

Calyculaglycosides

Research Plan

Natural products have been, and continue to be, a valuable source for pharmaceutical products. One of the problems with natural products is that some are produced in very small quantities that do not allow for adequate study. An example of this shortcoming is the Calyculaglycosides, a new type of terpene glycosides, which were isolated and identified in 1997 by Rodriguez and colleagues (Cobar, O.M., Rodriguez, A.D., Padilla, O.L., and J.A. Sanchez. 1997. The Calyculaglycosides: dilophol-type diterpene glycosides exhibiting antiinflammatory activity from the Caribbean Gorgonian *Eunicea* sp. *Journal of Organic Chemistry* 62:7183-7188.) The Calyculaglycosides are made up of three members – A, B and C, are similar in structure to the fucosides, and differ only in the structure of the sugar moiety that is attached to the aglycon. The identity of the sugar substituent influences the conformation of the molecules, which then greatly influences the biological activity of the compounds. A picture of Calyculaglycoside A in its most stable conformation is given below (**FIGURE**). The Calyculaglycosides (CLG-A, CLG-B, and CLG-C) were isolated from octocorals of the order Gorgonecea, but comprised only 0.08 %, 0.14 % and 0.06 % of the chloroform/methanol (1/1) extract, respectively.

The CLGs have three main structural areas that can be explored for their effects on activity: the cyclodecadiene ring, the spacer group, and the sugar moiety. The difficult to synthesize cyclodecadiene portion of CLG derivatives will be synthesized via new ring closing metathesis techniques that allow for formation of ten-membered and other rings (Nevalainen, M., and A.M.P. Koskinen. 2002. Total synthesis of nor-1,6-Germacradien-5-ols *Journal of Organic chemistry* 67:1554-1560). Once the CLG's have been synthesized, they will be tested in assays designed by investigators in the St. Jude Small Molecule Therapeutics Program. These assays will indicate which portions of the compounds are most important for their anti-inflammatory and anti-cancer activities. These studies will allow us to identify structure-activity relationships that may be important for the rational design of more potent analogs of the CLGs in the future.

