Oxime Cross-Linkable, Dopamine Containing, Adhesive Polymeric Brushes via ROMP for Biomedical Applications

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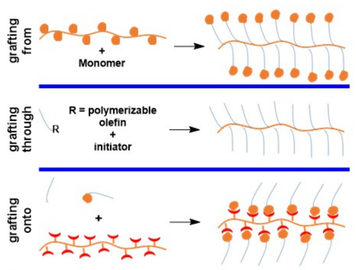
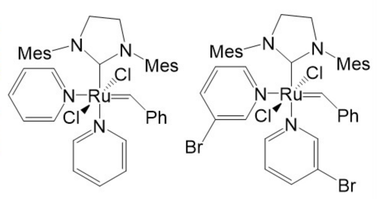
Background Information on Key Features of Design

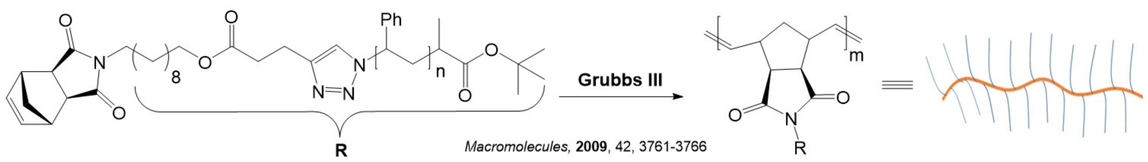
Brush polymers can be prepared using "grafting through". "grafting from" and "grafting onto approaches. Macromonomer approach (grafting through) provides the best degree of control over the exact chemical structure. Grubbs 3rd generation catalysts are currently most effective in achieving these transformations.



Chem Ing. Tech., **2014**, 86, 12, 2195-2214

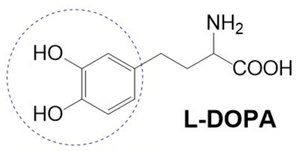


Grubbs 3rd generation catalysts commonly used in grafting through approach



Macromolecules, **2009**, 42, 3761-3766

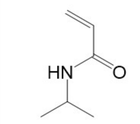
Source: https://en.wikipedia.org/wiki/Mussel
Content: image of *Mytillus sp.*



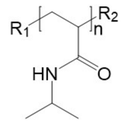
adhesive catechol component

L-DOPA

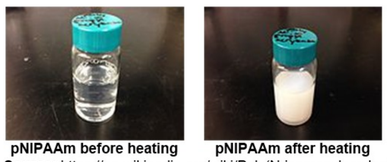
Sea mussels from genus *Mytillus* produce adherent mussel-foot-proteins (Mfp's), which contain amino acid L-DOPA. Catechol group in L-DOPA helps mussels to adhere to surfaces under water.This discovery inspired the use of catechol synthetic adhesives by many research groups.



N-isopropylacrylamide



poly-N-isopropylacrylamide (pNIPAAm)



pNIPAAm before heating **pNIPAAm after heating**
Source: https://en.wikipedia.org/wiki/Poly(N-isopropylacrylamide)

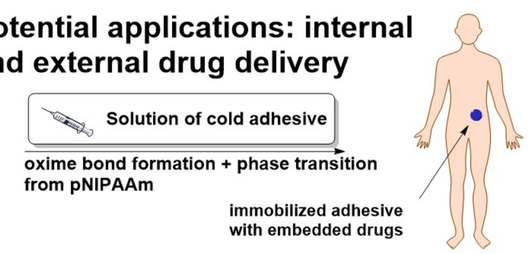
Content: pNIPAAm prepared via RAFT

Solution of Poly-N-isopropylacrylamide can act as thermosensitive hydrogel which has a lower critial solution temperature (LCST) of ~32ºC. It can expell whater and undergo phase transition when heated above LCST. The fact that LCST of pNIPAAm is higher than room temperature, but lower than human body temperature makes it attractive for biological application since the phase transition can occur at body temperature, but the solution can potentially be stored at room temperature.

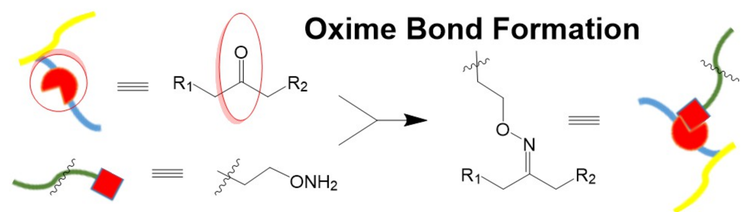
Design of Adhesive

Bioadhesives are important class of polymers which are either derived from or used in biological sys- tems. To make the use of adhesives efficient for internal delivery of drugs it desirable to have adhesives that are liquid before administration (i. e. can be injected via syringe) and become more stiff after injection, since this would ensure that the drug stays localized in the target location. We use rational design approach to solve this problem. Our proposed brush polymer has terminal catechol groups to enhance adhesion, pNIPAAm as a side chain of the bush to provide source for physical crosslinking and an additional ketone close to the oore of the brush to provide additional crosslinking via oxime bond formation.

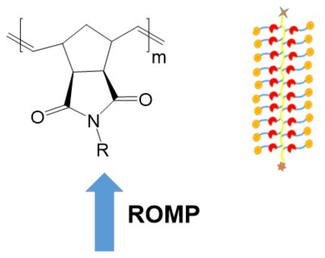
Potential applications: internal and external drug delivery



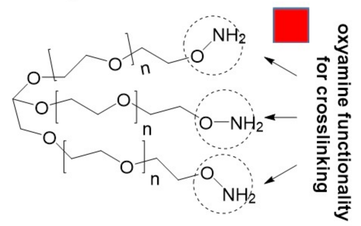
Oxime Bond Formation

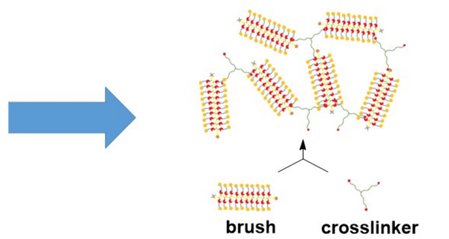


Multifunctional Brush



Oxyamine Crosslinker





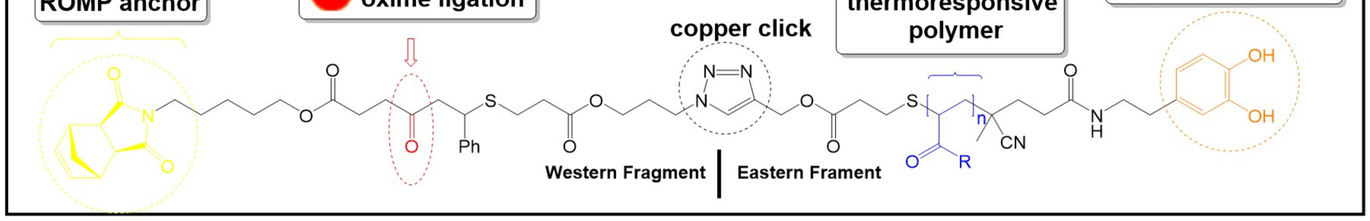
ROMP anchor

ketone for oxime ligation

Macromonomer

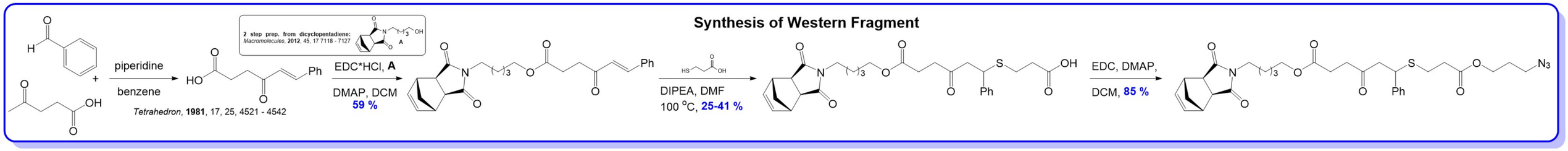
thermoresponsive polymer

catechol based adhesion



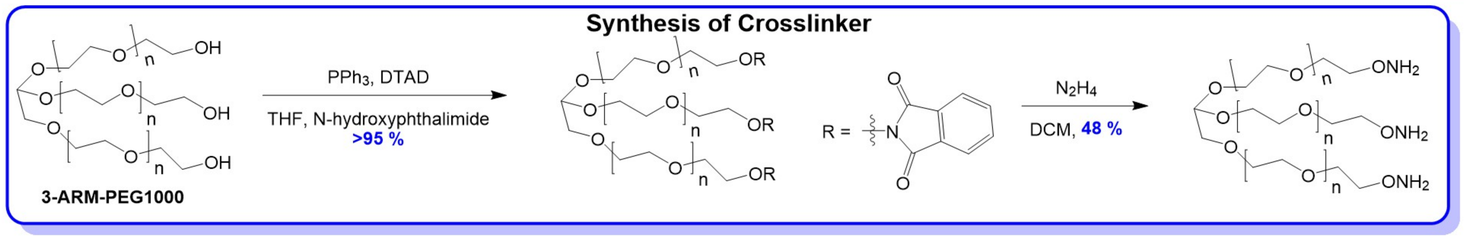
Progress Towards The Synthesis of the Brushes

Synthesis of Western Fragment

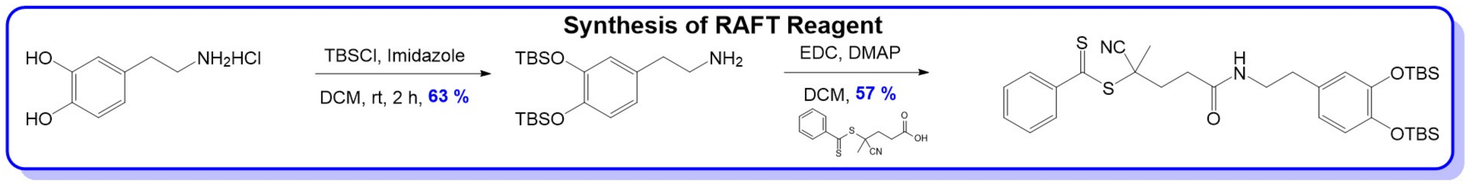


Tetrahedron, **1981**, 17, 25, 4521 - 4542

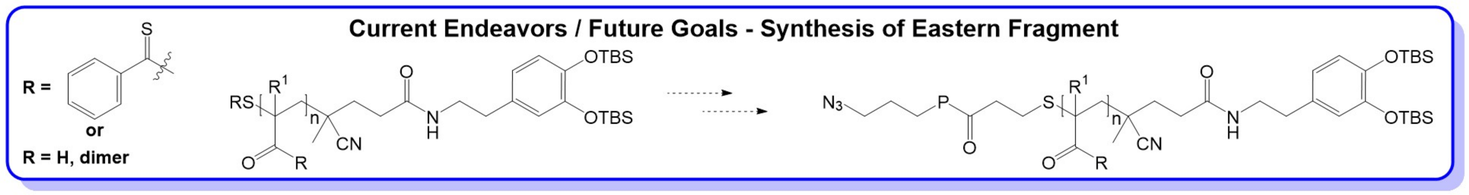
Synthesis of Crosslinker



Synthesis of RAFT Reagent



Current Endeavors / Future Goals - Synthesis of Eastern Fragment



Synthesis of Polymers