A divergent synthesis of α-galactosylceramide analogues

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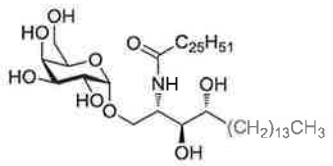
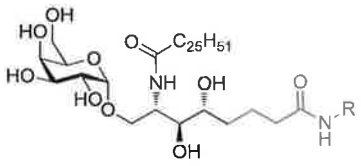
Screening of marine natural products for antitumor activities led to the discovery of glycolipids termed agelasphines, from wich α-GalCer (**1**) was obtained by structural optimization. α-GalCer is presented by CD1d-molecules on antigen presenting cells to the TCR of *i*NKT cells, which upon activation rapidly secrete Th1 and Th2 cytokines. Th1 cytokines mediate protective immune functions like tumor rejection, antiviral and antibacterial effects, while Th2 cytokines mediate regulatory immune functions to ameliorate autoimmune diseases. The fact that Th1 and Th2 cytokines antagonize each other's effect is believed to be responsible for the limited clinical benefit obtained with α-GalCer.[1] Hence, analogues that are capable of polarising the cytokine response to either Th1 or Th2 are of great interest.

In this poster a divergent synthetic pathway is described to afford α-GalCer analogous containing an amide moiety in the poorly investigated phytosphingosine chain.



1 α-GalCer



[1] P. B. Savage, L. Teyton., A. Bendelac, Chem. Soc. Rev. (2006), ***35***, 771-779.