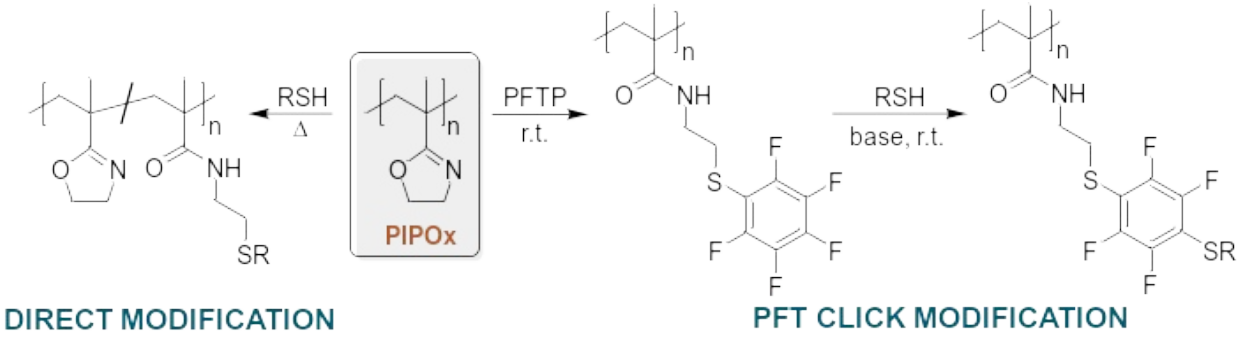
Synthesis of Functional (Co)Polymers Through the Post-Polymerization Modification of Poly(2-Isopropenyl-2-Oxazoline) with Thiols

S. Gupta, M. Janata, A. Mahun, V. Raus*

Institute of Macromolecular Chemistry, Czech Academy of Sciences, Heyrovského nám. 2, 162 00, Prague 6, Czech Republic
**raus@imc.cas.cz*

The great potential of poly(2-isopropenyl-2-oxazoline) (PIPOx) as a versatile platform for post-polymerization modifications has been recently realized.[1,2] Well-defined PIPOx can be prepared via different polymerization methods from a commercial monomer,[3] and the polymer features many favorable characteristics, including solubility in both water and organic solvents, thermal and hydrolytic stability, non-cytotoxicity, biocompatibility, and immunomodulation and non-fouling properties. Importantly, PIPOx provides catalyst- and byproduct-free, orthogonal ring-opening addition reactions, yielding functional poly(methacrylamide)s that find important applications, particularly in the biomedical field.[2] However, until recently, only relatively sluggish PIPOx reactions with carboxylic acids have been routinely exploited.

In this contribution, we will present the significant extension of the PIPOx post-polymerization modification platform in two directions. Firstly, we will summarize the results of our very recent comprehensive investigation of PIPOx reactivity with aliphatic and aromatic thiols, revealing that these reactions are dramatically accelerated in water, affording high degrees of modification faster and/or under milder reaction conditions than in organic solvents.[4] Secondly, we will demonstrate for the first time that the clean and rapid reaction with 2,3,4,5,6-pentafluorothiophenol transforms PIPOx into a highly reactive precursor for efficient *para*-fluoro-thiol (PFT) click reactions.[5] Within both these directions, we evaluated in detail the reactivity of a wide range of commercially available thiols, showing that numerous useful functionalities (e.g. charged groups, fluorescent tags, polymers, amino acids, peptides...) can be easily introduced into the polymeric precursor in an orthogonal fashion while maintaining a high degree of stoichiometric control over the composition of the final functional (co)polymer. These developments make the PIPOx platform an ideal tool for precision synthesis of large functional (co)polymer libraries.



Scheme 1. Synthesis of functional poly(methacrylamides) via PIPOx modification with thiols.

References

[1] Kopka, B.; Kost, B.; Basko, M. Poly(2-isopropenyl-2-oxazoline) as a reactive polymer for materials development. *Polym. Chem.* **2022**, *13 (33)*, 4736-4746.

[2] Kronek, J.; Minarčíková, A.; Kroneková, Z.; Majerčíková, M.; Strasser, P.; Teasdale, I. Poly(2-isopropenyl-2-oxazoline) as a Versatile Functional Polymer for Biomedical Applications. *Polymers* **2024**, *16 (12)*, 1708.

[3] Raus, V.; Hološ, A.; Kronek, J.; Mosnáček, J. Well-Defined Linear and Grafted Poly(2-isopropenyl-2-oxazoline)s Prepared via Copper-Mediated Reversible-Deactivation Radical Polymerization Methods. *Macromolecules* **2020**, *53 (6)*, 2077-2087.

[4] Gupta, S.; Janata, M.; Raus, V. Postpolymerization Modification of Poly(2-isopropenyl-2-oxazoline) with Thiols: Scope and Solvent Effects. *Macromolecules* **2025**, 58 (4), 2125–2134.

[5] Gupta, S.; Mahun, A.; Janata, M.; Raus, V. *Manuscript in preparation.*