Organic Synthesis of a Small Novel Molecule to Target Prostate Cancer

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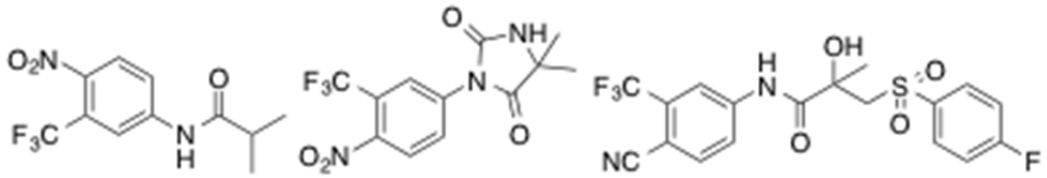
Introduction

I have focused my research on organic synthesis of a small novel molecule to target prostate cancer. This has consisted of performing multiple organic synthesis reactions as well as various biological assay's. Beyond performing organic synthesis and biological assay's, sufficient background research has been conducted on current forms of treatment as well as prostate cancer. Through the biological assay's we have found multiple molecules to show possible success in targeting prostate cancer.

Designing of these molecules is conducted in collaboration with Mr. Sravan K. Jonnalagadda, Ms. Shirisha Gurrapu, and Dr. Venkatram R Mereddy. These molecules of design consist of various derivatives of the current three forms of treatment. The three current forms are flutamide, nilutamide, and bicalutamide. These three molecules are displayed below in Figure 1.

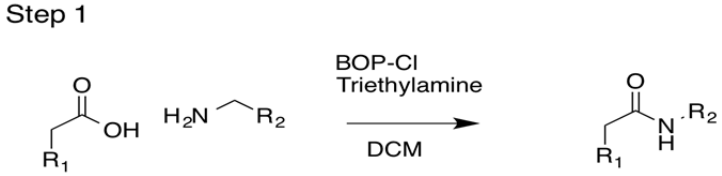
Figure 1.



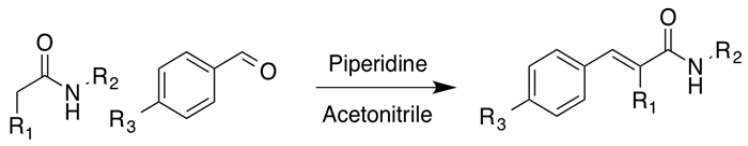
These three current forms of treatment are antiandrogen molecules that bind the androgen receptors (AR). This essentially causes the AR to become inactive therefore inhibiting excessive cell proliferation through competitive binding with Dihydrotestosterone.

Methods:

The organic synthesis procedures consist of the following basic steps:



Step 2



The first step is a Bop-Cl amide coupling reaction followed by a condensation reaction between an amide and carboxylic acid. After these two basic mechanisms are carried out, various derivatives are synthesized. Approximately 15 derivatives were synthesized.

The biological assay conducted on the compounds consisted of a cytotoxicity assay. LNCaP androgen positive prostate cancer cell line was used to carry out these toxicity evaluations on each compound. The cells were grown in appropriate media and plated in 24- well plates. After cells were plated the compound was implemented and the cells were allowed to grow for 72 hours. After 72 hours of growth, absorbance measurements were taken. The controls used for normalizing absorbance measurements consisted of growth media, taxol, and DMSO. After absorbance measurements were taken on each compound the data was analyzed.

The cytotoxicity assay was or will be conducted three times on each compound for repeatability. The molecules that show limited toxicity will be taken to further assays.

Results

Through synthesis and cytoxicity tests several of the designed molecules showed limited general toxicity towards cells. These compounds that have shown to be successful will be repeated in cytoxicity tests in various dilutions. The basic functional groups and molecular shape of successful molecules has been noted.

Conclusion

The organic synthesis of several small molecules has shown limited general toxicity towards LNCaP cells. These molecules that have shown to be successful will be taken through further research. Continued synthesis will take place mimicking these molecules. After multiple toxicity assay’s have been conducted and successful results documented, these molecules will be taken further into proliferative binding assay tests with the presence of Dihyrotestosterone.