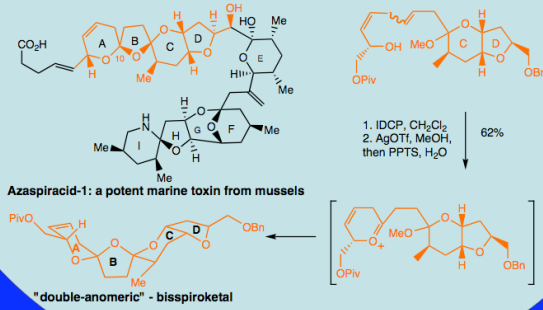
Mootoo Research Projects

Glycomimetics & Related Natural Products: Synthesis & Biomechanistic Applications

Synthesis of the ABCD trioxadispiroketal subunit of azaspiracid-1: An iodoetherification-dehydroiodination strategy for complex spiroketals

Org. Lett. **2007**, *9*, 4303-4306

An unusual spiroketalization strategy in which a hydroxyalkene serves as the synthetic equivalent of a cyclic enol ether was applied to the synthesis of the ABCD trioxadispiroketal subunit of azaspiracid-1. The trioxadispiroketal product, which represents a double anomeric effect was obtained as a single trioxadispiroketal diastereomer.

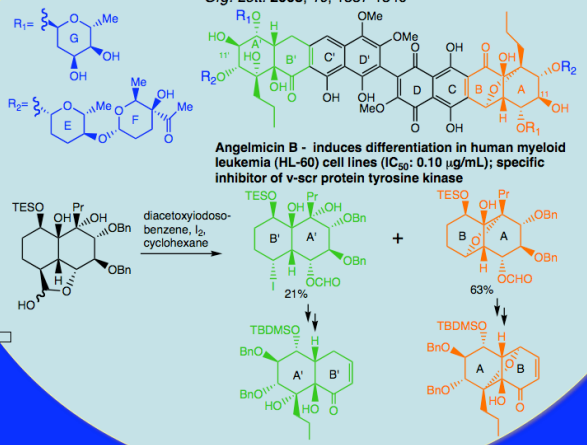


Azaspiracid-1: a potent marine toxin from mussels

"double-anomeric" - bisspiroketal

Synthesis of the AB and A'B' subunits of angelmicin B through the radical fragmentation of a central decalin-lactol precursor

Org. Lett. **2008**, *10*, 1337-1340

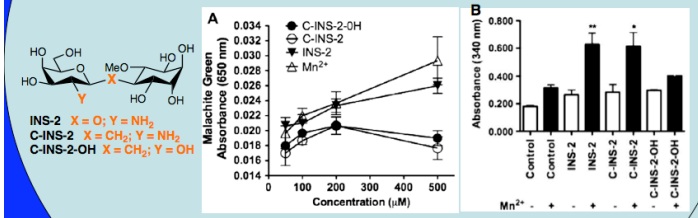


Angelmicin B - induces differentiation in human myeloid leukemia (HL-60) cell lines (IC_{50}: 0.10 μg/mL); specific inhibitor of v-scr protein tyrosine kinase

Synthesis of C-Glycoside Analogues of β-Galactosamine-(1->4)-3-O-Methyl-D-Chiro-Inositol and Assay as Activator of Protein Phosphatases PDHP and PP2Cα

Bioorg. Med. Chem. **2010**

INS-2 injected intravenously in rats is both insulin-mimetic and insulin-sensitizing. This bioactivity is attributed to allosteric activation of pyruvate dehydrogenase phosphatase (PDHP) and protein phosphatase 2Cα (PP2Cα). C-INS-2 activates PDHP comparable to INS-2, but failed to activate PP2Cα. C-INS-2-OH was inactive against both phosphatases.

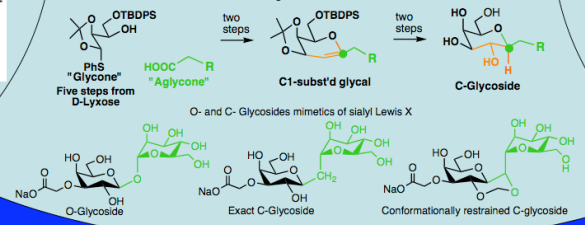


INS-2 X = O; Y = NH_2
C-INS-2 X = CH_2; Y = NH_2
C-INS-2-OH X = CH_2; Y = OH

(A) PP2C activity. Phosphopeptide as substrate with increasing concentrations of $MnCl_2$, INS-2, C-INS-2-OH or C-INS-2.
(B) PDHP assay. INS-2, C-INS-2 and C-INS-2-OH ±5 mM Mn^{2+}

C-Glycosides as probes for carbohydrate recognition

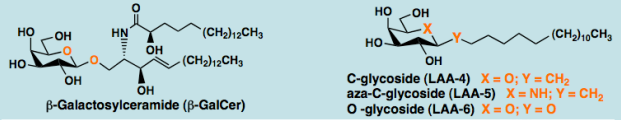
Eur. J. Org. Chem. **2008**, 645-654



Glycoside analogues of β-galactosylceramide, a novel class of small molecule antiviral agents that inhibit

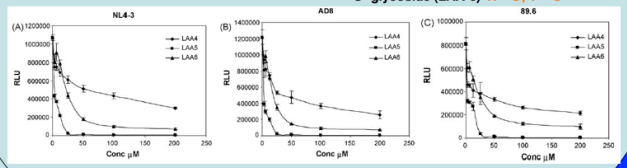
Antiviral Res. **2008**, *80*, 54-61

All three analogues showed similar binding as β-GalCer in a monolayer assay using a HIV-1 (IIIB) V3-loop specific peptide and also inhibited HIV Env-mediated cell-to-cell fusion and viral entry. The O- and C- glycoside did not show significant cytotoxicity.



β-Galactosylceramide (β-GalCer)

C-glycoside (LAA-4) X = O; Y = CH_2
aza-C-glycoside (LAA-5) X = NH; Y = CH_2
O -glycoside (LAA-6) X = O; Y = O



Glycoside analogs of GalCer inhibit virus infection in a coreceptor independent manner. TZM cells were infected with X4 tropic (A) or R5 tropic NLAD8 (B) or dual tropic 89.6 (C) virus in the presence of varying concentrations of test compounds