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

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Supporting Information

Experimental

Materials

1-Methoxy-1(trimethylsiloxy)-2-methyl propene (MTS, initiator, 99%), sodium metal, 2,2-diphenyl-1-picrylhydrazyl hydrate (DPPH, free radical inhibitor, 99%), methyl methacrylate, (MMA, 99%), and poly(ethylene glycol) methyl ether methacrylate (PEGMA, MW = 300 $gmol^{-1}$, monomer) were purchased from Aldrich, UK. Tetrabutylammonium hydroxide (40% in water), basic alumina (Al_2O_3, 95%), potassium metal, DMAEMA (monomer, 99%) and BuMA (monomer, 99%) were purchased from Acros Organics, UK. Tetrahydrofuran (THF, polymerisation solvent, 95%) and *n*-hexane (precipitation solvent, 95%) were purchased from Fisher Scientific.

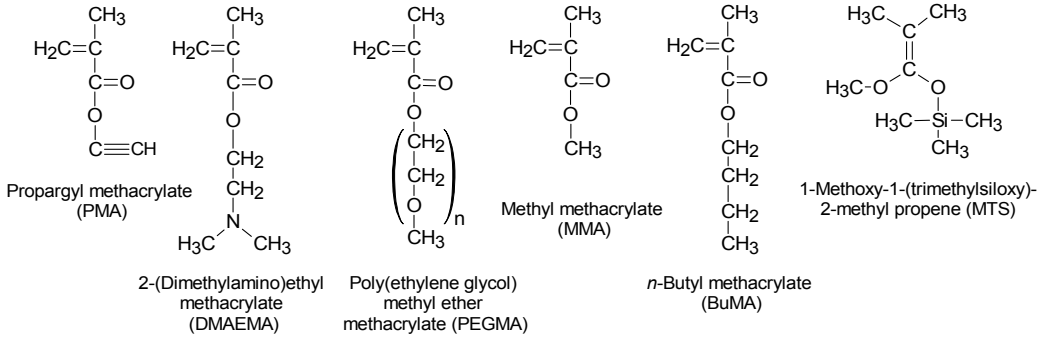

Figure 1: Chemical structures of main monomers used as well as the group transfer polymerisation initiator (shown on the right).

DMAEMA, MMA and BuMA monomers (shown in Fig. 1) were passed twice through basic alumina to remove inhibitors and protic impurities and stirred over CaH_2 for 3 hours in the

presence of DPPH. All three monomers were kept refrigerated until distillation before use. PEGMA was passed twice through basic alumina as a 50% v/v solution in THF and stirred overnight over CaH_2. No DPPH was added to the PEGMA monomer solution due to the inability to distil PEGMA prior to use. The solution was refrigerated until the polymerisation and it was filtered directly into the reaction flask with a 0.45μm syringe filter.

The initiator was distilled once before polymerisation and kept sealed under argon until use. Tetrabutylammoniumbibenzoate (TBABB) was the polymerisation catalyst and was synthesised by the reaction of tetrabutylammonium hydroxide and benzoic acid, as described by Dicker et al.[1] The catalyst was dried and stored under vacuum until use. THF was refluxed over a potassium/sodium amalgam for 3 days to dry before polymerisation. All glassware was dried overnight at 140°C and assembled hot under dynamic vacuum before use.

Synthesis

Synthesis of propargyl methacrylate (PMA)

Propargyl methacrylate was synthesised by the reaction of propargyl alcohol with methacryloyl chloride in THF in the presence of triethylamine. A 250mL two neck flask was fitted with a septum and dropping funnel and purged with argon. To this 75.0 mL of freshly distilled THF, 10.0 mL of propargyl alcohol (9.70g, 0.172 mol) and 75.0 mL of freshly distilled anhydrous triethylamine (54.9g, 0.542 mol) were added. The flask was placed in an ice bath at 0 °C and stirred. To the dropping funnel was added 25.0 mL of methacryloyl chloride (27.0g, 0.258 mol) which was added dropwise to the reaction mixture over 30 minutes. The reaction was left to stir for 3 hours at 0 °C. The product was passed through basic alumina to remove any unreacted methacryloyl chloride, methacrylic acid and triethylamine hydrochloride salt and then distilled to obtain pure propargyl methacrylate monomer. The chemical structure was confirmed with proton NMR

(methacrylate methyl group protons at 1.96 ppm, double bond protons at 5.6 and 6.2 ppm, protons next to the triple bond at 4.77 ppm and the acetylenic proton at 2.49 ppm).

Kinetic studies

Kinetic studies where performed at different temperatures. GTP is very fast (as it can be observed in the kinetics graphs) so it was very difficult to obtain good results at room temperature or higher. The reaction is exothermic and when low molecular weight monomers like MMA and PMA are polymerising, the temperature increases quite rapidly. So the best results were obtained when the reaction flask was immersed in cool water (15^{o}C). The monomer (PMA or MMA) was injected with a rate of 1 mL/min to a flask under argon that contained anhydrous THF (solvent), TBABB(catalyst) and the GTP initiator,MTS. Samples for gel permeation chromatography were taken out from the flask at regular intervals.

GTP Copolymerisation of PMA

All polymerisation reactions (including GPC and NMR) results are listed in Table 1 of Supporting Information. A typical GTP[2-5] procedure is described below for Polymer 4, MMA_{20}-*b*-PMA_5-*b*-MMA_{20}. Note that GTP is an exothermic polymerisation and the temperature was monitored during the polymerisation in order to monitor the reaction.

Freshly distilled THF (46 mL) and MTS (0.50 mL, 0.43 g, 2.46mmol) were syringed into a 250 mL round bottom flask containing TBABB (~10 mg) previously sealed with a septum and purged with argon. Then MMA was added (5.2 mL, 4.9 g, 49.2mmol) using a syringe. The temperature rose by 2.6 °C. After 10 minutes the exothermic reaction had abated and two 0.1 mL aliquots of the reaction solution were extracted for GPC and ^{1}H NMR analysis. Then the PMA monomer (1.6 mL, 1.5 g, 12.3mmol) was added using a syringe and the temperature increased by 2.2 °C. Subsequently, two more 0.1 mL aliquots were collected for GPC and ^{1}H NMR analysis. Finally, MMA (5.2 mL, 4.9 g, 49.2mmol) was added again. However, the

temperature did not rise, indicating that the final set of the polymerisation was not successful as it was later confirmed by GPC and ^{1}H NMR.

To produce random copolymers, the PMA was copolymerised with the second monomer. For polymer 3 and 6 the two monomers were added first in the polymerisation flask and the initiator was added later. On the other hand, for polymers 7 and 8 the initiator was added first and then the two monomers were added simultaneously and drop-wise to produce the random segment of the polymer. Thus there was a better control of the reaction and the temperature in the latter and that is why the PDI is lower (see Table 1).

Table 1: Molecular weights, composition 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		NMR	Succ?
			M_n	M_w/M_n	mol %	
1	PMA_{10}	1341	3100	1.42	100-0	Yes
	PMA_{10}-*b*-$PEGMA_{12}$	4941	3200	1.37	45-55	No
2	$PEGMA_{15}$	4600	4300	1.22	100-0	Yes
	$PEGMA_{15}$-*b*-PMA_2	4848	6100	1.27	83-17	Yes
3	$PEGMA_{15}$-*co*-PMA_4	5096	5300	1.33	80-20	Yes
4	MMA_{20}	2102	2600	1.12	100-0	Yes
	MMA_{20}-*b*-PMA_5	2723	3300	1.12	81-19	Yes
	MMA_{20}-*b*-PMA_5-b-MMA_{20}	4725	3300	1.12	N.D.	No
5	PMA_5	720	1700	1.28	100-0	Yes
	PMA_5-*b*-MMA_{20}	2623	1700	1.27	N.D.	No
	PMA_5-*b*-MMA_{20}-*b*-PMA_5	3242	1700	1.27	N.D.	No
6	MMA_{20}-*co*-PMA_5	2623	4200	1.27	79-21	Yes
7	$BuMA_{14}$-*co*-PMA_4	2487	3900	1.14	78-22	Yes
	($BuMA_{14}$-*co*-PMA_4)-*b*-DMA_{19}	5574	Multiple Peaks		N.D.	No
8	DMA_{19}	3087	4200	1.11	100-0	Yes
	DMA_{19}-*b*-($BuMA_{10}$-*co*-PMA_4)	5574	6900	1.07	56-33-11	Yes

* N.D. : not determined because it was clear that the polymerisation was not successful.

Click reaction of PEGMA$_{15}$-co-PMA$_4$ with azide 4-azidobenzoic acid (Fig. 2)

PEGMA$_{15}$-*co*-PMA$_4$, (0.2 g, 4.4 ×10^{-5} moles) was dissolved in THF(20mL) in a 100mL round bottom flask. To this solution, copper sulphate pentahydrate, 0.05g (2.00 × 10^{-4} moles), and sodium ascorbate, 20mg (1.01x10^{-4} moles) were added. The solution obtained a yellow colour as the copper catalyst was activated. Subsequently, 50mg (2.96 × 10^{-4} moles) of 4-azidobenzoic acid was added. The reaction was left to stir over night. The solution was filtered and then passed through asephadex LH20 columnto collect the polymer. The resulting modified polymer had a red colour, indicating the successful reaction. The chemical structure was confirmed with by proton NMR spectroscopy. Specifically, the peak at 2.5ppm in the starting polymer, corresponding to the alkyne ≡H was not present in the product and new peaks corresponding to aromatic protons close to 8ppm were observed. Also, the peak of the protons next to the ester group, O-CH$_2$- was shifted from 2.49 ppm to 5.2 ppm.

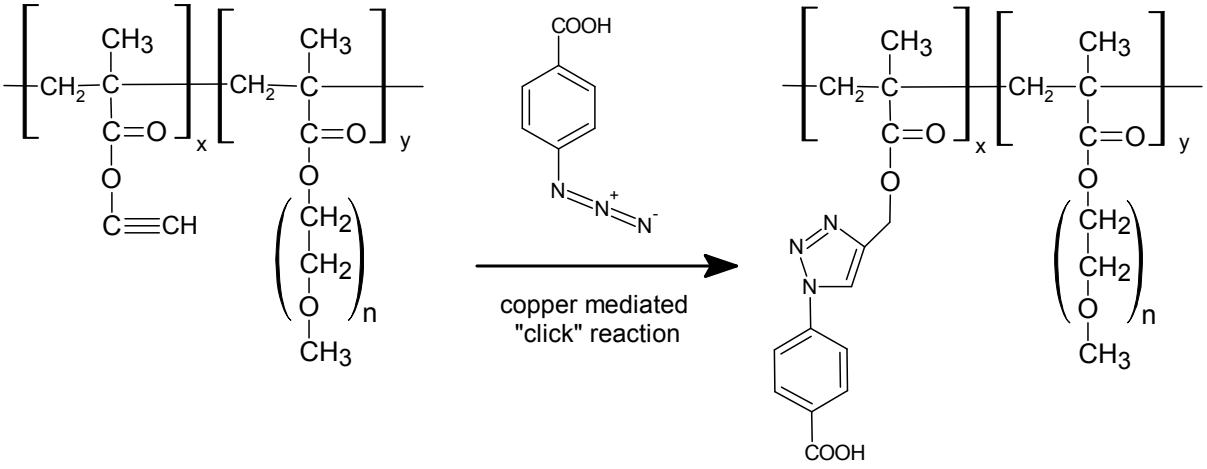

Figure 2: "Click" reaction of the poly[propargylmethacrylate-*co*-(polyethylene glycol methacrylate)] polymer with 4-azidobenzoic acid.

Characterisation

Gel Permeation Chromatography

The MWs and the MWDs of all the linear precursors to the copolymers and the copolymers were determined by gel permeation chromatography (GPC) using two PL-Mixed "E"

Polymer Laboratories columns. THF containing 5 vol.%triethylamine was the mobile phase and was pumped with a flow rate at 1 mL min^{-1} using a Viscotek vt7510 pump. A Viscotek 3580 differential refractometer was used to measure the refractive index signal. The calibration curve was based on nine narrow MW linear poly(methyl methacrylate)s (PMMAs) with MWs of 690, 5720, 1020, 1200, 1960, 4000, 8000, 13300 and 20010 $gmol^{-1}$.

Proton Nuclear Magnetic Resonance Spectroscopy (^{1}H-NMR)

A JEOL 400 MHz spectrometer instrument was used to acquire the ^{1}HNMR spectra of the copolymers and their precursors in $CDCl_3$.

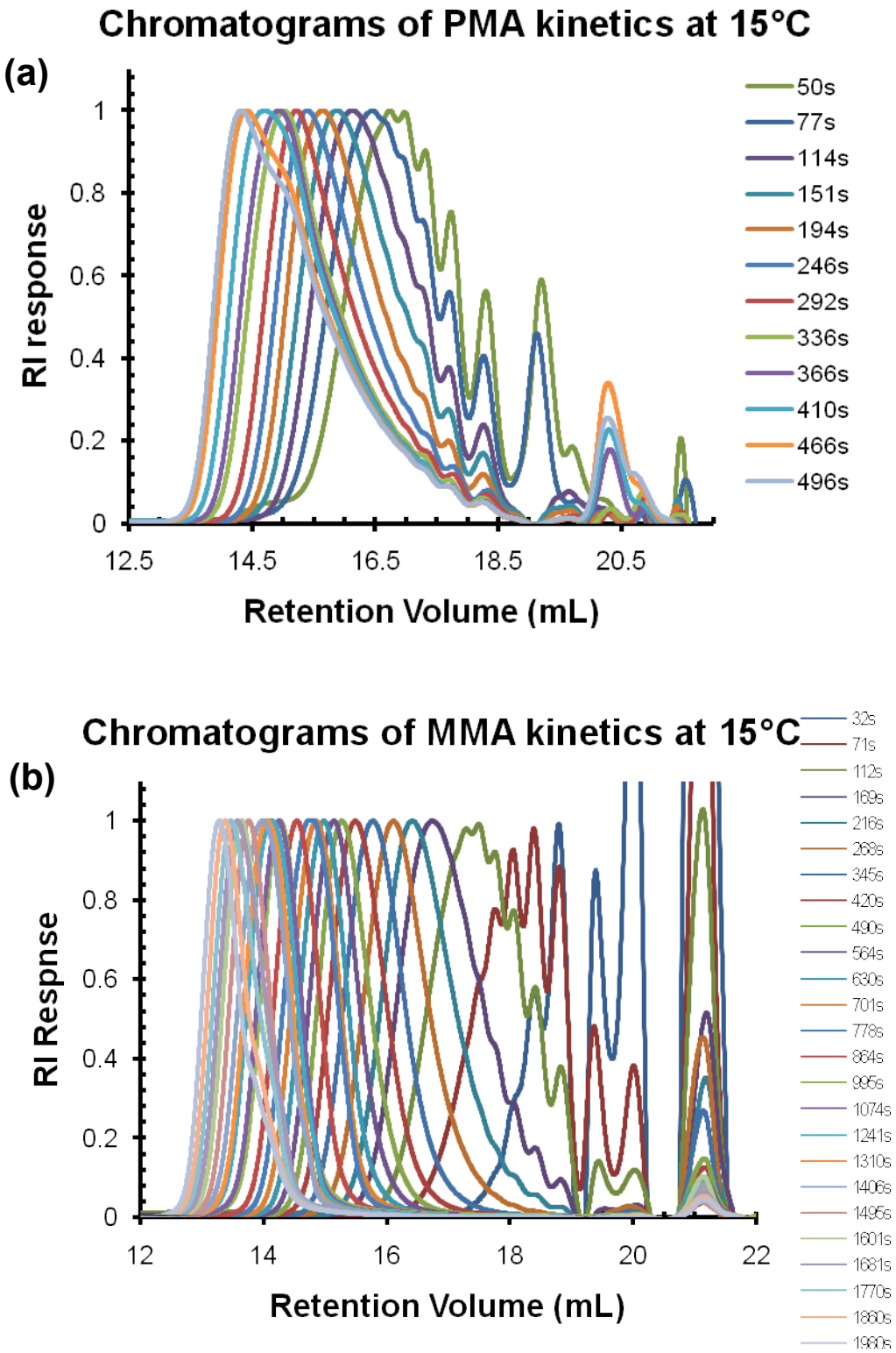

Figure3: GPC chromatograms of the polymerisation kinetics of PMA (a) and MMA (b).

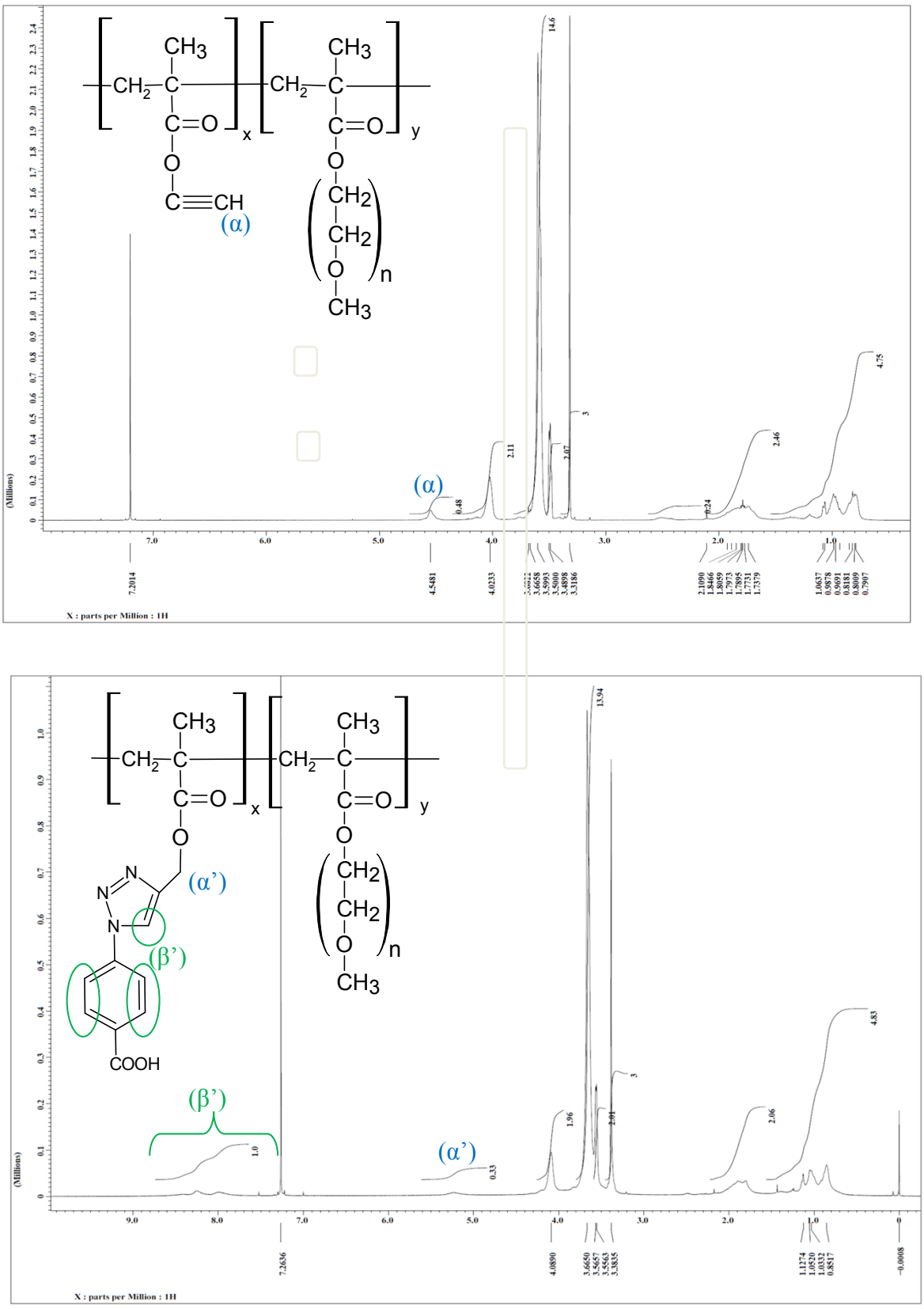

Figure 4: NMR spectra of PEGMA$_{15}$-*co*-PMA$_4$ with azide 4-azidobenzoic acid before (a) and after (b) the click reaction.

References

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