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Synthesis and investigation of multiblock copolymers and their anionic brush derivatives

SUMMARY OF DOCTORAL DISSERTATION

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VILNIAUS UNIVERSITETAS

FIZINIŲ IR TECHNOLOGIJOS MOKSLŲ CENTRAS

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Multiblokinių kopolimerų ir jų anijoninių šepetinių darinių sintezė bei tyrimas

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1. INTRODUCTION

Relevance of the work. RAFT polymerization, which effectively controls molecular weight and dispersity of the polymers, has been widely used in recent years for the synthesis of block copolymers. For the synthesis of multiblock copolymers, it is necessary to isolate and purify the intermediates (diblock, triblock copolymers, etc.), which reduces efficiency of the synthesis, increases dispersity of the copolymers and reduces functionality of the polymer chain ends. Synthesis of multiblock copolymers can be facilitated by one-pot polymerization methods. Unfortunately, there are only few publications describing the synthesis of multiblock copolymers by one-pot technique, and they concern mainly copolymers with short or very short blocks. In order to synthesize multiblock copolymers with relatively long blocks (degree of polymerization DP 50 or 100), it is necessary to find optimal polymerization conditions (suitable chain transfer agent (CTA), the ratio of CTA to the initiator and the monomer, suitable solvents, reaction temperature, etc.). This is a difficult task that becomes even more difficult if the used monomers are different in their polarity and solubility. The synthesis of block brush copolymers is even more complicated, as it is necessary to evaluate some additional factors, such as conditions for purification and modification of intermediates, interactions between the side chains, formation of polymeric nanostructures, etc.

Development of well - defined multiblock and multiblock brush copolymers with appropriate properties is a real challenge for polymer chemists. Such copolymers are of interest for many applications; for example, stimulus responsive copolymers have high potential in nanotechnology and biomedicine as diagnostic materials, carriers for controlled drug and gene transfer, materials for tissue matrix development in reproductive medicine, etc.

The aim of the present work was to synthesize and investigate amphiphilic and hydrophilic pentablock copolymers and their anionic pentablock brush derivatives bearing poly(acrylic acid) side chains.

The objectives of the research were the following:

1. To find optimal conditions for the RAFT polymerization of methacrylates suitable for the synthesis of block copolymers with relatively long blocks by one-pot RAFT polymerization.
2. To synthesize hydrophilic or amphiphilic triblock and pentablock copolymers with low dispersity.
3. To synthesize anionic pentablock brush copolymers with poly(acrylic acid) (pAA) side chains.
4. Evaluate properties of pentablock copolymers such as thermal transitions, wettability and aggregation in various solvents and water.
5. Evaluate properties of anionic pentablock brush copolymers such as ionization and aggregation in aqueous solutions.

Scientific novelty and practical value

Bifunctional RAFT CTA ethylene glycol di((1-butyl)sulfanylthiocarbonylsulfanyl-4-cyanopentanoate) has been synthesized for the first time which provides polymer chain grow to two directions and good control of one-pot RAFT polymerization of methacrylates (butyl methacrylate (BMA), (2-dimethylamino)ethyl methacrylate (DMAEMA), and 2-hydroxyethyl methacrylate (HEMA)) yielding multiblock copolymers.

Amphiphilic pentablock copolymers containing the blocks of pHEMA and pBMA, and hydrophilic pentablock copolymers containing the blocks of pHEMA and pDMAEMA with DP of each block at least 50 and low dispersity were synthesized via one-pot RAFT polymerisation method for the first time. The properties of pentablock copolymers, including thermal transitions, wettability and aggregation in various solvents and water, were studied.

Anionic pentablock brush copolymers, in which brush blocks are separated by linear hydrophobic blocks, are synthesized using RAFT polymerization method for the first time. The properties of anionic pentablock brush copolymers, including ionization and aggregation in aqueous solutions, were studied.

Defensive statements:

1. One-pot RAFT polymerization carried out in the presence of a bifunctional RAFT CTA, in an appropriate solvent and at appropriate

temperature is a suitable method for the synthesis of pentablock copolymers with low dispersity and relatively long blocks (DP > 50).

2. Hydrophilic pentablock copolymers containing the blocks of pHEMA and pDMAEMA have two aggregation temperatures. Aggregation temperature depends on the position of the pHEMA block and amount of HEMA units in the pentablock copolymer.

3. RAFT *grafting from* is a suitable method for the synthesis of anionic pentablock brush copolymers with low dispersity.

4. Acidic properties of anionic multiblock brush copolymers depend on their architecture and chemical composition.

Approbation of the research results. Results of the research were presented in 4 scientific papers in the journals included into the database of Clarivate Analytics Web of Science. Results were also reported at 5 international conferences.

Structure of the doctoral dissertation. The doctoral dissertation is written in Lithuanian and contains the following chapters: Introduction with the motivation of the research objectives, Literature Survey, Experimental Part, Results and Discussions, Conclusions, List of References (317 entries) and List of Scientific Publications. Materials of the dissertation are laid out in 146 pages, including 16 schemes, 41 figures and 10 tables.

2. MATERIALS AND METHODS

Main materials. 2-Hydroxyethyl methacrylate (HEMA, 96%), 2-(dimethylamino)ethyl methacrylate (DMAEMA, 98%), butyl methacrylate (BMA, 96%) and acrylic acid (AA, 99%) were distilled under reduced pressure before use. Azobisisobutyronitrile (AIBN) was recrystallized from methanol twice. 1,4-Dioxane (DO, ≥95%), dichloromethane (≥99%), and ethylene glycol (≥99%) were purified according to standard procedures. Other reagents were of analytical reagent grade and were used as received.

Synthesis of multiblock copolymers.

HEMA, AIBN and bifunctional RAFT CTA were dissolved in NMP (or in another solvent), the solution was purged with argon for 30 min. and then the flask was sealed with rubber septum. RAFT polymerization was carried out at 65 ºC for appropriate time, and then the flask via gas-tight syringe was replenished by a degassed solution of BMA and AIBN in NMP (or in another solvent). The same procedure of replenishing the flask was repeated before building the third block. At the end of polymerization, the block copolymer was precipitated by pouring the solution into a large amount of hexane/(ethyl acetate) (8/2, v/v) (twice) and dried under vacuum at 20 °C for at least 24 h.

Synthesis of brush copolymers.

pHEMA blocks present in multiblock copolymers were modified by attaching trithiocarbonate (TTC) moieties. The modified multiblock copolymers bearing TTC groups were dissolved in NMP, than the monomer AA and the initiator 4,4′-azobis(4-cyanovaleric acid) were added to the solution. The solution was purged with argon for 30 min, then the flask was sealed with rubber septum. RAFT graft polymerization of AA was carried out at 65 ºC. Multiblock brush copolymer was precipitated by pouring the solution to diethyl ether (twice) and dried under vacuum at room temperature for 24 h.

Characterization of copolymers.

Composition of the copolymers was determined by NMR spectroscopy, molecular weight (M_n) and dispersity (Đ) by SEC with quadruple detection, and thermal transitions by DSC. Aggregation and/or ionization behaviour of multiblock copolymers and their anionic brush derivatives in water were studied by potentiometric titration, DLS and SEM.

3. RESULTS AND DISCUSSIONS

3.1 Synthesis and study of multiblock copolymers

3.1.1. Solvent effect on RAFT polymerization of HEMA, BMA and DMAEMA

Organic solvents - butanol (BuOH), dioxane (DO), *N,N*-dimethyl formamide (DMF), dimethyl sulfoxide (DMSO), isopropanol (*i*-PrOH) and *N*-methyl 2-pyrrolidone (NMP) - were used as media for one-pot RAFT polymerization of HEMA, BMA and DMAEMA. These solvents differ by polarity, viscosity and complexing ability. FT-IR and NMR spectroscopies were used to study interactions in the solutions containing the monomers. Fragments of FT-IR spectra of HEMA and BMA dissolved in several solvents used for one-pot RAFT polymerization are presented in Fig. 1.

FT-IR spectra confirmed, that all the solvents formed complexes with the monomers, which increased electron density on both carbonyl and vinyl double bonds of the methacrylates. Unfortunately, absorption bands of methacrylates were partially overlapping with the absorption bands of NMP and DMF making the effect quantitatively imponderable.

A dependence of the chemical shifts in ^{1}H and ^{13}C NMR spectra attributed to vinyl carbons and vinyl protons on the used solvents proved that solvents had a certain effect on electronic structure of the monomers. A shift upfield indicated an increased electron density on the double bond of a monomer. A monomer with increased electron density on its double bond is considered as less active. On the contrary, activity of the radicals produced from inactive monomers is high, and this could be a determinant factor explaining faster polymerization of HEMA and BMA in NMP compared to DMF.

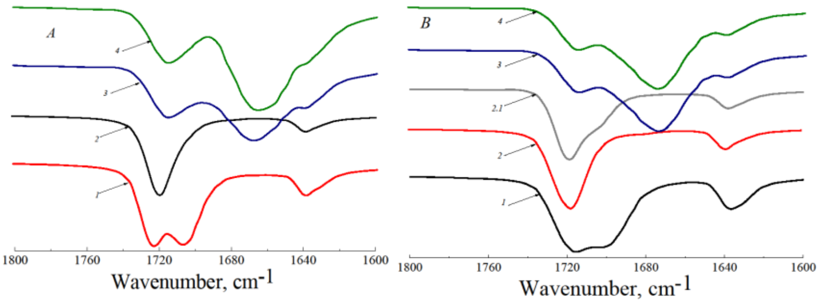


Fig. 1. Fragments of FT-IR spectra (region of carbonyl absorption) of HEMA (A) and BMA (B) in the solutions of BuOH (1), DO (2), DO/BuOH (1/1, v/v) (2.1), DMF (3) and NMP (4).

An alternative explanation of the solvent effect on propagation rate in RAFT polymerization was based on differences in local monomer concentrations. Because of differencies in molar volumes, local monomer concentration in close vicinity to the macroradical chain end is reduced, compared to the bulk conditions, and this effect is more evident using DMF as asolvent. Thus, according to the local monomer concentrations, the fastest polymerisation is expected in NMP and DO, which is in accord with kinetic data.

RAFT polymerization of HEMA mediated by bifunctional RAFT CTA was carried out in several organic solvents in the presence of AIBN as an initiator varying the monomer concentration, temperature, and the ratio of the CTA to the initiator.

Conversion of the monomers during polymerization was monitored by ^{1}H NMR spectroscopy. It was determined that the molar ratio of CTA to the initiator equal to 5/1 was sufficient to efficiently control the RAFT polymerization. Conversion of HEMA during the synthesis of the first block was rather high using any of the selected solvents (Figure 2 A). HEMA polymerization in DMF practically stopped after 15 hours, in DO and BuOH – after 20 hours. RAFT polymerization of HEMA in NMP became very slow at high monomer conversions but was still proceeding reaching nearly 100 mol % conversion. Conversion of BMA during the extention of pHEMA block in NMP was 97 mol % and in BuOH 92 mol % (Fig. 2B).

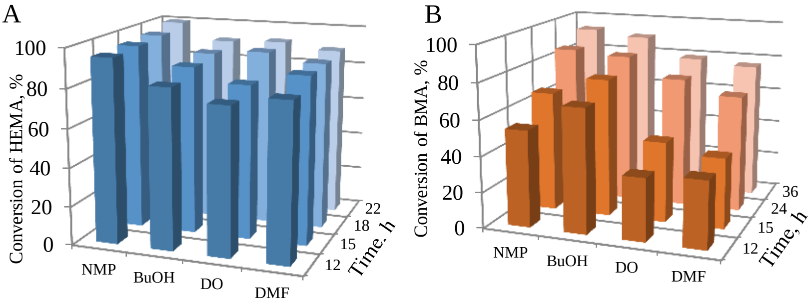


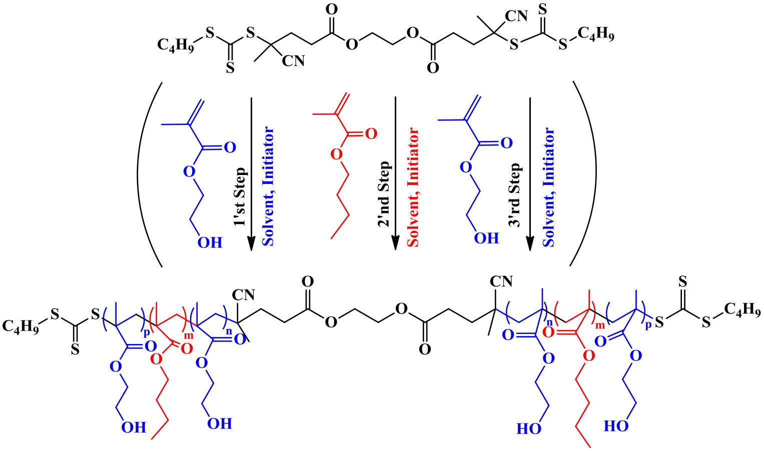
Fig. 2. Conversion of the monomers HEMA (A) and BMA (B) versus time during the first (A) and the second (B) stages of one-pot RAFT polymerization; $[M]_0 = 2.2$ mol/L, T = 65 °C.

RAFT polymerization of DMAEMA was studied in *i*-PrOH, DO, DMSO, and NMP. Irrespective of the solvent used, dispersity of the polymers was low ($Đ < 1.2$). Contrarily, conversion of the monomer after 12 hours of polymerization was solvent dependent, and varied from 59 mol % in *i*-PrOH to 97 mol % in NMP. Very high monomer conversion (over 97 mol %) after 12 hours of polymerization was reached in NMP; similar conversion was in DO as well but after 24 hours of polymerization. An increase of the molar ratio

[DMAEMA]/[CTA] from 50/1 to 80/1 under polymerization in DO had small effect on the monomer conversion but increased dispersity of the polymer.

3.1.2. Synthesis of pentablock copolymers by one-pot RAFT polymerization

Pentablock copolymers were synthesized by one-pot RAFT polymerization in three steps (Scheme 1). At the end of each step, when conversion of a monomer was very high, a new portion of a monomer, initiator and solvent was added, which resulted in extension of the polymer chain. This is a great advantage seeking to prepare triblock BAB or pentablock ABABA copolymers in two or three steps without separation of intermediate products.



Scheme 1. Synthesis of amphiphilic pentablock copolymers by three-step one-pot RAFT polymerization of HEMA and BMA

Results of successive one-pot RAFT polymerization of HEMA and BMA are presented in Table 1. Obviously, the highest conversion of the monomers during all three steps of polymerization was in NMP (96 - 99 mol %). In most of the solvents, the polymerization was well controlled resulting in the copolymers with dispersity Đ in the range 1.11 - 1.29. Molecular weight of the copolymers after each step of polymerization determined by SEC

(Fig. 3) was close to that calculated according to the ratio [CTA]/[I] (Table 1).

Table 1. Results of one-pot successive RAFT polymerization of HEMA and BMA in various solvents yielding homopolymers (1st step), triblock (2nd step) and pentablock (3rd step) copolymers. [M]/[CTA]/[I] = 100/1/0.4, T = 65ºC, $[M]_o$= 2.2 mol L^{-1}

No	Step	Polymer	Solvent	q, mol %	$M_{n,}\cdot10^{-3}$, g/mol	Đ
1	1	$HEMA_{89}$	DMF	89.0	14.5	1.12
	2	BMA_{44}-$HEMA_{89}$-BMA_{44}		87.0	28.9	1.12
	3	$HEMA_{74}$-BMA_{44}-$HEMA_{89}$-BMA_{44}-$HEMA_{74}$		83.5	46.9	1.24
2	1	$HEMA_{100}$	NMP	99.9	16.9	1.10
	2	BMA_{49}-$HEMA_{100}$-BMA_{49}		98.2	23.8	1.16
	3	$HEMA_{94}$-BMA_{49}-$HEMA_{100}$-BMA_{49}-$HEMA_{94}$		96.2	43.1	1.29
3	1	$HEMA_{92}$	DO	91.6	18.2	1.18
	2	BMA_{45}-$HEMA_{92}$-BMA_{45}		89.7	33.2	1.35
	3	$HEMA_{95}$-BMA_{45}-$HEMA_{92}$-BMA_{45}-$HEMA_{95}$		96.7	63.5	1.21
4	1	$HEMA_{96}$	BuOH	95.9	14.9	1.11
	2	BMA_{44}-$HEMA_{96}$-BMA_{44}		89.1	22.5	1.15
	3	$HEMA_{100}$-BMA_{44}-$HEMA_{96}$-BMA_{44}-$HEMA_{100}$		95.2	50.6	1.18

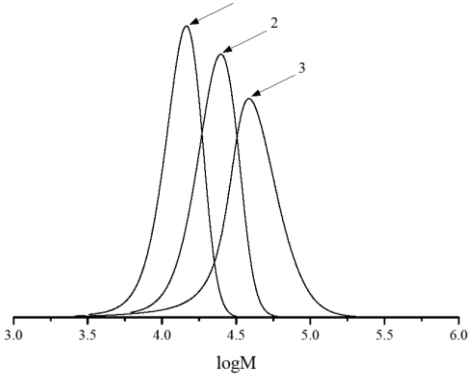
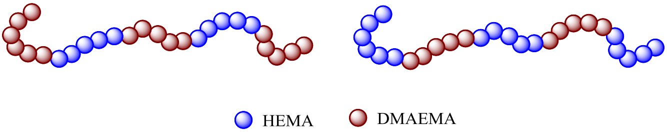


Fig. 3. Molecular weight distribution curves of amphiphilic pentablock copolymers after the first (1), second (2) and third (3) steps of one-pot RAFT polymerization (Table 1, No 2).

Pentablock copolymers with alternating blocks of pBMA and p(BMA-*st*-HEMA) were synthesized and used as the main chain for the synthesis of brush copolymers. During the synthesis of p(BMA-*st*-HEMA), an equimolar ratio of HEMA and BMA was used, and the polymerization was carried out in NMP. Monomers conversion was 96 - 99 mol % in all three steps of the polymerization yielding pentablock copolymers with low dispersity (1.23 - 1.28).

Two types of hydrophilic pentablock copolymers were synthesized - with similar length (DP 50-80) of pHEMA and pDMAEMA blocks and with significantly longer blocks of pDMAEMA (the molar ratio of DMAEMA/HEMA was from 3.5 to 9).



Scheme 2. Hydrophylic pentablock copolymers with different outer blocks.

Synthesis of hydrophilic pentablock copolymers was started either from pHEMA block or from pDMAEMA block giving pentablock copolymers with different outer blocks (Scheme 2). The blocking efficiency during the chain extension from the both pHEMA and pDMAEMA blocks was very similar. In the both cases, monomer conversion was nearly completed within 24 hours during the first and the second steps of polymerizations which is of extraordinary importance getting almost pure blocks of pentablock copolymers. In the third step, conversion of the monomers was lower (in some cases, 81 - 89 mol %) but sufficient to get predicted DP of the block.

During the synthesis of the block copolymers containing longer pDMAEMA blocks (Table 2), HEMA conversion in the first step was almost 100 mol %, but the conversion of DMAEMA in the second step was less than 90 mol %. Low dispersity of the polymers (blocks) and rather good agreement between theoretical and experimental molecular weights confirmed that all steps of successive one-pot RAFT polymerization of DMAEMA and HEMA in NMP were efficiently controlled.

Table 2. Results of one-pot successive RAFT polymerization of HEMA and DMAEMA in NMP yielding homopolymers (1st step), triblock (2nd step) and pentablock (3rd step) copolymers.
T = 65ºC, τ = 24 h, $[M]_o$= 2.2 mol L^{-1}

No	Step	Polymer	q, mol%	$M_{n,}\cdot 10^{-3}$, g/mol	Đ
1	1	pHEMA$_{50}$	99	7.7	1.10
	2	pDMAEMA$_{79}$-pHEMA$_{50}$-pDMAEMA$_{79}$	99	31.3	1.05
	3	pHEMA$_{77}$- pDMAEMA$_{79}$-pHEMA$_{50}$-pDMAEMA$_{79}$-pHEMA$_{77}$	98	48.0	1.19
2	1	pHEMA$_{80}$	99	10.9	1.12
	2	pDMAEMA$_{79}$-pHEMA$_{80}$-pDMAEMA$_{79}$	99	36.6	1.10
	3	pHEMA$_{70}$- pDMAEMA$_{79}$-pHEMA$_{80}$-pDMAEMA$_{79}$-pHEMA$_{70}$	95	57.5	1.17
3	1	pDMAEMA$_{49}$	98	11.2	1.10
	2	pHEMA$_{78}$-pDMAEMA$_{49}$-pHEMA$_{78}$	97	29.1	1.28
	3	pDMAEMA$_{73}$-pHEMA$_{78}$-pDMAEMA$_{49}$-pHEMA$_{78}$-pDMAEMA$_{73}$	95	43.6	1.52
4	1	pDMAEMA$_{78}$	98	12.3	1.12
	2	pHEMA$_{78}$-pDMAEMA$_{78}$-pHEMA$_{78}$	98	33.6	1.34
	3	pDMAEMA$_{71}$-pHEMA$_{78}$-pDMAEMA$_{78}$-pHEMA$_{78}$-pDMAEMA$_{71}$	94	42.3	1.53

3.1.3. Bulk properties of amphiphilic multiblock copolymers

Fig. 4 presents DSC heating curves of pHEMA, pBMA, and diblock and multiblock copolymers containing those blocks. T_g of pBMA was at 25 ºC while that of pHEMA at 44 ºC. The T_g value of the diblock copolymer pHEMA-*b*-pBMA was at 35 ºC and that of the triblock and pentablock copolymers at about 33 ºC. Thus, diblock, triblock and pentablock copolymers showed single glass transition temperature implying that the blocks were fully miscible forming homogeneous amorphous phase. Miscibility of the blocks can be explained by H-bonding between HEMA and BMA units.

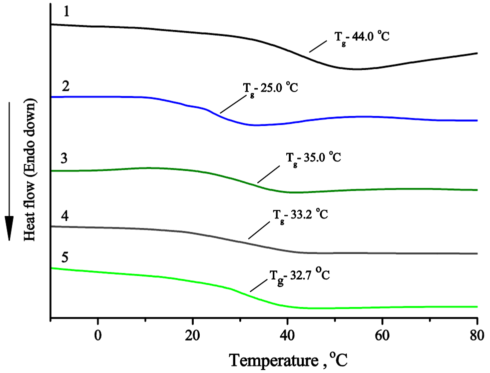


Fig. 4. DSC heating curves of pHEMA (1), pBMA (2) and block copolymers pHEMA-*b*-pBMA (3), pBMA-*b*-pHEMA-*b*-pBMA (4), and pHEMA-*b*-pBMA-*b*-pHEMA-*b*-pBMA-*b*-pHEMA (5).

Water contact angles (CA) on surfaces of homopolymers and block copolymers are presented in Table 3. Evidently, the most hydrophobic surfaces form polymer films cast from chloroform. Polymer films cast from ethanol are the most hydrophilic, and hydrophilicity of the films cast from DMF is medium. CA of pHEMA films is very low (33 to 36°), irrespective of the solvent. CA of pBMA films are much higher, and vary subject to the solvent from 64 to 94°. CA of the diblock copolymer films in most cases are slightly lower compared to pBMA films. The layers of triblock and pentablock copolymers were always slightly more hydrophobic than pBMA layers.

Table 3. Water contact angles (Θ) of the polymer films

Polymer	Θ				
	$CHCl_3$	DMF	Ethanol	Ethanol*	Ethanol**
pBMA	93.7	82.2	63.9	79.0	83.6
pHEMA	-	36.2	33.5	36.5	33.5
pBMA-*b*-pHEMA	92.4	80.7	66.9	73.9	77.0
pBMA-*b*-pHEMA-*b*-pBMA	100.8	86.8	72.3	80.0	85.0
pHEMA-*b*-pBMA-*b*-pHEMA-*b*-pBMA-*b*-pHEMA	100.4	86.3	64.8	85.5	82.3

* After annealing 24 h at 90 °C

** After annealing with CH_2Cl_2 vapour

Additionally, films of amphiphilic block copolymers spin-coated from ethanol solutions were annealed at 90 ºC for 24 hours. During annealing at a temperature higher than T_g of the polymer, mobility of the polymer segments increases. Almost the same results were observed after annealing the films in $CHCl_3$ vapours which swelled the film and effectively reduced T_g of the pBMA blocks. Thus, hydrophobic segments of pBMA can migrate to the air/polymer interface and minimize surface energy which results in increased values of CA.

3.1.4. Solutions properties of hydrophilic pentablock copolymers

In the present research, DLS, zeta potential measurements, and SEM were used to study self-assembly and aggregation of the multiblock copolymers in aqueous solutions upon heating from 15 °C to 65 °C.

Changes in intensity of the scattered light (A) and hydrodynamic radius of the particles (B) of the pentablock copolymers with different outer blocks during heating are presented in Fig. 5. The scattered light profiles and, especially, profiles of the hydrodynamic radius are similar but shifted in the temperature scale by 6 - 8 °C. The first step of aggregation of the pentablock copolymers upon heating starts at 26 °C for the pentablock copolymer with pHEMA outer blocks, and at 36 °C for the pentablock copolymer with pDMAEMA outer blocks (Fig. 5). Above these temperatures, the aggregates with an average hydrodynamic radius of 150 - 200 nm (the copolymer D_{72}-H_{78}-D_{49}-H_{78}-D_{72}) and 400 - 450 nm (the copolymer H_{77}-D_{79}-H_{50}-D_{79}-H_{77}) were formed (Fig 5). At 41 - 44 °C, the aggregates formed by the copolymer with pDMAEMA outer blocks became very large, with hydrodynamic radius of about 1000 - 1500 nm. Upon further heating, above 59 °C for the pentablock copolymer with pHEMA outer blocks and 65 °C for the pentablock copolymer with pDMAEMA outer blocks, intensity of the scattered light was sharply increasing, and large aggregates with the hydrodynamic radius of about 1500 - 2000 nm were formed (Fig. 5).

In order to get more information about temperature-induced self-assembly of the pentablock copolymers, zeta potential of aqueous copolymer solutions was measured at various temperatures, and morphology of the aggregates was evaluated by SEM. At room temperature and at mild heating, zeta potential of the both pentablock copolymers was positive and close to 15 mV. Above 55 °C, zeta potential of both copolymer solutions sharply decreased to -10 mV. A shift of the zeta potential to negative values coincided well with the sharp increase of intensity of the scattered light. SEM analysis of the pentablock copolymer with terminal pDMAEMA blocks revealed that the morphology of self-assemblies of the pentablock copolymer was changing in respect to temperature. At 35 °C, the copolymer formed micellar aggregates with the diameter of 200 - 300 nanometers. At appropriate temperature (42 – 44 °C), multicore aggregates with the size of 2 - 3 micrometers were found. Finally, at 55 °C aggregates with the sizes of about 400 nm were detected.

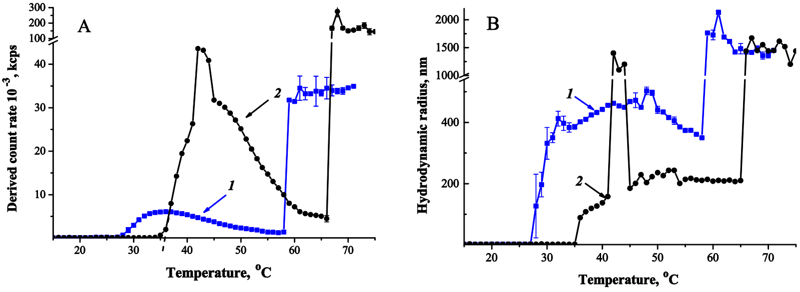
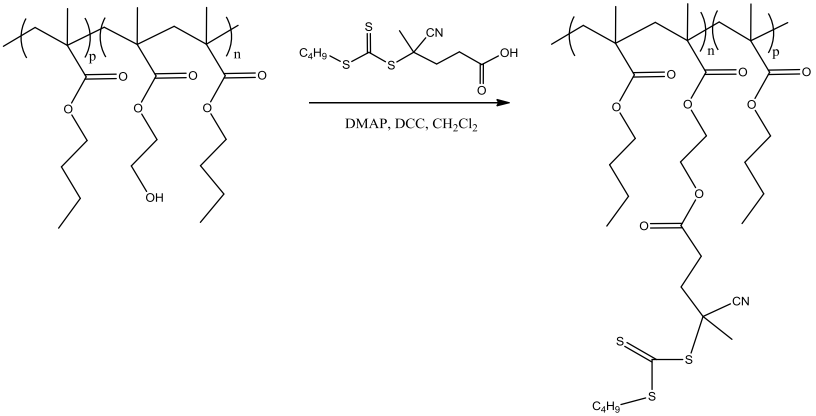


Fig. 5. Changes in intensity of the scattered light (A) and the hydrodynamic radius of the particles (B) of the pentablock copolymers H_{77}-D_{79}-H_{50}-D_{79}-H_{77} (1) and D_{72}-H_{78}-D_{49}-H_{78}-D_{72} (2) during heating.

3.2 Synthesis and study of multiblock brush copolymers

3.2.1. Decoration” of block copolymers by butylthiocarbonothioylthio groups

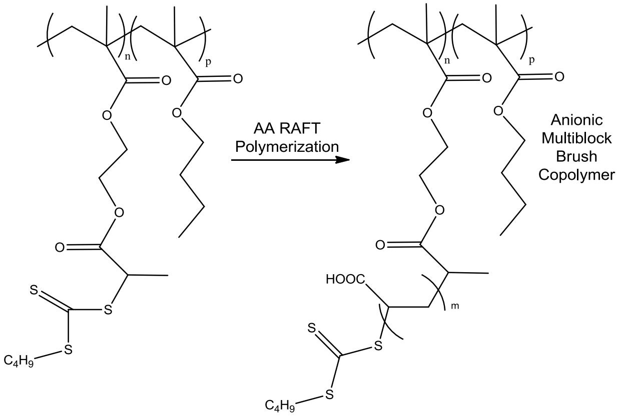
Modification of pHEMA blocks of multiblock copolymers by butylthiocarbonothioylthio fragments was carried out in two ways. The first one is based on esterification of pHEMA hydroxyl groups with 2-bromopropionyl bromide followed by substitution of the bromine atoms in the esterified derivatives with butylthiocarbonothioylthio groups. The second one is carbodiimide catalyzed esterification reaction between pHEMA hydroxyl groups and CTA carboxyl groups (Scheme 3). It was confirmed by ^{1}H NMR spectra that conversion of hydroxyl groups to trithiocarbonate (TTC) moieties in both cases was very high, nearly 100 %.



Scheme 3. Carbodiimide catalyzed esterification reaction between pHEMA hydroxyl groups and CTA carboxyl groups

3.2.2. Synthesis of multiblock brush copolymers containing poly(acrylic acid) side chains

Pentablock copolymers carrying TTC moieties attached by the first way have been used for RAFT *grafting from* polymerization of AA in order to prepare anionic molecular brushes (Scheme 4). At relatively low conversion of AA (about 20%), molecular weight distribution of the pentablock brush copolymers was rather narrow (Đ 1.7 - 2.3), and number average molecular weight M_n was close to that calculated according to the reaction scheme. At high conversion of AA (71.0 %), dispersity of copolymer was very large (Đ 3.3) and MWD curve broad showing considerable fractions of the macromolecules both with relatively low and very high molecular weights. The presence of the polymer fraction with very high molecular weight is related to intermacromolecular coupling reactions. Possibly, intermolecular chain coupling is unavoidable when polymer chains are growing in close vicinity one to another from the same backbone.



Scheme 4. Synthesis of anionic pentablock copolymers via RAFT *grafting from* method

Pentablock copolymers with alternating pBMA and p(BMA-*st*-HEMA) blocks decorated with TTC moieties by carbodiimide method also served as backbone for the synthesis of brush copolymers. The use of random copolymers p(BMA-*st*-HEMA) instead of pHEMA allowed to rarefy hydroxyl group carrying units and increase the distance between growing pAA chains. Further, trying to avoid intermacromolecular coupling reactions, an additional amount of CTA was added into the polymerization mixture.

Table 4. Parameters of anionic multiblock brush copolymers synthesized by *grafting from* RAFT polymerization of AA

No	pAA			Block brush copolymers				pK_a
	M_n g/mol	DP	Đ	$M_{theor.}$ g/mol	M_n g/mol	Đ	[1]φ_{AA} %	
1	800	8	1.19	187000	190000	1.28	33.8	5.27
2	860	9	1.22	139000	51000	1.50	40.0	4.87
3	1060	11	1.43	159000	177000	1.15	28.5	4.99
4	1100	12	1.37	292000	261000	1.22	55.0	5.55
5	1970	24	1.30	217000	419000	1.87	52.0	5.53
6	1780	21	1.44	240000	229000	1.33		

[1] The amount of AA, determined by potentiometric titration

The parameters of anionic multiblock brush copolymers are presented in Table 4. RAFT *grafting from* polymerization of AA was well controlled resulting in brush copolymers with rather low dispersity (Đ 1.15 - 1.87) and symmetrical and monomodal MWD curves.

3.2.3 Ionisation behaviour of multiblock brush copolymers

The degree of ionization of weak polyelectrolytes depends on the degree of neutralization, α, and therefore on pH. To compare the ionization behaviour of the multiblock brush copolymers with different length of pAA side chains, diluted solutions of these polyelectrolytes were titrated potentiometrically.

The curves of potentiometric titration of aqueous solutions of anionic multiblock brush copolymers (Table 4, No 1, 3, 4) are presented in Fig. 6.

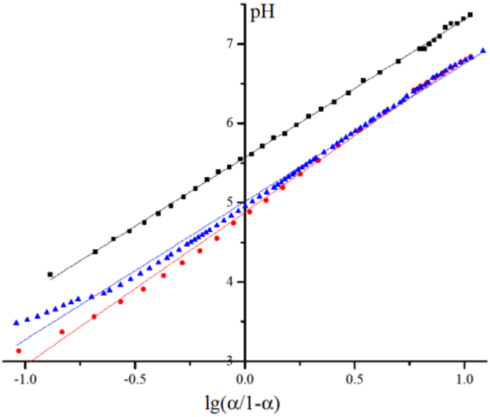


Fig. 6. The curves of potentiometric titration of aqueous solutions of anionic multiblock brush copolymers No 1 (●), No 3 (▲) and No 4 (■) (Table 4) plotted in the coordinates of the equation of Henderson and Hasselbalch.

Pentablock brush copolymer (Table 4, No 4) demonstrates a much weaker acidic properties (pK(α) is higher) compared to the triblock brush copolymer carrying nearly the same amount of pAA side chains of the same length (Table 4, No. 3) However, acidic properties of the triblock brush copolymer (Table 4, No 3) and pentablock brush copolymer with shorter pAA side chains (Table 4, No 1) are very similar (pK(α) values are close). Thus, acidic properties of multiblock brush copolymers are affected by their architecture and chemical composition.

The dependence of hydrodynamic radius (R_h) of anionic pentablock brush copolymers on the degree of neutralization (α) is presented in Fig. 7. In acidic medium most carboxyl groups are non-ionized ($\alpha < 0.05$). At such conditions, pentablock brush copolymers with relatively short pAA side chains are in compact coil conformation, with hydrodynamic diameter of the coils about 55 - 60 nm. At complete neutralization ($\alpha = 1$) of pAA carboxyl groups, pentablock brush copolymers are stretched, obtain cylindrical shape, and the size of the brush copolymers increases to 90 - 170 nm. Brush copolymers with similar length of pAA side chains (DP $\approx$ 8, Table 4, No 1 and 2), but different length of linear pBMA blocks form aggregates similar in size.

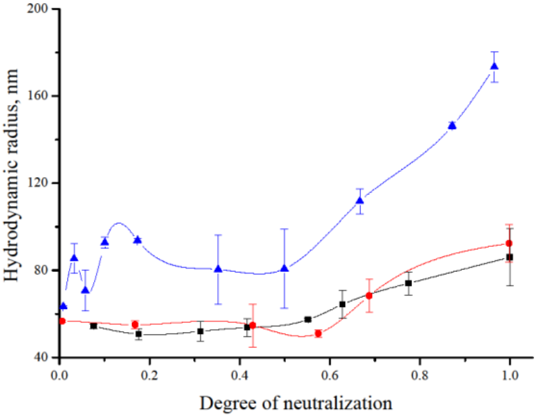


Fig. 7. The dependence of hydrodynamic radius on degree of neutralization of anionic pentablock brush copolymers No 1 (●), No 2 (■) and No 4 (▲) (Table 4).

CONCLUSIONS

1. The effect of four organic solvents - *N*,*N*-dimethyl formamide (DMF), *N*-methyl-2-pyrrolidone (NMP), 1,4-dioxane (DO) and butanol (BuOH) - on interactions inside reaction media and RAFT polymerisation of HEMA, BMA and DMAEMA was investigated by NMR and FT-IR spectroscopy, and kinetic methods. It was determined that polymerisation of methacrylates was the fastest in NMP where nearly full monomer conversion (97 - 99 mol %) was reached during 12 hours. Rate of polymerization of HEMA in NMP was more than twice, and that of BMA fourfold higher than in DMF. The effect of organic solvents on RAFT polymerisation of methacrylates is in accord with the theory of local monomer concentrations, but taking into account complexation of the monomers.
2. Amphiphilic pentablock copolymers containing units of HEMA and BMA were synthesized by one-pot RAFT polymerization in the presence of a difunctional RAFT CTA. The optimal solvent for the synthesis of multiblock copolymers was NMP, in which 96-99 mol % monomer conversion in every step of polymerization was achieved during 12 hours. Using other solvents, the monomer conversion was lower and insufficient to obtain well defined blocks during the synthesis of multiblock copolymers by one-pot RAFT polymerization. Pentablock copolymers were characterized by low dispersity (Đ 1,11 - 1,29) and contained negligible amount of HEMA units (1 - 2) in pBMA blocks.
3. Hydrophilic pentablock copolymers with iterative blocks of pHEMA and pDMAEMA were synthesized by one-pot RAFT polymerization. It was determined during the chain extension that almost all polymer chains remained „living“ even after third step of polymerization. Dispersity of hydrophilic pentablock copolymers synthesized in NMP, irrespective of the nature of the end blocks, was low (Đ 1,17 - 1,19).
4. Compatibility of pHEMA and pBMA blocks constituting amphiphilic multiblock copolymers is good. These copolymers have a single glass transition temperature which decreases upon increase of pBMA amount in the copolymers. The films of the

triblock and pentablock copolymers are more hydrophobic compared to those of pBMA and diblock copolymers.

5. Amphiphilic multiblock copolymers are soluble in DMSO but tend to form nanoaggregates in chloroform. In mixtures of organic solvents and deuterated water, the multiblock copolymers form micellar aggregates with outer hydrophilic corona. In mixtures of DMSO and deuterated water, pentablock copolymers with outer hydrophilic (pHEMA) blocks formed compact nanoaggregates of flower-like shape, and pentablock copolymers with outer hydrophobic (pBMA) blocks formed larger multicore aggregates.
6. Aqueous solutions of hydrophilic pentablock copolymers constituted of alternating pHEMA and pDMAEMA blocks demonstrated two aggregation temperatures at 26 - 36 °C and 59 - 65 °C, which were dependent on block position and amount of HEMA units. Pentablock copolymers with pHEMA outer blocks formed micellar aggregates of flower-like shape which upon increase of temperature became more uniform and smaller in size. Pentablock copolymers with pDMAEMA outer blocks formed micellar aggregates with intermicellar bridges which merged together to multicore aggregates at higher temperatures. Upon further heating, above 59 - 65 °C, poorly stabilized micellar aggregates of the pentablock copolymers stuck together forming very large aggregates with the diameter of ~2 μm.
7. For the decoration of the multiblock copolymers by butylthiocarbonothioylthio moieties, two methods were applied: two-step nucleophilic substitution reaction and carbodiimide catalysed esterification reaction. The carbodiimide catalysed reaction was superior since it was single-phase and faster, and the degree of modification of pHEMA hydroxyl groups was close to 100 %. During modification of the copolymers by nucleophilic substitution, some side reactions took place which resulted in partial crosslinking.
8. Anionic pentablock brush copolymers were synthesized differing in molecular weight (51 - 540 kg/mol) and length of pAA side chains (DP 4 - 41). Brush copolymers synthesized in the presence of multiCTA obtained by nucleophilic substitution reaction had high dispersity (Đ 1.66 - 3.2) and, in many cases, asymmetric MWD curves. Brush copolymers derived from the

pentablock copolymers with alternating pBMA and p(BMA-*st*-HEMA) blocks modified by carbodiimide method, had relatively low dispersity (Đ 1.15 - 1.87) and symmetric MWD curves. Although anionic brush copolymers derived from hydrophilic multiblock copolymers were visually soluble in organic solvents and water, they formed nanoaggregates with $R_h > 25$ nm.

9. Acidic properties of anionic multiblock brush copolymers depend on copolymer architecture and chemical composition. Pentablock brush copolymers with similar length and amount of pAA side chains are weaker acids compared to triblock brush copolymers of similar structure. It has been determined by DLS, that upon increase of the degree of neutralization, pentablock brush copolymers with longer side chains become more hydrophobic and form larger aggregates.

LIST OF SCIENTIFIC PUBLICATIONS ON THE THEME OF DISSERTATION

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1. T. Krivorotova, J. Jonikaite-Svegzdiene, P. Radzevicius, R. Makuska, Synthesis by RAFT polymerization and properties of anionic cylindrical molecular brushes bearing poly(acrylic acid) side chains, Reactive & Functional Polymers, 2014, 76, P. 32–40.

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Thesis of the international scientific conferences

1. P. Radzevičius, M. Steponavičiūtė, T. Krivorotova, R. Makuška, Synthesis of hydrophilic multiblock copolymers by one-pot RAFT copolymerization. *Programme and Proceedings of Baltic Polymer Symposium 2015*, Sigulda, Latvia, 2015.

2. P. Radzevičius, T. Krivorotova, R. Makuška. Solvent effect on molecular characteristics of multiblock copolymers synthesized by one-pot RAFT polymerization, *Baltic Polymer Symposium 2016, Programme and Abstracts*. Klaipėda, Lithuania, 2016.

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4. P. Radzevičius, T. Krivorotova, M. Steponavičiūte, M. Melinskas, R. Makuška. Synthesis by one-pot RAFT polymerization and study of stimuli responsive amphiphilic and hydrophilic ionizable pentablock copolymers. *Baltic Polymer Symposium 2017*. Tallinn, Estonia, 2017.

5. P. Radzevicius, M. Steponaviciute, T. Krivorotova, R. Makuska. Self-assembly in aqueous solutions of thermoresponsive pentablock copolymers synthesized by one-pot RAFT polymerization. *Baltic Polymer Symposium 2018*. Riga, Latvia, 2018.

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SANTRAUKA

Blokinių kopolimerų sintezei pastaruoju metu plačiai taikoma RAFT polimerizacija, kurią naudojant pavyksta efektyviai kontroliuoti blokų molekulinę masę ir jų dispersiškumą. Multiblokinių kopolimerų sintezės efektyvumas padidėja, naudojant “vieno indo” (angl. “*one pot*”) polimerizaciją, tačiau taikant šį metodą dažniausiai apsiribojama multiblokinių kopolimerų su trumpais ar labai trumpais blokais sinteze. Siekiant susintetinti multiblokinius kopolimerus su santykinai ilgais blokais, būtina parinkti optimalias polimerizacijos sąlygas – tinkamą grandinės perdavos agentą (GPA), jo santykį su monomeru ir iniciatoriumi, tirpiklį, temperatūrą, ir pan. Blokinių šepetinių kopolimerų sintezė dar sudėtingesnė, nes reikia įvertinti tarpinių produktų gryninimo bei modifikavimo sąlygas, sąveikas tarp šoninių grandinių, polimerinių nanostruktūrų susidarymą ir kt. Tikslios struktūros multiblokinių ir blokinių šepetinių kopolimerų sintezės metodikų kūrimas bei šių kopolimerų savybių tyrimas yra svarbūs, nes tokie kopolimerai gali būti naudojami nanotechnologijose ir biomedicinoje, pvz., kaip diagnostinės medžiagos, nešikliai kontroliuojamai vaistų ir genų pernašai ir kt.

Pagrindinis šio darbo tikslas – susintetinti „vieno indo“ RAFT polimerizacijos metodu ir ištirti hidrofilinius ir amfifilinius pentablokinius kopolimerus bei anijoninius šepetinius jų darinius.

Svarbiausi šio darbo rezultatai, atspindintys naujumą, originalumą ir svarbą:

Pirmą kartą ištirta tirpiklių įtaka metakrilatų RAFT polimerizacijai. Pirmą kartą naudojant difunkcinį RAFT GPA “vieno indo” RAFT polimerizacijos metodu susintetinti mažo dispersiškumo amfifiliniai pentablokiniai HEMA ir BMA kopolimerai ir hidrofiliniai pentablokiniai HEMA ir DMAEMA kopolimerai. Optimalus tirpiklis tokių multiblokinių kopolimerų sintezei yra NMP. Monomerų konversija kiekvienoje polimerizacijos stadijoje (sintetinant kiekvieną bloką) siekia 96 – 99 mol %, be to, dauguma kopolimero grandinių išlieka "gyvybingos" visą polimerizacijos laiką.

Multiblokinių amfifilinių kopolimerų pHEMA ir pBMA blokai yra tarpusavyje gerai suderinami, mikrofazės neatsiskiria. Tokie kopolimerai turi vieną stiklėjimo temperatūrą, kuri mažėja didėjant pBMA kiekiui kopolimeruose. Triblokinių ir pentablokinių kopolimerų plėvelės yra hidrofobiškesnės nei pBMA ir diblokinių kopolimerų plėvelės.

Pirmą kartą nustatyta, kad pentablokiniai hidrofiliniai kopolimerai, sudaryti iš pHEMA ir pDMAEMA blokų, turi dvi agregacijos temperatūras ties 26 – 36 °C ir 59 – 65 °C; agregacijos temperatūra priklauso nuo pHEMA bloko padėties ir HEMA grandžių kiekio pentablokiniame kopolimere. Temperatūrai pakilus virš 59 – 65 °C, silpnai stabilizuoti pentablokinių kopolimerų miceliniai agregatai sulimpa tarpusavyje ir sudaro labai didelius agregatus, kurių skersmuo ~2 μm.

Pirmą karta *skiepijimo nuo* būdu susintetinti mažo dispersiškumo anijoniniai pentablokiniai šepetiniai kopolimerai, besiskiriantys šoninių pAR grandinių ilgiu (PL 7 – 24). Optimalūs šepetinių kopolimerų rodikliai gauti naudojant pentablokinius kopolimerus su alternuojančiais pBMA ir p(BMA-*st*-HEMA) blokais, modifikuotais TTK grupėmis karbodiimidiniu būdu ir į reakcijos mišinį papildomai įdėjus mažamolekulio GPA.

Anijoninių šepetinių multiblokinių kopolimerų rūgštinės savybės priklauso nuo jų struktūros bei cheminės sudėties. Panašų šoninių pAR grandinių ilgį ir jų skaičių turinčio šepetinio pentablokinio kopolimero rūgštinės savybės yra silpnesnės nei analogiškos struktūros šepetinio triblokinio kopolimero.

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