Synthesis of Fluorine-containing ganglioside analogues

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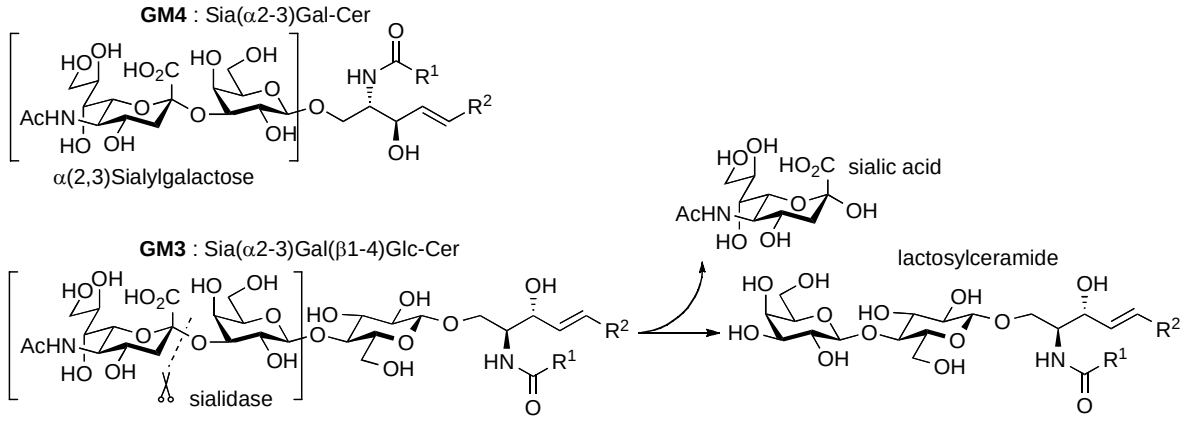
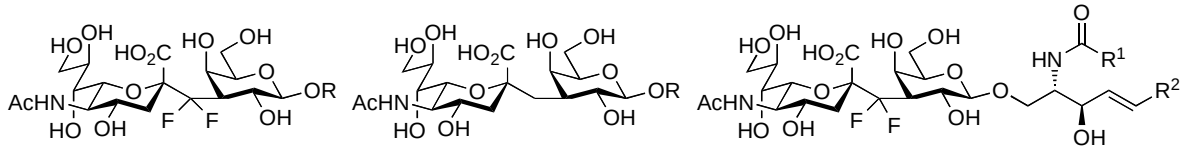
The α(2,3)sialylgalactose structure is widely found at the nonreducing end in glycoproteins and glycolipids and is recognized as one of the most important units in carbohydrate molecules. For example, sialyl Lewis^x and sialyl Lewis^a, which are ligands of L-, E-, and P-selectin, are composed of this structure. Gangliosides also contain the same structure, and are thought to make important contributions to cell signaling and cell surface interactions. But, the physiological roles of this structure are still not fully clarified. Dynamic metabolism of α-sialosides in living cells, involving hydrolysis of α-sialoside linkages by sialidases and their formation by sialyltransferases, is associated with complex signal networks. Therefore biologically stable analogues would be useful as chemical probes for clarifying the biological functions of these molecules.



C-Glycoside analogues of α(2,3)sialylgalactose structure (*C*-sialoside), in which the anomeric oxygen atom of sialic acid is replaced by a carbon atom, are particularly attractive candidate molecules as mimics of native *O*-sialoside. We recently established the methodologies based on Ireland-Claisen rearrangement for the stereocontrolled synthesis of CF_2-linked[1)] and CH_2-linked α(2,3)sialylgalactose[2)] analogues (**1** and **2**), which were designed as novel types of sialidase-resistant α(2,3)sialylgalactose mimics. The CF_2-linked GM4 (**3**) was synthesized and found to act as GM4 mimic on human lymphocyte.



CF_2-linked α(2,3)sialylgalactose (**1**)

CH_2-linked α(2,3)sialylgalactose (**2**)

CF_2-linked GM4 (**3**, $R^1 = {}^nC_{17}H_{35}$, $R^2 = {}^nC_{15}H_{31}$)

References:
(1) Hirai, G.; Watanabe, T.; Yamaguchi, K.; Miyagi, T.; Sodeoka, M.: Stereocontrolled and Convergent Entry to CF_2-Sialosides: Synthesis of CF_2-linked Ganglioside GM4. *J. Am. Chem. Soc.* **2007**, *129*, 15420-15421.
(2) Watanabe, T.; Hirai, G.; Kato, M.; Hashizume, D.; Miyagi, T.; Sodeoka, M.: Synthesis of CH_2-linked α(2,3)Sialylgalactose Analogue: On the Stereoselectivity of the Key Ireland-Claisen Rearrangement. *Org. Lett.* **2008**, *10*, 4167-4170.