Synthesis of Two Potent Rexinoids at the Gram Scale for In-Vivo Cancer Studies

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Introduction

Bexarotene is an antineoplastic agent approved by the U.S. Food and Drug Administration in late 1999 to treat Cutaneous T Cell Lymphoma. It falls under a class of medications classified as Retinoids. Retinoids are drugs that are relatives of Vitamin A. Retinoids control normal cell growth, and cell differentiation. This medication is used to halt the growth of cancer cells but comes with major side effects. These side effects include blood test abnormalities, rash, lowered white blood cell count, nausea, infection, and an increase of fat in the blood (cholesterol and triglycerides).

Background

In this study, we examine two analogue rexinoids that have a similar INOS suppression to compound LG100268. The purpose in examining the percentage of INOS and SREBP is to better identify rexinoids with potency that is more clinically acceptable and with a lower SREBP induction (fewer side effects) for patients of cancer. The analogues we examined have a very close INOS suppression to LG100268 (an INOS suppression of 15%), lower in scale than Bexarotene. On the other hand, Bexarotene has a lower percentage of SREBP then LG100268. The importance in targeting a molecule like LG100268 is to regulate the triglyceride levels and other alarming side effects in those who have weak immune systems. With the data down below, we examined the potency of our compounds that will later be introduced to mouse models. Synthesizing these rexinoids will help bring greater awareness and ‘design new rexinoids with appropriate interactions with coactivators and corepressors...'(12, Zhang) that will minimize side effects in cancer patients treated with these drugs.

Hypothesis

We will be able to make between 4 and 5 grams of two different target molecules to have a collaborator be able to examine them in mouse models of human cancer (lung and breast).

First Target Molecule Intermediate Reaction Scheme and Details:

![Reaction Scheme 1](image1)

Crude Reaction TLC of 7

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Second Target Molecule Intermediate Reaction Scheme and Details:

![Reaction Scheme 2](image2)

Crude Reaction TLC of 11

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Results

![TLC Plate](image3)

![HNMR Scan](image4)

Yields were comparable to yields found in prior studies. A proton nuclear magnetic resonance scan (figures 3 and 4) and a thin layer chromatography test (figure 2) proved purity. Future research includes testing compounds 7 and 11 in mouse models of human cancers, potentially lung and breast. These studies help with better understanding the mechanisms of rexinoids in cancer that will be clinically effective and accessible to those in need.

References


Acknowledgements

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*Both investigators contributed equally to this project.