Poster #29

Studies Toward the Synthesis of Potential Estrogen Mimics

Ashton T. Hamme[1], Jun Wang[1], Erick Ellis[1], Tiffany Cook[1], and Tom Wiese[2]
[1]Department of Chemistry, Jackson State University[2]College of Pharmacy, Xavier University

Naturally occurring compounds such as flavanoids and isoflavones, which are found in green tea, soybeans, and fish, have been shown to be beneficial in breast cancer treatment through binding to estrogen receptors. Other natural products such as 11-deoxyfistualrin-3 are cytotoxic against estrogen dependant MCF-7 breast cancer tissue.[1] The investigation of 11-deoxyfistularin-3, and the synthesis of closely related analogues, can determine if this compound is an estrogen mimic, and which functional groups may be responsible for the biological response. The purpose of this project was to model 11-deoxyfistualrin-3 with known breast cancer pharmaceutical compounds, such as Raloxifene[2], to determine if there is any overlap of the functional groups in the estrogen receptor active site. If any overlap is present between the two compounds, then analogues of the natural product would be synthesized for *invitro* estrogen receptor binding studies. FlexS and FlexX molecular modeling programs were used to study the natural product and the pharmaceutical compound. The synthesis of the 4,5-dihydroisoxazole precursor to an analogue of 11-deoxfistularin-3 was accomplished by using 1,3-dipolar cycloaddition with a functionalized enone. The cycloaddition of Methyl 2-(bromomethyl)acrylate with (4-Methoxyphenyl)hydroximoyl chloride using triethylamine in chloroform afforded only the 5,5 disubstituted 4,5-dihydroisoxazole regioisomer. The 1,3-dipolar cycloaddition of 3- chloro-2-chloromethyl propene with aromatic hydroximoyl chlorides also gave rise to one regioisomeric cycloadduct. Both of these compounds will be used as precursors to 11-deoxyfistularin-3 analogues.

Contact Information:
e-mail: ashton.t.hamme@jsums.edu
phone: (601) 979-3713
fax: (601) 979-3674