Synthesis of Thiolated Precursors for Drug Delivery Applications

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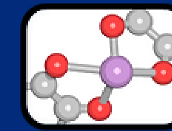

Introduction

Tumor cells have 10 – 100 times more GHS receptors than healthy cells. It plays many roles in cellular respiration. Oversaturation with disulfide bonds interrupts cellular respiration and causes disulfidptosis[1]. Covalent organic frameworks (COFs) are a class of porous crystalline materials with covalent bonds between linkers[2]. These connections could be made by reversable disulfide bonds; a COF linked with disulfide bonds applied as a nanoparticle (NP) chemotherapeutic could target and kill cancer cells. Crystalline NPs are ideal for drug delivery of this material to maximize active cite surface area.

Intracellular Glutathione (GSH) Redox

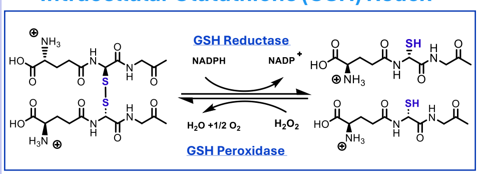

Figure 1: Non-enzymatic cell reduction and oxidation pathway from glutathione disulfide (GSSG) to GSH

Methods

Monomer Synthesis: Products are synthesized from base materials via radical halogenation[3], and pallidum catalyzed fourfold cross coupling phenyl bromide groups[4].

Crystal formation: Recrystallized solids are dissolved in chloroform in a vapor diffusion chamber. The antisolvent, acetone, diffuses into the inner jar. Highly pure and crystalline solids slowly grow as solubility decreases. When equilibrium is reached, white needle like crystals form.

Vapor Diffusion Chamber

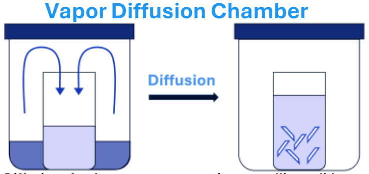

Figure 2: Diffusion of solvent vapors generating crystalline solids

Monomer Synthesis

Synthesis of Tetrakis(4-bromo-[1,1'-biphenyl]-4-yl methane)

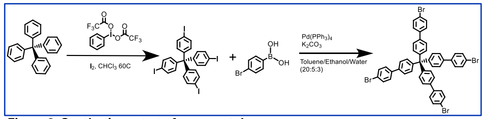

Figure 3: Synthetic route to form crystal monomer

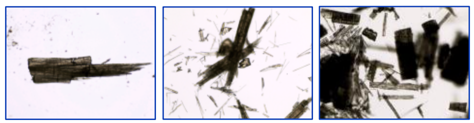

Figure 4: Crystalline Solids Under Optical Microscope

Fourfold Suzuki Miyaura Cross Coupling

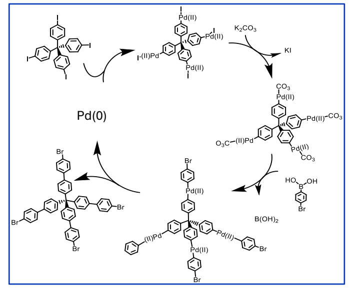

Figure 5: Catalytic mechanism to generate monomer

Purification and Characterization

Sample Purification

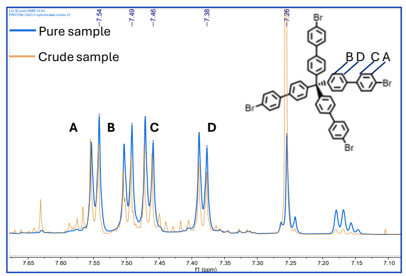

Figure 6: H[1] NMR of LG-30 before (blue) and after (orange) purification

Structure Absorption Quantification

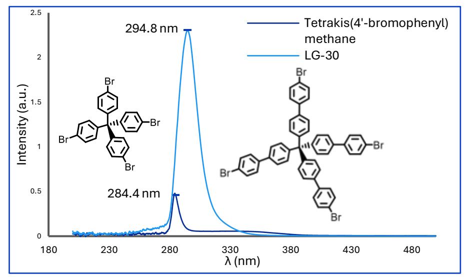

Figure 7: UV-Vis of single and double bromo-phenyl ring monomers

Powder X-Ray Diffraction

PXRD Results

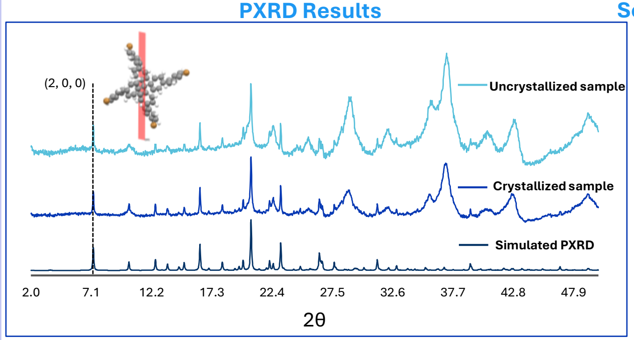

Figure 8: Tetrakis(4-bromo-[1,1'-biphenyl]-4-yl methane) Monomer Conformations

Solved Crystal Structure

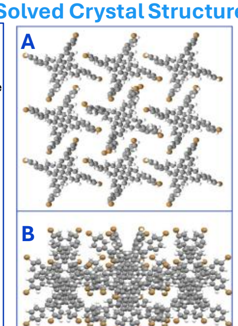

Figure 9: Crystal Packing Formation

Conclusions

Investigations of the final product represents confirmation of synthesis and crystalline character. PXRD spectra of experimental materials align with simulated diffraction patterns. The vapor diffused morphology displays greater crystallinity than than amorphous precursors. Its CIF structure file suggests possible interatomic distance between bromines capable of hosting disulfide bonds. All characterization and figures confirm the successful synthesis of Tetrakis (4-bromo-[1,1'-biphenyl] -4-yl methane).

Future work

Thiolating final products could generate monomer with a similar CIF. Heterogeneous oxidation would change the thiols to disulfides without solvation[5]. Cell studies can determine the material's effectiveness on tumor cells.

Thiolation of Coupled Product

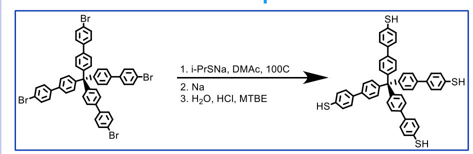

Figure 10: Projected Synthesis of Tetrakis(4'-thio-[1,1'-biphenyl]-4-yl)methane

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References

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