Synthesis of a ^{99m}Tc Flutamide System for Imaging Androgen Expression in Prostate Cancer

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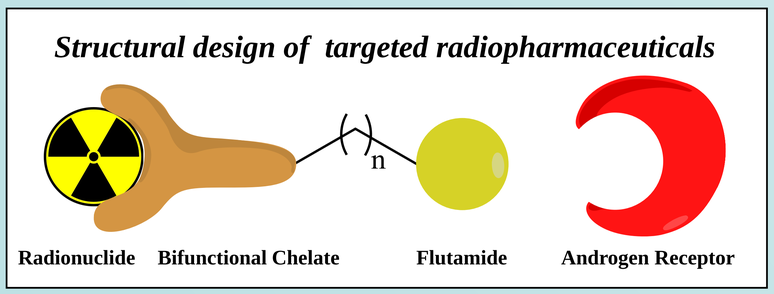
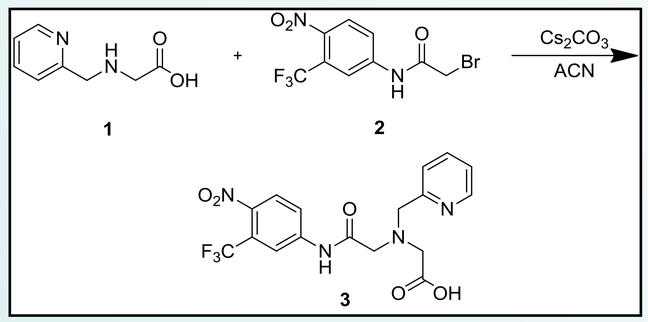
Introduction

Approximately 230,000 men in the U.S. are diagnosed with prostate cancer (PC) each year. Current preliminary diagnostic methods are severely limited in detailed molecular information surrounding the development of PC. Development of an alternative diagnostic tool for early detection of PC would provide physicians with cellular and organ function information that would improve the treatment options and potentially increase the survival rate.

The androgen receptor (AR) is a well known nuclear shuttle protein responsible for testosterone transport into the nucleus. In early stages of PC, the AR is over-expressed on the surface and in cyctoplasm, which presents an ideal motif for targeting. Non-steroidal antagonists, such as Flutamide (**2**), are potent inhibitors of AR function. By modifying Flutamide with a bifunctional chelator specific for ^{99m}Tc, the potency of Flutamide can be combined with an imaging component to yield a novel radiopharmaceutical agent for diagnosing AR expression in PC.

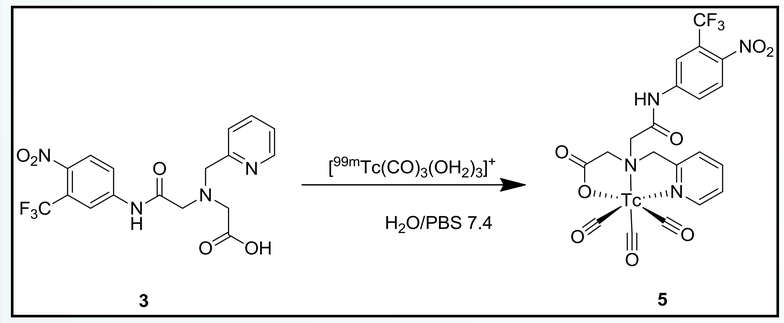


Ligand Synthesis

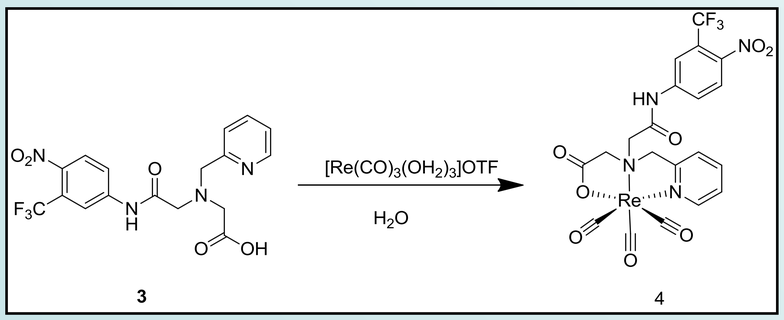


Compound **1** was prepared by dissolving methyl 2-((pyridin-2-ylmethyl)amino)acetate (46 mg, 0.26 mmol) in methanol and 1.0 M lithium hydroxide (3 mL, 3:1) in methanol (9 mL) at room temperature overnight while stirring. The solution was then rotovapped to dryness and the crude product was purified HPLC.

Technetium Complexation and Cell Study



Rhenium Complexation



Compound **3** (95 mg, 0.23 mmol) was dissolved in water (10 mL). 0.1 M $[Re(CO)_3(OH_2)_3]$OTF (2.3 mL, 0.23 mmol) was added to the solution. The solution was stirred at room temperature overnight. The product precipitated out of solution and was collected by filtering the reaction mixture through a sintered funnel. The filtrate was rotovapped to dryness and redissolved in methano. A new precipitate formed, was filtered off with a sintered funnel, and combined with the first precipitate collected.

Conclusion

Acknowledgements

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