

Synthesis and Crystallization of the 5'-Benzoyl Guanosine Derivative

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Abstract

The overall goal of this project was to successfully synthesize a specific derivative of Guanosine, 5'-Benzoyl-2',3'-isopropylidene Guanosine, and subsequently establish a method which will result in the creation of large, clear crystals of the hexadecamer form of the compound. Guanosine derivatives self-organize into quartets, forming a primarily planar ring. Through additional chemical manipulation these rings can then be forced to stack on top of one another, with one symmetrical pair in the middle, and the surrounding two planes being symmetrical to one another. These crystals were then analyzed via x-ray crystallography to determine the exact molecular structure, and to characterize the types of interactions between layers. Prior to my success in this project, this derivative had never been successfully characterized by x-ray crystallography

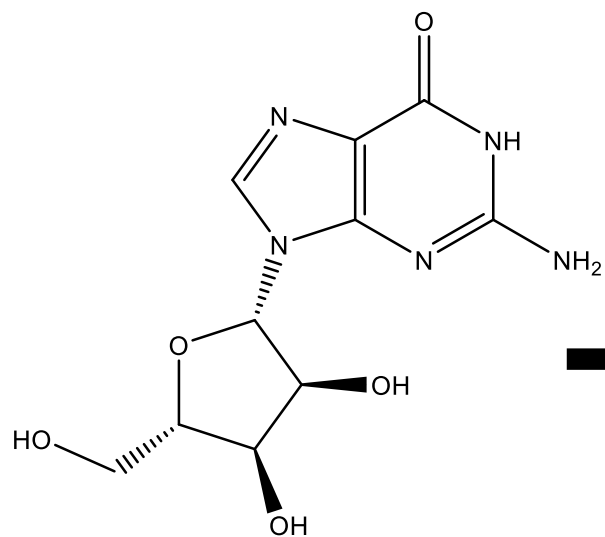
Questions I'm looking at

- How can the 5'-benzoyl-2',3'-isopropylidene Guanosine derivative be synthesized?
- Can the hexadecamer of 5'-benzoyl-2',3'-isp-G be crystallized?

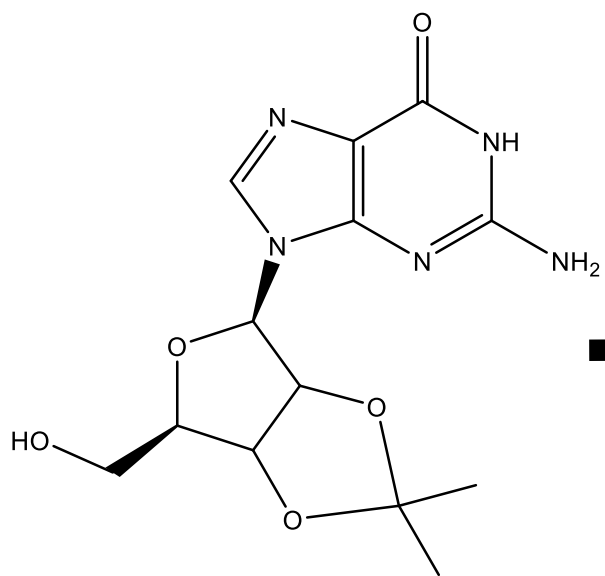
Progress made (Success!)

- Synthesis of 5'-benzoyl derivative from Guanosine
- Crystallization of 5'-benzoyl derivative

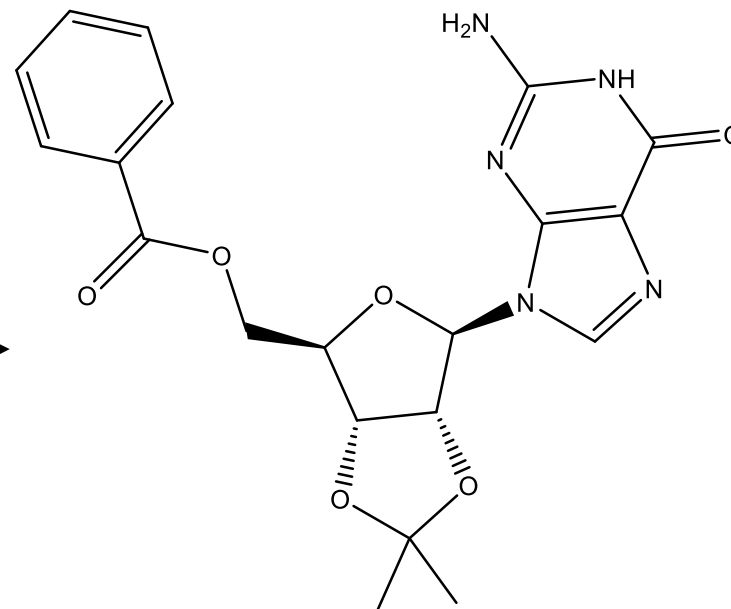
Starting Material



Guanosine



2',3'-isopropylidene
Guanosine



5'-benzoyl-2',3'-isopropylidene
Guanosine

End Product

How do we make the Hexadecamer?

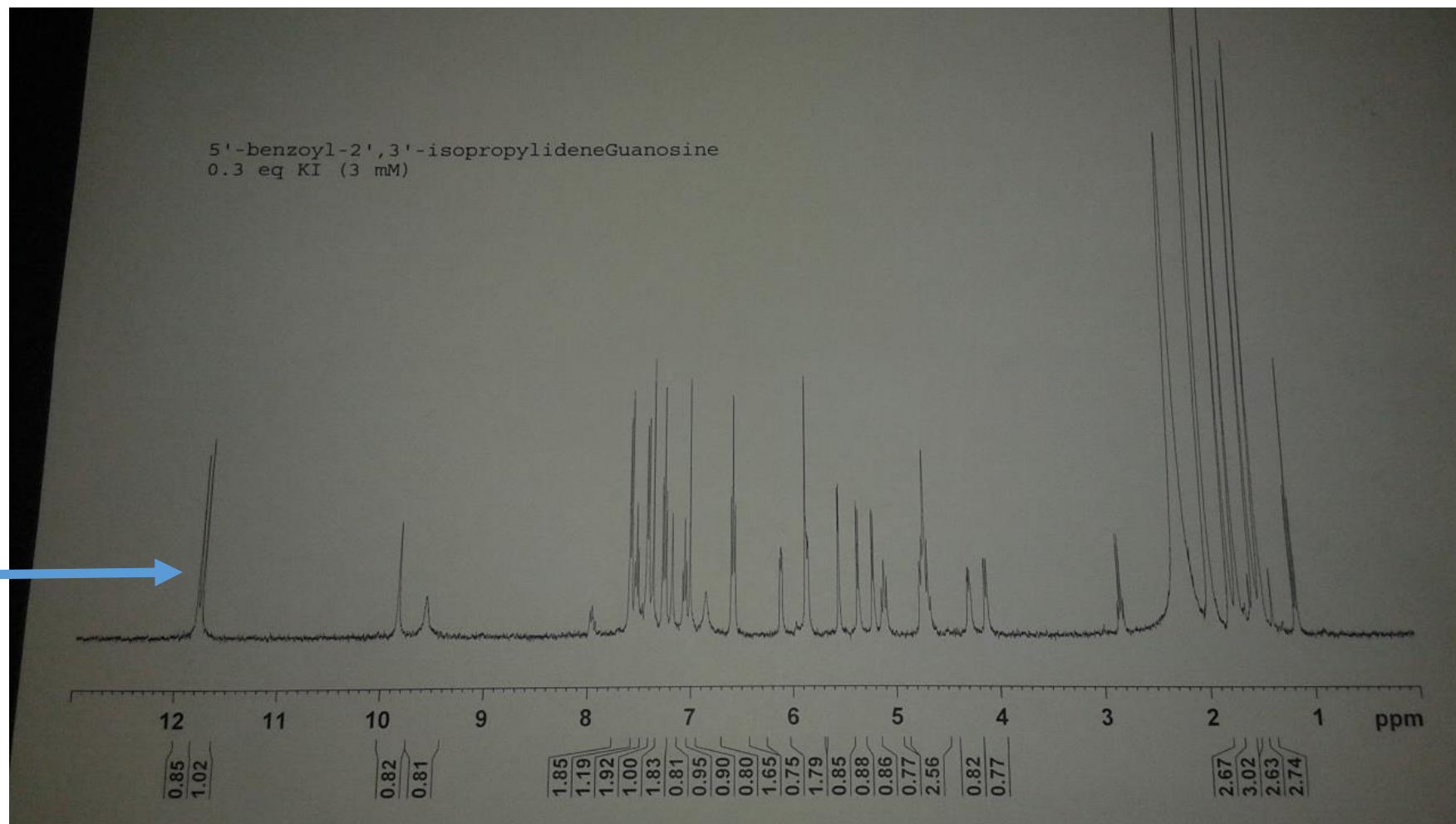
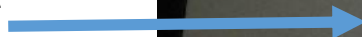
- Aqueous KI Solution or K-DNP solution is dried out in a vial
- Some number of equivalents of G-Derivative are added with Deuterated Chloroform or Deuterated Acetonitrile
- Sonication, and stirring overnight
- Test to see if the 16-mer structure formed via NMR400

16-mer Conditions

- Tested a number of different conditions with 100mg/1mL Potassium Iodide Solution or K-DNP Solution
 - 1:1 equivalents
 - 1:3 equivalents ← Big Winner!
 - 2:1 equivalents
 - Etc.

16-Mer NMR (Successful Solutions!)

Characteristic
16-mer NMR
Peaks

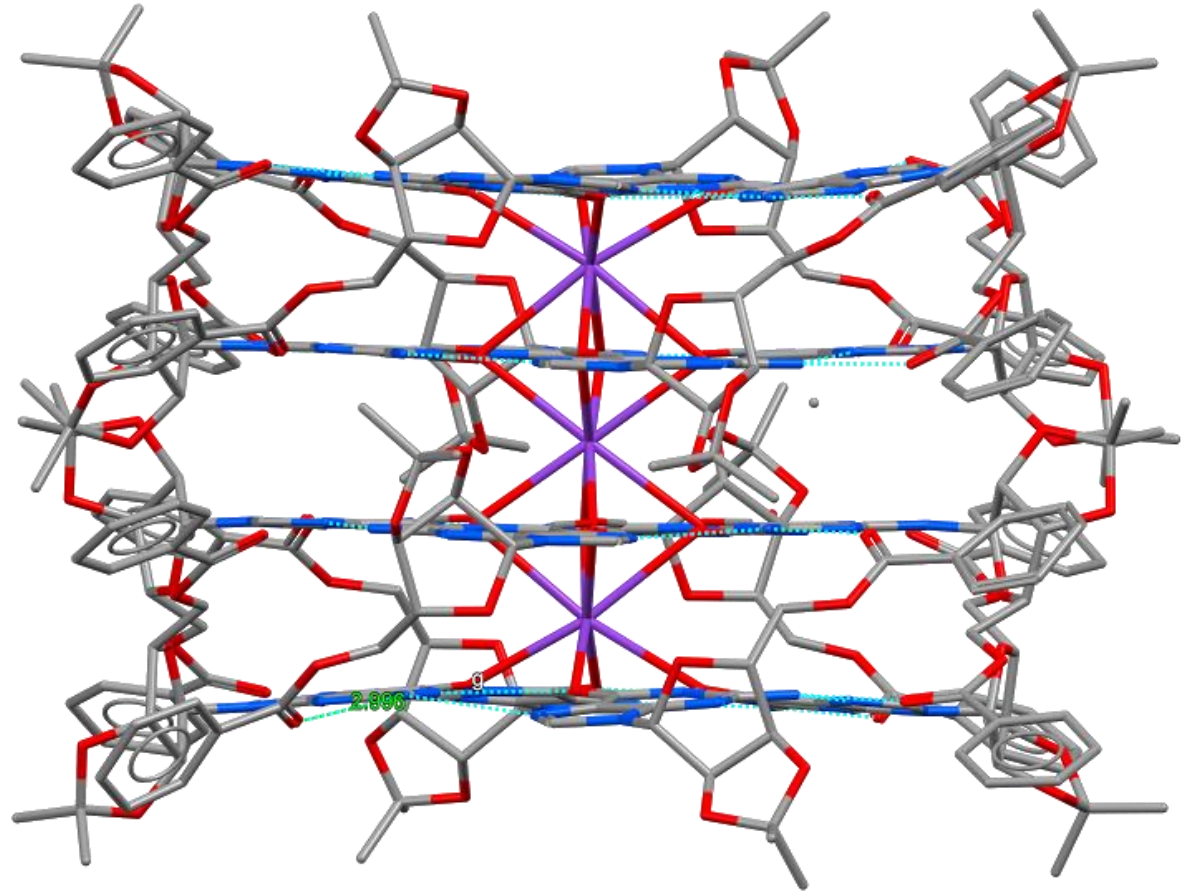
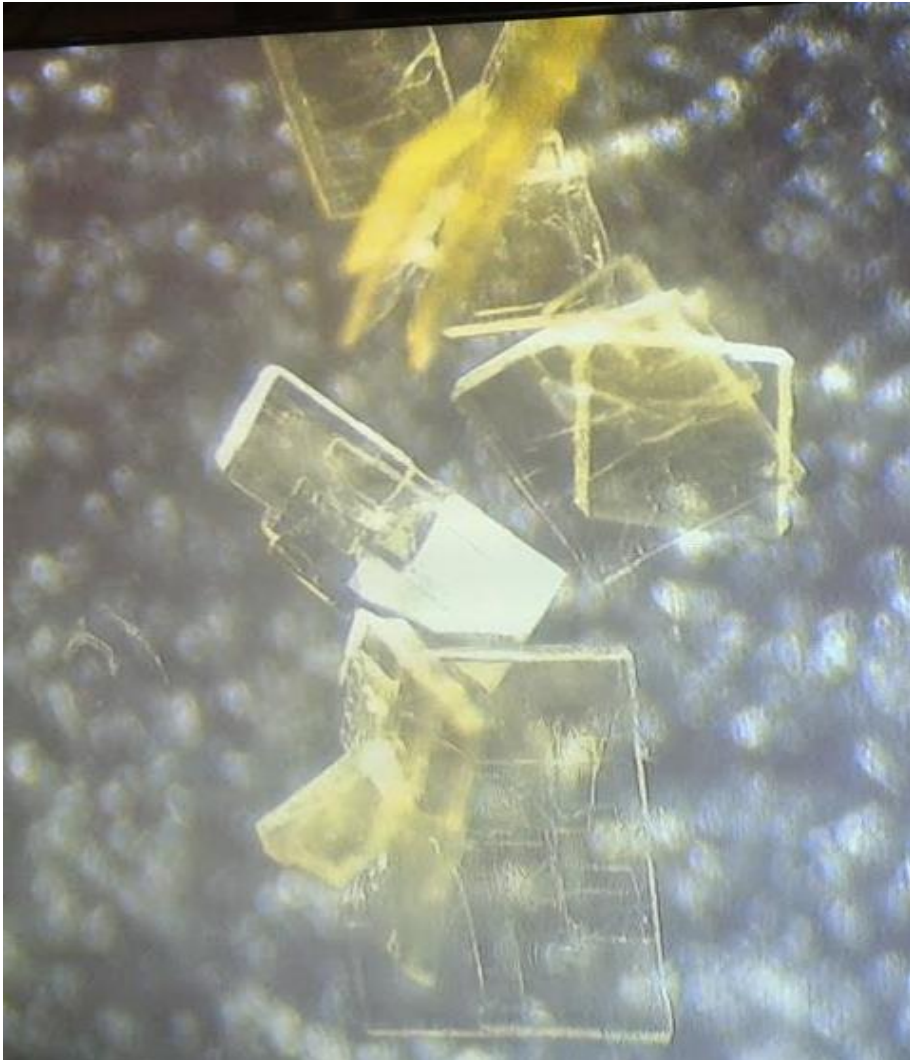


Tested Crystallization Techniques

- Slow Evaporation
 - Room Temperature
 - Inside and outside of Dessicator
- Solvent Diffusion
 - Room Temperature
 - With and without Benzene co-crystallization agent
 - Refrigerator
 - With and without Benzene co-crystallization agent

Success!

Grown crystals in solution!



Crystal Structure determined by Dr. Zavalij of the X-Ray Crystallography Facility

Problems

- K-DNP did not form exclusively 16-mer
 - Formed a mixture of 8-mer and 16-mer, unusable for my purposes
- Room temperature crystallization flat-out didn't work
- Crystallization had to be done in the fridge
 - Increases the amount of time needed between trials, makes it difficult to see what didn't work

Future Directions

- Pi-Stacking Compounds
 - Organic soluble dyes
 - I plan on working on this next semester
- DNA Intercalating Compounds

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