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Pearl Necklace Architecture: New Threaded Star-Shaped Copolymers

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ABSTRACT: The synthesis of star-shaped polymers, which are threaded regularly along a common backbone, is described. Thus, two different approaches for preparation of so-called pearl necklace polymers (synonyms: multigraft copolymers, barbwire or centipedes polymers, multiple dumbbells or star-oligomers) are presented. Poly(ethylene oxide) (PEO) was used as a thread and poly(dimethylaminoethyl methacrylate) (PDMAEMA) stars were used as pearls. In the first approach, a polycondensation reaction of PEO macromonomers with partly protected dipentaerythritol leads first to a multiblock PEO. Afterward, the protected hydroxy groups of dipentaerythritol, which is situated at the junction points of the blocks, can be released for the anchoring of PDMAEMA chains. In the second approach, anionic polymerization of ethylene oxide leads directly to a diblock PEO with an interior dipentaerythritol unit. The chain ends can be modified with further dipentaerythritols, giving access after selective deprotection to either star dimers or star trimers. PDMAEMA was either attached by "grafting from" procedure using atom transfer radical polymerization or "grafting to" approach using click chemistry. The advantages and disadvantages of the different approaches are discussed.

Introduction

Star-shaped polymers belong to the class of branched polymers. They possess several polymer chains linked to a common core. In general, these chains can even be of different chemical nature, yielding so-called miktoarm or heteroarm stars. A huge number of studies have been performed in order to obtain different star-shaped molecules.[1−16] Star-shaped polymers can be even linked together. Therefore, dumbbell-shaped polymers can be regarded as two star-shaped polymers connected by a common backbone.[17−22] However, an extension of this idea was hardly addressed so far: several stars can be threaded along a common backbone, leading to pearl necklace polymers (PN polymers). This notion is in analogy to the pearl necklace structures of polyelectrolytes in poor solvents.[23−26] Either the (star-shaped) pearls can freely move along the backbone (polyrotaxane-type of PN polymers)[27−29] or the pearls are glued onto the thread. Here, we just regard the latter case, since our pearls are covalently attached to the backbone. Pioneering work in this area of multigraft polymers was performed by Mays et al. leading to combs, centipedes, and barbwires.[30−32] They used anionic polymerization together with chlorosilane-based coupling reactions in a "grafting through" fashion. As a disadvantage of their attempt, polymeric monofunctinal and trifunctional linking agents, which develop during the preparation of the desired difunctional silanes, could lead to irregular structures.[31] In this paper, two new routes via functional multiblock polymers and consecutive "grafting to" or "grafting from" approaches are presented. They employ Williamson ether synthesis/anionic polymerization, protection group chemistry and controlled radical polymerization. Thus, well-defined structures are expected.

Actually, linked star-shaped polymers are ubiquitously encountered during preparation of polymer stars. They can be formed as a mixture of side products during synthesis of polymer stars with help of controlled radical polymerization using the core-first attempt[33] or even with help of the arm-fist approach (leading to brush-like aggregates).[34] Recombination of growing chains of two different stars can lead to star−star coupling. However, irregular products are expected, since a common, linear backbone cannot be guaranteed for these structures. These side products were only sparsely investigated, since polymer chemists usually try to minimize the number of coupled stars during synthesis of star-shaped polymers. In contrast, macroscopic cross-linking of star-shaped polymers can be easily achieved and might lead to interesting gel-like materials.[35,36] Between these two extremes it is quite difficult to control the structure of the coupled stars. One attempt was recently given.[37] A bifunctional linking agent led to a mixture of bridged stars (dimers, linear/cyclic trimers and different tetrastar aggregates besides variable amounts of star unimers) during preparation of star-shaped polymers in terms of an arm-first synthesis. Therefore, residual star unimers need to be separated from the linked stars. The limited number of bridged stars confines this approach. Thus, this paper will provide two pathways to obtain these PN structures. Our approach presents the exclusive preparation of linearly threaded dimer and trimer stars. It will also address the preparation of PN polymers with a higher number of stars per molecule. In both cases, the length of the spacers between the star-shaped moieties can be varied over more than 1 order of magnitude. At the same time different types of polymers in spacer and arms were utilized.

In previous work we have already synthesized and characterized miktoarm stars based on poly(ethylene oxide) (PEO) and poly(dimethylaminoethyl methacrylate) (PDMAEMA).[38,39] As a proof of principle, we concentrate again on PEO, which is in

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a multiblock-fashion decorated with dipentaerythritol units. Multiblock, multifunctional polymers with interior hydroxyl groups have been already prepared.[40−45] However, to our best knowledge no further modification of the hydroxyl groups with polymers has been performed so far. Thus, the final PN product was generated by either "grafting from" in terms of direct atom transfer radical polymerization ATRP[2] or by "grafting to" in terms of click coupling[46−49] of preformed arms. Before, the backbone was built by a polycondensation reaction between reactive PEO and partly protected dipentaerythritol (Williamson ether synthesis).

This PN type of polymers can be even regarded as multiple dumbbells or star oligomers. On the other hand, their architecture approaches the structure of molecular bottle brushes in case of short spacers and long arms.[16] It has been shown earlier that star-shaped polymers can align under certain conditions into worm-like micelles.[50] It can be therefore expected that the prealignment of stars in PN polymers might facilitate the formation of anisotropic aggregates. In addition, the PN polymers could serve as a model for comparison with the pearl necklace structures of polyelectrolytes in poor solvents.[23,26] Finally, PN polymers might become an interesting research topic in nanoscience, since the threaded structure of the stars can be used as templates for aligned nanoparticles.[51,52]

Experimental Part

Materials. *N,N*-Dimethylaminoethyl methacrylate (DMAEMA; purified by filtration over basic alumina) and molecular sieves (3 Å, 8 to 12 mesh) were purchased from Acros Organics, Geel, Belgium. Sodium hydride (50% in paraffin oil), dioxan and formic acid were obtained from Merck (Darmstadt, Germany). Dichloromethane (DCM), dimethylformamide (DMF), chloroform, tetrahydrofuran (THF; distilled over sodium/benzophenone) and *n*-hexane were purchased from Lab-Scan (Poland) or VWR. Methanesulfonyl chloride was obtained from Riedel-de Haën. Sodium hydroxide, sodium chloride, anhydrous diethyl ether (Et_2O), methanol (MeOH) and acetone were bought from J.T. Baker (Holland). Hex-5-ynoyl chloride was obtained from ChemCollect, Germany. Dipentaerythritol, *N,N*-dimethyl-4-pyridinamine (DMAP), dimethyl sulfoxide (DMSO), LiCl, tetrabutylammonium bromide (TBAB), triethylamine, 2-bromo-2-methylpropanoyl bromide, CuCl, $CuCl_2$, CuBr, *N,N,N′,N″,N‴,N‴*-hexamethyltriethyltriamine (HMTETA), anisole (purified by filtration over basic alumina), trimethylsilyldiazomethane in diethyl ether (2 M), 2,2′-bipyridyl, dithranol, and *trans*-3-indoleacrylic acid (IAA) and methyl iodide (MeI) were bought from Aldrich. Poly(ethylene oxide) (PEO, poly(ethylene glycol) of molecular weight 4000 and 20000 g/mol), acetic acid, *N,N′*-dicyclohexylcarbodiimide (DCC), triethylamine, and α-cyano-4-hydroxycinnamic acid (CHCA) was obtained from Fluka. HCl (1.0 M) was obtained from Oy FF-Chemicals Ab, Finland. Regenerated cellulose dialysis membranes (Cellu Sep H1, molecular weight cut off MWCO 1000; Cellu Sep T1, MWCO 3500; Cellu Sep T2, MWCO 6000−8000) were purchased from Membrane Filtration Products, Inc., Seguin, Texas. Reagents were bought in the highest purities available and were used as delivered (except where otherwise stated). Dendritic initiator fragment 2,2-bis(2-bromoisobutyroyloxymethyl)propionic acid was synthesized according to literature.[53] Dipentaerythritoldiformal (2′,2″,6′,6″-di-*O*-methylene-2,2,6,6-tetrahydroxymethyl-4-oxa-1,7-heptandiol) was synthesized according to literature[54] and dried in desiccator under vacuum for 18 h. 2-(2-Azidoethoxy)ethyl bromoisobutyrate was obtained according to the literature.[48] THF (Merck, p.a.) for anionic polymerization of ethylene oxide was purified by successive distillation over CaH_2 and potassium and kept under dry nitrogen before use. Ethylene oxide (Linde, 3.0) was condensed onto CaH_2 and stirred at 0 °C for 3 h before being transferred into glass ampules for storage. Prior to use ethylene oxide was additionally purified over *n*-BuLi and condensed into a sampling ampule. The phosphazene base t-BuP_4 (Fluka, 1 M in hexane) was used as received.

Synthesis. As an example, we describe the synthesis of pearl necklace polymers with PEO spacers of molecular weight 4000 g/mol applying a polycondensation process of macromonomers. Following recipes were also applied for PEO (M_n = 20000 g/mol) after taking the new stochiometry into account.

Preparation of Bismesylated PEO (*e.g., Mes−*PEO_{91}*−Mes, Poly*(*ethylene oxide*) *α,ω-Dimethanesulfonate*). This was prepared adopting procedures reported in the literature:[38,55] hydroxytelechelic PEO (60 g; $M_n \sim 4000$ g/mol) was dissolved in DCM (200 g) and triethylamine (11 g; 110×10^{-3} mol), before molecular sieve was added. After 1 h, the sieve was taken out of the mixture and it was cooled under stirring at 0 °C. Then, methanesulfonyl chloride (6 g; 5 mL; 52×10^{-3} mol) was added dropwise and the mixture was slowly allowed to warm up to room temperature (RT) for 16 h. Then the orange mixture was filtrated over silica and dried with molecular sieve. Then it was concentrated in vacuo. The polymer was precipitated twice from DCM solution in diethyl ether. The precipitate was washed with *n*-hexane to gain after drying in vacuum a white powder (31 g; NMR shows attachment of the mesylate).

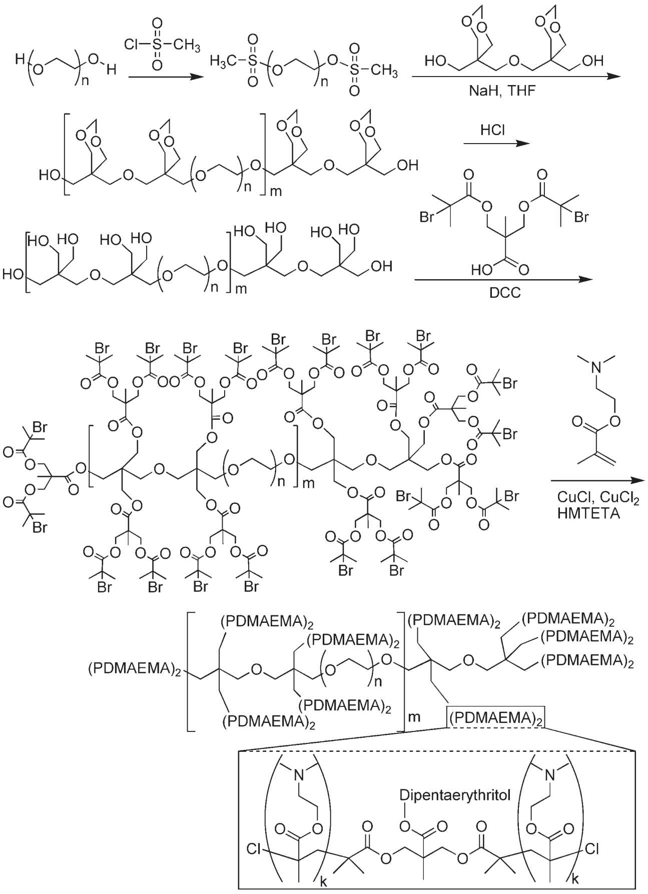
For mesylated PEO (4000 g/mol; Mes−PEO_{91}−Mes): SEC (DMF, 1 g/L LiBr, PEO calibration): M_n = 3600 g/mol; PDI = 1.09; δ_H (200 MHz; $CDCl_3$; Me_4Si) 4.35 (4H, m, PEO), 3.97 (2H, m, PEO), 3.73 (4H, m, PEO), 3.8−3.5 (m, PEO−H), 3.3 (2H, m, PEO), 3.06 (6H, s, $-OSO_2CH_3$); δ_C (50.3 MHz; $CDCl_3$; Me_4Si) 70.7 (main signal PEO), 69.5, 69.2 (PEO), 37.9 (OSO_2CH_3).

For mesylated PEO (20000 g/mol; Mes−PEO_{454}−Mes): SEC (DMF, 1 g/L LiBr, PEO calibration): M_n = 18000 g/mol; PDI = 1.09.

Preparation of Multiblock PEO (*e.g., Protected*[PEO_{91}*-dipentaerythritol*]$_4$). The acetal dipentaerythritoldiformal (669 mg; 2.4×10^{-3} mol) was dissolved (after being reprecipitated from $CHCl_3$-solution by use of *n*-hexane and dried in vacuum desiccator) in 20 mL of THF (distilled over Na/benzophenone) after NaH (200 mg, 8×10^{-3} mol; equals 400 mg crude 50% NaH in paraffin oil) was added under nitrogen-counterflow at RT. Hereby the dry flask was equipped with a narrow gas outlet connected to a water trap ($CaCl_2$). After 1 h of stirring, a solution of 10.00 g of mesylated PEO in 60 mL of THF (2.40×10^{-3} mol, $M_n \sim 4160$ g/mol; dissolved under nitrogen; PEO has been reprecipitated from $CHCl_3$ solution by use of anhydrous Et_2O and dried in vacuum exsiccator) was added slowly over 20 min with help of a syringe (flask with polymer solution was washed twice with 20 mL of THF and added to the reaction mixture). After 2 h of reaction, the setup was equipped with a condenser (equipped with water trap) and the mixture was refluxed for 3 h before 300 mg of a crude NaH mixture was added. Then the mixture was refluxed for another hour before further 60 mg of acetal were added in order to endfunctionalize unreacted end groups. This required refluxing for another 30 min, before the mixture was stirred at RT for 3 days. Then 10 mL of MeOH were added and the mixture was concentrated. It was dialyzed against MeOH for 1 day (MWCO 6000) and then precipitated from diethyl ether. The precipitate was taken up in water (30 mL) to be dialyzed against water for 1 night. Then the solution was freeze-dried (5.6 g of obtained). Then the polymer was dissolved in 250 mL of DCM and 100 mL of hexane before the polymer was fractionated by "partial precipitation" adding mL-wise *n*-hexane to the mixture. Six fractions were collected, were the first three fractions showed almost no traces of diblock and monoblock PEO by size exclusion chromatography SEC (together 3 g; 30% overall yield).

For multiblock polymer with PEO (4000 g/mol) as spacer (protected [PEO_{91}-dipentaerythritol]$_4$): SEC (DMF, 1 g/L LiBr, PEO calibration): M_n = 17000 g/mol, PDI = 1.35; δ_H (200 MHz; $CDCl_3$; Me_4Si) 4.77 (4n H, 2 overlapping d, $J \sim 6$ Hz, O−CH_2−O acetal), 3.98 (2n H, m, PEO), 3.72 (8nH, m, dioxane

Scheme 1. Reaction Pathway toward Pearl Necklace Polymers with Short Spacers



side ring −C−CH_2−O−CH$_2$−O−CH_2−C− of dipentaerythritol), 3.7−3.5 (360*n*H, main peak PEO-*H*), 3.43 (4*n*H, s, main chain −O−CH_2−C− of dipentaerythritol), 3.40 (4*n*H, s, main chain −O−CH_2−C- of dipentaerythritol), 3.28 (2n H, s, PEO); δ_C (50.3 MHz; CDCl$_3$; Me$_4$Si) 94.4 (O−*C*H$_2$−O acetal), 71.5−68.0 (PEO + dipentaerythritol signals), 40.0 (q, −*C*− dipentaerythritol).

For multiblock polymer with PEO (20000 g/mol) as spacer (protected [PEO$_{454}$-dipentaeryhthritol]$_3$): SEC (DMF, 1 g/L LiBr, PEO calibration): M_n = 58500 g/mol, PDI = 1.5.

Preparation of Hydroxy-Functionalized Multiblock PEO (e.g., [PEO$_{91}$-dipentaerythritol]$_4$). Three grams of fractionated multiblock PEO (1.4 × 10^{-3} mol acetal groups) was dissolved in 100 mL of 1 M HCl and placed for 18 h at 90 °C. Then the mixture was concentrated in vacuo, before the viscous residue was again dissolved in 50 mL of water and dialyzed against water for 2 days (MWCO 12000) and then freeze-dried (to yield 2.5 g; 80% yield). NMR showed >90% removal of protecting acetal groups.

For multiblock polymer with PEO (4000 g/mol) as spacer ([PEO$_{91}$-dipentaerythritol]$_4$): SEC (DMF, 1 g/L LiBr, PEO calibration): M_n = 14000 g/mol; PDI = 1.42; δ_H (200 MHz; CDCl$_3$; Me$_4$Si) 4.0−3.4 (overlapping PEO and dipentaerythritol signals), δ_C (50.3 MHz; CDCl$_3$; Me$_4$Si) 74−67 (overlapping PEO and dipentaerythritol signals), 64.6 (most probably C−*C*H$_2$−OH), 62.0 (most probably residual O−CH$_2$−*C*H$_2$−OH), 45.7 (q, −*C*− dipentaerythritol).

Preparation of Initiator-Functionalized Multiblock PEO (e.g., [PEO$_{91}$−IniBr$_6$]$_4$). The hydroxy-functionalized multiblock PEO (1 g; 9.5 × 10^{-4} mol OH-groups) was dissolved in 10 mL of DCM and dried with molecular sieve. The sieve was taken out after 1 h and then all components were mixed (0.6 g of ATRP-initiator fragment 2,2-bis(2-bromoisobutyroyl-oxymethyl)propionic acid, 1.4 × 10^{-3} mol; 0.34 g of DCC, 1.7 × 10^{-3} mol; 11 mg DMAP, 1 × 10^{-4} mol) and stirred for 5 days. Then the precipitate was filtered off and the remaining solution was precipitated twice by use of diethyl ether. Then the precipitate was taken up in 10 mL of DMF and dialyzed against DMF (MWCO 12000). After dialysis for 24 h the solution was again precipitated twice by use of diethyl ether (second time from DCM solution). Drying in vacuum yielded 1.1 g of polymer (NMR showed 80% conversion yielding 75% total modification).

For multiblock polymer with PEO (4000 g/mol) as spacer ([PEO$_{91}$−IniBr$_6$]$_4$): SEC (DMF, 1 g/L LiBr, PEO calibration): M_n = 15400 g/mol; PDI = 1.43; δ_H (200 MHz; CDCl$_3$; Me$_4$Si) 4.41 (6*n*H, d, J ~ 11 Hz, C−CH_2−O−COCBr), 4.28 (6*n*H, d, *J* ~ 11 Hz, C−CH_2−O−COCBr), 4.19 (6n H, s, C−CH_2−O−COC(CH$_3$)(CH$_2$−OCOCBr)$_2$), 3.98 (2H, m, PEO), 3.8−3.35 (370*n*H, PEO and dipentaerythritol), 3.27 (2H, m, PEO), 1.90 (36n H, s, OC=OC(CH_3)$_2$Br), 1.33 (9n H, s, C−CH$_2$−O−COC(CH_3)(CH$_2$−OCOCBr)$_2$); δ_C (50.3 MHz; CDCl$_3$; Me$_4$Si) 171.9 (C−CH$_2$−O−*C*(=O)C(CH$_3$)(CH$_2$−OC(=O)CBr)$_2$), 171.0 (O*C*(=O)C(CH$_3$)$_2$Br), 74−67 (overlapping PEO and dipentaerythritol signals), 66.1 (C−*C*H$_2$−O−C(=O)C(CH$_3$)(*C*H$_2$−OC(=O)C(CH$_3$)$_2$Br)$_2$), 64.1 (most probably residual C−*C*H$_2$−OH), 55.6 (OC(=O)*C*(CH$_3$)$_2$Br), 47.0 (O−C(=O)*C*(CH$_3$)(CH$_2$−OC(=O)C(CH$_3$)$_2$Br)$_2$), 44.3 (q, C of dipentaerythritol), 30.8 (−OC(=O)C(*C*H$_3$)$_2$Br), 18.2 (O−C(=O)C(*C*H$_3$)(CH$_2$−OC(=O)C(CH$_3$)$_2$Br)).

For multiblock polymer with PEO (20000 g/mol) as spacer ([PEO$_{454}$−IniBr$_6$]$_3$): SEC (DMF, 1 g/L LiBr, PEO calibration): M_n = 57000 g/mol; PDI = 1.65.

Preparation of Pearl Necklace Polymer with PEO Thread and PDMAEMA Pearls (e.g., [PEO$_{91}$-b-(PDMAEMA$_{140}$)$_{3.6}$]$_4$). The multiblock PEO macroinitiator (49.8 mg; M_n(repeating unit) ~ 5500 g/mol; 5.5 × 10^{-5} mol initiation groups), CuCl (13.8 mg; 1.4 × 10^{-4} mol) and CuCl$_2$ (2 mg; 1.5 × 10^{-5} mol) were mixed in anisole (3.4 g) and deoxygenated. Then the ligand HMTETA (29 mg; 1.25 × 10^{-4} mol) and the monomer DMAEMA (1.78 g; 0.011 mol) was also mixed and deoxygenated and then introduced to the macroinitiator mixture at 60 °C under stirring. Therefore, 1.81 g of a mixture containing HMTETA (50 mg) and DMAEMA (3.1 g) were introduced after deoxygenation. After 140 min the reaction was stopped by dilution with THF (5 mL) and the conversion was 42% according to NMR ($P_{n,theo,arm}$ ~ 84). Then the polymer was filtrated over silica and then reconcentrated before it has been precipitated from hexane. The precipitate was taken up with DMF and dialyzed against DMF for 18 h (MWCO 12000) and against THF for another 24 h. Then a third of the mixture (4 mL; ~ 200 mg polymer) were treated with 0.4 g of MeI at RT, whereas in 5 min gelation occurred (under formation of the corresponding quaternized PN polymer with poly{[2-(methacryloyloxy)ethyl] trimethylammonium iodide} arms: [PEO$_{91}$-*b*-(PMETAI$_{140}$)$_{3.6}$]$_4$). This mixture was left for standing at RT for 3 days (this quaternized PDMAEMA containing polymer was then dissolved in excess water and dialyzed against water and freeze-dried −300 mg). Another third of the PDMAEMA containing PN polymer was precipitated from hexane (using a Teflon beaker) and dried in vacuum whereas the last third of the THF solution was stored (200 mg).

For PN polymer with PEO (4000 g/mol) as spacer ([PEO$_{91}$-*b*-(PDMAEMA$_{140}$)$_{3.6}$]$_4$): SEC (DMF, 1 g/L LiBr, PEO calibration): M_n = 59200 g/mol; PDI = 1.65; M_n(NMR) = 370000 g/mol; δ_H (200 MHz; CDCl$_3$; Me$_4$Si) 4.3−3.9 (O−CH_2CH$_2$−N), 3.8−3.5 (PEO−*H*), 2.7−2.4 (OCH$_2$CH_2−N), 2.4−2.1 (−N(CH_3)$_2$), 2.1−1.6 (PDMAEMA backbone CH_2), 1.2−0.7 (PDMAEMA backbone CH_3).

For PN polymer with PEO (20000 g/mol) as spacer ([PEO$_{454}$-*b*-(PDMAEMA$_{90}$)$_{3.3}$]$_3$): SEC (DMF, 1 g/L LiBr, PEO calibration): M_n = 60800 g/mol; PDI = 1.77; M_n(NMR) = 190000 g/mol.

Cleavage of Arms. A 40 mg sample of quaternized pearl necklace polymer was dissolved in 1 mL of concentrated aqueous NaOH solution (additional water was added since a homogeneous solution was obtained) and kept at 85 °C for 5 days. The cooled solution was carefully brought to pH 3 with concentrated HCl (precipitation of insoluble PEO/poly(methacrylic acid) (PMAA) complex is observed) and freeze-dried. Then the residue was dialyzed against water for 1 day (MWCO 1000) and freeze-dried in order to extract the dry residue with 10 mL of methanol (containing 1 g/L NaOH) for 7 days at RT. The supernatant methanol was then rejected, whereas the residue was the sodium salt of poly(methacrylic acid) PMAA. The PMAA was therefore dissolved in 2 mL of pH 3 HCl and dialyzed for 1 day before 1 mL of 0.1 M HCl was added into the dialysis tube. The dialysis was continued for 6 h against water (MWCO 1000), before the mixture was finally freeze-dried. Then the dried protonated PMAA was dissolved in 0.2 mL of water and 2 mL of THF before 0.1 mL of 2 M trimethylsilyldiazomethane in diethyl ether was added (additional water was dropwise added until the original PMAA solution is homogeneous; in course of the reaction, THF was added dropwise to ensure homogeneous solution also for developing poly(methyl methacrylate) or PMMA). The addition of diazomethane was continued until the solution remains yellowish for more than an hour under stirring at RT. Then the solution was dialyzed against THF (MWCO 1000) for 3 days and then dried in vacuo (5 mg of PMMA).

PMMA from pearl necklace polymer with PEO spacer (4000 g/mol; $[\mathrm{PEO}_{91}\text{-}b\text{-}(\mathrm{PMETAI}_{140})_{3.6}]_4$): M_n(MALDI−ToF, matrix dithranol) = 14200 g/mol; PDI(MALDI−ToF) = 1.06; P_n(arm) = 138, $P_{n,\mathrm{theo}}$(arm) = 84 (obtained by conversion times monomer to initiator ratio); initiator efficiency $f = 0.6$.

PMMA from pearl necklace polymer with PEO spacer (20000 g/mol; $[\mathrm{PEO}_{454}\text{-}b\text{-}(\mathrm{PMETAI}_{90})_{3.3}]_3$): M_n(MALDI−ToF, matrix dithranol) = 9500 g/mol; PDI(MALDI−ToF) = 1.06; P_n(arm) = 93; $P_{n,\mathrm{theo}}$(arm) = 50; initiator efficiency $f = 0.55$.

PMMA: δ_H(200 MHz; $CHCl_3$, Me_4Si; mainsignals) 3.7−3.5 (O−CH_3), 2.1−1.6 (PMMA backbone CH_2); 1.2−0.6 (PMMA backbone CH_3).

The following recipes describe the preparation of PN polymer's smallest representatives in terms of repeating units (quasi-monodisperse star dimer, which is a dumbbell polymer, and a star trimer). However, the overall dimensions of the products are large, since a long PEO spacer was applied:

Preparation of Dipentaerythritoldiacetoneketal (*oxybis{methylene-[2,2-dimethyl-5-(hydroxymethyl)-1,3-dioxan-5-ylidene]}*).[56] Dipentaerythritol (10 g of 80% technical grade; 31 × 10^{-3} mol), para-toluenesulfonic acid monohydrate (0.7 g; 4 × 10^{-3} mol) and acetone (70 mL; 1 mol; technical grade) were mixed in a round-bottom flask equipped with a condenser (together with 15 g of dry molecular sieve). Then the mixture was stirred under reflux for 4 days (at 70 °C), before the residual reactant was filtered off. The acid was neutralized by adding ~3 g of K_2CO_3 and letting it stand overnight before filtration and concentration (2.5 g of crude product). Then the crude product (2 g) was adsorbed on 4 g of silica, and it was purified by column chromatography (200 g of silica 60 mesh 230−400; eluent: ethyl acetate/acetone 100:1; $R_f = 0.4$) in order to obtain 1.5 g of pure ketal after concentration (12% yield).

δ_H(200 MHz; DMSO-d_6; Me_4Si) 4.60 (2H, t, $J \sim 4.5$ Hz, $-CH_2-O-H$), 3.61 (8H, s, dioxane side ring $-C-CH_2-O-C-(CH_3)_2-O-CH_2-C-$ of dipentaerythritol), 3.38 (4H, d, $J \sim 4.5$ Hz, $-CH_2-O-H$), 3.29 (4H, s, $-CH_2-O-CH_2-$), 1.31 (6H, s, CH_3-C-CH_3 ketal), 1.29 (6H, s, CH_3-C-CH_3 ketal); δ_C (50.3 MHz; DMSO-d_6; Me_4Si) 97.3 (CH_3-C-CH_3 ketal), 70.6 ($C-CH_2-O-CH_2-C$), 61.7 (dioxane side ring $-C-CH_2-O-C(CH_3)_2-O-CH_2-C-$ of dipentaerythritol), 60.4 ($-CH_2-OH$), 38.7 (q. C), 24.2 (CH_3-C-CH_3 ketal), 23.3 (CH_3-C-CH_3 ketal).

Preparation of Azido-Terminated PDMAEMA.[48] Initiator 2-(2-azidoethoxy)ethyl bromoisobutyrate (0.40 g, 1.43 × 10^{-3} mol), CuCl (0.132 g; 1.33 × 10^{-3} mol), $CuCl_2$ (45 mg; 0.33 × 10^{-3} mol), the monomer DMAEMA (7.5 g; 47.6 × 10^{-3} mol; filtered over basic alumina) and the ligand HMTETA (0.38 g; 1.66 × 10^{-3} mol) were weighed into a flask and then degassed by bubbling nitrogen. Then the solution was put to 60 °C under stirring and the initiator (0.40 g; 1.43 × 10^{-3} mol) was added with help of a syringe. After 10 min, the solution was poured into chloroform and the conversion was 42% according to NMR. The copper compounds were retained by filtration over silica, and then the polymer was concentrated in vacuo. The viscous solution was precipitated from cold hexane and then the precipitate was dialyzed against dioxane (MWCO 1000). After freeze-drying, 1.3 g of PDMAEMA were retained. The permeate gave another 1 g of crude product after freeze-drying (P_n(NMR) = 17).

SEC (DMF, 1 g/L TBAB, PMMA calibration): M_n = 900 g/mol, PDI = 1.2; M_n(NMR) = 2800 g/mol; M_n(MALDI−ToF, matrix CHCA) = 3500 g/mol, PDI(MALDI−ToF) = 1.10; δ_H(200 MHz; $CDCl_3$; Me_4Si) 4.3−3.8 ($O-CH_2CH_2-N(CH_3)_2$), 3.7−3.5 ($-CH_2-O-CH_2-$), 3.4−3.2 ($-CH_2-CH_2-N_3$), 2.7−2.4 (OCH_2CH_2-N), 2.4−2.1 ($-N(CH_3)_2$), 2.1−1.6 (PDMAEMA backbone CH_2), 1.2−0.7 (PDMAEMA backbone CH_3).

Preparation of PEO with Interior Protected Dipentaerythritol Groups (*HO−PEO$_{670}$−dipentaeryth.−PEO$_{670}$−OH*). PEO with an internal protected dipentaerythritol group was synthesized by anionic polymerization of ethylene oxide in THF at 45 °C using dipentaerythritoldiformal as bifunctional initiator. Prior to the reaction the dipentaerythritoldiformal was dried under high vacuum (ca. 10^{-4} mbar) at 100 °C overnight in order to remove traces of water, which might act as initiating sites, too. The dried dipentaerythritoldiformal was dissolved in dry THF followed by activation of the hydroxy-groups for anionic polymerization of ethylene oxide by deprotonation using the phosphazene base t-BuP_4 at room temperature for 1 h. Subsequently, the desired amount of ethylene oxide was added, and the polymerization was conducted at 45 °C for 2 days, before being terminated with a mixture of acetic acid/methanol = 1/5 v/v.

SEC (DMF, 1 g/L TBAB, PEO calibration): M_n = 59000 g/mol; PDI = 1.1; M_n(NMR) = 55000 g/mol; M_n(MALDI−ToF, matrix IAA) = 58400 g/mol, PDI(MALDI−ToF) = 1.00; δ_H (200 MHz; $CDCl_3$; Me_4Si) 4.78 (4 H, m, $-O-CH_2-O-$), 4.0−3.2 (5400 H, PEO and dipentaerythritol).

Preparation of Bismesylated PEO (*Mes−PEO$_{1340}$−Mes, Poly(ethylene oxide) α,ω-Dimethanesulfonate*). The hydroxy-terminated PEO (1 g of HO−PEO$_{670}$−dipentaeryth.−PEO$_{670}$−OH; $M_n \sim 59000$ g/mol; 3.39 × 10^{-5} mol OH) was dissolved in DCM (6 g) and triethylamine (0.2 g; 2.0 × 10^{-3} mol), before 10 grains of molecular sieve were added. After 1 h, the sieve was taken out of the mixture and it was cooled under stirring to 0 °C. Then, methanesulfonyl chloride (0.06 g, 0.04 mL; 5 × 10^{-4} mol) was added dropwise and the mixture was slowly allowed to warm up to RT for 5 h hours. Then, the orange mixture was filtrated over silica and dried with molecular sieve and then it was concentrated in vacuo. The polymer was precipitated twice from DCM solution once in diethyl ether and once in hexane in order to gain after drying in vacuum a white powder (0.6 g; 60% yield).

SEC (DMF, 1 g/L TBAB, PEO calibration): M_n = 44000 g/mol; PDI = 1.11; SEC (DMF, 1 g/L TBAB, PMMA calibration): M_n = 97000 g/mol, PDI = 1.14; M_n(NMR) = 50000 g/mol; δ_H (200 MHz; $CDCl_3$; Me_4Si) 4.78 (4 H, m, $-O-CH_2-O-$), 4.39 (4 H, m, PEO), 4.0−3.2 (5400 H, PEO and dipentaerythritol), 3.08 (6H, m, mesylate CH_3).

Preparation of PEO with Protected Dipentaerythritol End Groups. The dipentaerythritoldiacetoneketal (500 mg; 1.5 × 10^{-3} mol) and NaH (50 mg, 2 × 10^{-3} mol; equals 100 mg of crude 50% NaH in paraffin oil) were weighed into a flask, which was purged with nitrogen. Then 12 mL of THF (distilled over Na/benzophenone) were added. Another 13 mL of THF were used to dissolve the mesylated PEO under gentle heating (0.55 g, $M_n \sim 59000$ g/mol; 9.3 × 10^{-6} mol) and the solution was injected to the dipentaerythritol suspension after degassing. Then, the mixture was refluxed for 1 h and was stirred for 16 h at RT. Then further 150 mg of NaH were added and the mixture was stirred under reflux for 5 h. Then, the viscous solution was diluted (30 mL) with THF and the suspension was centrifuged. Acetic acid was added slowly to the supernatant until the solution became neutral (as seen by dropping one drop on wet pH paper). Then the THF solution was precipitated in diethyl ether. Precipitation in diethyl ether gave 0.42 g of polymer, which were dissolved in methanol and dialyzed for 4 days against methanol (MWCO 6000) and precipitated again in diethyl ether. NMR showed the right ratio of integrals after dialysis and SEC is monomodal.

SEC (DMF, 1 g/L TBAB, PEO calibration): M_n = 49900 g/mol; PDI = 1.08; M_n(NMR) = 53000 g/mol; M_n(MALDI−ToF, matrix IAA) = 59500 g/mol, PDI(MALDI−ToF) = 1.01; δ_H (200 MHz; $CDCl_3$; Me_4Si) 4.78 (4 H, m, $-O-CH_2-O-$), 4.0 −3.2 (5400 H, PEO and dipentaerythritol), 1.40 (12H, s, ketal CH_3), 1.39 (12H, s, ketal CH_3).

Preparation of PEO with Dipentaerythritol End Groups (*dipentaeryth.−PEO*$_{1340}$*−dipentaeryth.*). The PEO with protected dipentaerythritol end groups (0.3 g) was dissolved in 18 mL of aqueous solution of acetic acid (5 wt %) and formic acid (0.5 wt %). This mixture was allowed to stand for 4 days before the solution was dialyzed against water (MWCO 6000; 8 h) and freeze-dried to obtain 0.29 g of polymer. NMR showed basically full deprotection of the acetoneketals and intact formal groups. SEC monomodal.

SEC (DMF, 1 g/L TBAB, PEO calibration): M_n = 49200 g/mol; PDI = 1.10; M_n(NMR) = 63000 g/mol; M_n(MALDI−ToF, matrix IAA) = 59000 g/mol, PDI(MALDI−ToF) = 1.00; δ_H (200 MHz; $CDCl_3$; Me_4Si) 4.78 (4 H, m, $-O-CH_2-O-$), 4.0−3.2 (5400 H, PEO and dipentaerythritol).

Preparation of PEO with Telechelic Alkyne Groups (*alkyne*$_5$*−PEO*$_{1340}$*−alkyne*$_5$). The solution of PEO with dipentaerythritol end groups (0.1 g; 1.7×10^{-6} mol; 1.7×10^{-5} mol of OH) and DMAP (1 mg; 1×10^{-4} mol) in $CHCl_3$ (2 mL; dried over molecular sieves) and triethylamine (0.5 mL; dried over molecular sieves) was cooled with ice. Then hex-5-ynoyl chloride (60 mg; 4.6×10^{-4} mol) was added dropwise over 5 min with help of syringe and septum. Under stirring, the solution was left to warm up for 16 h to RT before the solution was filtered over basic alumina and concentrated and precipitated in diethyl ether. Then the polymer was dialyzed against methanol for 6 h and against dioxane for 3 d (MWCO 6000). Then it was freeze-dried (90 mg) and the integrals showed basically 10 alkyne units per molecule.

SEC (DMF, 1 g/L TBAB, PEO calibration): M_n = 36000 g/mol; PDI = 1.29; M_n(NMR) = 53000 g/mol; M_n(MALDI−ToF, matrix IAA) = 59000 g/mol, PDI(MALDI−ToF) = 1.00; δ_H (200 MHz; $CDCl_3$; Me_4Si) 4.76 (4 H, m, $-O-CH_2-O-$), 4.09 (20H, s, $C-CH_2-O-C(=O)-$), 4.0 - 3.2 (5400 H, PEO and dipentaerythritol), 2.44 (20H, t, J ∼ 8 Hz, $-O-C(=O)-CH_2-CH_2-CH_2-CC-H$), 2.25 (20H, dt, J ∼ 6 Hz, J ∼ 2 Hz, $-O-C(=O)-CH_2-CH_2-CH_2-CC-H$), (10H, t, J ∼ 2 Hz, $-O-C(=O)-CH_2-CH_2-CH_2-CC-H$), (20H, m, $-O-C(=O)-CH_2-CH_2-CH_2-CC-H$).

Preparation of Dumbbell Polymer with PEO Linker and PDMAEMA Arms (($PDMAEMA_{19})_5-PEO_{1340}-(PDMAEMA_{19})_5$). The alkyne modified PEO (0.076 g; 1.29×10^{-6} mol; M_n ∼ 60000 g/mol), the azide modified PDMAEMA (0.076 g; 2.5×10^{-5} mol; M_n ∼ 3000 g/mol), CuBr (2.00 mg, 1.4×10^{-5} mol) and bipyridyl (4.2 mg; 2.7×10^{-5} mol) were introduced to one flask and deoxygenated by N_2 counterflow, before deoxygenated THF (1 mL; distilled over Na/benzophenone) was introduced (slight heating to solubilize polymer). Then the mixture was stirred at RT for 40 h. The mixture was diluted and filtrated over silica and concentrated before the crude product has been dissolved in 3 mL of chloroform and precipitated in 100 mL of diethyl ether (the supernatant contained 25 mg of 90% PDMAEMA). This precipitation procedure was repeated twice until the precipitate's composition according to ^1H NMR does not change anymore. The precipitate was then freeze-dried from dioxan to yield 75 mg of dumbbell polymer.

SEC (DMF, 1 g/L TBAB, PEO calibration): M_n = 35000 g/mol; PDI = 1.38; M_n(NMR) = 97000 g/mol; M_n(osmometry) = 52000 g/mol; M_n(MALDI−ToF, matrix CHCA) = 105000 g/mol, PDI(MALDI−ToF) = 1.12; M_n(expected) = 95000 g/mol; δ_H (200 MHz; $CDCl_3$; Me_4Si) 7.44 (10H, s, triazole H), 4.77 (4H, s, $-O-CH_2-O-$), 4.3−3.9 (380H, $O-CH_2CH_2-N$), 3.8 - 3.5 (5400H, PEO-H), 2.7−2.4 (380H, OCH_2CH_2-N), 2.4 - 2.1 (1140H, $-N(CH_3)_2$), 2.1−1.6 (380H, PDMAEMA backbone CH_2), 1.2−0.7 (570H, PDMAEMA backbone CH_3).

Preparation of the Star Trimer. For this, please refer to the Supporting Information.

The characterization of all polymers is summarized in Table S1 and S2 in the Supporting Information.

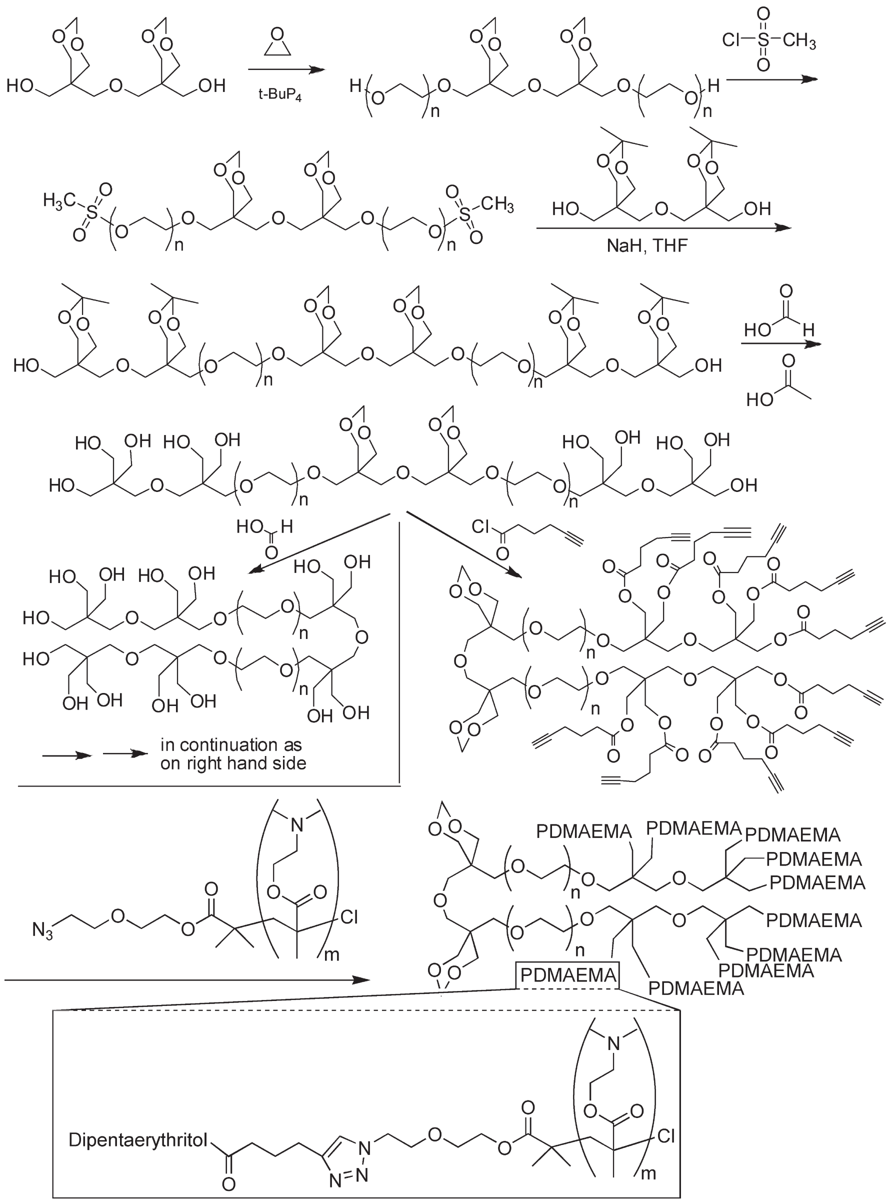
Polymer Characterization. *NMR Spectroscopy*. The NMR spectra were measured with a 200-MHz Varian Gemini 2000 NMR spectrometer (operating at 200 MHz for ^1H and at 50.3 MHz for ^{13}C) using $CDCl_3$ or deuterated DMSO as solvent (usually 10 mg/mL). In some cases (for the preparation of the star trimers) a different NMR spectrometer was used: Bruker DRX 400 spectrometer. The chemical shifts are presented in parts per million downfield from the internal TMS standard. Simulations were performed with ACD/HNMR and ACD/CNMR Predictor Ver.3.00. For determination of M_n(NMR) (^1H NMR end group analysis), the sum of all integrals of signals, which were assigned to the polymer above 4 ppm and below 3.2 ppm, were used to divide this sum by the number of protons used for integration and compared to the signals of PEO. In order to make meaningful end group analysis special care was taken for proper phasing and adjustment of the baseline.

Size Exclusion Chromatography (*SEC*). The SEC analyses were performed with a Waters instrument equipped with Waters Styragel HR 6, HR 4 and HR 2 columns (7.8 × 300 mm each), and Waters 2487 UV and Waters 2410 RI detectors. Dimethylformamide with either 1 g/L LiBr or 1 g/L TBAB was used as an eluent at a flow rate of 0.8 mL/min. In some cases (for the preparation of the star trimers) a different SEC setup was used: SEC analyses were carried out at 30 °C using a high pressure liquid chromatography pump (Bischoff 2250) and a refractive index detector (Jasco). The eluting solvent was again dimethylformamide (DMF) with 1 g/L LiBr and a flow rate of 1.0 mL/min. Four columns with PSS GRAM material were applied. The length of the precolumn was 50 mm and the diameter 8 mm. The remaining three columns had a length of 300 mm, diameter of 8 mm, particle size of 10 mm, and the nominal pore widths were 100, 1 000 and 1 000Å. PEO samples were carefully heated with a fan to accelerate the dissolution process. Conventional calibrations were performed with poly(methyl methacrylate) or poly(ethylene oxide) (Polymer Laboratories, Amherst, MA).

Matrix Assisted Laser Desorption Ionization−Time of Flight (*MALDI−ToF*) *Mass Spectrometry*. MALDI−ToF mass spectrometry was performed on a Bruker microflex equipped with 337 nm N_2 laser in the reflector mode for determination of molecular weight of linear and modified PDMAEMA arms (PMMA) and in the linear mode for PEO precursors and dumbbells (accelerating voltage 20 kV, pressure 5×10^{-6} mbar). THF solutions of dithranol or IAA (20 μL of 20 g/L), sodium trifluoroacetate (0.5 μL of 10 g/L) and analyte (5 μL of 10 g/L PMMA or PEO) were mixed and 0.5 μL were applied on sample plate. For PDMAEMA-containing polymers CHCA was used as matrix (45 μL of 10 g/L in DMSO) mixed with polymer solution in THF (5 μL of 10 g/L).[57] This mixture was applied on a sample plate and dried in vacuo (1 μL). In case of overlapping peaks (e.g., double charged species), Gaussian curve fitting was performed in order to calculate number-average molar mass and polydispersity index.

Osmometry. A membrane osmometer (Osmomat 090, Gonotec GmbH, Berlin, Germany) with regenerated cellulose membrane

Scheme 2. Reaction Pathway toward Dumbbell Polymers and Star-Trimers with Long Spacers



(Gonotec two layer membrane 90.9.0010; cut off 20000 Da) was used for the determination of the molecular weight of dumbbell polymer. Solutions with different concentrations in THF were injected to extrapolate to zero concentration. The cell was kept at 30 °C. To rinse the measurement cell with a new sample, approximately 0.7 mL of sample solution was injected three times.

Atomic Force Microscopy. Three drops of an aqueous solution of quaternized $[(\mathrm{PDMAEMA}_{140})_{3.6}\text{-}b\text{-}\mathrm{PEO}_{91}]_4$ (0.0005 g/L) was spincasted (2000 rpm) on freshly cleaved mica. The sample was analyzed under ambient air using a Veeco's MultiMode V AFM in tapping mode. Simultaneous topographic and phase imaging was carried out at a scanning frequency of 0.5 Hz. The probe was TESP-SS (Super Sharp: 42 N/m, 320 kHz, 2−5 nm ROC, no coating). No image processing except flattening was done.

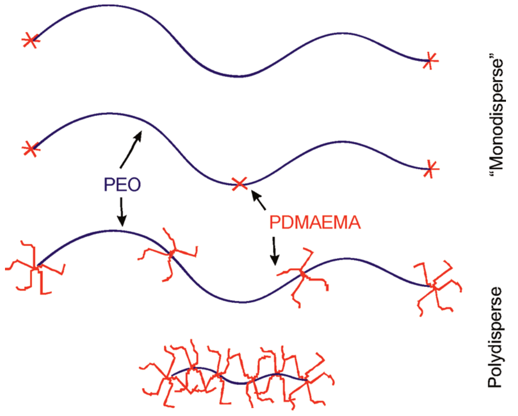
Results and Discussion

We have developed two different approaches in order to prepare linked star polymers (star oligomers), which are threaded along a common backbone. Hereby, we have concentrated on pearl necklace polymers with a poly(ethylene oxide) (PEO) backbone and poly(dimethylaminoethyl methacrylate) (PDMAEMA) side arms. The first approach employs a polycondensation reaction utilizing a Williamson ether synthesis of bismesylated, telechelic PEO macromonomer. The PEO forms a polydisperse multiblock polymer upon mesylate substitution with help of an equimolar amount of a small bifunctional alcohol, possessing further protected hydroxygroups to be released after the condensation reaction. This alcohol was chosen to be dipentaerythritol, partly protected with help of formaldehyde-based acetal (formal) or an acetone-based ketal (see Schemes 2 and 3 and Schemes 1, 2, 4 and 5 in the Supporting Information). After acid catalyzed deprotection, the released hydroxy functions could be modified with initiators for atom transfer radical polymerization (ATRP). Thus, polymerization of dimethylaminoethyl methacrylate (DMAEMA) gave the desired products. Similarly, the second approach employs also a Williamson-type condensation reaction of a preformed, bismesylated PEO, now reacting with an excess of partly protected dipentaerythritol (ketal).

This allows full modification of the end groups. The PEO was prepared by anionic polymerization of ethylene oxide, starting from a bifunctional initiator with four protected hydroxyl functions (dipentaerythritol formal). High molecular weight was targeted, yielding a PEO with interior, protected anchor groups for a star moiety, which is situated in the middle of the chain. Selective deprotection releases the hydroxyl groups for modification with polymer. In contrast to the first approach, we chose to apply an arm-first route in order to obtain high arm-numbers with short arms. This was achieved by a Huisgen 1,3-dipolar cycloaddition ("click chemistry"). Thus, we could obtain star dimers (dumbbell polymer) and trimers as smallest representatives of the pearl necklace (PN) polymers.

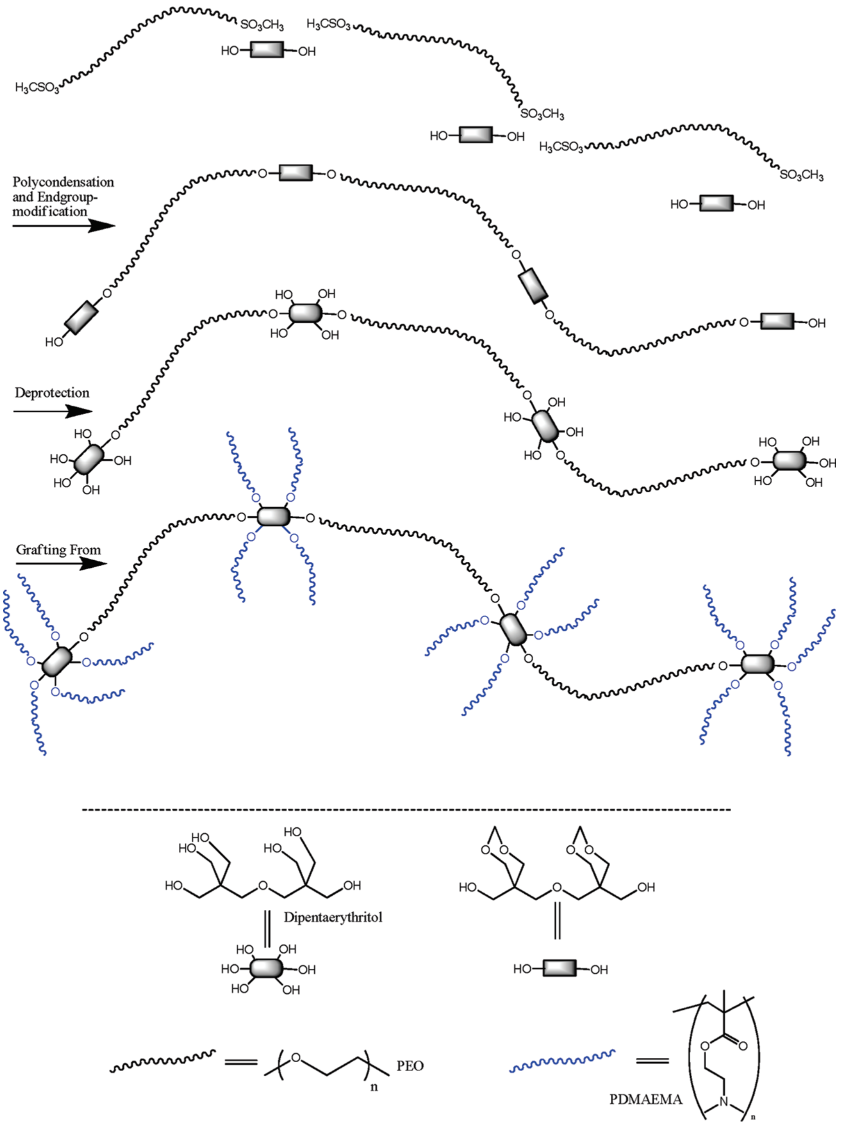
Scheme 3 depicts all the PN polymers prepared and gives also an impression on the dimensions of the products. A comparison of both approaches reveals both advantages and disadvantages. Whereas the first attempt can yield polymers with a high number of stars incorporated into one molecule, the resulting polydisperse product consists of a mixture of different star oligomers. In addition, the spacer molecular weight is limited, when aiming for higher star numbers. This is true, since the polycondensation reaction becomes less and less favorable for increasing PEO molecular weight (equimolarity of reactants is hard to adjust and reaction times get unfavorably long). In contrast, the second approach results in star dimers and trimers, but high molecular weight spacers can be applied without changes in the reactivity. In addition, the resulting polymers are expected to be narrow distributed. In the following we describe in detail the preparation of this new class of polymers

Scheme 3. Representation of Synthesized Pearl Necklace Polymers[a]

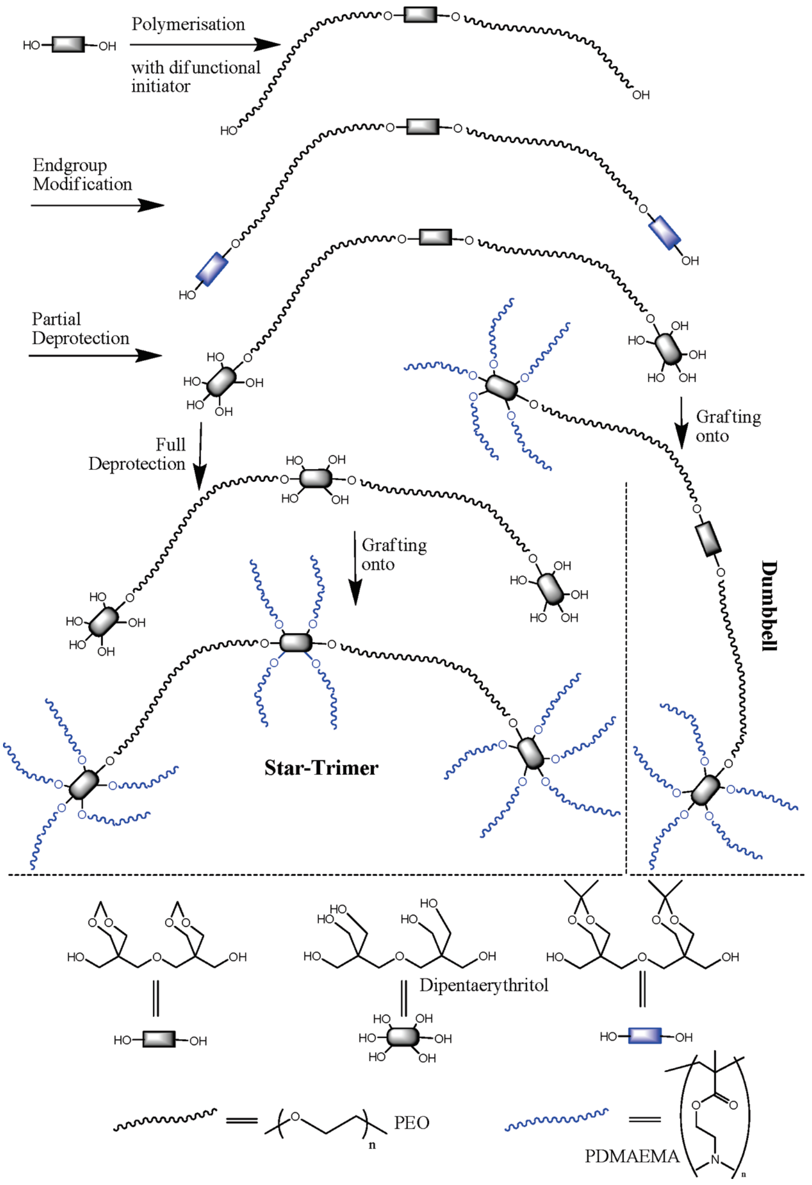


[a] These are drawn approximately to scale; the longer poly(ethylene oxide) (PEO) backbones have degree of polymerizations $P_n \sim 1300$, whereas the shortest poly(dimethylaminoethyl methacrylate) (PDMAEMA) chains have $P_n \sim 19$); the last two polymers were prepared from multiblock PEO prepared by a polycondensation reaction.

Scheme 4. schematic description of preparation pathway toward star oligomers (pearl necklace polymers)



Scheme 5. Schematic Description of Preparation Pathway toward Star Dimers and Trimers



(all steps are summarized in Scheme 1 and 2 and in Table S2 in the Supporting Information). The schematic procedure is given in Scheme 4 and 5.

Synthesis of Pearl Necklace Polymers by Polycondensation Reaction. Above mentioned polycondensation route toward PN polymers (multiple dumbbells) could be successfully performed using a protected acetal of dipentaerythritol (2′,2″,6′,6″-di-*O*-methylene-2,2,6,6-tetrahydroxymethal-4-oxa-1,7-heptandiol), which has been prepared according to literature.[54] This dipentaerythritoldiformal still has two reactive hydroxy groups, suitable for etherification reactions, whereas four hydroxy groups are protected for future anchoring of the initiator moieties for atom transfer radical polymerization (ATRP). A similar procedure has already been used for preparation of miktoarm star polymers.[38,39] Two different hydroxy-telechelic PEO samples ($M_n \sim 4000$ g/mol and 20000 g/mol) were converted into the respective fully mesylated species, similar as described in literature.[55] Then, several attempts were taken to link the dipentaerythritol derivative with the mesylated PEO in dry THF with sodium hydride as base under reflux. E.g. a slow addition of the polymer with help of a syringe pump was tried, in order to achieve at a certain point equimolarity of the reactants. However, this attempt did not give high molecular weight products probably due to ring formation at low polymer concentration. However, when a stoichiometric ratio 1:1 for both reactants was tried to be established already at the beginning of the reaction, we could always see an increase in molecular weight by means of size exclusion chromatography (SEC) (see Figure 2).

Also NMR gives a clear indication of the successful preparation of a multiblock PEO (see Figure 1).

According to SEC, some attempts gave directly multiblock polymers with a number of blocks ranging from 2 up to 40 (see Figure 2). In some cases, remnants of the precursor PEO were still left. The precursor could be removed by fractionated precipitation. Hereby crude PEO product was dissolved in dichloromethane and iterated dropwise addition of *n*-hexane finally led to precipitation of high molecular weight fractions, which were collected. Using only the fractions of the highest molecular weight would allow getting PN polymers with a considerable number of stars. But, the yield of the high molecular fraction is only limited. Therefore, we united the best fractions in order to get a reasonable amount of material for the preparation of PN polymers.

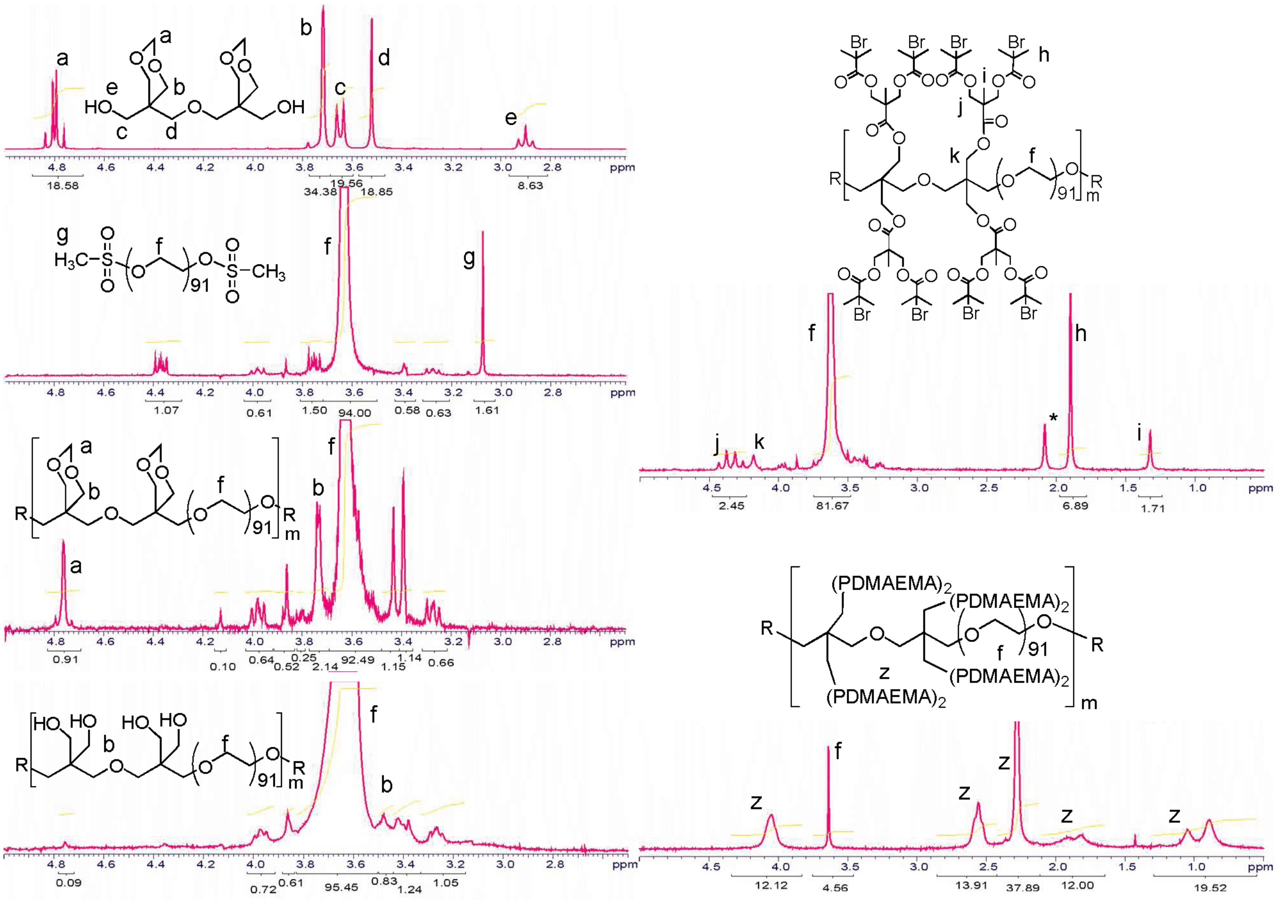


Figure 1. ^{1}H NMR spectra (in $CDCl_3$) of all intermediates toward pearl necklace polymer $[PEO_{91}\text{-}b\text{-}(PDMAEMA_{140})_{3.6}]_4$ (using a polycondensation process) and the final product.

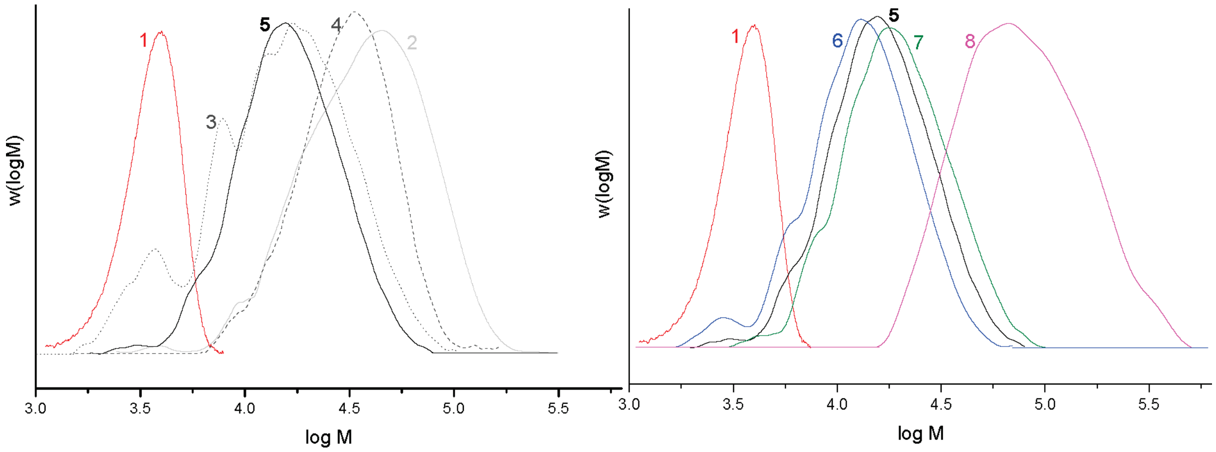


Figure 2. Molecular weight distributions of poly(ethylene oxide) (PEO) derivatives toward pearl necklace (PN) polymers obtained by size exclusion chromatography (PEO standards); left-hand side: multiblock PEO (precursor PEO: number-average molecular weight M_n = 4000 g/mol; red, no. 1) obtained by different attempts; best result for condensation reaction (M_n = 26000 g/mol, polydispersity index PDI = 1.61; in gray, no. 2) and distributions of a bigger batch before (crude product; M_n = 10400 g/mol, PDI = 1.84; dotted, dark gray line, no. 3) and after fractionated precipitation (best fraction: M_n = 23000 g/mol, PDI = 1.31, dashed, dark gray line, no. 4; united good fractions used for further reactions: M_n = 17000 g/mol, PDI = 1.35, black line, no. 5); right-hand side: all the intermediates toward pearl necklace polymer (red, no. 1: precursor PEO M_n = 4000 g/mol; black, no. 5: united good fractions of protected multiblock PEO, M_n = 17000 g/mol, PDI = 1.35; blue, no. 6: deprotected multiblock PEO, M_n = 14000 g/mol, PDI = 1.42; green, no. 7: macroinitiator, M_n = 15000 g/mol, PDI = 1.44; pink, no. 8: PN polymer $[(PDMAEMA_{140})_{3.6}\text{-}b\text{-}PEO_{91}]_4$, M_n = 59000 g/mol, PDI = 1.65).

As a next step, the protecting acetal groups needed to be removed from the polymer in order to get accessible hydroxy groups. This was achieved by treatment of the multiblock PEO with 1 N HCl at 85 °C overnight. Then 90% of the protective groups could be removed without substantial harm to the polymeric backbone, as seen by NMR and as seen by only a minor shift of the molecular weight distribution in SEC (which could be also due to adsorption of OH groups on the column). However, fractionation after deprotection might be the preferable procedure.

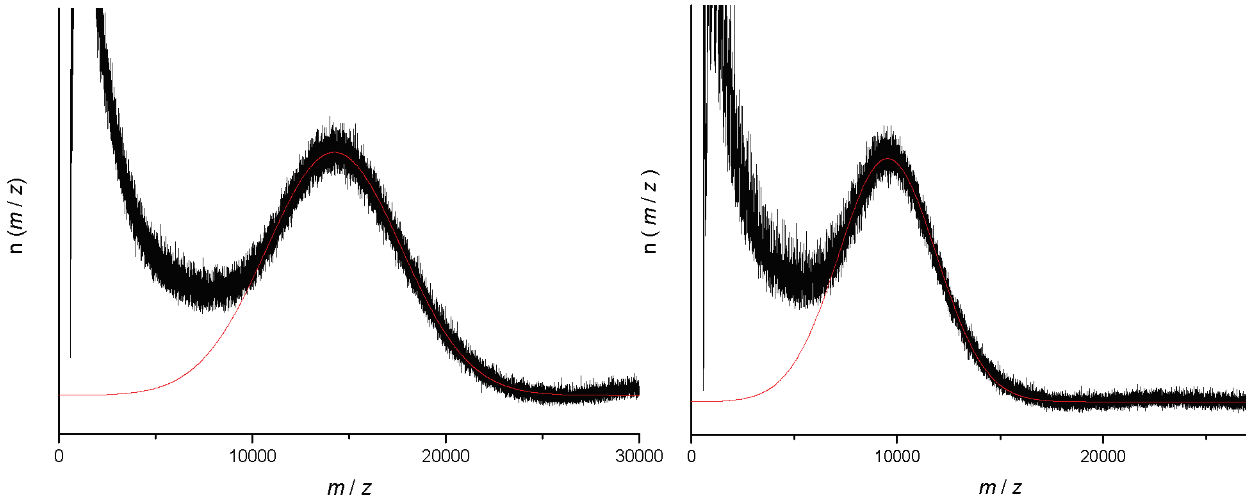


Figure 3. Matrix assisted laser desorption ionization−time-of-flight (MALDI−ToF) mass spectra of cleaved off and modified poly(dimethylaminoethyl methacrylate) (PDMAEMA) arms (equals poly(methyl methacrylate)) of pearl necklace polymers (red curves are Gaussian fits: left-hand side, $[(\mathrm{PDMAEMA}_{140})_{3.6}\text{-}b\text{-}\mathrm{PEO}_{91}]_4$ gives M_n = 14300, P_n = 137, PDI = 1.05; right-hand side, $[(\mathrm{PDMAEMA}_{90})_{3.3}\text{-}b\text{-}\mathrm{PEO}_{460}]_3$ gives M_n = 9500, P_n = 91, PDI = 1.06).

Then the deprotected multiblock PEO was esterificated with a dendritic ATRP initiator fragment, namely 2,2-bis-(2-bromoisobutyroyloxymethyl)propionic acid, using DCC as coupling reagent (see Figure 1). This dendronizing agent, containing two initiation sites per free carboxy group, was prepared according to literature.[53] The advantage of this branched initiating group is the increase in arm number. ^{1}H NMR analysis showed that 75% of all formerly protected hydroxy goups bear a bifunctional initiator moiety after esterification, enabling the grafting of stars with on average six arms. 75% of esterification yield is typical for all those reactions (even at prolonged reaction times), indicating a hindered attack of further acid after partial esterification. The same result was already encountered in the esterification of a diblock PEO with central hydroxy groups.[38]

Those macroinitiators were then used for the ATRP of DMAEMA, yielding a pearl necklace structure with basic pearls (consisting of the weak polyelectrolyte PDMAEMA) and a neutral thread. The polymerizations were performed in anisole to low/medium conversions yielding products with two different spacer lengths (see Table S1, Supporting Information). Assuming full initiation, the expected formulas according to conversion times molar ratio of monomer to initiation sites would be $[(\mathrm{PDMAEMA}_{80})_6\text{-}b\text{-}\mathrm{PEO}_{91}]_4$ and $[(\mathrm{PDMAEMA}_{50})_6\text{-}b\text{-}\mathrm{PEO}_{460}]_3$ (with $[(\mathrm{PDMAEMA}_n)_x\text{-}b\text{-}\mathrm{PEO}_k]_m$ and n assigning number-average degree of polymerization per arm, x assigning number-average arm number per segment, k assigning number-average degree of polymerization of each spacer, and m assigning the number-average star number per molecule). These formulas are slightly simplified, since at both ends of the PN polymer star moieties are expected as well. In addition, a decreased initiation site efficiency is expected, leading to longer arms and a lower arm number per star unit. This was proven by cleavage of the arms and analysis of the arm's molecular weight. After quaternization of PDMAEMA and alkaline hydrolysis of all ester moieties, the resulting poly(methacrylic acid) (PMAA) could be separated from the PEO backbone. The PMAA was methylated and the final poly(methyl methacrylate) (PMMA) was subjected to mass spectrometry (Figure 3). As a result, we found a 40−50% lowered initiation site efficiency. Therefore, the polymers should be assigned following formulas: $[(\mathrm{PDMAEMA}_{140})_{3.6}\text{-}b\text{-}\mathrm{PEO}_{91}]_4$ and $[(\mathrm{PDMAEMA}_{90})_{3.3}\text{-}b\text{-}\mathrm{PEO}_{460}]_3$. The incomplete initiation was observed earlier during preparation of miktoarm stars,[38] since the dendritic initiation fragment can yield only approximately 50% initiation efficiency at the conditions used for PDMAEMA polymerization. Actually, there are even more resemblances between the PN polymers and the miktoarm stars, which were prepared earlier. Those miktoarm stars, which have on average either three or four PDMAEMA and 2 PEO arms, can be regarded as one associating star unit of our pearl necklace polymers.

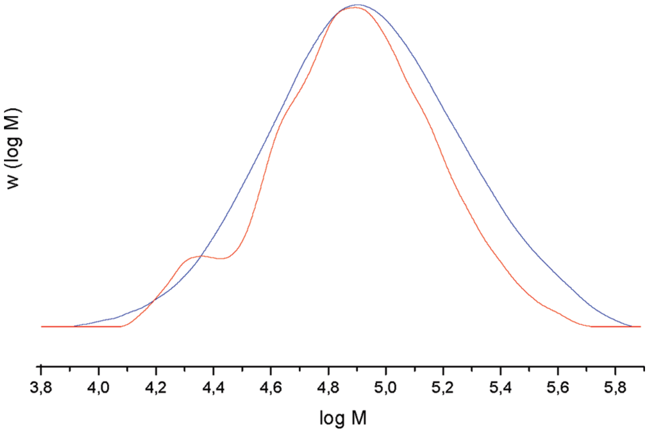


Figure 4. Molecular weight distribution of multiblock poly(ethylene oxide) (PEO) macroinitiator (red; spacer: number-average molecular weight M_n = 20000 g/mol; M_n(SEC; PEO calibration) = 57100 g/mol, polydispersity index PDI(SEC) = 1.65) and of its pearl necklace polymer with poly(dimethylaminoethyl methacrylate) (PDMAEMA) arms $[(\mathrm{PDMAEMA}_{90})_{3.3}\text{-}b\text{-}\mathrm{PEO}_{454}]_3$ (blue; $M_{n,\mathrm{app}}$(SEC; PEO calibration) = 60800 g/mol, $\mathrm{PDI}_{\mathrm{app}}$(SEC, PEO calibration) = 1.77; $M_{n,\mathrm{theo}}$(conversionNMR) = 190000 g/mol); molecular weight distribution was obtained by size exclusion chromatography using PEO standards.

SEC analysis of the PN polymers showed that the hydrodynamic volume grows considerably when just using a small PEO spacer (Figure 2). This is expected, since the polymer occupies a larger volume due to the dense decoration of the backbone with long arms, whose length is almost in the order of the backbone. However using a larger PEO spacer, the overall dimensions of the macromolecule do not change considerably, since the dimensions of the arms are rather small compared to the length of the backbone (see Figure 4). However, the polydispersity increases slightly during ATRP in both cases.

We were also able to visualize quaternized [(PDMAEMA$_{140}$)$_{3.6}$-*b*-PEO$_{91}$]$_4$ by means of atomic force microscopy (AFM) on mica. Structures were seen, where several stars align into one molecule along with star dimers and monomers (Figure 5). The corresponding other polymers could not be visualized as single molecules by AFM probably due to the increased PEO content (only the cationic polyelectrolyte adsorbs strongly to the negatively charged mica surface; the PEO tends to crystallize on the surface, which might aggravate the AFM analysis).

Synthesis of Pearl Necklace Polymers and Dumbbells from Preformed Linker Polymer. As mentioned above, the smallest representatives of PN polymer—star dimer and star trimer—can be obtained by using the same etherification reactions on a PEO with central dipentaerythritol moiety (Scheme 5). This diblock PEO can be obtained by anionic polymerization of ethylene oxide, using partly protected dipentaerythritol (dipentaerythritoldiformal) as a bifunctional initiator. Again, the four protected hydroxy groups can be used for further anchoring of polymer side chains after deprotection. By adjusting the monomer to initiator ratio, we targeted for rather high molecular weight ($M_n \sim$ 60000 g/mol). After termination with acetic acid, the hydroxy-telechelic diblock PEO was mesylated in order to attach on each end additional partly protected dipentaerythritol units using the same Williamson ether synthesis attempt as mentioned above. We also tried to perform the synthesis in equimolar amounts, in order to obtain again multiblock PEOs with high molecular weight spacers (see above). As already mentioned, the polycondensation reaction using PEO macromonomers gets increasingly difficult with increasing molecular weight of the spacer molecule. Therefore, we did not manage to obtain considerable amounts of coupled product. But an excess of dipentaerythritoldiacetoneketal (see also Figure 11 for NMR) allowed full modification of the chain ends.[56] Then we could selectively deprotect the exterior dipentaerythritol units under rather mild conditions in aqueous acetic and formic acid. The selective deprotection is feasible, since the outer acetone-based ketal groups are much more labile than the formaldehyde-based interior acetal groups. The interior acetal groups were then removed by prolonged stirring in formic acid in order to obtain the

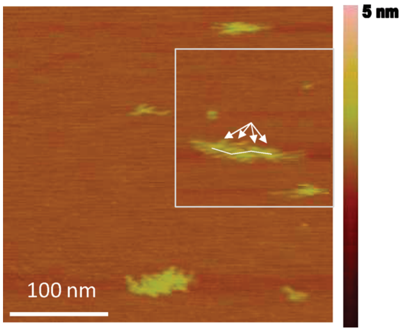


Figure 5. Atomic force microscopy (AFM) height image of quaternized [(PDMAEMA$_{140}$)$_{3.6}$-*b*-PEO$_{91}$]$_4$ (spincasted at 2000 rpm, from 0.0005 g/L solution on mica).

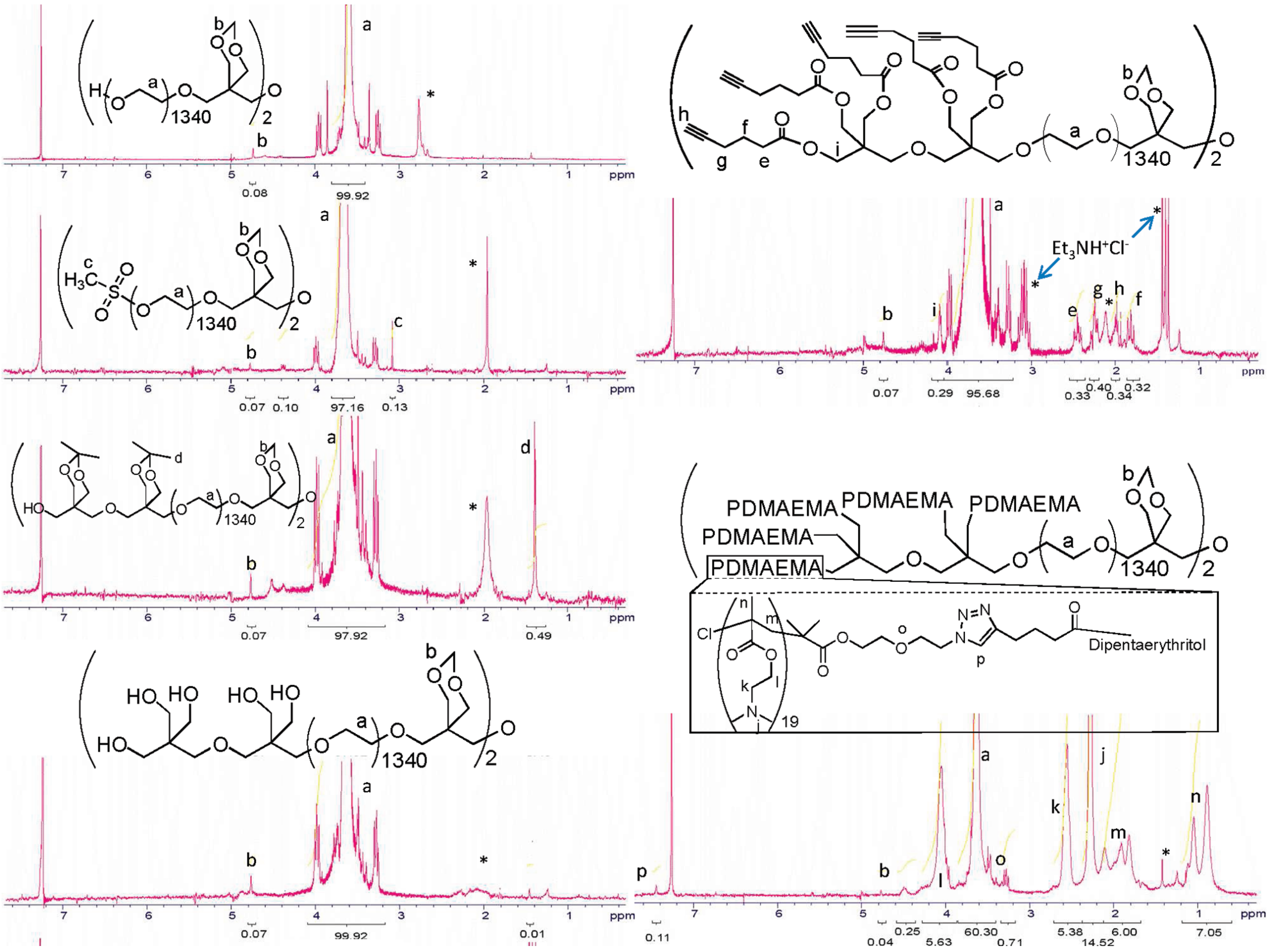


Figure 6. ^{1}H NMR spectra (in CDCl$_3$) of all intermediates toward the dumbbell polymer and the final product (PDMAEMA$_{19}$)$_5$–PEO$_{1340}$–(PDMAEMA$_{19}$)$_5$.

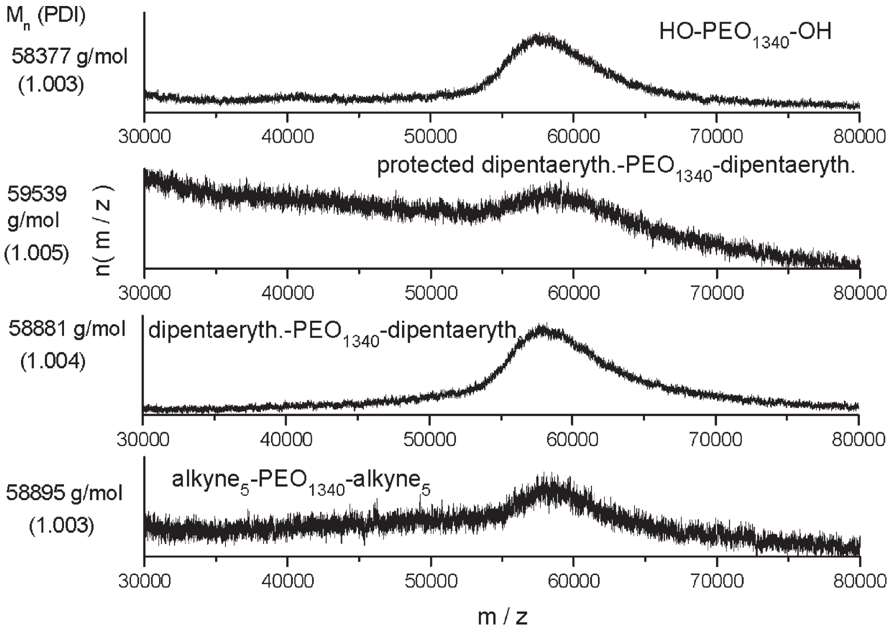


Figure 7. Matrix assisted laser desorption ionization−time-of-flight (MALDI−ToF) mass spectra of poly(ethylene oxide) (PEO) precursors of dumbbell polymer $(PDMAEMA_{19})_5$−PEO_{1340}−$(PDMAEMA_{19})_5$.

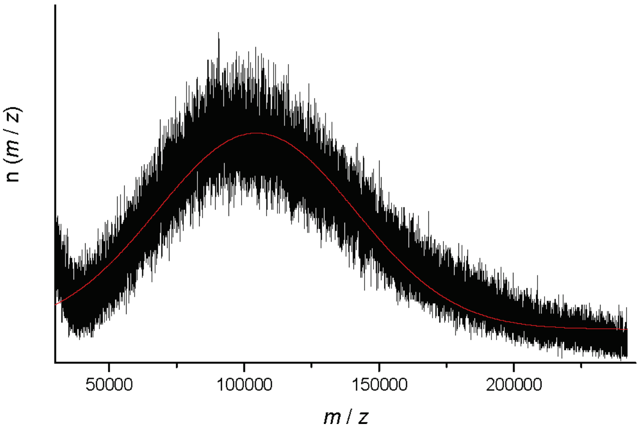


Figure 8. Matrix assisted laser desorption ionization−time-of-flight (MALDI−ToF) mass spectra of $(PDMAEMA_{19})_5$−PEO_{1340}−$(PDMAEMA_{19})_5$ dumbbell polymer (red curve: Gaussian fit yielding number-average molecular weight M_n = 105000 g/mol and polydispersity index PDI = 1.12).

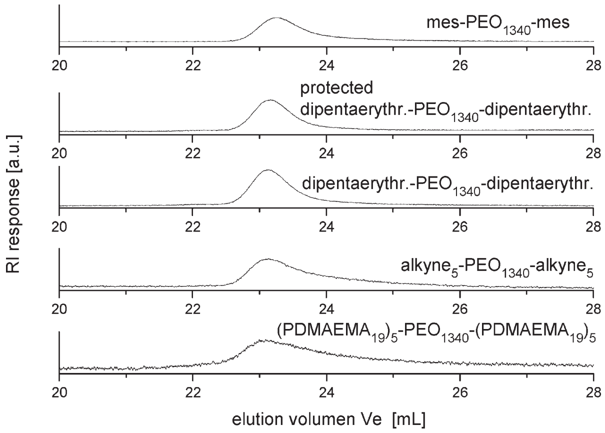


Figure 9. Size exclusion chromatography eluograms of poly(ethylene oxide) (PEO) precursors of dumbbell polymer $(PDMAEMA_{19})_5$−PEO_{1340}−$(PDMAEMA_{19})_5$ together with final product.

precursor for the star trimer. We describe all further modification steps in case of the star dimer (dumbbell). All modifications were followed by ^{1}H NMR (Figure 6).

Hereby one needs to pay special attention to proper phasing and baseline adjustment and of course to the right choice of delay times and pulse widths, since NMR end group analysis becomes increasingly difficult for the molecular weights used. However, the simplicity of PEO NMR spectra with its sharp peak is beneficial for end group analysis. Therefore, the important groups could be easily detected without overlap with PEO. The spectra are compiled in Figure 6. The integrals over the characteristical peaks coincide well with the expected values.

The overall molecular weight was also checked by matrix assisted laser desorption ionization−time-of-flight (MALDI−ToF) mass spectrometry and SEC (Figures 7, 8, and 9).

During all the modifications of the PEO the molecular weight does not change considerably, as seen by mass spectrometry and SEC. MALDI−ToF MS gives a real increase in the molecular weight only for the final dumbbell polymer (Figure 8), whereas the elution volume of the peak value hardly changes in SEC (Figure 9).

These results are expected, taking the long PEO spacer and the short PDMAEMA arms into account. The dumbbell was prepared by introduction of alkyne functions into the end groups of the PEO and consecutive click-coupling of short, azide-functionalized PDMAEMA. The advantage of the “grafting to” of short PDMAEMA is the introduction of a higher arm number, whereas “grafting from” gives usually considerable longer arms and a lower arm number due to lowered initiation site efficiency. Therefore, the deprotected hydroxy functions of the telechelic PEO were reacted with hex-5-ynoyl chloride, yielding five triple bonds on each end. The azide-functionalized PDMAEMA was prepared by ATRP using 2-(2-azidoethoxy)ethyl bromoisobutyrate as initiator. The successful synthesis was proven by SEC, NMR and MALDI−ToF MS (see Figures 10 and 11). We aimed for short chains with low degree of polymerization ($P_n \sim 20$). The final preparation of the dumbbell was established by copper chloride catalyzed Huisgen 1,3-dipolar cycloaddition with a slight excess of linear PDMAEMA.

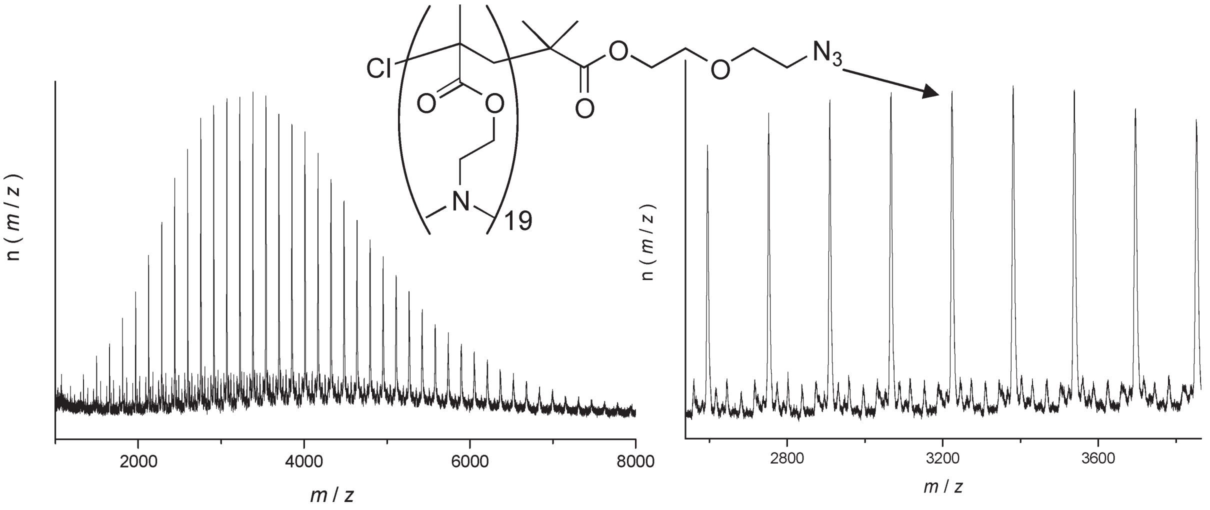


Figure 10. Matrix assisted laser desorption ionization−time-of-flight (MALDI−ToF) mass spectra of linear, azide-modified poly(dimethylaminoethyl methacrylate) (PDMAEMA) arms (number-average molecular weight M_n = 3500 g/mol, polydispersity index PDI = 1.10). Right-hand side: enlargement of spectra (the peak at m/z = 3223 can be assigned to the protonated species with degree of polymerization P_n = 19 and following formula: $C_{160}H_{300}N_{22}O_{41}Cl_1^+$).

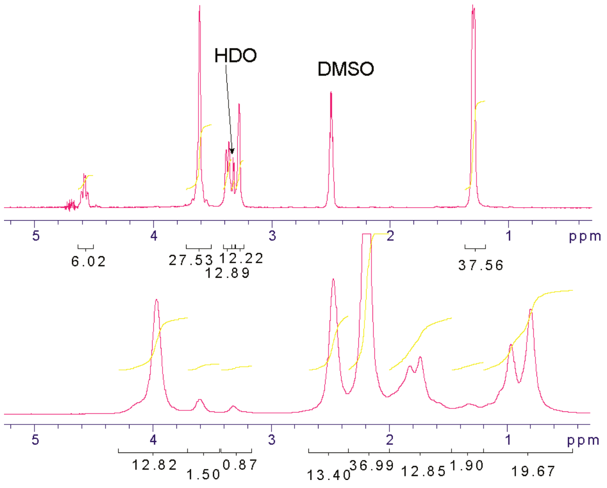


Figure 11. ^{1}H NMR spectra of dipentaerythritoldiacetoneketal (top, in deuterated DMSO) and azide-modified poly(dimethylaminoethyl methacrylate) PDMAEMA$_{19}$ (dissolved in $CDCl_3$).

After separation of unreacted PDMAEMA, the successful preparation of the dumbbells was proven by ^{1}H NMR, showing the development of the aromatic triazole protons in the right integration ratio (Figure 6). This proves high conversion and the attachment of five short PDMAEMA arms on each end. During the reaction, the molecular weight increases by approximately 50%. MALDI−ToF MS showed only one peak with the expected molecular weight (Figure 8). However, according to MALDI−ToF, the polydispersity seems to have slighty increased during the reaction. The reason is not totally clear but the CHCA matrix, which needs to be used for PDMAEMA containing polymers, may have an influence. An increase in polydispersity was also seen in SEC. However, limited adsorption of the PDMAEMA containing polymer might lead to a broadened response in the eluogram, which shows some extent of tailing (which leads to a decreased M_n). In contrast, the peak value only slightly changes as compared to the other polymers (see Figure 9). Hence, one should be aware that the dimensions of the macromolecule hardly change due to the short PDMAEMA arms (see Scheme 3). Actually we have prepared a large polymer ($P_{n,\text{spacer}}$ = 1340) with small polymeric end groups ($P_{n,\text{arm}}$ = 19). The successful synthesis is also corroborated by the molecular weight obtained by osmometry, though it is 40% lower than expected ($M_{n,\text{Osmometry}}$ = 52000 g/mol). By selecting certain injections during the measurement, we could even obtain $M_{n,\text{Osmometry}}$ up to 70000 g/mol. One should be aware that only one left over PDMAEMA chain (M_n ~ 3000 g/mol) per dumbbell (M_n ~ 90000 g/mol) would decrease the molecular weight-average by almost 50%. Since we used an excess of PDMAEMA during click coupling and removed free PDMAEMA after reaction, it is hardly possible to retain 100% of the linear chains. The impurities are in the range of 3 wt %, assuming one leftover PDMAEMA chain per dumbbell. Thus, we have successfully synthesized a star dimer.

Accordingly, we prepared also a star trimer after almost full deprotection of all acetal groups. The interior formal groups were removed upon prolonged treatment of the polymer with formic acid at RT. According to NMR, the conversion was 70% after 5 weeks (see Supporting Information). Short, harsh treatment with 1 M HCl at 85 °C would lead to an almost complete deprotection, but at the same time partial decomposition of the diblock PEO was observed. Thus, the gentle deprotection procedure was preferred. Then, the same steps were performed as for the preparation of the star dimer (dumbbell). Finally, a molecule with an average overall PDMAEMA arm number of 12 was prepared. This and therefore the successful preparation of a pearl necklace polymer with three star-units was evidenced by NMR and SEC (Supporting Information).

Conclusions

Two different approaches for preparation of pearl necklace (PN) polymers with fixed pearls have been developed. Poly(ethylene oxide) (PEO) was used as a thread and poly(dimethylaminoethyl methacrylate) (PDMAEMA) stars were used as pearls. The pearls are threaded along the backbone equidistantly. The first approach, employing a polycondensation reaction of macromonomers, is especially suitable for preparation of PN polymers with higher star numbers (number of pearls) and shorter spacers. This leads to a polydisperse mixture of PN polymers. In contrast, basically unimodal, quasi-monodisperse PN polymers can be obtained by modification of a preformed diblock PEO with an interior dipentaerythritol moiety. This allows the preparation of the smallest representatives of PN molecules in terms of star number (star dimer, which is a dumbbell, and star trimer) with rather long PEO spacers. The attachment of PDMAEMA was either achieved by a "grafting from" approach using ATRP or by a "grafting to" approach using click chemistry. Again, the advantage of the "grafting from" is the introduction of longer PDMAEMA chains, whereas the arm number is usually decreased due to lowered initiation site efficiency. The clicking of short, azide-terminated PDMAEMA is especially feasible for the achievement of a higher arm number.

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Supporting Information Available: Text giving the experimental procedures and discussion of data regarding the star trimer, tables of ATRP reactions and molecular weight characteristics, and figures showing ^{1}H NMR spectra and SEC eluograms. This material is available free of charge via the Internet at http://pubs.acs.org.

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