon, *Mar. Environ. Res.*, 2001, **52**, 231.
37 R. C. Schoenfeld, S. Conova, D. Rittschof and B. Ganem, *Bioorg. Med. Chem. Lett.*, 2002, **12**, 823.
38 K. Hanssen, G. Cervin, R. Trepos, J. Petitbois, T. Haug, E. Hansen, J. Andersen, H. Pavia, C. Hellio and J. Svenson, *Mar. Biotechnol.*, 2014, **16**, 684.
39 S. Tsukamoto, H. Kato, H. Hirota and N. Fusetani, *Tetrahedron*, 1996, **52**, 8181.
40 S. Tsukamoto, H. Kato, H. Hirota and N. Fusetani, *J. Org. Chem.*, 1996, **61**, 2936.
41 R. M. Van Wagoner, J. Jompa, A. Tahir and C. M. Ireland, *J. Nat. Prod.*, 1999, **62**, 794.
42 N. Pénez, G. Culioli, T. Pérez, J.-F. Briand, O. P. Thomas and Y. Blache, *J. Nat. Prod.*, 2011, **74**, 2304.
43 J. A. Diers, H. K. Pennaka, J. Peng, J. J. Bowling, S. O. Duke and M. T. Hamann, *J. Nat. Prod.*, 2004, **67**, 2117.
44 V. Ladmiral, G. Mantovani, G. J. Clarkson, S. Cauet, J. L. Irwin and D. M. Haddleton, *J. Am. Chem. Soc.*, 2006, **128**, 4823.
45 W. H. Binder and R. Sachsenhofer, *Macromol. Rapid Commun.*, 2007, **28**, 15.
46 D. D. Díaz, S. Punna, P. Holzer, A. K. McPherson, K. B. Sharpless, V. V. Fokin and M. G. Finn, *J. Polym. Sci. A Polym. Chem.*, 2004, **42**, 4392.
47 B. Wang, M. Liu, Z. Chen, R. Liang, S. Ding, S. Chen and S. Jin, *Int. J. Pharm.*, 2007, **331**, 19.
48 R. J. Thibault, K. Takizawa, P. Lowenheilm, B. Helms, J. L. Mynar, J. M. J. Fréchet and C. J. Hawker, *J. Am. Chem. Soc.*, 2006, **128**, 12084.
49 H. Nulwala, K. Takizawa, A. Odukale, A. Khan, R. J. Thibault, B. R. Taft, B. H. Lipshutz and C. J. Hawker, *Macromolecules*, 2009, **42**, 6068.
50 H. Nulwala, D. J. Burke, A. Khan, A. Serrano and C. J. Hawker, *Macromolecules*, 2010, **43**, 5474.
51 M. Hetzer, G. Chen, C. Barner-Kowollik and M. H. Stenzel, *Macromol. Biosci.*, 2010, **10**, 119.
52 S. Beghdadi, I. Abdelhedi Miladi, H. Ben Romdhane, J. Bernard and E. Drockenmuller, *Biomacromolecules*, 2012, **13**, 4138.
53 S. Beghdadi, I. A. Miladi, D. Addis, H. B. Romdhane, J. Bernard and E. Drockenmuller, *Polym. Chem.*, 2012, **3**, 1680.
54 H. Mori, K. Ishikawa, Y. Abiko, Y. Maki, A. Onuma and M. Morishima, *Macromol. Chem. Phys.*, 2012, **213**, 1803.
55 B. J. Adzima, S. C. Taylor, H. He, D. R. Luebke, K. Matyjaszewski and H. B. Nulwala, *J. Polym. Sci. A Polym. Chem.*, 2014, **52**, 417.
56 M. Meldal and C. W. Tornøe, *Chem. Rev.*, 2008, **108**, 2952.
57 D. Linares, O. Bottzeck, O. Pereira, A. Praud-Tabariès and Y. Blache, *Bioorg. Med. Chem. Lett.*, 2011, **21**, 6751.
58 C. Barner-Kowollik and S. Perrier, *J. Polym. Sci. A Polym. Chem.*, 2008, **46**, 5715.
59 C. G. Hardy, L. Ren, T. C. Tamboue and C. Tang, *J. Polym. Sci. A Polym. Chem.*, 2011, **49**, 1409.
60 J. Chiefari, Y. K. Chong, F. Ercole, J. Krstina, J. Jeffery, T. P. T. Le, R. T. A. Mayadunne, G. F. Meijs, C. L. Moad, G. Moad, E. Rizzardo and S. H. Thang, *Macromolecules*, 1998, **31**, 5559.
61 C. Barner-Kowollik, in *Handbook of RAFT Polymerization*, Wiley-VCH Verlag GmbH & Co. KGaA, 2008, pp. 1.
62 G. Moad, E. Rizzardo and S. H. Thang, *Aust. J. Chem*, 2009, **62**, 1402.
63 B. Chong, G. Moad, E. Rizzardo, M. Skidmore, S.H. Thang, *Aust. J. Chem*., 2006, **59**, 755.



A series of bromotyramine-based 4 -acryloyl-1,2,3- triazole monomers and polymers using click chemistry and RAFT polymerization