TITLE: Synthesis of Pyridine Derivatives as Antagonists of Chemokine Receptor CXCR4

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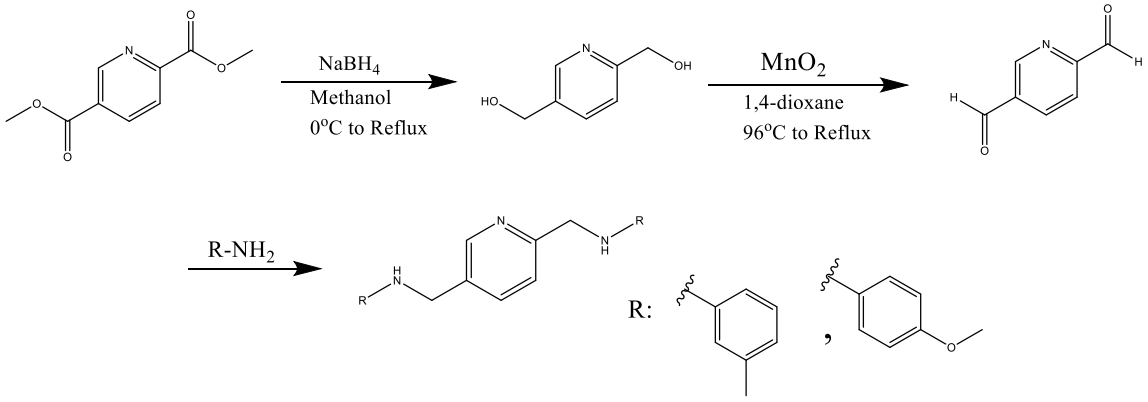
Introduction: Cancer is a disease that involves abnormal cell growth that has the potential to migrate from the origin and reproduce in other parts of the body. CXCR4 is a chemokine receptor which has interactions with the CXCL12 ligand to promote the progression of diseases such as HIV, cancer cell metastasis and inflammation. Inhibition of the receptor and its ligand has shown to decrease the progression of these diseases.

Purpose: The purpose for this research is to synthesize potent antagonist to inhibit the interaction between CXCR4 and CXCL12.

Method: 2,5-dimethoxypyridine was used to synthesize 2,5-dicarbaldehydepyridine in a two-step reaction: a reduction of the two ester groups into primary alcohols and an oxidation of the alcohols into aldehydes. 2,5-Dicarbaldehydepyridine is the starting compound for the synthesis of the CXCR4 antagonist analogs through a reductive amination process. The synthesized small molecules were analyzed in a series of preliminary assays to determine the biding affinity for the CXCR4 receptor.



Results: Two pyridine analogs were synthesized and tested in two preliminary assays: a binding affinity assay and a matrigel invasion assay. These assays demonstrate how well the molecules are at binding to CXCR4. The 3-methyl analog proved successful in both assays, a binding affinity of 1nM concentration and 58% invasion through the matrigel membrane.

Conclusions: The assays imply that the pyridine analogs are successful at binding to the CXCR4 receptor. Further synthesis of these analogs are being produced for analysis.