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Graft Copolymers Based on Functional Polyesters

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Summary: Graft copolymers with a polyester backbone and PMMA side chains were successfully prepared in a two and a three step approach. In the two step approach, functional polyesters were prepared via polycondensation using hexane diol and bromosuccinic acid as building blocks and methyl methacrylate (MMA) was grafted from the resulting poly(hexamethylene bromosuccinate) (PHMBS), here the initiating group is linked directly to the polyester backbone. In the second approach hexane diol and malic acid were used as bilding blocks giving poly(hexamethylene malate) (PHMM). The hydroxyl groups of PHMM were transferred with 2-bromo-2-propionylbromide into an ATRP-initiator. Then the grafting of MMA from poly(hexamethylene malate) bromopropionate (PHMM-BrP) was investigated.

Keywords: atom transfer radical polymerization (ATRP); biodegradable graft copolymers; functional polyester; polycondensation

Introduction

Much interest in current research is focussed on biocompatible and biodegradable polymers.[1–3] Especially aliphatic polyesters fulfil the requirement for these biopolymers. But the mechanical properties are not always acceptable for certain applications. Graft copolymers with PMMA grafts of low molecular weight can improve the mechanical properties, and if the PMMA chains are on an oligomeric length scale, the biodegradability is still warranted due to the possibility of excreting PMMA oligomers from the human body without degradation.[4]

Synthetic Strategy

Oligomeric polyesters were prepared via polycondensation of hexane diol and either malic acid or bromosuccinic acid. From the resulting poly(hexamethylene bromosuccinate) (PHMBS) and from poly(hexamethylene malate)bromopropionate (PHMM-BP), which was prepared from poly(hexamethylene malate) (PHMM), MMA was grafted (Scheme 1).

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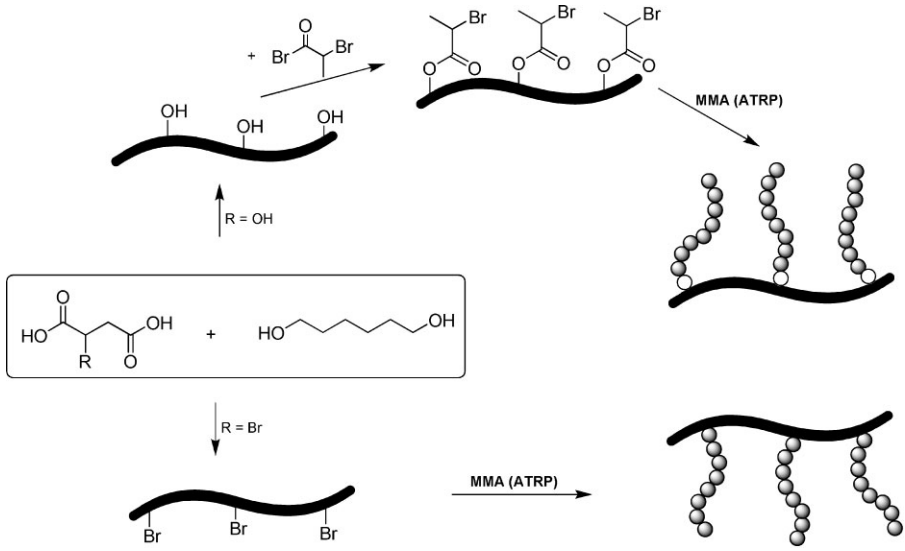
Experimental Part

Materials

THF ($\geq$ 99.9% p.a., Merck) was distilled over sodium. Poly(hexa-methylene malate) (PHMM, $\overline{M}_n = 1\ 300$ g/mol, D = 2.03) was prepared as described in literature.[5] Acetonitrile (99.5% p.a., Merck), 2,2'-bipyridine (99 + %, Acros-Organics), 2-bromo-2-propionylbromide (98%, Riedel-deHaen), bromosuccinic acid (BSA, 96%, ABCR), 2-butanone (99,5%, Fluka), copper (I) bromide (CuBr, 98%, Fluka), 1,6-hexane diol (HD, $\sim$ 97%, Fluka), methylmethacrylate (MMA, $\geq$99%, Fluka), pyridine (99,8%, Fluka), and scandium (III) trifluoromethanesulfonate [$Sc(OTf)_3$, 99%, Aldrich] were used without further purification.

Graft polymerisations were performed under nitrogen atmosphere, which was passed over molecular sieves (4 Å) and finely dispersed potassium on aluminium oxide before use.



Scheme 1.
Graft copolymers with a polyester backbone and PMMA side chains.

Synthesis of Poly(hexamethylene bromosuccinate) (PHMBS)

1,6-Hexane diol (HD; 5.00 mmol, 609 mg) and bromosuccinic acid (BSA; 5.00 mmol, 1.03 g) were dissolved in acetonitrile (4 mL). To this solution $Sc(OTf)_3$ (50.0 μmol, 24.6 mg), dissolved in acetonitrile (1 mL), was added and heated to 60 °C. Then the solvent was removed under reduced pressure (100 mbar) and the reaction was continued in vacuo (10^{-2} mbar) for 22 h. The resulting product, a colourless high viscous liquid, was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.32–1.46 (br, C*H*$_2$CH$_2$CH$_2$O), 1.55–1.73 (br, C*H*$_2$CH$_2$O), 2.50–2.90 (br, O*H*), 2.97 (dd, CH*H*-CHBr), 3.25 (dd, C*H*H-CHBr), 3.63 (t, C*H*$_2$OH), 4.02–4.26 (m, C*H*$_2$OCO), 4.55 (dd, C*H*Br) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.3 (*C*H$_2$CH$_2$CH$_2$O), 25.4 (*C*H$_2$CH$_2$CH$_2$O), 28.2 (*C*H$_2$CH$_2$O), 28.3 (*C*H$_2$CH$_2$O), 38.2 (*C*H$_2$CHBr), 39.6 (*C*HBr), 65.1 (*C*H$_2$O), 66.0 (*C*H$_2$O), 169.0 (*C*OCHBr), 169.7 (*C*OCH$_2$) ppm. SEC in THF: $\overline{M}_n$ = 7 300 g/mol, D = 2.02.

Synthesis of Poly(hexamethylene malate)bromopropionate (PHMM-BP)

PHMM [3.00 mmol (according to OH groups), 563 mg] was dissolved in THF (4 mL), pyridine (6.10 mmol, 483 mg) was added and the solution was cooled to 0 °C. Under stirring a solution of 2-bromo-2-propionylbromide (6.00 mmol, 130 mg) in THF (1 mL) was added dropwise over 30 min and reacted for another 15 min. Aqueous work up yielded a highly viscous yellowish liquid (921 mg, 94%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.31–1.44 (br, C*H*$_2$CH$_2$CH$_2$O), 1.58–1.71 (br, C*H*$_2$CH$_2$O), 1.79–1.91 (m, C*H*$_3$), 2.84–3.05 (br, CO-C*H*$_2$-CHO), 4.07–4.24 (br, C*H*$_2$O), 4.32–4.49 (br, C*H*Br), 5.47–5.54 (br, CO-C*H*O-CH$_2$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, selected peaks): δ = 21.4 (*C*H$_3$), 25.2 (*C*H$_2$CH$_2$CH$_2$O), 28.1 (*C*H$_2$CH$_2$O), 39.9 (*C*HBr, term.), 40.1 (*C*HBr), 69.2 (CO-*C*H$_2$-CHO), 168.2 (*C*O-CHBr, term.), 168.9 (*C*O-CHBr), 170.2 (*C*O-CHO), 173.9 (*C*O-CH$_2$CHO) ppm. SEC in THF: $\overline{M}_n$ = 1 800 g/mol, D = 1.74.

Grafting of MMA from PHMM-BP

CuBr (1.20 mmol, 172 mg), 2,2'-bipyridine (2.40 mmol, 375 mg) and MMA (destabilised over Al_2O_3, 12.0 mmol, 1.20 g) were transferred into a Schlenk tube and dissolved in 2-butanone (4 mL). Then, PHMM-BP [1.20 mmol (per Br-atom), 353 mg], dissolved in 2-butanone (6 mL),

was added and the reaction mixture was degassed. Polymerisation was carried out at 60 °C for 20 h. Aqueous work up yielded a colourless solid (1.29 g, 83%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.76–0.88 [(br, C-C*H*$_3$ (rr)], 0.95–1.04 [(br, C-C*H*$_3$ (mr)], 1.16–1.29 [(br, C-C*H*$_3$ (mm)], 1.29–1.50 (br, C*H*$_2$CH$_2$CH$_2$O), 1.50–1.70 (br, C*H*$_2$CH$_2$O), 1.70–2.06 (br, C*H*$_2$CHCH$_3$), 2.79–2.93 (br, CO-C*H*$_2$ -CHO), 3.40–3.66 (br, OC*H*$_3$), 3.96–4.18 (br, OC*H*$_2$), 5.32–5.52 (br, CO-C*H*O-CH$_2$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 14.1, 22.6, 31.5, 44.5, 44.8, 51.7, 177.8 ppm. SEC in THF: $\overline{M}_n$ = 15 000 g/mol, D = 6.02.

Grafting of MMA from PHMBS

CuBr (0.880 mmol, 127 mg), 2,2'-bipyridine (1.72 mmol, 278 mg) and MMA (destabilised over Al_2O_3, 12.0 mmol, 1.20 g) were transferred into a Schlenk tube and dissolved in 2-butanone (3 mL). Then, PHMBS [880 μmol (per Br-atom), 254 mg], dissolved in 2-butanone (2.5 mL), was added and the reaction mixture was degassed. Polymerisation was carried out at 40 °C for 2 h. Aqueous work up yielded a colourless solid (805 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.78–0.88 [(br, C-C*H*$_3$ (rr)], 0.95–1.08 [(br, C-C*H*$_3$ (mr)], 1.17–2.17 [(br, C-C*H*$_3$ (mm)], 1.32–1.48 (br, C*H*$_2$CH$_2$CH$_2$O), 1.55–1.74 (br, C*H*$_2$CH$_2$O), 1.75–2.00 (br, C*H*$_2$CHCH$_3$), 2.97 [dd, C*H*H-CHBr (unreacted)], 3.26 [dd, CH*H*-CHBr (unreacted)], 3.53–3.67 (br, OC*H*$_3$), 4.00–4.25 (br, OC*H*$_2$), 4.52–4.60 [m, C*H*Br (unreacted)], 6.84 [s, C*H* = C*H* (elimination main product)]. SEC in THF: $\overline{M}_n$ = 33 000 g/mol, D = 21.0.

Results and Discussion

The polycondensation of hexane diol and malic acid, as well as of hexane diol and bromo-succinic acid was carried out in an equimolar ratio in bulk at 60 °C under vacuum with scandium triflate (0.01 eq.) as catalyst. With this catalyst secondary OH-groups do not react under these reaction conditions[6,7] as well as other functional groups do not disturb the polycondensation. The molecular weight and the molecular weight distribution of PHMM with $\overline{M}_n$ = 1 300 g/mol and D = 2.03 as well as of PHMBS with $\overline{M}_n$ = 7 300 g/mol and D = 2.02 is acceptable for a polycondensation (compare Fig. 1a and 2a; all SEC-analyses were performed in THF using PMMA standards). The reaction of PHMM with 2-bromo-2-propionylbromide, which was carried out under argon atmosphere with pyridine as base at 0 °C, can be easily followed by size exclusion chromatography, where the series of oligomers shifts to higher elution volumes, as expected (Fig. 1b).

The ATRP of MMA from these two macroinitiators (PHMBS and PHMM-BP) was carried out under argon atmosphere using standard Schlenk technique with CuBr/bipyridine as catalytic system and ethylmethylketone as solvent at 60 °C.

The reaction is very fast, and in principle the polymerisation itself works perfectly. With PHMM-BrP as macroinitiator a well defined graft copolymer is obtained. The relative high molecular weight distribution of D = 6.02 can be explained through the most probable distribution of the macroinitiator (D = 2.02). Macroinitiators with only two functional groups will obviously start only two PMMA side chains, macroinitiators with 20 functional groups can start 20 side chains and therefore the distribution will expand to a large extend.

The observation of a characteristic peak in the ^{1}H NMR ($CDCl_3$; δ = 6.82 ppm) indicates, that for PHMBS as initiator, beside chain growth reaction (grafting from) also an elimination of hydrobromic acid via a radical mechanism is taking place, forming C,C-double bonds within the polyester backbone, which are stabilised by two carbonyl groups (Scheme 2). These C,C-double bonds of the formed fumarate unit can also participate in the ATRP leading first to a branched and later to a cross-linked polymer.

The size exclusion chromatogram (Fig. 2b) shows, that at low monomer conversion – 9.3% (at 30 min) and 20.1%

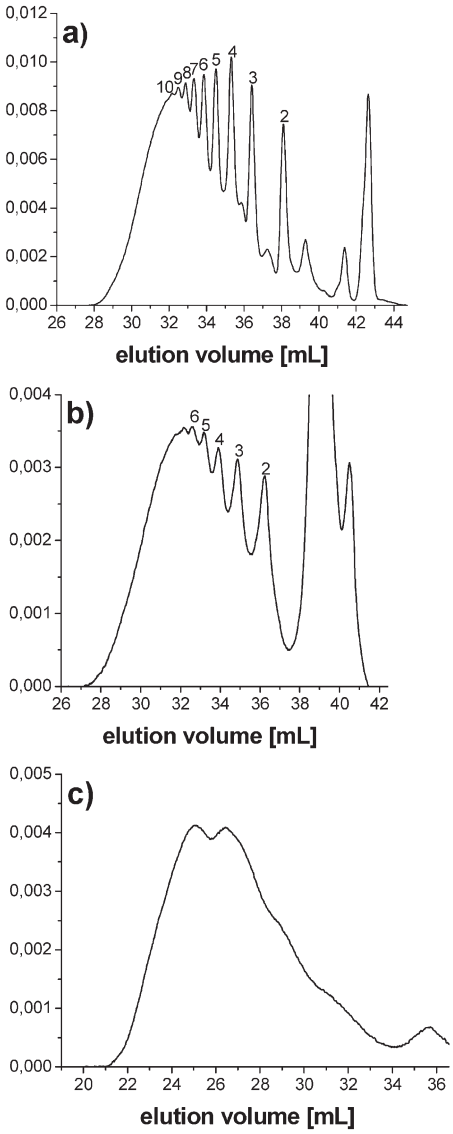


Figure 1.
Size exclusion chromatograms of a) PHMM ($\overline{M}_n$ = 1 300 g/mol, D = 2.03), b) PHMM-BrP ($\overline{M}_n$ = 1 800 g/mol, D = 1.74) and c) PHMMP-*graft*-PMMA ($\overline{M}_n$ = 15 000 g/mol, D = 6.02).

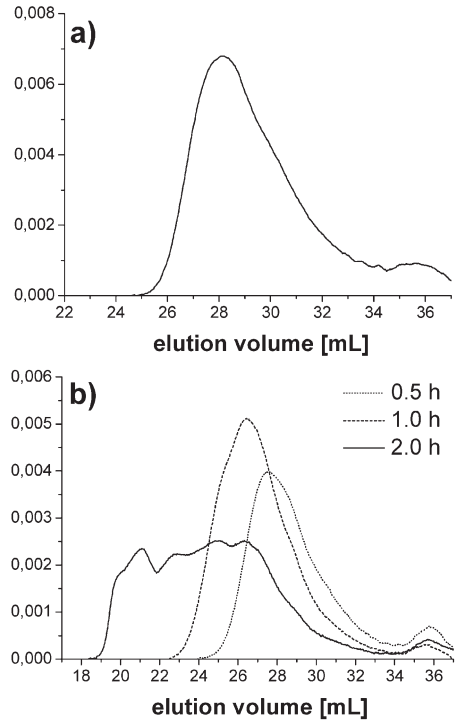
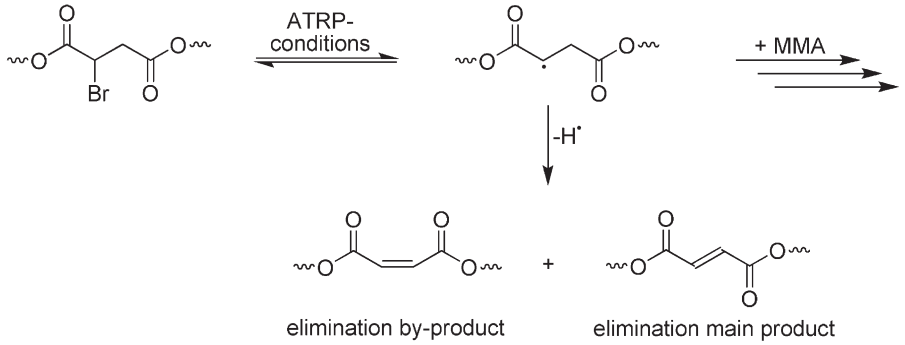


Figure 2.
Size exclusion chromatograms of a) PHMBS ($\overline{M}_n$ = 7 300 g/mol, D = 2.02) and b) PHMS-*graft*-PMMA (0.5 h: $\overline{M}_n$ = 9 800 g/mol, D = 2.00; 1.0 h: $\overline{M}_n$ = 16 800 g/mol, D = 2.78; 2.0 h: $\overline{M}_n$ = 33 000 g/mol, D = 21.0).

(at 60 min) – grafting is the main reaction occurring while the C,C-double bonds of the backbone are not participating in the reaction. The molecular weight distribution increases only slightly with D = 2.00 at 30 min to D = 2.78 at 60 min. After two hours at a monomer conversion of 52.7%, the molecular weight distribution increases to 21.0 and after that gelation is observed.

In the beginning both reactions – elimination of HBr by formation of a fumarate unit and grafting from – are taking place. Then due to a relative low concentration of fumarate repeating units compared to the concentration of MMA at the beginning of the reaction grafting from prevails. After two hours when ca. 50% of MMA is consumed the fumarate C,C-double bonds start participating in the radical chain process leading to chain coupling reaction. First a soluble polymer with a high polydispersity is obtained and later a polymer network is formed. Thus, if the reaction is stopped at low monomer conversion, a graft copolymer can be obtained with an unsaturated polyester backbone and PMMA grafts.



Scheme 2.
ATRP of MMA using PHMBS as macroinitiator: Grafting from and elimination of hydrobromic acid (occurring as side reaction during the ATRP).

At high monomer conversion ($[MMA]_t/[MMA]_0 < 0.5$) a degradable polymer network is obtained. The cross-link density can be adjusted by the reaction conditions and the ratio of MMA to initiating sites. This might be of interest for special biomedical applications.

Conclusion

Functional polyesters with hydroxyl or bromine substituents were prepared using hexane diol and malic acid or bromosuccinic acid as monomers and scandium triflate as catalyst. Via polymer analogous reactions the polyester backbone was grafted with PMMA. These biodegradable building blocks combine the degradability of aliphatic polyesters with the specific properties of the methyl methacrylate used for grafting. Moreover, by using PHMBS as macroinitiator for the grafting from reaction, an unsaturated polyester backbone grafted with PMMA is obtained. Depending on the reaction conditions linear, branched, highly branched or cross-linked biodegradable polymers (materials) can be obtained.

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