UNIVERSIDAD DE LA RIOJA

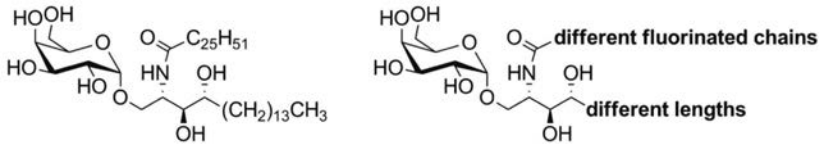
XI CARBOHYDRATE SYMPOSIUM

Synthesis of fluorinated analogues of KRN7000

David Collado, M. Isabel Matheu, and Omar Boutureira

Departament de Química Analítica i Química Orgànica, Facultat de Química, Universitat Rovira I Virgili, 43007 Tarragona, Spain; e-mail: david.collado@urv.cat

Glycosphingolipids are important biomolecules commonly found in eukaryotic cell membranes. They play a critical role in cell communication, growth, differentiation and programmed cell death and have also shown promising activities against diverse pathologies.[1] For example, the complex formed by the association of α-glycosphingolipid KRN7000 and CD1d proteins interacts with a component of the immune system, the Natural Killer T (NKT) cells, and upon its activation, NKT cells release cytokines, which are signaling molecules involved in cellular communication and immune response.[2] Several KRN7000 analogues have been synthesized featuring modifications in both the sugar and the lipid moieties, all of which with the aim of developing new structures for clarifying and exploring their biological role and therapeutic potential. Particularly relevant examples are those incorporating fluorine moieties in their structure, which are known to confer some interesting properties such as higher metabolic stability, binding and lipophilicity and membrane permeability.[3] Although several fluorinated KRN7000 analogues at the carbohydrate moiety have been synthesized as well as those with partial fluorination of the lipid portion, the preparation of derivatives with fully or partially perfluorinated acyl chains able to modulate the lipid-receptor interaction is unprecedented. Here we describe our progress on the development of a diversity-oriented synthesis approach to perfluorinated analogues of KRN7000 at the ceramide moiety to gain insight into the underlying mechanisms of glycolipid-protein interactions.



α-GalCer (KRN 7000)

[1] Banchet-Cadeddu, A.; Hénon, E.; Dauchez, M.; Renault, J.-H.; Monneaux, F.; Haudrechy, A. *Org. Biomol. Chem.* **2011**, *9*, 3080.
[2] Yu, K. O. A.; Porcelli, S. A. *Immunology Letters* **2005**, *100*, 42.
[3] Ojima, I. *J. Org. Chem.* **2013**, *78*, 6358.