

Synthesis of Cephalostatin Analogs with anti-Lymphoma Activity

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Cephalostatin is one of the most potent anti-cancer agents ever been tested in the National Cancer Institute, belongs to the cephalostatins family. This family consists from 19 compounds, which have been isolated from *Cephalodiscus gilchristi*, a microorganism living in the Indian Ocean, by Pettit's group at the Arizona State University.⁽¹⁻⁴⁾

As part of our work, we are concerned in the synthesis of analogs to cephalostatins, hoping to prepare potent anti-cancer pro-drugs. One of the routes, which we have selected, was the hydroboration of the exo-cyclic double bond at carbon-12 of the steroid moiety. This resulted in a mixture of diastereomers of hydroxymethylene derivative with a large enhancement of the biological activity. The efforts were concentrated on diastereoselective hydroboration using different borane complexes. This process gave, in the cases of catechol-borane complex and D-(N-tosyl) valine-borane complex, F-ring opened products instead of hydroborated products.⁽⁵⁾

In this study we have development a method with chemo-, regio- and stereoselective F-Ring opening.^(5,6) Several bis-steroids have been synthesized and the biological activity for some compounds was evaluated against 60-cell lines (NCI-Testing). Others were tested against three-selected cancer cell lines (stomach adenocarcinoma, hepatocellular carcinoma and breast adenocarcinoma), tested in the Medizinische Hochschule Hannover (MHH)/ Germany. Some of these compounds have shown a remarkable activity against different cell lines and others will be tested later.

References:

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