VERSATILE SYNTHESIS OF C-5" AND C-6"-MODIFIED α-GALCER ANALOGUES AS NEW iNKT CELL LIGANDS

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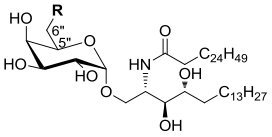
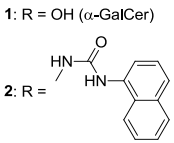
α-Galactosylceramide (**1**) is known as the prototypical antigen for iNKT cells. Following complexation with the antigen presenting glycoprotein CD1d, α-GalCer is recognized by iNKT-cells, which, after activation, produce a rapid burst of Th1 and Th2 cytokines. The fact that both kinds of cytokines antagonize each other's effect is seen as a considerable drawback for therapeutic applications. Hence, much research efforts are directed towards the identification of α-GalCer analogues capable of skewing the iNKT cell responses towards a more biased Th1 or Th2 profile.

Based on the interesting Th1 biased in vivo response induced by analogue **2** and the recently obtained crystal structure of this compound complexed to mCD1d and the TCR[1] we synthesized a diverse set of derivatives modified at the C-5" or C-6"-position of the galactopyranosyl ring.





[1] S. Aspeslagh, Y. Li, E. D. Yu, N. Pauwels, M. Trappeniers, E. Girardi et al., The EMBO Journal (2011), **30**, 2294-2305.