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Synthesis of the Acetal free analogue of the KRN 7000 glycosphingolipid

Michael Amjad Qaqish
University of Windsor, qaqis112@uwindsor.ca

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Michael Qaqish, Michael Reynolds, John F. Trant

Carbohydrates fulfill many roles in biological systems including (but not limited to): acting ascellular structural support, mediating cellsignaling and acting as an energy supply. They can also act as “superantigens” for the immune system whenpart of certain fat molecules called glycosphingolipids. These molecules are able to activateinvariant Natural Killer T-Cells (iNKT cells); white blood cells that mount a dangerous, non-specificsystemic immune response potentially leading to cell death. However, this same immune response (if controlled), has promise to act as a last line antiviral and/or a potential anticancer agent by potentially turning the immune system against a previously ignored virus, infection or tumour. The identification and synthesis of such immunoactive agents for clinical and mechanistic applications is of great interest in carbohydrate immunology. KRN7000 is of particular interest. It was first isolated from a marine sponge, and is the most potent activator of iNKT cells. However, if almost any part of the molecule is modified, all biological activity is lost. One of the few exceptions, is that the enzymatically-sensitive bond attaching the sugar to the lipid can be replaced with a stable carbon linkage. However, the synthesis is too long to be commercially useful. We wish to discuss our approach towards this molecule that attempts to streamline the approach by very subtly modifying KRN7000 in a new way. The synthesis, and its implications for biological activity, will be discussed.