Special Considerations in Polymer-Polymer Conjugation via Radical Thiol-Ene and Thiol-Yne Reactions

Benjamin D. Fairbanks¹,², Kristi S. Anseth¹,³ and Christopher N. Bowman¹

¹University of Colorado, Department of Chemical and Biological Engineering
²CSIRO Materials Science and Engineering
³Howard Hughes Medical Institute

Block copolymers are often prepared by sequential chain polymerization reactions, although often such an approach is precluded because of incompatible polymerization mechanisms and reaction conditions. Highly efficient “click” reactions, such as the azide alkyne cycloaddition¹ and thiol-maleimide Michael addition², have been employed to couple preformed polymer blocks together, permitting the synthesis of novel copolymers. While the radical thiol-ene reaction has been shown to be robust and efficient in bulk polymerizations, post polymerization conjugation has been attempted and heretofore proven ineffective³. Herein we demonstrate the successful conjugation of polymer chains via radical thiol-ene and thiol-yne additions initiated photochemically and via reduction oxidation. Reactions are performed in solution, in non-purged atmosphere and at ambient temperatures. All reactive groups on polymers are stoichiometrically balanced (1:1 thiol:ene or 2:1 thiol:yne). Reactions were monitored via proton NMR and products analyzed by dynamic light scattering. We demonstrate that particular considerations must be made when performing the radical thiol-ene reactions in dilute conditions, including appropriate alkene selection and initiator concentration. Conjugation of thiol modified poly(ethylene glycol) (PEG) to norbornene or pentynoate modified PEG is achieved with 93% (Fig. 1) and 85% π bond conversion respectively. Disubstituted polycaprolactone (PCL) was employed to synthesize PEG-PCL-PEG triblock copolymer with > 90% conversion. These results demonstrate that the radical thiol-ene and thiol-yne reactions can be applied as a tool for polymer-polymer conjugation.

![Figure 1](image_url)

**Figure 1.** Depletion of norbornene-associated proton peaks and simultaneous and proportional emergence of proton alpha to sulfur on thioether product following reaction of PEG-thiol with PEG-norbornene. Photochemically initiated (red) and reduction oxidation initiated (blue).


Benjamin Fairbanks
Research Associate
University of Colorado, Department of Chemical and Biological Engineering, USA

OCE Post-Doctoral Fellow
CSIRO Materials Science and Engineering, Australia
Phone: 1+ 303 492 2997  E-mail: bend@ou.edu