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Guanidine and Biguanide Modified Adsorptive Antimicrobial Blockcopolymers

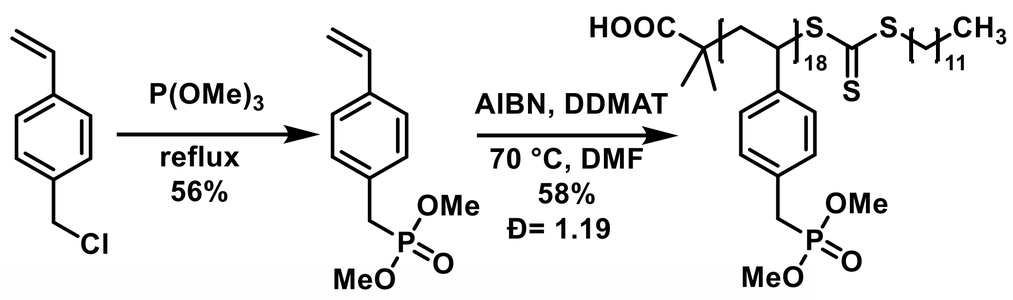
Motivation and Aim

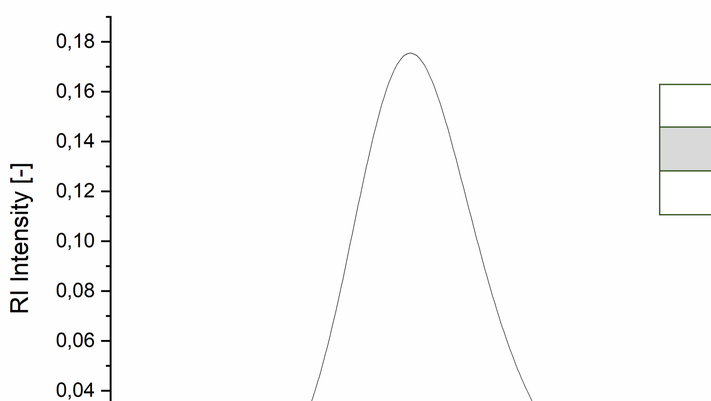
Due to over- and misuse of common antibiotics an increased development of resistance in pathogens has been observed, often resulting in difficulties treating respective infections. Antimicrobial polymers, designed to mimic natural antimicrobial peptides, have shown promising results regarding gram-positive and negative bacterial strains with resistances towards antibiotics. One important field of application are dental implants. Since dental implants don't have a fibrous connection to the surrounding gum tissue, gaps start to form, which are prone for infections. By coating the titanium socket with an adsorptive antimicrobial polymer, infections and the following treatment with antibiotics can be prevented. Since guanidine and biguanide moieties show antimicrobial activity on their own and phosphonic acids are established molecular anchors for titanium surfaces, they are promising candidates for such polymers.[1-4]

Figure 1: Comparison between a healthy tooth and the socket of a dental implant.

Synthesis Concept

a) Phosphonic Acid Block

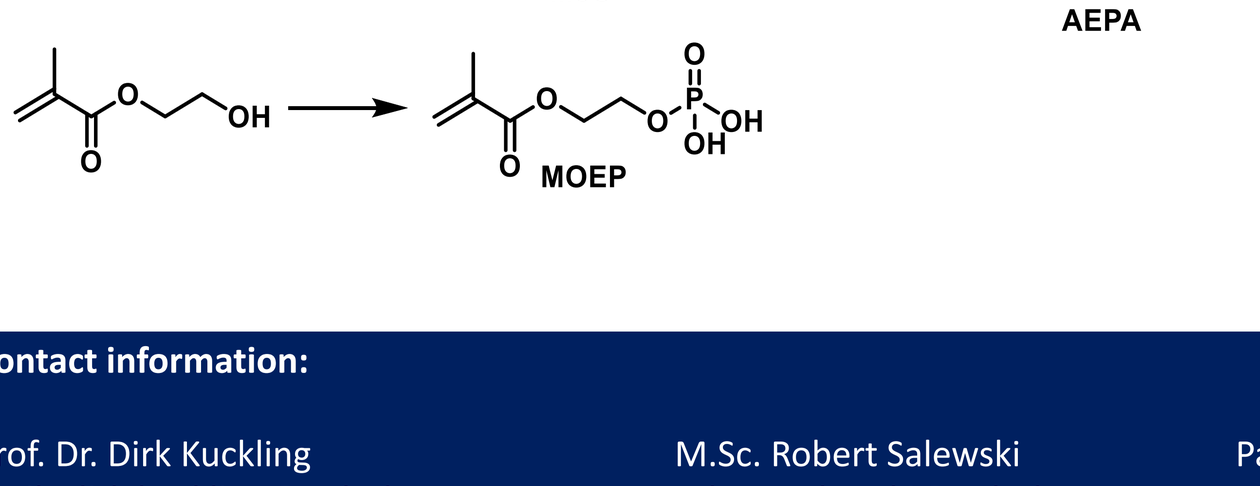




M_n	2400 g/mol
M_w	2800 g/mol
Đ	1.19

Figure 2: Synthesis and SEC curve of Polydimethylvinylbenzylphosphonate (P-DMVBP) in HFIP with BHT as internal standard and a PMMA calibration curve.

The synthesized P(DMVBP) can be used as a macro-CTA for further RAFT polymerisations to add the antimicrobial block. However, the purification procedure is tedious and the phosphonic ester needs to be hydrolyzed. In the future, different phosphonic or phosphoric acid based monomers are planned to be polymerised as well.



b) Guanidine Based Monomers

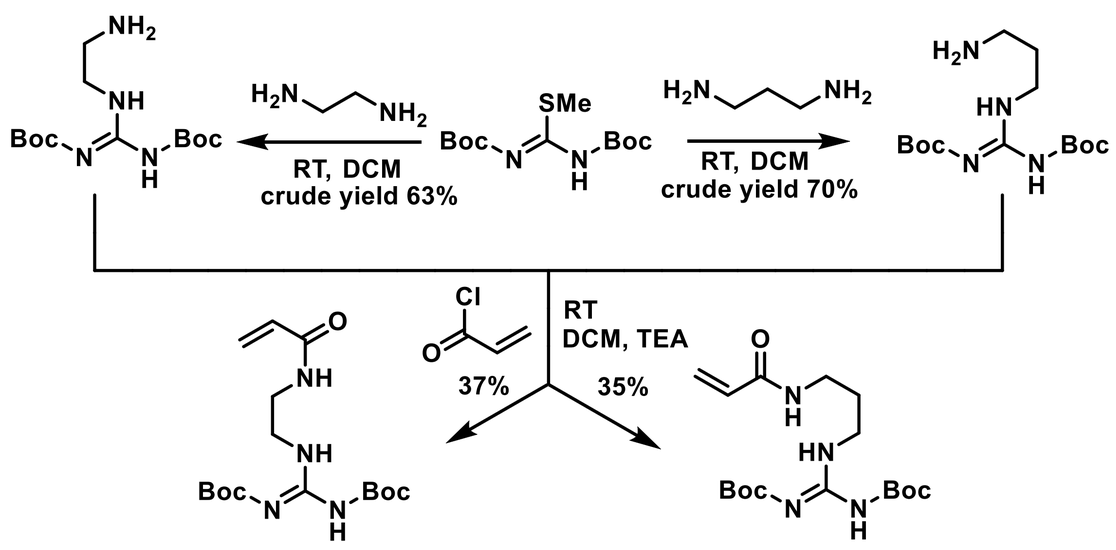


Figure 3: Synthesis of Diboc-GEA and Diboc-GPA published by *Martin et al. (2018).*

According to the procedure of *Martin et al. (2018)* DiBoc-GEA was synthesized. Based on these results, propylenediamine was used to synthesize DiBoc-GPA. By copolymerising both monomers with the already existing phosphonic acid based macro-CTA, a diblockcopolymer can potentially be synthesized. After a simultanious hydrolysis of the phosphonic ester and deprotection of the guanidine moiety the polymer has the potential to show antimicrobial activity and can be grafted onto titantium surfaces. By varying the length of the alkyl chain of the guanidine monomer, the influence on the antimicrobial activity can be determined.

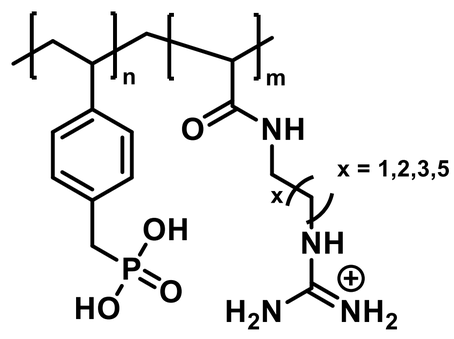


Figure 4: Concept of the block copolymer containing a guanidine-modified block with varying alkyl chain lengths, a phosphonic acid-based anchor block.

c) Biguanidine Based Monomers

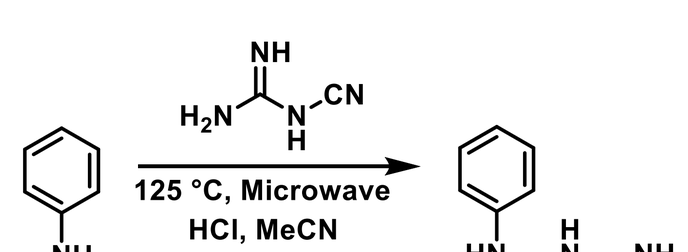


Figure 5: Microwave-assisted conversion of aniline into phenylbiguanidine utilizing concentrated hydrogen chloride and cyanoguanidine.

Based on the successful microwave-assisted conversion of aniline it is planned to conduct the same synthesis with different aniline derivatives that allow for the addition of a vinylgroup.

Figure 6: Concept of microwave-assisted two-step synthesis of *p*-biguanidine-phenyl acrylate

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[2] Methling, R.; Greiter M., Al-Zwaity J.; Müller, M.; Schönherr, H.; Kuckling, D., Salt-Responsive Switchable Block Copolymer Brushes with Antibacterial and Antifouling Properties, Macromol. Biosci. 2025, 25, 2400261. DOI:10.1002/mabi.202400261
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[4] Zhang, H.; Liu, Y.; Luo, T.; Zhao, Q.; Cui, K.; Huang, J.; Jiang, T.; Ma, Z., Synthesis of novel guanidine-based ABA triblock copolymers and their antimicrobial honeycomb films, Polym. Chem., 2018, 9. DOI:10.1039/C8PY00732B.

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