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Well-defined "Click-able" Copolymers in One-Pot Synthesis

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Well-defined "click-able" homo- and co-polymers were synthesised using a living polymerisation technique. Specifically propargyl methacrylate was successfully homo- and co-polymerised using Group Transfer Polymerisation, GTP. This one-pot synthesis was performed without the need to protect the acetylenic group. Finally it was confirmed that the acetylenic functional group was unaffected by the polymerisation by clicking with azide 4-azidobenzoic acid.

Due to the high yields and simple reaction conditions "click" chemistry has become a very useful and popular tool for polymer chemists in the last two decades.[1] One of the most common "click-able" groups is the acetylenic.[2] However, introducing acetylenic moieties on a polymer while keeping the molecular weight distribution, MWD (polydispersity, PDI=M_w/M_n) of the polymer narrow is quite challenging.

Specifically, propargyl methacrylate (PMA) and propargyl acrylate (PA) can be easily directly (co)polymerised with free radical polymerisation[3, 4]but this produces polymers with high PDIs (1.6 to 7.3). In order to produce well-defined polymers (polymers with narrow PDI) living or controlled polymerisation methods must be used but the direct polymerisation of PMA or PA with these methods is more challenging. Consequently, when using living or controlled polymerisation techniques the propargyl-group is usually protected and then de-protected after the polymer is recovered.[5-20]

For example when using Atom-Transfer Radical Polymerisation, ATRP to polymerise the protected form of PMA (trimethylsilyl-PMA, TMSPMA) a homopolymer of PDI=1.20 was produced,[18] while direct homopolymerisation of PMA resulted in polymers with very high PDIs (>3) and crosslinked networks.[21] When PA was copolymerised with N-isopropylacrylamide, NIPAm using an ATRP and a poly(ethylene glycol), PEG-macroinitiator a copolymer of narrow PDI=1.09 was produced.[22] However, it should be pointed out that the molar % of PA was very low (<0.02%).

Direct Reversible Addition-Fragmentation Chain-Transfer, RAFT polymerisation of PMA produced a polymer with relatively broad PDI, M_w/M_n =1.64[23] but when the propargyl-monomer was copolymerised at a relatively low molar % (<20%) the polydispersity of the polymers was narrower.[24] Specifically NIPAm-PA,2-(dimethylamino)ethyl methacrylate-PA(DMAEMA-PA), and methyl methacrylate-PMA (MMA-PMA) random copolymers of M_w/M_ns = 1.23-1.29, 1.32-1.52 and 1.12-1.37, respectively, have been reported.[24-26] When random terpolymers were synthesised by RAFT polymerisation using a higher molar % (27%) of PMA the polymers with PDIs between 1.59 and 1.99 were produced.[27] In general, when producing lower molecular weight polymers at low propargyl-monomer compositions the PDI is narrower. Similar observations were made when single electron transfer initiator and propagation through RAFT (SET-RAFT) was used to homopolymerise PMA.[28] Polymers of relatively narrow M_w/M_n< 1.55 were produced when lower concentration and conversion rates were used and the results were considered better than when ATRP or RAFT was performed.[28]

In this study PMA was homo- and co-polymerised using GTP, a living polymerisation technique that has the advantage of being fast, easy and cost-effective.[29, 30] Firstly, the PMA was homopolymerised at room temperature but the temperature increased too rapidly resulting to un-controlled polymerisation. When the temperature was reduced at 15°C the polymerisation was easier to control. Polymerisation kinetics were carried out for PMA as well as MMA for comparison purposes (Fig 1 – more details in Supporting Information).

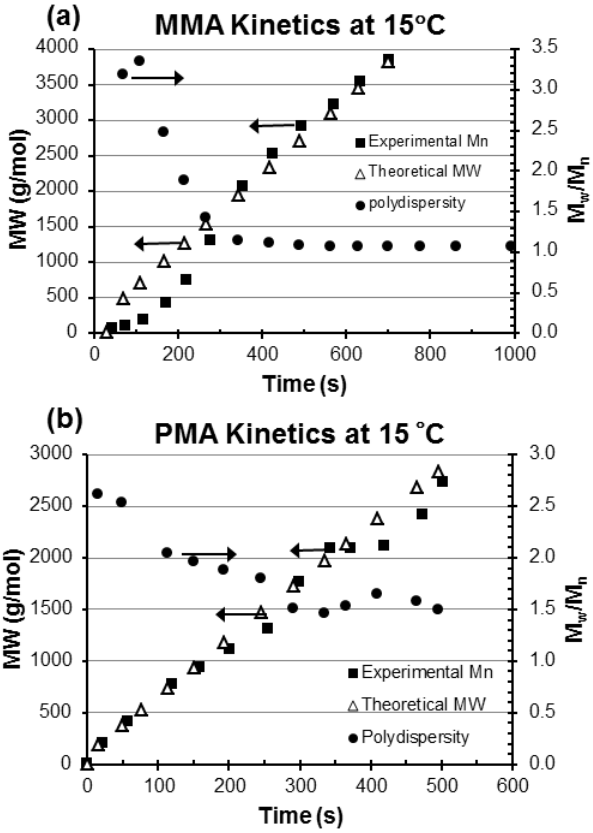

Fig. 1 Polymerisation kinetics of MMA (a) and PMA (b). The theoretically calculated molecular weight, the M_n and the polydispersity are shown in triangles, squares and circles, respectively.

As it can be observed in Fig 1, GTP is very rapid and each polymerisation step only takes between 10 to 15 minutes,[31] depending on the monomer and the degree of polymerisation. Furthermore normally the monomer is fully converted to the polymer which makes GTP an excellent technique to produce multiblock copolymers.[32-37] So in just 345 s and 336 s polymers with number average molecular weights, M_ns close to 2000 g/mol (2050 and 2090 g/mol for pMMA and pPMA, respectively) were obtained. The M_w/M_n decreased as the M_n increased, as it is expected for a living polymerisation technique, for both monomers until this M_n(~2000 g/mol) but after this the PDI for pPMA homopolymers did not remain as narrow. It should also be pointed out that overall the polymerisation of MMA was more controlled than the one of PMA with narrower PDIs (as low as 1.07). However, the PDIs of the PMA homopolymers via GTP were still better when compared with those reported when using controlled free radical polymerisation methods.

PMA was also copolymerised using GTP with a variety of different monomers. Specifically DMAEMA, MMA, poly(ethylene glycol) methyl methacrylate (PEGMA), and *n*-butyl methacrylate (BuMA) were used as the comonomer. Sequential as well as simultaneous GTP polymerisation was performed to produce block and random copolymers. The results are summarised in Table 1 with the last column indicating if the polymerisation step was successful or not.

Table 1: Molecular weights and molecular weight distributions of all the polymers and their precursors. The last column indicates if the polymerisation was successful or not.

No	Polymer	Theor. MW g/mol	GPC Results		Succ?
			M_n	M_w/M_n	
1	PMA_{10}	1341	3100	1.42	Yes
	PMA_{10}-*b*-$PEGMA_{12}$	4941	3200	1.37	No
2	$PEGMA_{15}$	4600	4300	1.22	Yes
	$PEGMA_{15}$-*b*-PMA_2	4848	6100	1.27	Yes
3	$PEGMA_{15}$-*co*-PMA_4	5096	5300	1.33	Yes
4	MMA_{20}	2102	2600	1.12	Yes
	MMA_{20}-*b*-PMA_5	2723	3300	1.12	Yes
	MMA_{20}-*b*-PMA_5-b-MMA_{20}	4725	3300	1.12	No
5	PMA_5	720	1700	1.28	Yes
	PMA_5-*b*-MMA_{20}	2623	1700	1.27	No
	PMA_5-*b*-MMA_{20}-*b*-PMA_5	3242	1700	1.27	No
6	MMA_{20}-*co*-PMA_5	2623	4200	1.27	Yes
7	$BuMA_{14}$-*co*-PMA_4	2487	3900	1.14	Yes
	($BuMA_{14}$-*co*-PMA_4)-*b*-DMA_{19}	5574	Multiple Peaks		No
8	DMA_{19}	3087	4200	1.11	Yes
	DMA_{19}-*b*-($BuMA_{10}$-*co*-PMA_4)	5574	6900	1.07	Yes

[a] PEGMA, MMA, BuMA, PMA and DMA are abbreviations formethoxy poly(ethylene glycol) methacrylate, methyl methacrylate, *n*-butyl methacrylate, propargyl methacrylate and 2-(dimethylamino)ethyl methacrylate , respectively.

[b] Theoretical, expected molecular weight of the polymer. Calculated using this formula: $MW_{polymer}=DP_A\times MW_A+ DP_B\times MW_B+ DP_C\times MW_C+100$ g/mol, where MW and DP stand for molecular weight and degree of polymerisation, and A, B, C correspond to the three different monomers used. Note that 100 g mol^{-1} the MW of initiator fragment that is attached on the end of each polymer chain.

[c]The calibration curve was based on nine narrow molecular weight linear poly(methyl methacrylate)s (PMMAs) with MWs of 690, 5720, 1020, 1200, 1960, 4000, 8000, 13300 and 20010 g mol^{-1}.

The results of the PMA copolymerisations are very interesting. Specifically when the PMA is polymerised first (see Polymer 1 and Polymer 5) it does not allow any further sequential polymerisation. However when the comonomer is polymerised first the PMA can be sequentially polymerised to obtain a diblock copolymer as it can be observed for Polymers 2 and 4. It is noteworthy that these are the first reported *block* copolymers when using either PMA or PA unless a macroinitiator is used.

When the PMA was simultaneous copolymerised with another monomer the synthesis was successful (Polymers 3 and 6) with quite narrow PDIs <1.33. It should be mentioned though that the PDIs can be improved if the two monomers are added slowly and drop-wise in the flask after the addition of the initiator and not before the addition of the initiator as it was done in this study.

Finally, more complex polymers were also tried to be synthesised, Polymer 7 and 8, were the PMA was simultaneous copolymerised with one monomer after or before the homopolymerisation of another monomer.

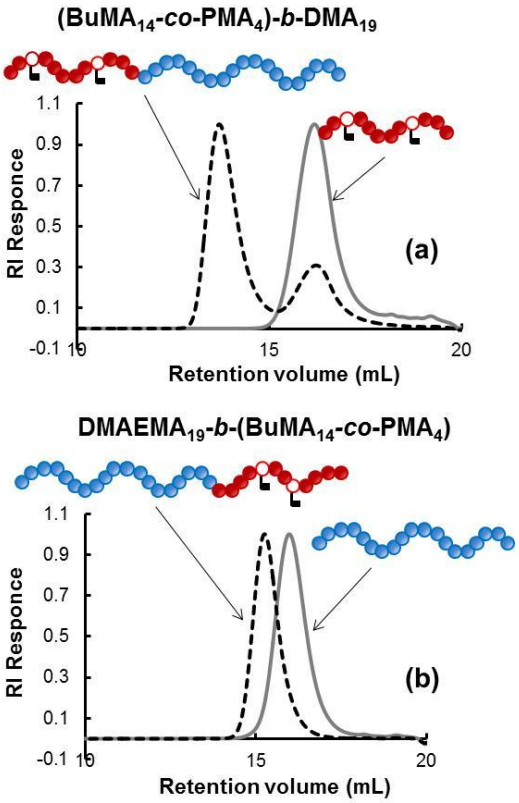

Fig. 2: GPC chromatographs of (a) P7: ($BuMA_{14}$-*co*-PMA_4)-*b*-DMA_{19} and (b) P8: DMA_{19}-*b*-($BuMA_{10}$-*co*-PMA_4) and their precursors. The polymers are also schematically illustrated with PMA, DMAEMA and BuMA coloured in white, blue and dark red, respectively.

Similarly to the previous results when PMA was copolymerised first it did not allow further controlled growth of the polymer chain (see Fig 2(a)). On the other hand as it can be seen in Fig 2.bPMA could easily be copolymerised to comprise the second block of the polymer and produce a diblock copolymer where the second block is a random polymer segment of PMA with BuMA (Polymer 8). The PDI of Polymer 8, $DMAEMA_{19}$-*b*-($BuMA_{10}$-*co*-PMA_4)is very narrow, M_w/M_n=1.07. BuMA assisted to have more controlled polymerisation when it was simultaneously

copolymerised with PMA since the temperature did not increase as much and as rapidly (higher molecular weight monomers polymerised slower and the reaction GTP is less exothermic[38-40]). Furthermore it is important to notice that the PDI of the diblock copolymer is narrower compared to the first DMAEMA block, as it is expected for a living polymerisation technique. Therefore, well-defined diblock copolymers with acetylenic functionalities can be successfully synthesised in one pot synthesis without the need of protecting the propargyl group of the monomer. These type of polymers can be used as precursors for "click" chemistry reactions and produce more complex and functional polymer or/and polymer conjugates.

In order to confirm that the acetylenic group is still intact after the polymerisation a "click" reaction of Polymer 3, $PEGMA_{15}$-*co*-PMA_4 with azide 4-azidobenzoic acid was performed. Nuclear magnetic resonance (NMR) spectroscopy confirmed that the acetylenic group is still functional and the "click" reaction was carried out successfully (see supporting information).

Conclusions

An acetylenic containing monomer was homo- and co-polymerised for the first time using GTP. Homopolymerisation was successful and worked better when the temperature was decreased, producing polymers with relatively narrow PDI < 1.5. Sequential polymerisation was only successful when the acetylenic monomer was added last. However this enabled for the first time the synthesis of *block* copolymers (instead of just random copolymer) containing triple bond functionalities which can later be used for "click" chemistry. Thus, novel well-defined acetylenic copolymers of block architectures with PDIs < 1.37 were synthesised with an easy and fast, one-pot procedure.

Notes and references

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‡ Footnotes should appear here. These might include comments relevant to but not central to the matter under discussion, limited experimental and spectral data, and crystallographic data.

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