Alternative Hydrogen Sulfide Delivery Molecule for Oxidative Stress Mitigation: Synthesis of t-butyloxycarbonyl-protected thioglutamic acid

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Research Background

- Tissue engineering technologies are based on this biological triad and consist of:
  - A scaffold promotes tissue's physical form
  - Cells that will form the tissue
  - Biological signalling mechanisms (such as growth factors, bioreactors, or simple signaling molecules.

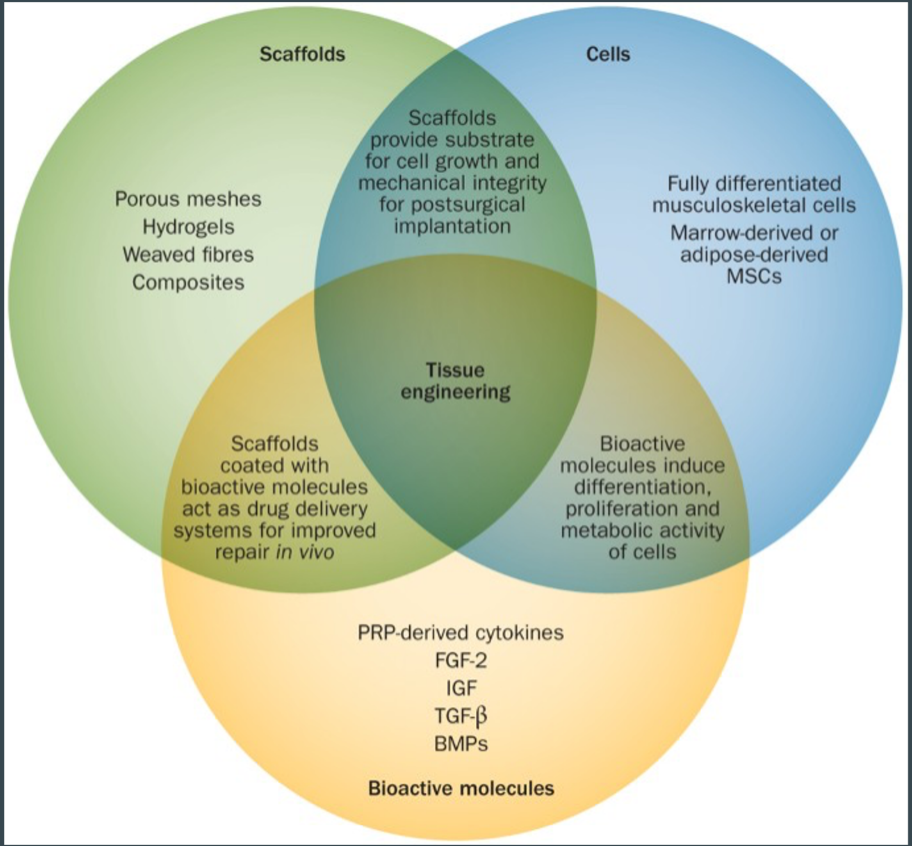


Image adapted from Smith, B., Grande, D. The current state of scaffolds for musculoskeletal regenerative applications. *Nat Rev Rheumatol* **11,** 213–222 (2015). https://doi.org/10.1038/nrrheum.2015.27

Research Background Cont.

- Hydrogen sulfide (H2S) has been shown as a novel neuro-modulator and neuroprotective agent
- Prospects of synthetic degradable polymer glutamate polyester and polyanhydride backbone
- Previously demonstrated H2S releasing molecule Thioglutamic acid (GluSH)

Research Goal: To develop a new synthesis pathway to enable monomer creation.

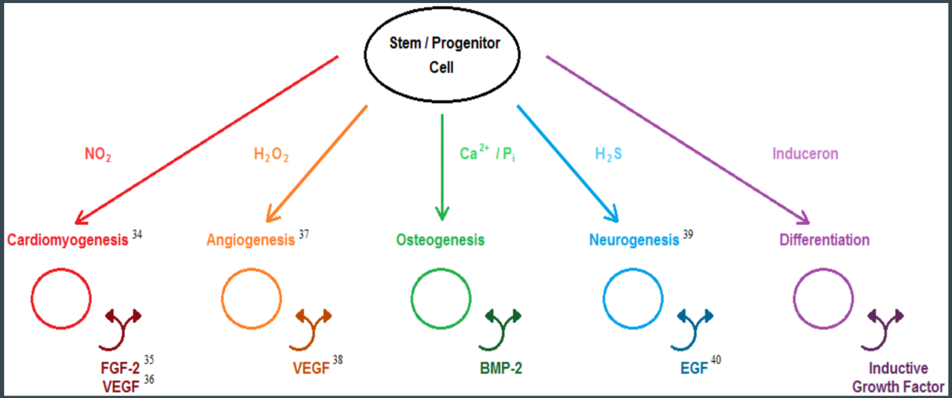
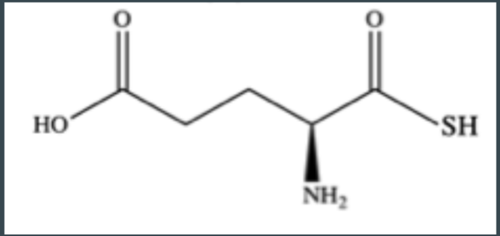


Figure adapted from Cushnie EK, Ulery BD, Nelson SJ, Deng M, et al. (2014) Simple Signaling Molecules for Inductive Bone Regenerative Engineering. *PLoS ONE* 9(7): e101627.

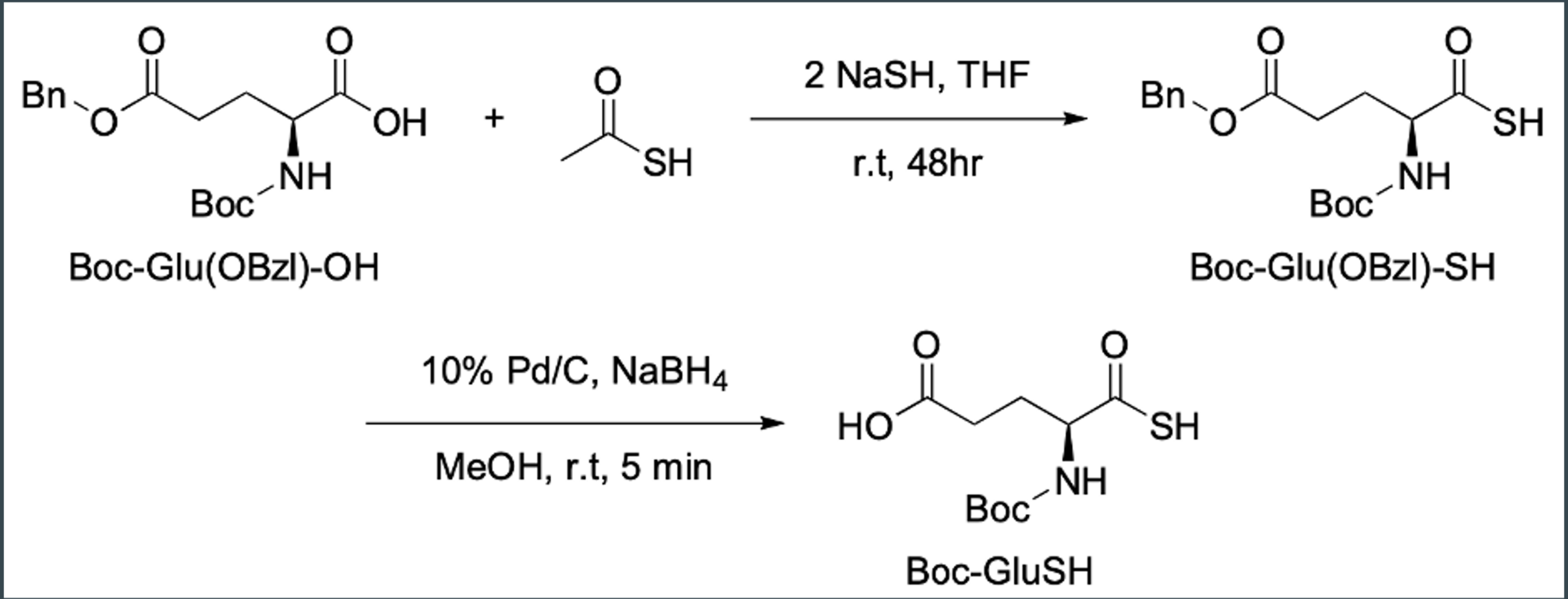


GluSH molecule

Research Goals and Methods:

- Develop alternative synthesis pathway for amine protected GluSH
- Product detection through thin layer chromatography (TLC)
- Separation through column chromatography
- Identification of products by Fourier transform infrared spectroscopy (FTIR) and proton (1H) as well as carbon (13C) nuclear magnetic resonance (NMR) spectroscopy techniques.

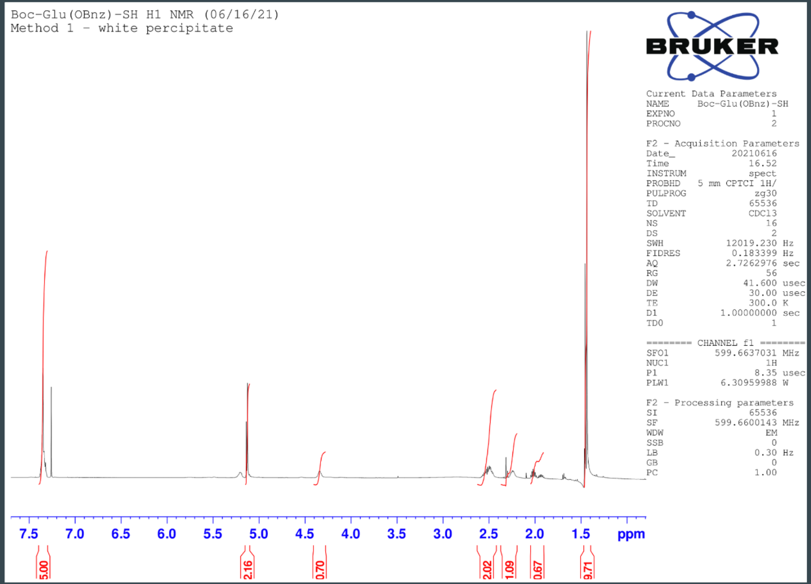
Synthesis Scheme

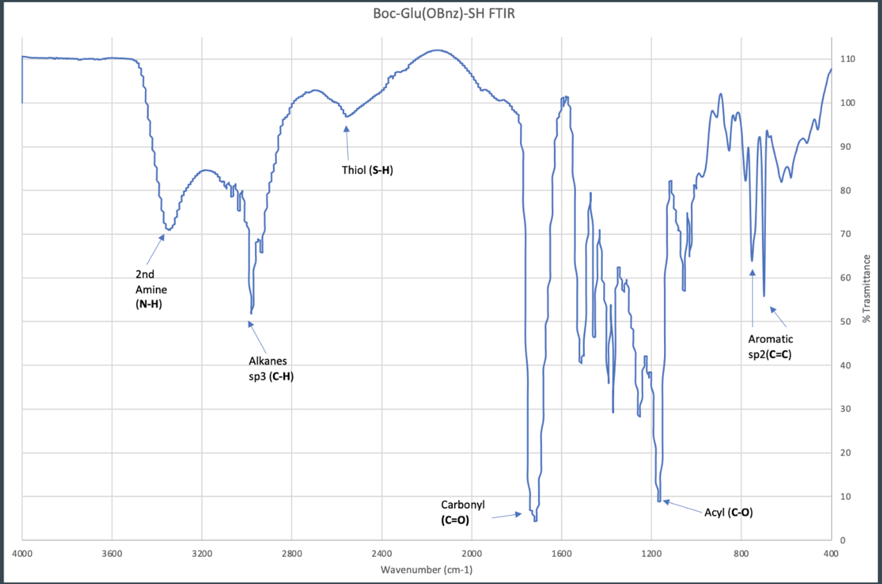


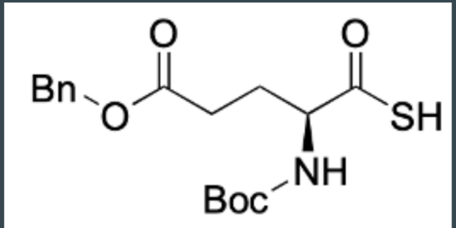
Synthesis Experiments

Scale	Reaction conditions	Yield % (crude)	Yield % (separated)
0.01 mols (3.374g)	Standard reaction conditions	61.5	28.6
0.005 mols (1.687g)	Standard (2x solvent)	62.3	36.2
0.01 mols (3.374g)	Standard, followed by subsequent iodine oxidation rxn	46.2	15.3
0.01 mols (3.374g)	Standard (air sealed), refined workup	84%	TBD
0.01 mols (3.374g)	Standard (open air), refined workup	96%	TBD

FTIR and H1 NMR







Boc-Glu(OBzl)-SH

Future Work

- Synthesis pathway of monomer with 2-(Boc-GluSH) glutaric ester and N-(Boc-GluSH) glutamic amide
- Polyester and polyanhydride synthesis
- Material characterization of polymers
- *In Vitro* Cellular Impact Assessment

Acknowledgements

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