

SELECTIVE INHIBITORS OF GALECTIN-3

CROSS-REFERENCE TO A RELATED APPLICATION

[0001] This disclosure claims priority from U.S. provisional application number 63/605,083 filed on December 1, 2023 which is incorporated herein by reference in its entirety.

TECHNICAL FIELD

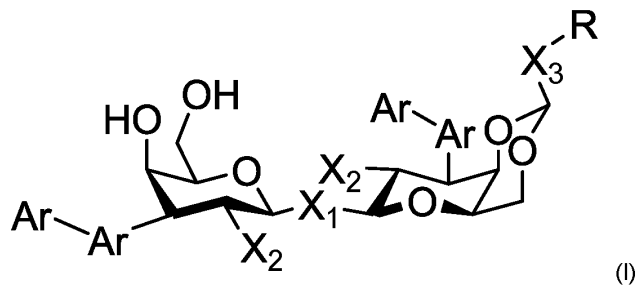
[0002] This disclosure relates to the field of galectin-3 inhibitors, methods using same and methods for producing same.

BACKGROUND OF THE ART

[0003] Galectins are proteins that bind to galactoside residues and their natural ligands are glycoconjugates having a non-reducing galactopyranoside terminus. Galectins have the ability to regulate numerous biological process, including neoplastic transformation, tumor cell survival processes, angiogenesis, and tumor metastasis. Galectin inhibitors or galectin antagonists are thus desired for the treatment of disease with upregulated galectin. Galectin-3 in particular, is a therapeutic target for medical interventions for example for lung and liver fibrosis. Since galectins perform many vital functions, a selective inhibitor to galectin-3 is desired to avoid affecting other galectins such as galectin-1. Indeed, galectin-1 is expressed in many tissues and has structural homology with galectin-3. In addition, cellular penetration is required to inhibit galectin-3 effectively. The current inhibitors and antagonists have poor pharmacokinetic properties and poor cell penetration. They also lack specificity to galectin-3 and inhibit both galectin-1 and galectin-3 similarly. Accordingly, there is a need for galectin-3 inhibitors that have improved specificity to galectin-3 and improved pharmacokinetic properties.

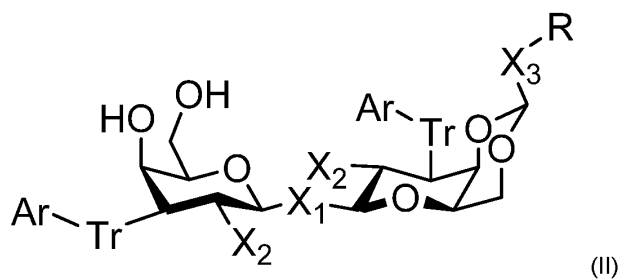
SUMMARY

[0004] In one aspect, there is provided a compound of formula I



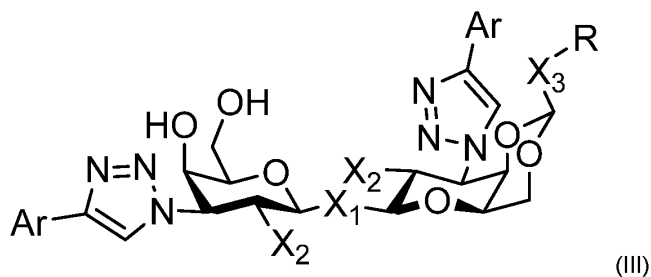
[0005] X_1 is O or S, X_2 is OH or a halogen, X_3 is O, S, N(J) or is absent, wherein J is H or R, R is a branched or linear alkyl, a cycloalkyl, an aryl or a heteroaryl that is optionally substituted with one or more of a halogen, an alkyl, -O-alkyl, or -NH-alkyl, and Ar are each independently an aryl or a heteroaryl that is optionally substituted with one or more of a halogen, an alkyl, -O-alkyl, or -NH-alkyl.

[0006] In some embodiments, the compound of formula I is of formula II



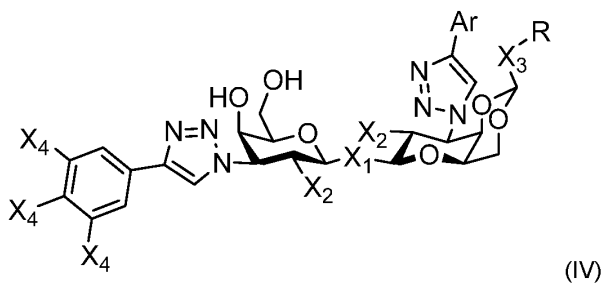
[0007] wherein X_1 , X_2 , X_3 , R and Ar are as defined in claim 1 and wherein Tr is a triazole that is optionally substituted with one or more of a halogen, an alkyl, -O-alkyl, or -NH-alkyl.

[0008] In some embodiments, the compound of formula I is of formula III



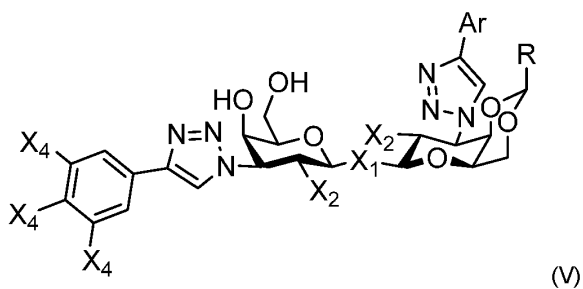
[0009] wherein X_1 , X_2 , X_3 , Ar and R are as defined above.

[0010] In some embodiments, the compound of formula I is of formula IV



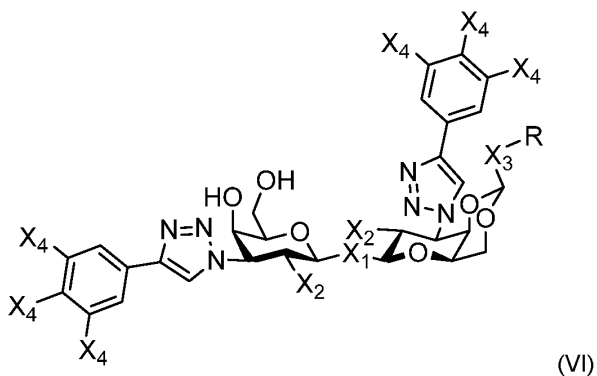
[0011] wherein X_1 , X_2 , X_3 , Ar and R are as defined above, and wherein each of X_4 is independently a halogen or a hydrogen.

[0012] In some embodiments, the compound of formula I is of formula V



[0013] wherein X_1 , X_2 , Ar and R are as defined above, and wherein each of X_4 is independently a halogen or a hydrogen.

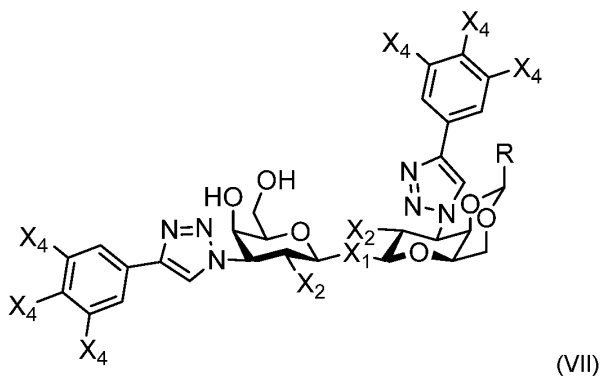
[0014] In some embodiments, the compound of formula I is of formula VI



(VI)

[0015] wherein X_1 , X_2 , X_3 , and R are as defined above, and wherein each of X_4 is independently a halogen or a hydrogen.

[0016] In some embodiments, the compound of formula I is of formula VII



(VII)

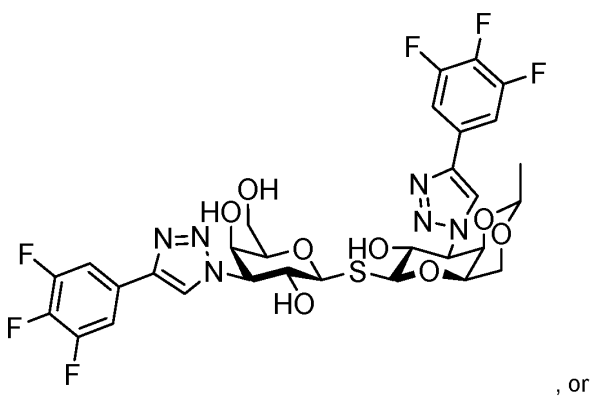
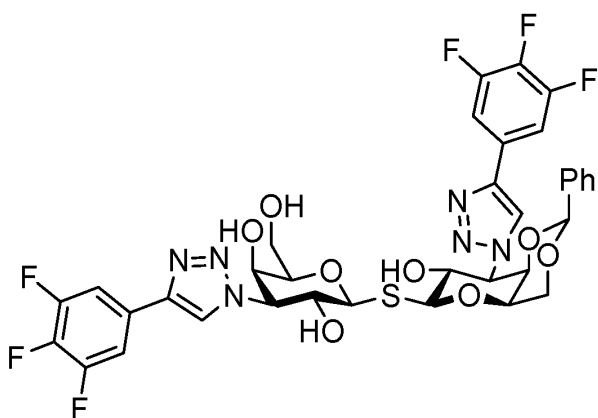
[0017] wherein X_1 , X_2 , and R are as defined above, and wherein each of X_4 is independently a halogen or a hydrogen.

[0018] In some embodiments, the halogen is F, Br or Cl.

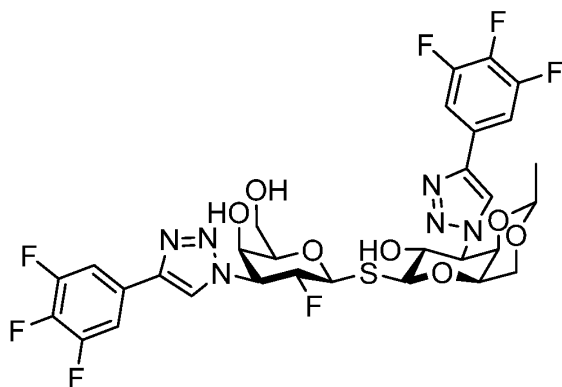
[0019] In some embodiments, for R the branched or linear alkyl is a C_1 - C_6 .

[0020] In some embodiments, X_1 is S.

- [0021] In some embodiments, the cycloalkyl is a C₃-C₆ cycloalkyl.
- [0022] In some embodiments, the aryl for formulas II-VII is phenyl.
- [0023] In some embodiments, the heteroaryl is pyridine or pyrimidine.
- [0024] In some embodiments, R is methyl or phenyl.
- [0025] In some embodiments, the alkyl of the alkyl or -O-alkyl substituents is a C1-C7 branched or linear alkyl.
- [0026] In some embodiments, the compound is



, or

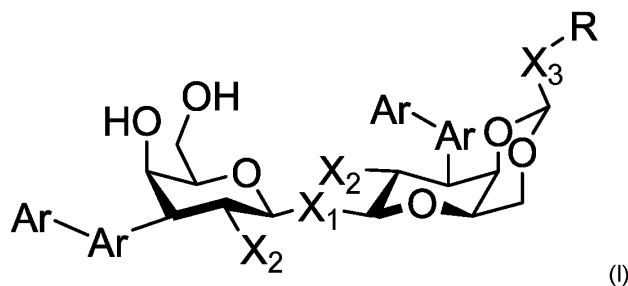


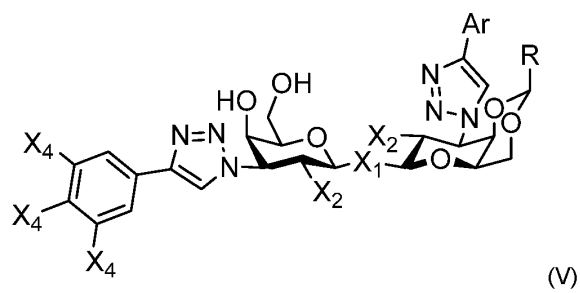
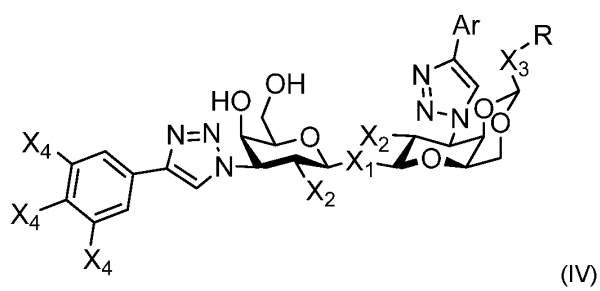
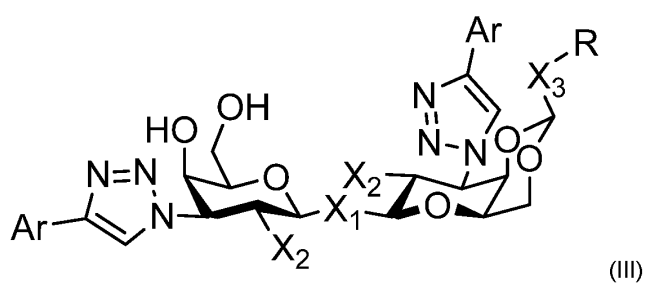
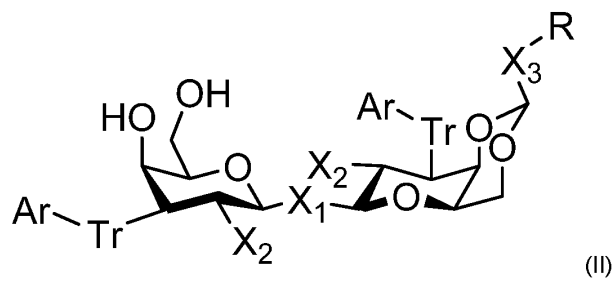
[0027] In a further aspect, there is provided a method for treating fibrosis or cancer in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of the compound as defined herein. In a further aspect, there is provided the use of the compound as defined herein, for treating fibrosis or cancer in a subject in need thereof. In some embodiments, the cancer is selected from lymphoma, glioblastoma, pulmonary metastasis in breast or colon cancer, lung carcinoma, lung adenocarcinoma, breast cancer, prostate cancer, bladder cancer, melanoma, thyroid cancer colon cancer, ovarian cancer, pancreatic carcinoma, gastric cancer, hepatocellular carcinoma, or oral squamous cell carcinoma.

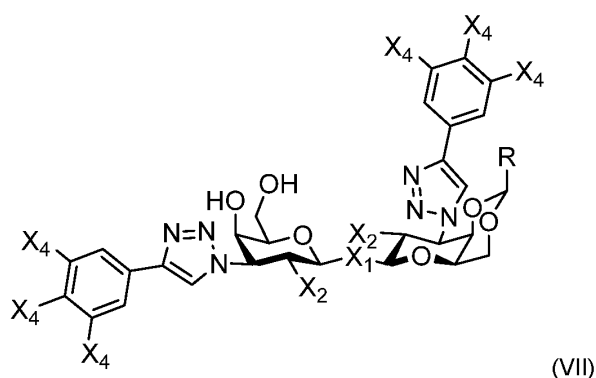
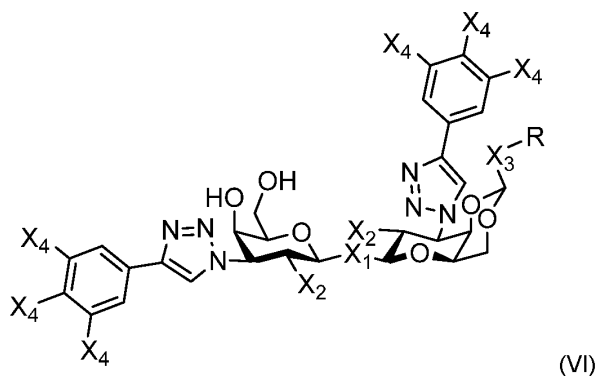
[0028] Many further features and combinations thereof concerning the present improvements will appear to those skilled in the art following a reading of the instant disclosure.

DETAILED DESCRIPTION

[0029] There is provided a compound of formula I, II, III, IV, V, VI, or VII:



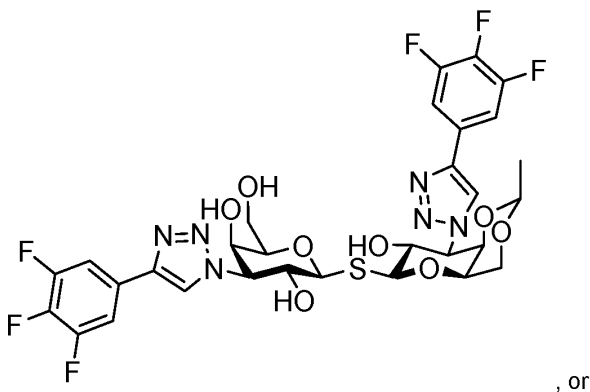
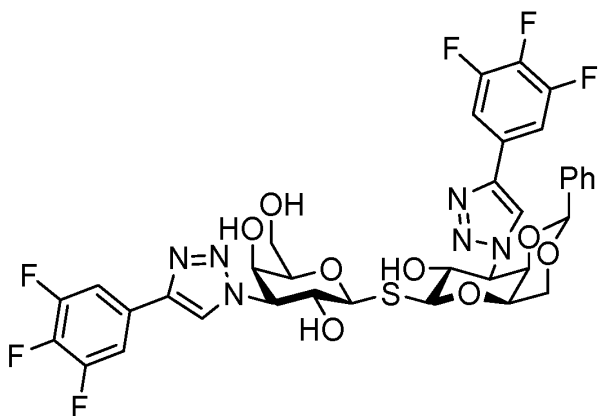




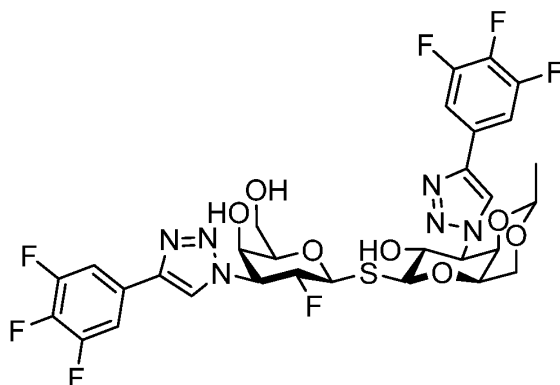
[0030] X₁ is O or S. X₂ is OH, or a halogen. The halogen is for example selected from F, Br, and Cl. X₃ is O, S, N(J) or is absent where J is H or R. Each of X₄ is independently a halogen or a hydrogen. The halogen is preferably F. R is a branched or linear alkyl, a cycloalkyl, an aryl or a heteroaryl. Ar is an aryl or a heteroaryl. Tr is a triazole. Ar, Tr and/or R are optionally substituted with one or more substituents. Examples of substituents include but are not limited to halogen, -O-alkyl, alkyl and -N(J)-alkyl. Tr is for example mono-fluorophenyl triazole, di-fluorophenyl triazole, or tri-fluorophenyl triazole. The substituents on R are preferably but not limited to hydrophobic substituents such as methyl, methoxy, ethyl, ethoxy, and alkanolamine. The substituents are more preferably apolar for example a C₁-C₇ linear or branched alkyl such as methyl, ethyl, propyl, butyl, hexyl, and heptyl. The branched or linear alkyl is for example a linear or branched C₁-C₆, preferably C₁-C₄ such as methyl, ethyl, propyl, isopropyl, isobutyl sec-butyl, and *tert*-butyl. The cycloalkyl is for example a C₃-C₆ cycloalkyl such as cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl. The aryl group is for example phenyl. The heteroaryl is for example a 5 or 6 membered aromatic ring with at least one carbon atom and one or more heteroatoms

selected from N, O or S. Examples of heteroaryl include but are not limited to pyridine, pyrimidine, diazine, triazine, tetrazine, diazole, pyrazole, pyrrole, triazole, tetrazole, thiophene, thiazole, imidazole, isoxazole, oxazole, isothiazole, thiadiazole, oxadiazole, selenazole, selenadiazole, furan and oxazole that are each independently substituted or unsubstituted with one or more of the substituents described herein.

[0031] In some embodiments, the compound is selected from



, or



[0032] The compound of formulas I, Ia, Ib, Ic and Id are a disaccharide where the two saccharides are linked by X_1 which is O or S and one of the saccharides has adjacent -OH and -CH₂-OH groups. This part of the compound is responsible, at least in part, for the antagonistic properties of the molecule (antagonist of galectin-3). The other saccharide in contrast has the formerly -OH and -CH₂-OH groups (that have lost the hydrogen of the hydroxyl and each of the oxygen atoms) forming a covalent bond with the same carbon atom thereby forming a 6 membered cyclic structure. This hydrophobicity on one side of the compound improves the compound's capacity to enter the lipophilic cell membrane. A reduced or lack of polarity also increases the compound's ability to cross the cell membrane. In preferred embodiments, the compounds are selective inhibitors of galectin-3 (compared to galectin-1). This is an advantage for the treatment of conditions where galectin-3 is upregulated but not galectin-1. Receiving an antagonist of galectin-1 can have severe side effects because it plays a role in sensitizing resting T lymphocytes to Fas (CD95)-mediated cell death via mitochondrial hyperpolarization, budding, and fission. Moreover, galectin-1 is expressed in many different tissues therefore non-selective galectin antagonists can lead to cell apoptosis in various tissues that are otherwise healthy.

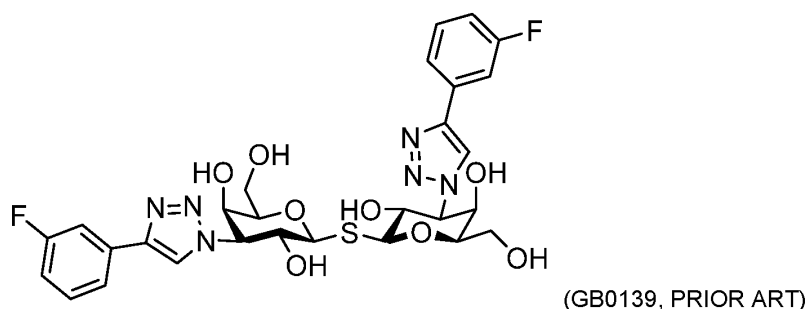
[0033] Accordingly, the compounds of the present disclosure are useful for the treatment of fibrosis (such as idiopathic pulmonary fibrosis), non-alcoholic fatty liver disease, non-alcoholic hepatic steatosis, non-alcoholic steatohepatitis, and cancers where galectin-3 is upregulated. Indeed, galectin-3 is a tumour suppressor because it has anti-apoptotic activity. Cancers where galectin-3 is dysregulated are described in Laderach, D. J., & Compagno, D. (2023). Inhibition of galectins in cancer: Biological challenges for their clinical application. *Frontiers in Immunology*, 13, 1104625. In some embodiments, the cancer is a lung cancer. The cancer, however, can be a lymphoma, glioblastoma, pulmonary metastasis in breast or colon cancer, lung

carcinoma, lung adenocarcinoma, breast cancer, prostate cancer, bladder cancer, melanoma, thyroid cancer colon cancer, ovarian cancer, pancreatic carcinoma, gastric cancer, hepatocellular carcinoma, or oral squamous cell carcinoma.

[0034] The compounds of the present disclosure can be formulated in pharmaceutical compositions with an excipient. The compounds can be administered as part of combination therapies, particularly for cancer. For example, the compounds can be administered in combination with chemotherapy.

EXAMPLE

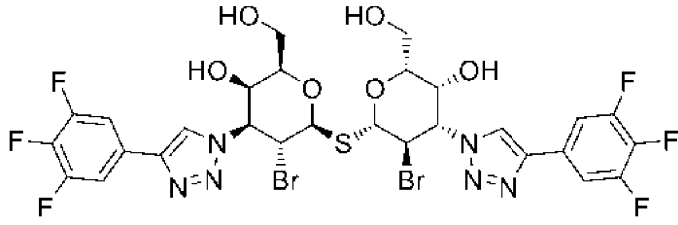
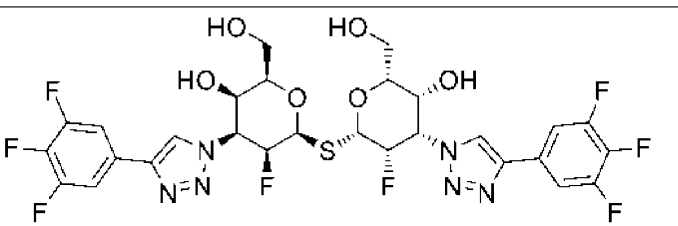
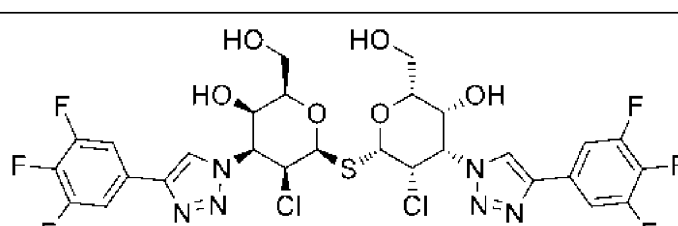
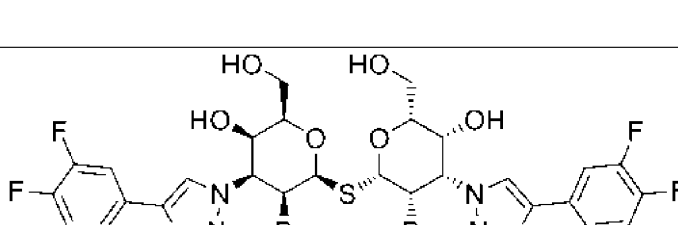
[0035] GB0139 (3,3'-dideoxy-3,3'-bis-[4-(3-fluorophényl)-1H-1,2,3-triazol-1-yl]-1,1'-sulfanediyl-di-β-D-galactopyranoside; also referred to as TD139) is a thiodigalactopyranoside inhibitor of galectins-1 and -3, which has reached Phase IIb clinical trials for the treatment of idiopathic pulmonary fibrosis. However, the properties of GB0139 are not optimal when compared to monosaccharide inhibitors. Indeed, GB0139 is not transported efficiently across the cell membrane and improvements are needed.

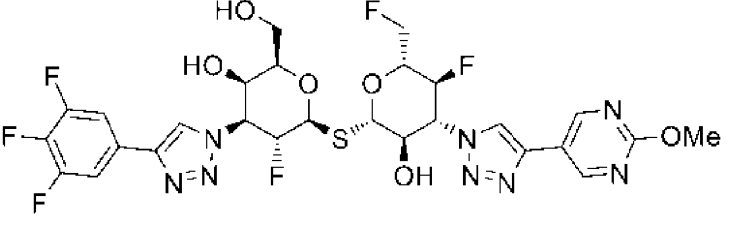
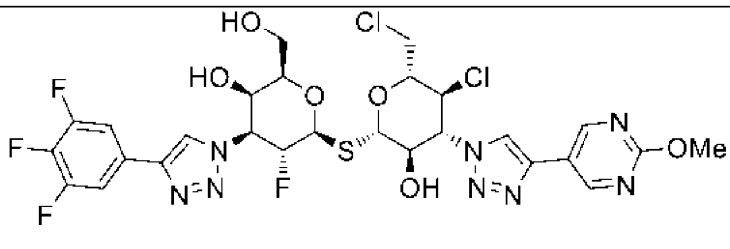
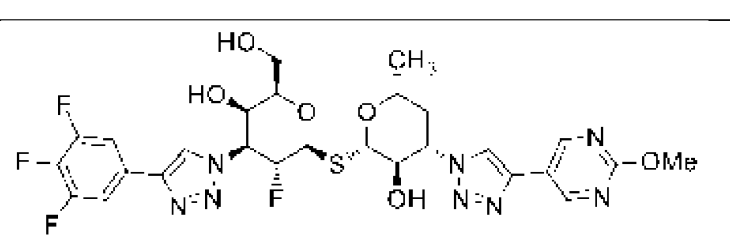
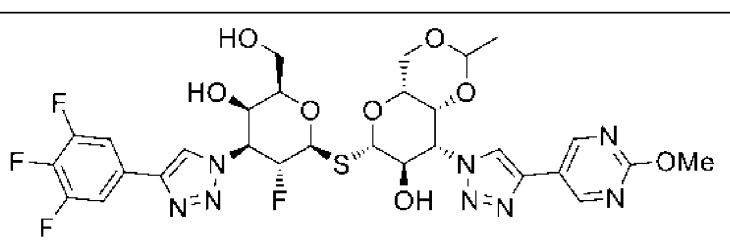
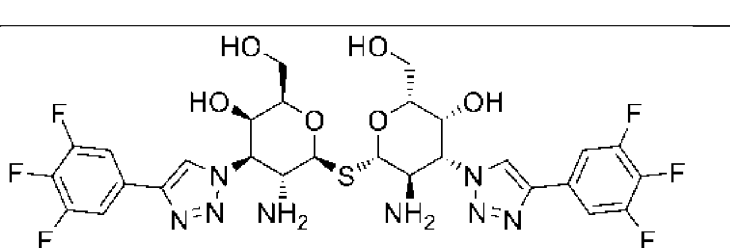


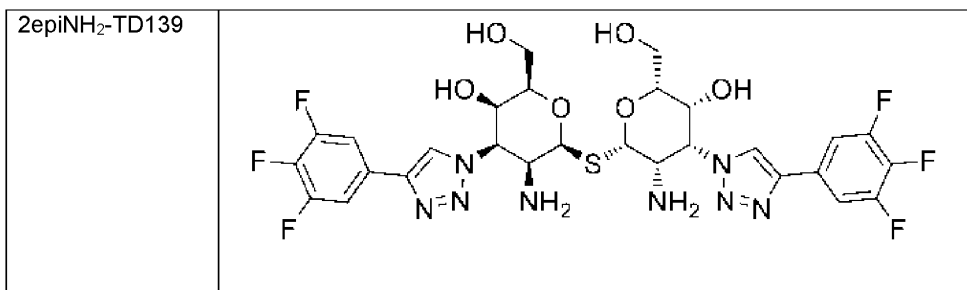
[0036] A comparative *in silico* study of the interaction of halogenated and non-halogenated compounds analogous to GB0139 with galectin-1 and -3 was carried out. A total of 14 compounds, including halogenated analogues of GB0139 (2X-GB0139) and other molecules were tested (Table 1).

Table 1. Initial compound for in silico screening

Name	Structure
TD139 or GB0139 (prior art)	
TD139-triF	
2F-TD139	
2Cl-TD139	

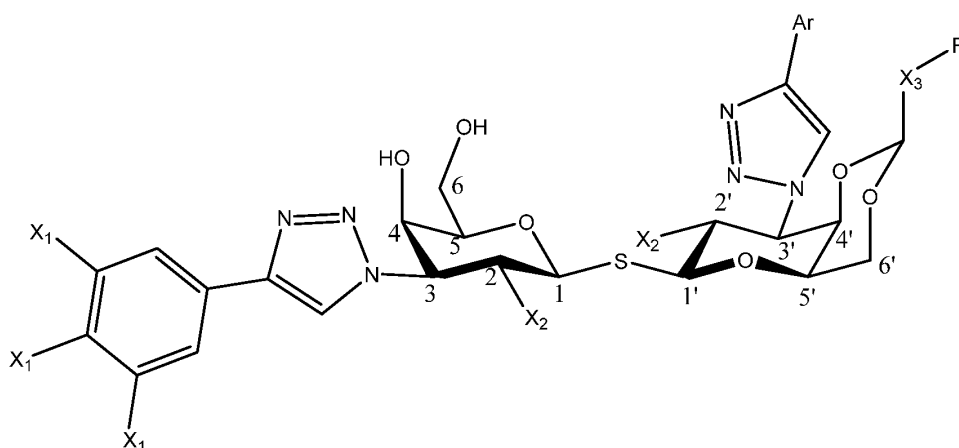
2Br-TD139	
2epiF-TD139	
2epiCl-TD139	
2epiBr-TD139	

Hyb-F	
Hyb-Cl	
Hyb-H	
Hyb-Ethy	
2NH ₂ -TD139	



[0037] Experimental structures for testing the *in silico* activity against gal-1 and gal-3 were used (PDB 4Y24 for Gal-1, and PDB 5E89, 5H9P and 6RZI for Gal-3) and the optimal binding conditions for TD139 on these experimental structures were determined. Binding results indicated that 2Br-TD139, 2Cl-TD139 and 2F-TD139-triF molecules have a lower potential affinity for galectin 1 and galectin 3, since the replacement of a hydroxyl group by a halogen weakens the binding of specific interactions through the loss of an H-bond between the ligand and gal-3. Also, the molecular docking of Hyb-Ethy suggests a high affinity with gal-3.

[0038] These initial results with GB0139 derivatives demonstrated that the central sugars of the molecule are responsible for most of the specific interactions directing molecule binding, while the ends, having a more dominant non-polar character, are responsible for non-specific interactions in galectin binding.



[0039] Among the 2X-GB0139 candidate molecules, the binding results indicate that the 2Br-GB0139-triF, 2Cl-GB0139-triF and 2F-GB0139-triF molecules have a lower potential affinity for

gal-1 and gal-3, since the replacement of a hydroxyl group by a halogen weakens the binding of specific interactions through the loss of an H-bond between the ligand and galectin. The halogen of the 1st sugar (bound to carbon 2 see above) is completely exposed to the solvent and does not interact with galectin, so its presence does not influence the docking pose obtained. On the other hand, the halogen atom on the second sugar (bound to carbon 2' see above) replaces oxygen O, which is involved in 4 H-bonds with the galectin. The loss of these bonds leads to a loss of affinity between these molecules and the galectin. In contrast, the binding of the 2NH₂-GB0139-triF molecule to gal-1 and gal-3 proteins indicates a potential affinity of the same order of magnitude as for the original ligand, and the presence of an amine group stabilizes the ligand's bound conformation, favoring good affinity.

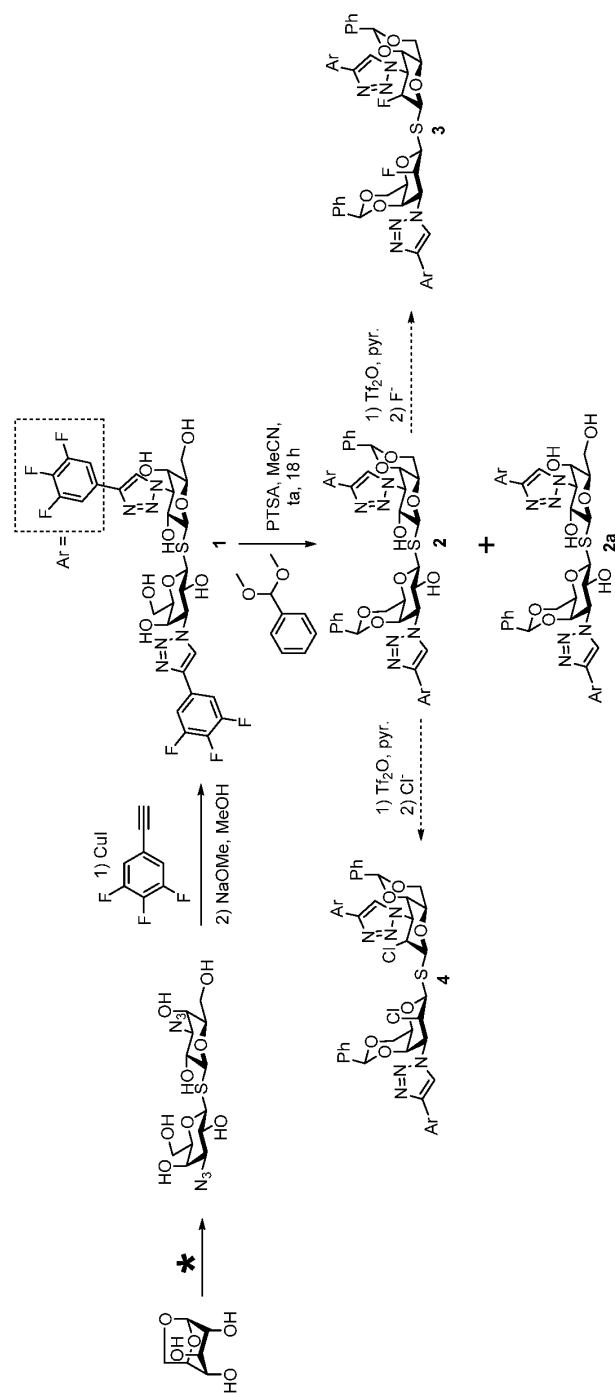
[0040] The molecular bonding of Hyb-Ethy showed a high affinity with galectin. Indeed, the terminal methyl of the "Ethy" group is positioned less than 4 angstrom from an NH₂ of Arg74, and a COO of Asp54 (sequence from the protein data bank (PDB) labeled 5E89, 5H9P or 6RZI for Gal-3).

[0041] Following these *in silico* studies, derivatives of GB0139 were synthesized (schemes 1-3 and Table 2). Initially, the synthesis pathway of scheme 1 was evaluated. Scheme 1 leverages the pathways previously developed and described in WO2020248068. This synthetic route allowed the preparation of bis-(2,4,6-tri-O-acetyl-3-azido-3-deoxy-β-D-galactopyranosyl)-sulfane from levoglucosane. Compound 1 (see scheme 1) was prepared which has 3 fluorine atoms on each of the aromatic groups after click and deprotection. Selective protection of the hydroxyl groups at positions O4/O4' and O6/O6' generated compound 2. Interestingly, as a by-product, a compound with a single protecting group (compound 2a) was generated. All attempts to install halogens in the C2/C2' positions failed. It was not possible to generate compounds 3 and 4 according to scheme 1. However, compounds 5 and 6, which resulted in the protection of diols at positions O4/O4' and O6/O6' in the form of ethylidene were successfully synthesized (see scheme 2). Scheme 3 demonstrates the synthesis of compounds where F replaces the hydroxyl attached to C2 of the saccharide. In one case, a compound incorporated 2 fluorine atoms at C2 and C2' (compound 14). The protection of analogue 17 as ethylidene yielded compound 18 and 19.

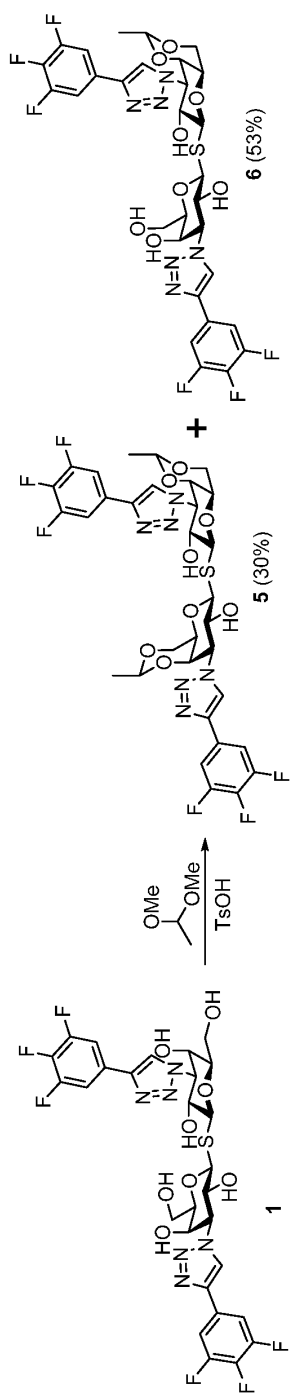
[0042] The specific protocol for the synthesis of the compounds as per Schemes 1-3 is presented in greater details below) The compounds produced were characterized by spectroscopy (notably nuclear magnetic resonance (NMR)) and high-resolution mass spectrometry (HRMS).

Scheme 1.

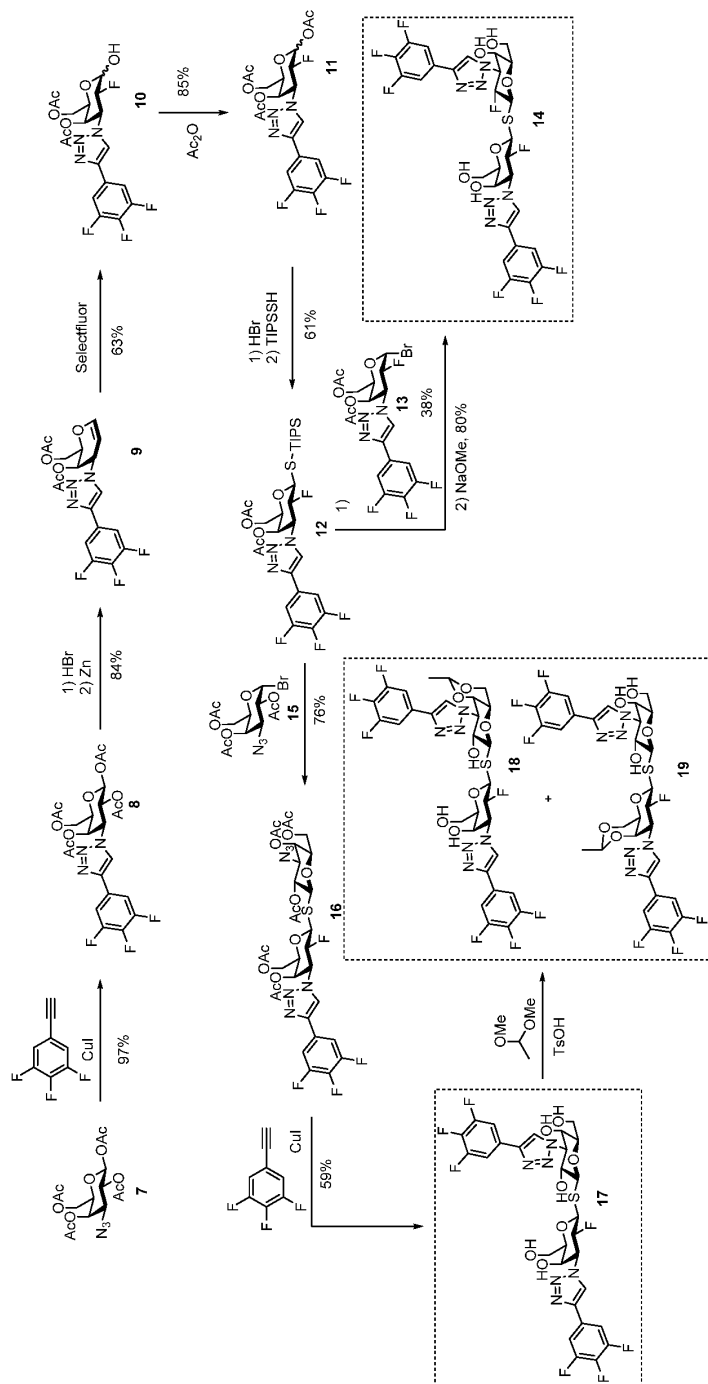
* = reaction conditions as per WO2020248068



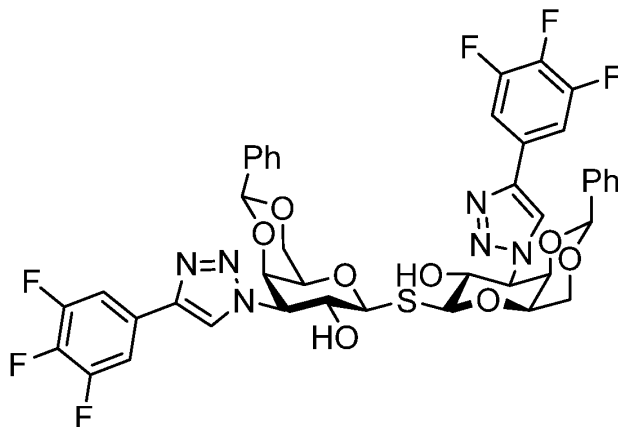
Scheme 2.



Scheme 3



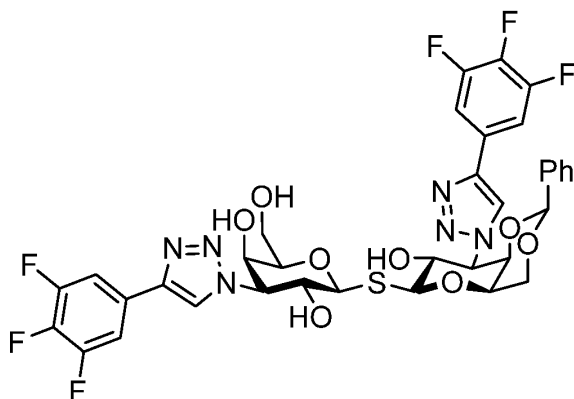
[0043] Bis-(4,6-di-O-benzylidene-3-deoxy-3-[4-(3,4,5-trifluorophenyl)-1H-1,2,3-triazol-1-yl]- β -D-galactopyranosyl)sulfane (**2**):



[0044] To a stirred solution of 3, 3'-di-deoxy-1,1'-sulfanediyl-3,3'-[4-(3,4,5-trifluorophenyl)-1H-1,2,3-triazol-1-yl]-di- β -D-galactopyranoside (265.2 mg, 0.3680 mmol) in MeCN (7 mL) was added benzaldehyde dimethyl acetal (220 μ L, 1.4722 mmol, 4 equiv.) and *p*-toluenesulfonyl chloride (*p*-TsOH) (14 mg, 0.07361 mmol, 0.2 equiv). The reaction was stirred at room temperature for 24h. The reaction was concentrated under reduced pressure and purified by flash chromatography (silica gel, MeOH/dichloromethane (DCM), 1:19 to 3:17) to give **2** as a white amorphous solid (196.4 mg, 0.219 mmol, 60 % yield) and **2a** as a white amorphous solid (54.2 mg, 0.0648 mmol, 18 % yield). Analytical data for **2**; R_f : 0.78 (MeOH/DCM, 1:9); $[\alpha]_D^{25} = -37$ (*c* 0.5, CHCl₃); ¹H NMR (500 MHz, acetone) δ 8.69 (d, ⁴*J*_{triazole-H3} = 1.8 Hz, 2H, triazole), 7.68 (m, 4H, Ar), 7.48 – 7.33 (m, 6H, Ar), 7.27 (m, 6H, Ar), 5.58 (t, ⁴*J*_{benzylidene-H6a} = ⁴*J*_{benzylidene-H6b} = 2.0 Hz, 2H, CHPh), 5.26 (dd, ³*J*_{H1-H2} = 9.5 Hz, ⁴*J*_{H1-H5} = 1.8 Hz, 2H, H-1), 5.24 (ddd, ³*J*_{H3-H2} = 10.1 Hz, ³*J*_{H3-H4} = 3.3 Hz, ⁴*J*_{H3-triazole} = 1.9 Hz, 2H, H-3), 4.90 (br, 2H, OH-2), 4.63 (dt, ³*J*_{H4-H3} = 3.2 Hz, ³*J*_{H4-H5} = ³*J*_{H4-H6b} = 1.5 Hz, 2H, H-4), 4.56 (t, ³*J*_{H2-H1} = ³*J*_{H2-H3} = 10.0 Hz, 2H, H-2), 4.31 (dt, ²*J*_{H6a-H6b} = 12.6 Hz, ³*J*_{H6a-H5} = 1.7 Hz, 2H, H-6a), 4.24 (dt, ²*J*_{H6b-H6a} = 12.6 Hz, ³*J*_{H6b-H5} = ⁴*J*_{H6b-H4} = 1.9 Hz, 2H, H-6b), 4.09 (p, ³*J*_{H5-H6a} = ³*J*_{H5-H6b} = ³*J*_{H5-H4} = ⁴*J*_{H5-H1} = 1.8 Hz, 2H, H-5); ¹³C NMR (126 MHz, acetone) δ 152.3 (ddd, *J* = 247.6, 10.2, 4.2 Hz, 4C, Ar), 144.7 (q, *J* = 2.5 Hz, 2C, triazole), 139.7 (dt, *J* = 250.0, 15.3 Hz, 2C, Ar), 139.1 (s, 2C, CHPh), 129.5 (s, 2C, CHPh), 129.2 (td, *J* = 9.2, 4.8 Hz, 2C, Ar), 128.8 (s, 4C, CHPh), 126.9 (s, 4C, CHPh), 122.9 (s, 1C, triazole), 110.2 (dd, *J* = 17.7, 5.6 Hz, 4C, Ar), 101.2 (s, 2C, CHPh), 85.3 (s, 2C, C-1), 76.0 (s, 2C, C-4), 71.2 (s, 2C, C-5), 69.7 (s, 2C, C-6), 68.4 (s, 2C, C-2), 66.6 (s, 2C, C-3); ¹⁹F NMR (470 MHz, acetone) δ -136.1 (dd, *J* = 19.9, 9.9 Hz, 4F, F-Ar), -

164.5 (td, $J = 19.9, 16.6, 9.9$ Hz, 2F, F-Ar); HRMS calcd for $C_{42}H_{36}O_8N_6F_6S^+$ $[M + H]^+$ 897.2136, found 897.2097.

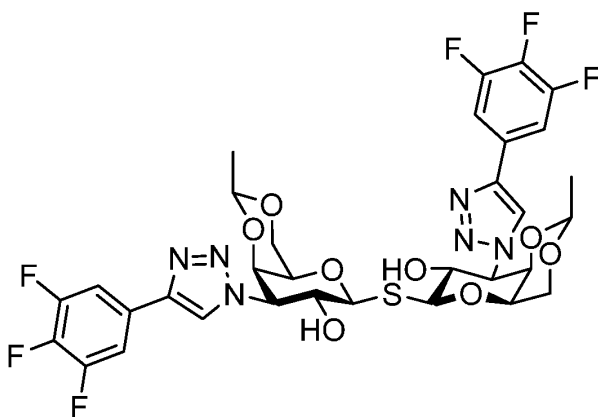
[0045] 4',6'-O-benzylidene-3, 3'-di-deoxy-1,1'-sulfanediyl-3,3'-[4-(3,4,5-trifluorophenyl)-1*H*-1,2,3-triazol-1-yl]-di-β-D-galactopyranoside (**2a**):



[0046] Analytical data for **2a**; R_f : 0.52 (MeOH/DCM, 1:9); $[\alpha]_D^{25} = -12$ (c 0.6, $CHCl_3$); 1H NMR (500 MHz, acetone) δ 8.59 (s, 1H, triazole'), 8.47 (s, 1H, triazole), 7.63 (dd, $J = 8.8, 6.7$ Hz, 2H, Ar'), 7.48 (dd, $J = 7.8, 1.3$ Hz, 2H, CHPh'), 7.44 (dd, $J = 8.8, 6.8$ Hz, 2H, Ar), 7.18 (q, $J = 7.6, 6.9$ Hz, 3H, CHPh'), 5.63 (s, 1H, CHPh'), 5.26 (dd, $^3J_{H3-H2} = 10.7$ Hz, $^3J_{H3-H4} = 3.9$ Hz, 1H, H-3'), 5.14 (d, $^3J_{H1-H2} = 9.5$ Hz, 1H, H-1'), 5.03 (d, $^3J_{OH4-H4} = 5.7$ Hz, 1H, OH-4), 5.00 (d, $^3J_{H1-H2} = 9.3$ Hz, 1H, H-1), 4.94 (dd, $^3J_{H3-H2} = 10.6$ Hz, $^3J_{H3-H4} = 2.9$ Hz, 1H, H-3), 4.85 (ddd, $^3J_{H2-H3} = 10.8$ Hz, $^3J_{H2-H1} = 9.5$ Hz, $^3J_{H2-OH2} = 4.7$ Hz, 1H, H-2'), 4.81 (td, $^3J_{H2-H3} = 10.9$ Hz, $^3J_{H2-H1} = 9.5$ Hz, $^3J_{H2-OH2} = 5.7$ Hz, 1H, H-2), 4.67 (dd, $^3J_{H4-H3} = 4.0$ Hz, $^3J_{H4-H5} = 1.8$ Hz, 1H, H-4'), 4.59 (d, $^3J_{OH2-H2} = 4.6$ Hz, 1H, OH-2'), 4.58 (d, $^3J_{OH2-H2} = 5.6$ Hz, 1H, OH-2), 4.41 (ddd, $^3J_{H4-OH4} = 5.3$ Hz, $^3J_{H4-H3} = 3.2$ Hz, $^3J_{H4-H5} = 1.3$ Hz, 1H, H-4), 4.40 (dd, $^2J_{H6a-H6b} = 12.3$ Hz, $^3J_{H6a-H5} = 1.8$ Hz, 1H, H-6a'), 4.32 (dd, $^2J_{H6b-H6a} = 12.6$ Hz, $^3J_{H6b-H5} = 1.3$ Hz, 1H, H-6b'), 4.23 (br, 1H, OH-6), 4.13 (td, $^3J_{H5-H6a} = ^3J_{H5-H4} = 1.8$ Hz, $^3J_{H5-H6b} = 1.4$ Hz, 1H, H-5'), 4.01 (ddd, $^3J_{H5-H6a} = 6.7$ Hz, $^3J_{H5-H6b} = 5.0$ Hz, $^3J_{H5-H4} = 1.5$ Hz, 1H, H-5), 3.88 (dd, $^2J_{H6a-H6b} = 11.2$ Hz, $^3J_{H6a-H5} = 6.7$ Hz, 1H, H-6a), 3.81 (dd, $^2J_{H6b-H6a} = 11.5$ Hz, $^3J_{H6b-H5} = 5.2$ Hz, 1H, H-6b); ^{13}C NMR (126 MHz, acetone) δ 152.3 (ddd, $J = 248.0, 10.2, 3.7$ Hz, 2C, Ar'), 152.1 (ddd, $J = 246.0, 9.9, 4.1$ Hz, 2C, Ar), 144.6 (q, $J = 2.6$ Hz, triazole'), 144.3 (q, $J = 2.8, 2.4$ Hz, triazole), 139.7 (dt, $J = 250.1, 15.3$ Hz, Ar'), 139.5 (dt, $J = 248.3, 15.3$ Hz, Ar), 138.8 (s, 1C, CHPh'), 129.5 (s, 1C, CHPh'), 129.1 (td, $J = 8.7, 4.9$ Hz, 2C, Ar/Ar'), 128.8 (s, 2C, CHPh'), 127.1 (s, 2C, CHPh'), 122.7 (s, 1C, triazole), 122.5 (s, 1C, triazole'), 110.2 (dd, $J = 17.4, 5.7$ Hz, 2C,

Ar'), 110.0 (dd, $J = 17.6, 5.2$ Hz, 2C, Ar), 101.8 (s, 1C, CHPh'), 86.2 (s, 1C, C-1), 86.1 (s, 1C, C-1'), 80.8 (s, 1C, C-5), 76.1 (s, 1C, C-4'), 71.5 (s, 1C, C-5'), 70.2 (s, 1C, C-6'), 69.9 (s, 1C, C-4), 68.3 (s, 2C, C-2/C-2'), 68.0 (s, 1C, C-3), 66.3 (s, 1C, C-3'), 62.4 (s, 1C, C-6); ^{19}F NMR (470 MHz, acetone) δ -136.1 (dd, $J = 19.9, 8.3$ Hz, 2F, Ar), -136.4 (dd, $J = 20.7, 9.1$ Hz, 2F, Ar), -164.5 (tt, $J = 19.9, 6.6$ Hz, 1F, Ar), -165.1 (tt, $J = 19.9, 6.6$ Hz, 1F, Ar); HRMS calcd for $\text{C}_{35}\text{H}_{31}\text{O}_8\text{N}_6\text{F}_6\text{S}^+ [\text{M} + \text{H}]^+$ 809.1823, found 809.1808.

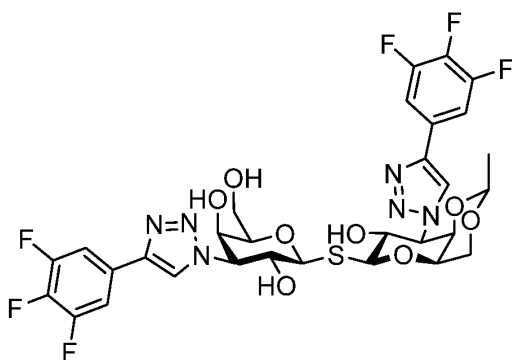
[0047] Bis-(4,6-di-O-ethylidene-3-deoxy-3-[4-(3,4,5-trifluorophenyl)-1*H*-1,2,3-triazol-1-yl]- β -D-galactopyranosyl)sulfane (**5**):



[0048] To a stirred solution of compound **1** (53 mg, 0.07355 mmol) in MeCN (1.5 mL) was added 1,1-diethoxyethane (11.5 μL , 0.0809 mmol, 1.1 equiv.) and *p*-TsOH (3 mg, 0.01467 mmol, 0.2 equiv). The reaction was stirred at room temperature overnight. The reaction was quenched with Et_3N (15 μL , 0.11 mmol, 1.5 equiv) and concentrated under reduce pressure. The crude mixture was purified by flash chromatography (silica gel, MeOH/DCM, 1:19 to 3:17) to give **5** as a white amorphous solid (16.1 mg, 0.0208 mmol, 30% yield) and **6** as a white amorphous solid (27.4 mg, 0.0367 mmol, 53% yield). Analytical data for **5**; R_f : 0.8 (MeOH/DCM, 1:9); $[\alpha]_{\text{D}}^{25} = -48$ (c 0.7, Acetone); ^1H NMR (500 MHz, acetone) δ 8.62 (s, 2H, triazole), 7.64 (dd, $J = 9.2, 6.7$ Hz, 4H, Ar), 5.28 (ddd, $^3J_{\text{H}2-\text{H}3} = 10.6$ Hz, $^3J_{\text{H}2-\text{H}1} = 9.9$ Hz, $^3J_{\text{H}2-\text{OH}2} = 4.4$ Hz, 2H, H-2), 5.06 (dd, $^3J_{\text{H}3-\text{H}2} = 10.9$ Hz, $^3J_{\text{H}3-\text{H}4} = 3.4$ Hz, 2H, H-3), 4.93 (d, $^3J_{\text{H}1-\text{H}2} = 9.3$ Hz, 2H, H-1), 4.86 (q, $J = 5.1$ Hz, 2H, CHCH₃), 4.58 (dd, $^3J_{\text{H}4-\text{H}3} = 3.5$ Hz, $^3J_{\text{H}4-\text{H}5} = 1.3$ Hz, 2H, H-4), 4.38 (dd, $^2J_{\text{H}6a-\text{H}6b} = 12.6$ Hz, $^3J_{\text{H}6a-\text{H}5} = 1.6$ Hz, 2H, H-6a), 4.25 (d, $^3J_{\text{OH}2-\text{H}2} = 4.6$ Hz, 2H, OH-2), 4.16 (dd, $^2J_{\text{H}6b-\text{H}6a} = 12.7$ Hz, $^3J_{\text{H}6b-\text{H}5} = 2.0$ Hz, 2H, H-6b), 4.08 (q, $^3J_{\text{H}5-\text{H}4} = ^3J_{\text{H}5-\text{H}6a} = ^3J_{\text{H}5-\text{H}6b} = 1.7$ Hz, 2H, H-5), 1.22 (d, $J = 5.1$ Hz, 6H,

CHCH₃); ¹³C NMR (126 MHz, acetone) δ 152.3 (ddd, *J* = 247.0, 10.0, 4.3 Hz, 4C, Ar), 144.0 (q, *J* = 2.2 Hz, 2C, triazole), 139.7 (dt, *J* = 249.4, 15.5 Hz, 2C, Ar), 129.2 (td, *J* = 9.0, 4.8 Hz, 2C, Ar), 123.2 (s, 2C, triazole), 110.1 (dd, *J* = 17.4, 5.4 Hz, 4C, Ar), 100.4 (s, 2C, CHCH₃), 86.9 (s, 2C, C-1), 76.0 (s, 2C, C-4), 71.6 (s, 2C, C5), 70.0 (s, 2C, C-6), 67.2 (s, 2C, C-2), 65.6 (s, 2C, C-3), 21.4 (s, 2C, CHCH₃); ¹⁹F NMR (470 MHz, acetone) δ -136.1 (dd, *J* = 19.7, 8.9 Hz, 4F, Ar), -164.6 (tt, *J* = 20.3, 6.6 Hz, 2F, Ar); HRMS calcd for C₃₂H₃₁O₈N₆F₆S⁺ [M + H]⁺ 773.1823, found 773.1803

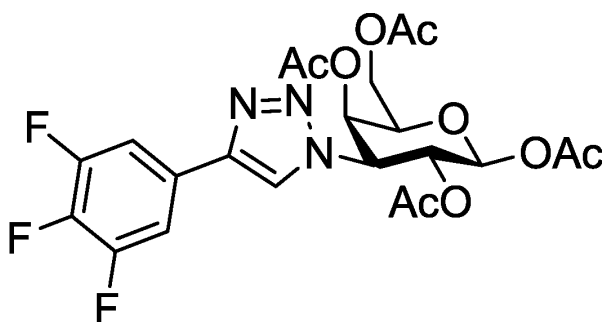
[0049] 4',6'-O-ethylidene-3, 3'-di-deoxy-1,1'-sulfanediyl-3,3'-[4-(3,4,5-trifluorophenyl)-1*H*-1,2,3-triazol-1-yl]-di-β-D-galactopyranoside (**6**):



[0050] Analytical data for **6**; R_f: 0.52 (MeOH/DCM, 1:9); [α]_D²⁵ = -1.1 (c 0.9, MeOH); ¹H NMR (500 MHz, acetone) δ 8.70 (s, 1H, triazole), 8.58 (s, 1H, triazole), 7.72 (td, *J* = 9.2, 6.7 Hz, 4H, Ar/Ar'), 5.14 (dd, ³*J*_{H3-H2} = 10.6 Hz, ³*J*_{H3-H4} = 3.5 Hz, 1H, H-3'), 5.08 (d, ³*J*_{H1-H2} = 9.4 Hz, 1H, H-1'), 4.99 (d, ³*J*_{H1-H2} = 9.4 Hz, 1H, H-1), 4.95 (dd, ³*J*_{H3-H2} = 10.6 Hz, ³*J*_{H3-H4} = 2.8 Hz, 1H, H-3), 4.93 (d, ³*J*_{OH4-H4} = 5.4 Hz, 1H, OH-4), 4.85 (ddd, ³*J*_{H2-H3} = 10.6 Hz, ³*J*_{H2-H1} = 9.4 Hz, ³*J*_{H2-OH2} = 5.4 Hz, 1H, H-2), 4.78 (q, *J* = 5.1 Hz, 1H, CHCH₃), 4.77 (ddd, ³*J*_{H2-H3} = 10.6 Hz, ³*J*_{H2-H1} = 9.6 Hz, ³*J*_{H2-OH2} = 5.0 Hz, 1H, H-2'), 4.62 (d, ³*J*_{OH2-H2} = 5.5 Hz, 1H, OH-2), 4.56 (d, ³*J*_{OH2-H2} = 5.1 Hz, 1H, OH-2'), 4.42 (ddd, ³*J*_{H4-OH4} = 5.1 Hz, ³*J*_{H4-H3} = 2.8 Hz, ³*J*_{H4-H5} = 1.0 Hz, 1H, H-4), 4.42 (dd, ³*J*_{H4-H3} = 3.5 Hz, ³*J*_{H4-H5} = 1.2 Hz, 1H, H-4'), 4.27 (br dd, ³*J*_{OH6-H6a} = 6.7 Hz, ³*J*_{OH6-H6b} = 4.7 Hz, 1H, OH-6), 4.23 (dd, ²*J*_{H6a-H6b} = 12.5 Hz, ³*J*_{H6a-H5} = 1.5 Hz, 1H, H-6a'), 4.04 (dd, ²*J*_{H6b-H6a} = 12.7 Hz, ³*J*_{H6b-H6a} = 1.9 Hz, 1H, H-6b'), 4.00 (q, ³*J*_{H5-H4} = ³*J*_{H5-H6a} = ³*J*_{H5-H6b} = 1.6 Hz, 1H, H-5'), 4.00 (ddd, ³*J*_{H5-H6a} = 6.3 Hz, ³*J*_{H5-H6b} = 4.7 Hz, ³*J*_{H5-H4} = 1.1 Hz, 1H, H-5), 3.89 (ddd, ²*J*_{H6a-H6b} = 10.9 Hz, ³*J*_{H6a-H5} = 6.3 Hz, ³*J*_{H6a-OH6} = 4.3 Hz, 1H, H-6a), 3.81 (ddd, ²*J*_{H6b-H6a} = 11.6 Hz, ³*J*_{H6b-OH6} = 6.5 Hz, ³*J*_{H6b-H5} = 4.8 Hz, 1H, H-6b), 1.19 (d, *J* = 5.1 Hz, 3H, CHCH₃); ¹³C NMR (126 MHz, acetone) δ 152.3 (ddd, *J* = 247.0, 10.0, 4.1 Hz, 4C, Ar/Ar'), 144.8 (q, *J* = 2.4 Hz, 1C, triazole), 144.4 (q, *J* = 2.4 Hz, 1C, triazole), 139.8 (dt, *J* =

249.7, 15.5 Hz, 1C, Ar/Ar'), 139.7 (dt, $J = 249.2, 15.7$ Hz, 1C, Ar/Ar'), 129.4 (td, $J = 9.2, 4.8$ Hz, 1C, Ar/Ar'), 129.3 (td, $J = 9.1, 4.8$ Hz, 1C, Ar/Ar'), 123.0 (s, 1C, triazole), 122.6 (s, 1C, triazole'), 110.3 (dd, $J = 17.2, 5.8$ Hz, 2C, Ar/Ar'), 110.2 (dd, $J = 17.1, 5.5$ Hz, 2C, Ar/Ar'), 99.7 (s, 1C, CHCH₃), 86.2 (s, 1C, C-1), 86.0 (s, 1C, C-1'), 80.8 (s, 1C, C-5), 75.3 (s, 1C, C-4'), 71.2 (s, 1C, C-5'), 69.9 (s, 1C, C-4), 69.5 (s, 1C, C-6'), 68.31 (s, 1C, C-2'), 68.28 (s, 1C, C-2), 68.2 (s, 1C, C-3), 66.3 (s, 1C, C-3'), 62.6 (s, 1C, C-6), 20.9 (s, 1C, CHCH₃); ¹⁹F NMR (470 MHz, acetone) δ -136.18 (dd, $J = 17.3, 8.3$ Hz, 2F, Ar/Ar'), -136.22 (dd, $J = 17.2, 8.3$ Hz, 2F, Ar/Ar'), -164.6 (tt, $J = 19.9, 6.6$ Hz, 1F, Ar/Ar'), -164.7 (tt, $J = 19.9, 5.8$ Hz, 1F, Ar/Ar'); HRMS calcd for C₃₂H₃₁O₈N₆F₆S⁺ [M + H]⁺ 747.1666, found 747.1651.

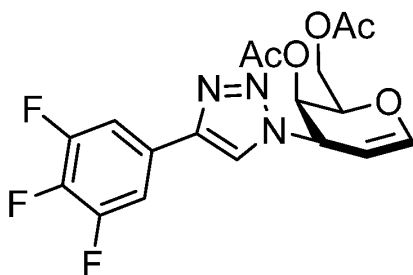
[0051] 1,2,4,6-tetra-*O*-acetyl-3-deoxy-3-[4-(3,4,5-trifluorophenyl)-1*H*-1,2,3-triazol-1-yl]- β -D-galactopyranose (**8**):



[0052] To a stirred solution of compound **7** (1 g, 2.6787 mmol) in N,N-Dimethylformamide (DMF) (27 mL) was added, in order, CuI (255 mg, 1.339 mmol, 0.5 equiv), 5-ethynyl-1,2,3-trifluorobenzene (830 μ L, 6.6968 mmol, 2.5 equiv.) and N,N-Diisopropylethylamine (DIPEA) (1.4 mL, 8.036 mmol, 3 equiv.). The reaction was heated at 60°C for 24h, then cooled down to rt and quench with the addition of sat. aq. NH₄Cl (60 mL). The solution was extracted with EtOAc (3 $\times$ 150 mL) and the combined organic phases were washed with water (150 mL) and brine (150 mL). The organic phase was dried over Na₂SO₄, filtered and concentrated under reduced pressure. The crude was purified by flash chromatography (silica gel, EtOAc/Hexanes, 3:7 to 1:1) to give **8** as a white amorphous solid (1.37 g, 2.585 mmol, 97% yield). R_f : 0.30 (EtOAc/Hexanes, 1:1); $[\alpha]_D^{25} = 66$ (c 0.4, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.75 (s, 1H, triazole), 7.46 – 7.38 (m, 2H, Ar), 6.51 (d, $^3J_{H1-H2} = 3.5$ Hz, 1H, H-1), 5.99 (dd, $^3J_{H2-H3} = 11.9$ Hz, $^3J_{H2-H1} = 3.6$ Hz, 1H, H-2), 5.62 (dd, $^3J_{H4-H3} = 3.1$ Hz, $^3J_{H4-H5} = 1.5$ Hz, 1H, H-4), 5.37 (dd, $^3J_{H3-H2} = 11.9$ Hz, $^3J_{H3-H4} = 3.1$ Hz, 1H,

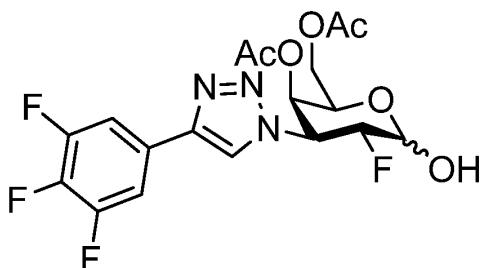
H-3), 4.52 (td, $^3J_{H5-H6a} = ^3J_{H5-H6b} = 6.8$ Hz, $^3J_{H5-H4} = 1.6$ Hz, 1H, H-5), 4.15 (dd, $^2J_{H6a-H6b} = 11.5$ Hz, $^3J_{H6a-H5} = 6.8$ Hz, 1H, H-6a), 4.10 (dd, $^2J_{H6b-H6a} = 11.4$ Hz, $^3J_{H6b-H5} = 6.5$ Hz, 1H, H-6b), 2.23 (s, 3H, OAc-1), 2.07 (s, 3H, OAc-4), 2.05 (s, 3H, OAc-6), 1.88 (s, 3H, OAc-2); ^{13}C NMR (126 MHz, CDCl_3) δ 170.5 (s, 1C, OAc-6), 169.7 (s, 1C, OAc-2), 169.1 (s, 1C, OAc-4), 168.8 (s, 1C, OAc-1), 151.8 (ddd, $J = 250.3, 10.3, 4.1$ Hz, 2C, Ar), 145.5 (q, $J = 2.7$ Hz, 1C, triazole), 139.9 (dt, $J = 252.6, 15.7$ Hz, 1C, Ar), 126.3 (td, $J = 8.8, 4.8$ Hz, 1C, Ar), 119.3 (s, 1C, triazole), 110.0 (dd, $J = 16.9, 5.5$ Hz, 2C, Ar), 89.3 (s, 1C, C-1), 69.2 (s, 1C, C-5), 68.6 (s, 1C, C-4), 65.4 (s, 1C, C-2), 61.3 (s, 1C, C-6), 58.4 (s, 1C, C-3), 21.0 (s, 1C, OAc-1), 20.8 (s, 1C, OAc-6), 20.5 (s, 1C, OAc-4), 20.4 (s, 1C, OAc-2); ^{19}F NMR (470 MHz, CDCl_3) δ -133.3 (dd, $J = 19.9, 8.3$ Hz, 2F, Ar), -160.1 (tt, $J = 21.6, 5.8$ Hz, 1F, Ar); HRMS calcd for $\text{C}_{22}\text{H}_{23}\text{O}_9\text{N}_3\text{F}_3^+$ $[\text{M} + \text{H}]^+$ 530.1381, found 530.1355.

[0053] 4,6-Di-O-acetyl-3-deoxy-3-[4-(3,4,5-trifluorophenyl)-1H-1,2,3-triazol-1-yl]-D-galactal (9):



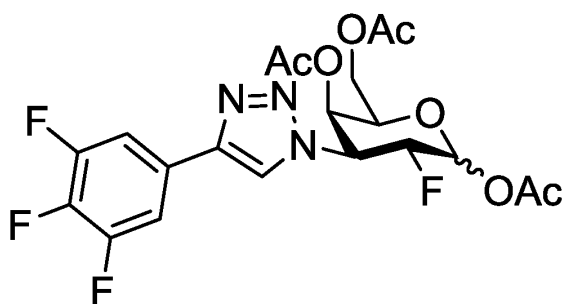
[0054] To a stirred solution of compound **8** (1.37 g, 2.585 mmol) in DCM (12 mL) was added HBr/AcOH 33% wt. (half of DCM, 6 mL). The reaction was stirred overnight at room temperature. The reaction was diluted with DCM (50 mL) and washed with water (2 × 50 mL), a saturated aqueous NaHCO_3 solution (50 mL) and brine (50 mL). The organic phase was concentrated under reduced pressure and the crude bromo was used without any further purification. The crude bromo was dissolved in MeCN (26 mL) then zinc dust (1,267 g, 19.3875 mmol, 7.5 equiv.) and NH_4Cl (1,037 g, 19.3875 mmol, 7.5 eq) were added. The reaction mixture was heated at 65°C for 1 h then filtered over celite pad, rinsed with MeCN and concentrated under reduced pressure. The crude solid was purified by flash chromatography (silica gel, EtOAc/Hexanes, 3:7 to 1:1) to give **8** as an amorphous white solid (893.4 mg, 2.172 mmol, 84% yield). The spectroscopic data derived from compound **8** matched those reported in WO2019075045.

[0055] 4,6-Di-O-acetyl-2,3-di-deoxy-2-fluoro-3-[4-(3,4,5-trifluorophenyl)-1*H*-1,2,3-triazol-1-yl]- α/β -D-galactopyranose (**10**):



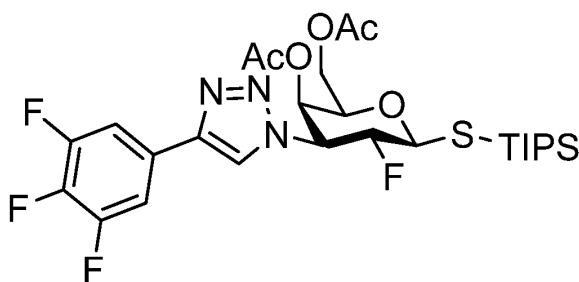
[0056] To a stirred solution of compound **9** (206.8 mg, 0.5028 mmol) in nitromethane (5 mL) was added Selectfluor™ (Sigma Aldrich) (213.7 mg, 0.6033 mmol, 1.1 equiv.) and the reaction mixture was stirred overnight. Water (3 mL) was added, and the reaction was heated at 90°C for 5h. After cooling to room temperature, nitromethane was removed under reduced pressure and the resulting aqueous phase was extracted with EtOAc (3 × 15 mL). The combined organic phases were washed with water (15 mL) and brine (15 mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude was purified by flash chromatography (silica gel, EtOAc/Hexanes, 1:4 to 3:2) to give **10** as an amorphous white solid (141.1 mg, 0.3163 mmol, 63% yield). The spectroscopic data derived from compound **10** matched those reported in WO2019075045A1.

[0057] 1,4,6-Tri-O-acetyl-2,3-di-deoxy-2-fluoro-3-[4-(3,4,5-trifluorophenyl)-1*H*-1,2,3-triazol-1-yl]- α/β -D-galactopyranose (**11**):



[0058] To a stirred solution of compound **10** (127.0 mg, 0.2839 mmol) in pyridine (6 mL) at 0°C was added acetic anhydride (Ac₂O) (268 µL, 2.839 mmol, 10 equiv.). The ice bath was removed, and the reaction was stirred at room temperature for 3h. Upon consumption of the starting material, the reaction was diluted in EtOAc (50 mL) and the resulting organic phase was washed with water (20 mL), a saturated aqueous NaHCO₃ solution (20 mL), an aqueous 1 M HCl solution (20 mL) and brine (20 mL). The organic phase was dried over Na₂SO₄, filtered, and concentrated under reduced pressure then purified by flash chromatography (EtOAc/Hexanes, 1:4 to 1:1) to give **11** as white amorphous solid (118.6 mg, 0.2424 mmol, 85% yield). The spectroscopic data derived from compound **11** match those reported in WO2019075045A1.

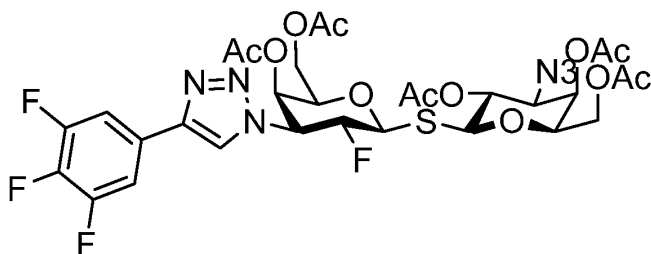
[0059] Triisopropyl 4,6-di-O-acetyl-2,3-dideoxy-2-fluoro-1-thio-3-[4-(3,4,5-trifluorophenyl)-1H-1,2,3-triazol-1-yl]-β-D-galactopyranoside (**12**):



[0060] To a stirred solution of compound **11** (60.5 mg, 0.1236 mmol) in dry DCM (1 mL) was added HBr/AcOH 33% wt (500 µL, half of DCM). The reaction was capped and stirred at room temperature overnight. The reaction was diluted with DCM (10 mL) and washed with water (5 mL), a saturated aqueous NaHCO₃ solution (5 mL) and brine (5 mL). The organic phase was dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude bromo was used without any further purification. To a stirred solution of the crude bromo in dry MeCN (previously nitrogen gas purged for 10 mins) (2 mL) was added K₂CO₃ (51.2 mg, 0.3708 mmol, 3 equiv) followed by triisopropylsilanethiol (TIPSSH) (53 µL, 0.2472 mmol, 2 equiv), and the mixture was stirred for 4h at rt. Upon completion of the reaction, the solvent was evaporated under reduced pressure. The residue was dissolved in CH₂Cl₂ (10 mL), washed with water (10 mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude was purified by flash chromatography (silica gel, EtOAc/Hexanes, 1:4 to 2:3) to give **12** as a white amorphous solid (46.6 mg, 0.07519 mmol, 61% yield). *R_f*: 0.55 (EtOAc/Hexanes, 2:3); [α]_D²⁵ = 35 (c 0.7, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.81 (s, 1H, triazole), 7.53 – 7.37 (m, 2H, Ar), 5.67 (td, ³J_{H4-}

^1H NMR (400 MHz, CDCl_3) δ 5.16 (ddd, $^2J_{\text{H2-F2}} = 48.3$ Hz, $^3J_{\text{H2-H3}} = 10.2$ Hz, $^3J_{\text{H2-H1}} = 9.0$ Hz, 1H, H-2), 4.96 (td, $^3J_{\text{H3-H2}} = ^3J_{\text{H3-F2}} = 10.5$ Hz, $^3J_{\text{H3-H4}} = 3.4$ Hz, 1H, H-3), 4.83 (dd, $^3J_{\text{H1-H2}} = 9.1$ Hz, $^3J_{\text{H1-F2}} = 2.5$ Hz, 1H, H-1), 4.17 (dd, $^2J_{\text{H6a-H6b}} = 10.7$ Hz, $^3J_{\text{H6a-H5}} = 5.0$ Hz, 1H, H-6a), 4.10 (dd, $^2J_{\text{H6b-H6a}} = 10.9$ Hz, $^3J_{\text{H6b-H5}} = 7.0$ Hz, 1H), 4.06 (ddd, $^3J_{\text{H5-H6b}} = 6.8$ Hz, $^3J_{\text{H5-H6a}} = 5.2$ Hz, $^3J_{\text{H5-H4}} = 1.0$ Hz, 1H, H-5), 2.05 (s, 3H, OAc-6), 2.04 (s, 3H, OAc-4), 1.33 (hept, $J = 7.5$ Hz, 3H, STIPS), 1.17 (d, $J = 7.3$ Hz, 9H, STIPS), 1.16 (d, $J = 7.5$ Hz, 9H, STIPS); ^{13}C NMR (126 MHz, CDCl_3) δ 170.5 (s, 1C, OAc-6), 169.3 (s, 1C, OAc-4), 151.8 (ddd, $J = 249.9, 9.7, 3.4$ Hz, 2C, Ar), 145.4 (q, $J = 2.7$ Hz, 1C, triazole), 139.9 (dt, $J = 253.2, 18.9$ Hz, 1C, Ar), 126.3 (td, $J = 8.7, 4.3$ Hz, 1C, Ar), 119.8 (s, 1C, triazole), 110.1 (dd, $J = 17.0, 5.2$ Hz, 2C, Ar), 88.5 (d, $^1J_{\text{C2-F2}} = 189.8$ Hz, 1C, C-2), 80.1 (d, $^2J_{\text{C1-F2}} = 23.8$ Hz, 1C, C-1), 75.8 (s, 1C, C-5), 69.1 (d, $^3J_{\text{C4-F2}} = 7.2$ Hz, 1C, C-4), 63.8 (d, $^2J_{\text{C3-F2}} = 19.6$ Hz, 1C, C-3), 62.0 (s, 1C, C-6), 20.8 (s, 1C, OAc), 20.6 (s, 1C, OAc), 18.5 (s, 1C, STIPS), 18.4 (s, 1C, STIPS), 13.1 (s, 1C, STIPS); ^{19}F NMR (470 MHz, CDCl_3) δ -133.4 (dd, $J = 20.3, 8.3$ Hz, 2F, F-Ar), -160.2 (tt, $J = 21.5, 7.2$ Hz, 1F, F-Ar), -191.6 (ddt, $^2J_{\text{F2-H2}} = 48.8$ Hz, $^3J_{\text{F2-H3}} = 10.7$ Hz, $^3J_{\text{F2-H1}} = ^4J_{\text{F2-H4}} = 2.5$ Hz); HRMS calcd for $\text{C}_{27}\text{H}_{38}\text{O}_5\text{N}_3\text{F}_4\text{Si}^+$ [M + H] $^+$ 620.2232, found 620.2260.

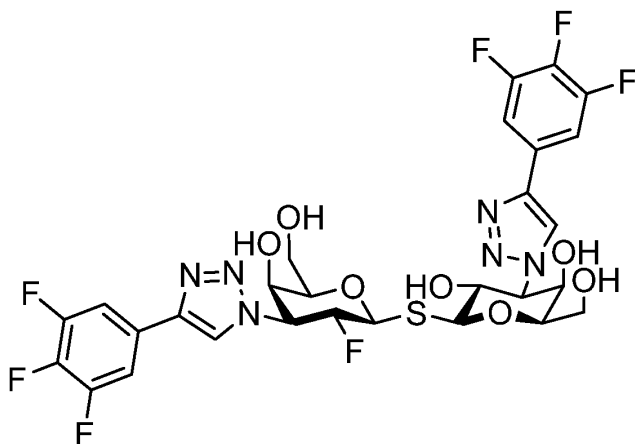
[0061] 2',4,4',6,6'-penta-O-acetyl-3'-azido-2, 3, 3'-tri-deoxy-2-fluoro-1,1'-sulfanediyl-3-[4-(3,4,5-trifluorophenyl)-1H-1,2,3-triazol-1-yl]-di- β -D-galactopyranoside (**16**):



[0062] To a stirred solution of compound **11** (29.8 mg, 0.06089 mmol) in dry DCM (1 mL) was added HBr/AcOH 33% wt (500 μL , half of DCM). The reaction was capped and stirred at room temperature overnight. The reaction was diluted with DCM (10 mL) and washed with water (5 mL), a saturated aqueous NaHCO_3 solution (5 mL) and brine (5 mL). The organic phase was dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The crude bromo **15** was used without any further purification. To a stirred solution of the crude bromo **15** in dry MeCN (previously nitrogen gas purged for 10 mins) (2 mL) was added compound **12** (31 mg, 0.06089 mmol). To the mixture was added a 1M TBAF solution in THF (91 μL , 0.09134 mmol, 1.5 equiv.)

dropwise and the reaction was stirred at room temperature for 15 mins. The reaction was concentrated under reduced pressure and purified by flash chromatography (silica gel, EtOAc/Hexanes, 1:9 to 2:3) to give **16** as a white amorphous solid (35.8 mg, 0.04609 mmol, 76% yield). R_f : 0.38 (EtOAc/Hexanes, 3:2); $[\alpha]_D^{25} = -6.7$ (c 1.0, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.86 (s, 1H, triazole), 7.66 – 7.34 (m, 2H, Ar), 5.68 (ddd, ³J_{H4-H3} = 3.0 Hz, ⁴J_{H4-F2} = 2.4 Hz, ³J_{H4-H5} = 1.1 Hz, 1H, H-4), 5.51 (dd, ³J_{H4-H3} = 3.4 Hz, ³J_{H4-H5} = 1.3 Hz, 1H, H-4'), 5.32 (dt, ²J_{H2-F2} = 48.6 Hz, ³J_{H2-H1} = ³J_{H2-H3} = 9.8 Hz, 1H, H-2), 5.28 (t, ³J_{H2-H1} = ³J_{H2-H3} = 10.0 Hz, 1H, H-2'), 5.05 (dd, ³J_{H1-H2} = 9.7 Hz, ³J_{H1-F2} = 2.2 Hz, 1H, H-1), 4.98 (td, ³J_{H3-H2} = ³J_{H3-F2} = 10.4 Hz, ³J_{H3-H4} = 3.3 Hz, 1H, H-3), 4.87 (d, ³J_{H1-H2} = 10.0 Hz, 1H, H-1'), 4.26 – 4.10 (m, 5H, H-6a/b, H-6a/b', H-5), 3.92 (td, ³J_{H5-H6a} = ³J_{H5-H6b} = 6.5 Hz, ³J_{H5-H4} = 1.3 Hz, 1H, H-5'), 3.70 (dd, ³J_{H3-H2} = 10.1 Hz, ³J_{H3-H4} = 3.4 Hz, 1H, H-3'), 2.19 (s, 3H, OAc), 2.17 (s, 3H, OAc), 2.09 (s, 3H, OAc), 2.06 (s, 3H, OAc), 2.05 (s, 3H, OAc); ¹³C NMR (126 MHz, CDCl₃) δ 170.7, 170.4, 170.1, 169.6, 169.2 (s, 5C, 5 × OAc), 151.8 (ddd, J = 250.1, 10.0, 5.0 Hz, 2C, Ar), 145.5 (q, J = 3.6 Hz, 1C, triazole), 139.9 (dt, J = 251.9, 16.0 Hz, 1C, Ar), 126.2 (td, J = 8.7, 3.4 Hz, 1C, Ar), 120.7 (s, 1C, triazole), 110.1 (dd, J = 17.2, 5.7 Hz, 2C, Ar), 85.5 (d, ¹J_{C2-F2} = 191.2 Hz, 1C, C-2), 81.3 (s, 1C' C-1'), 80.9 (d, ²J_{C1-F2} = 23.8 Hz, 1C, C-1), 75.8 (s, 1C, C-5'), 75.7 (s, 1C, C-5), 68.62 (s, 1C, C-2'), 68.59 (d, ³J_{C4-F2} = 6.2 Hz, 1C, C-4), 67.7 (s, 1C, C-4'), 63.7 (d, ²J_{C3-F2} = 19.1 Hz, 1C, C-3), 63.0 (s, 1C, C-3), 61.6 (s, 1C, C-6'), 61.2 (s, 1C, C-6), 20.94, 20.87, 20.81, 20.79, 20.5 (s, 5C, 5 × OAc); ¹⁹F NMR (470 MHz, CDCl₃) δ -133.4 (dd, J = 20.9, 7.8 Hz, 2F, Ar), -160.1 (tt, J = 20.3, 6.6 Hz, 1F, Ar), -194.8 (ddt, ²J_{F2-H2} = 48.3 Hz, ³J_{F2-H3} = 10.7 Hz, ³J_{F2-H1} = ⁴J_{F2-H4} = 2.3 Hz, 1F, F-2); HRMS calcd for C₃₀H₃₃O₁₂N₆F₄S⁺ [M + H]⁺ 777.1808, found 777.1835.

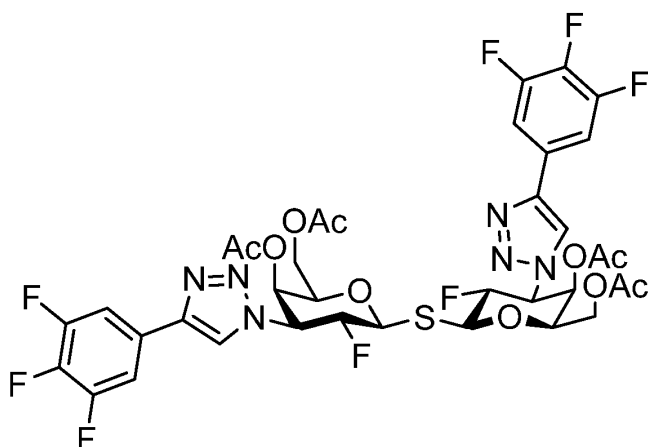
[0063] 2, 3, 3'-tri-deoxy-2-fluoro-1,1'-sulfanediyl-3, 3'-[4-(3,4,5-trifluorophenyl)-1*H*-1,2,3-triazol-1-yl]-di- β -D-galactopyranoside (**17**):



[0064] To a solution of compound **16** (35.8 mg, 0.04609 mmol) and CuI (4.4 mg, 0.023 mmol, 0.5 equiv) in MeCN (3 mL) was added 1-ethynyl-3-fluorobenzene (11.4 μ L, 0.09218 mmol, 2 equiv) and DIPEA (24 μ L, 0.1383 mmol, 3 equiv). The mixture was stirred 19h at 60 °C before cooling down to room temperature. A saturated aqueous NH_4Cl solution (3 mL) was added and the reaction mixture was stirred for 30 mins at room temperature. The organic solvent was evaporated under reduced pressure and the residue was diluted in water (15 mL) and extracted with EtOAc (3 x 15 mL). The combined organic solutions were dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The obtained crude was dissolved in MeOH (500 μ L) and DCM (1 mL) followed by addition of a 1.7 M solution of NaOMe in MeOH (2 drops, $\sim$ pH 9-10). The resulting solution was stirred 16 h and neutralized to pH $\approx$ 7 with acidic resin. The mixture was filtered and concentrated under reduced pressure. The product was purified by flash column chromatography (MeOH/DCM, 19:1 to 17:3) to give **17** as a white amorphous solid (19.5 mg, 0.02699 mmol, 59% yield). R_f : 0.23 (MeOH/DCM, 1:9); $[\alpha]_D^{25} = 140$ (c 0.5, acetone); ^1H NMR (500 MHz, acetone) δ 8.80 (s, 1H, triazole), 8.66 (s, 1H, triazole), 7.73 – 7.63 (m, 4H, Ar), 5.54 (dt, $^2J_{\text{H}2-\text{F}2} = 49.2$ Hz, $^3J_{\text{H}2-\text{H}1} = ^3J_{\text{H}2-\text{H}3} = 9.9$ Hz, 1H, H-2), 5.34 (td, $^3J_{\text{H}3-\text{H}2} = ^3J_{\text{H}3-\text{F}2} = 10.9$ Hz, $^3J_{\text{H}3-\text{H}4} = 3.0$ Hz, 1H, H-3), 5.33 (dd, $^3J_{\text{H}1-\text{H}2} = 9.5$ Hz, $^3J_{\text{H}1-\text{F}2} = 2.9$ Hz, 1H, H-1), 5.22 (d, $^3J_{\text{OH}4-\text{H}4} = 5.9$ Hz, 1H, OH-4), 5.06 (d, $^3J_{\text{H}1-\text{H}2} = 9.5$ Hz, 1H, H-1'), 4.97 (dd, $^3J_{\text{H}3-\text{H}2} = 10.6$ Hz, $^3J_{\text{H}3-\text{H}4} = 2.9$ Hz, 1H, H-3'), 4.94 (d, $^3J_{\text{OH}4-\text{H}4} = 5.9$ Hz, 1H, OH-4'), 4.71 (td, $^3J_{\text{H}2-\text{H}1} = ^3J_{\text{H}2-\text{H}3} = 10.2$ Hz, $^3J_{\text{H}2-\text{OH}2} = 5.7$ Hz, 1H, H-2'), 4.57 (d, $^3J_{\text{OH}2-\text{H}2} = 5.7$ Hz, 1H, OH-2'), 4.45 (dtd, $^3J_{\text{H}4-\text{OH}4} = 5.5$ Hz, $^3J_{\text{H}4-\text{H}3} = ^4J_{\text{H}4-\text{F}2} = 3.2$ Hz, $^3J_{\text{H}4-\text{H}5} = 1.0$ Hz, 1H, H-4), 4.33 (ddd, $^3J_{\text{H}4-\text{OH}4} = 6.0$ Hz, $^3J_{\text{H}4-\text{H}3} = 3.0$ Hz, $^3J_{\text{H}4-\text{H}5} = 1.0$ Hz, 1H, H-4'), 4.27 (br, 1H, OH-6), 4.13 (br, 1H, OH-6), 4.09 (ddd, $^3J_{\text{H}5-\text{H}6a} = 6.4$ Hz, $^3J_{\text{H}5-\text{H}6a} = 5.4$ Hz, $^3J_{\text{H}5-\text{H}4} = 1.1$ Hz, 1H, H-5), 3.98 (td, $^3J_{\text{H}5-\text{H}6a} = ^3J_{\text{H}5-\text{H}6b} = 5.9$ Hz, $^3J_{\text{H}5-\text{H}4} = 1.1$ Hz, 1H, H-5'), 3.93 –

3.76 (m, 4H, H-6a/b, H-6a/b'); ^{13}C NMR (126 MHz, acetone) δ 152.3 (ddd, $J = 247.0, 10.2, 4.1$ Hz, 2C, Ar), 152.29 (ddd, $J = 247.4, 10.1, 4.4$ Hz, 2C, Ar), 145.1 (q, $J = 2.9, 2.4$ Hz, 1C, triazole), 144.5 (q, $J = 2.9, 2.4$ Hz, 1C, triazole), 139.7 (dt, $J = 248.4, 18.1$ Hz, 2C, Ar), 129.4 (td, $J = 8.9, 4.8$ Hz, 1C, Ar), 129.0 (td, $J = 8.9, 4.8$ Hz, 1C, Ar), 122.4 (s, 1C, triazole), 122.2 (s, 1C, triazole), 110.3 (dd, $J = 17.6, 5.7$ Hz, 2C, Ar), 110.2 (dd, $J = 17.3, 5.2$ Hz, 2C, Ar), 88.0 (d, $^1J_{\text{C2-F2}} = 186.4$ Hz, 1C, C-2), 85.6 (s, 1C, C-1'), 81.6 (d, $^2J_{\text{C1-F2}} = 23.8$ Hz, 1C, C-1), 80.6 (s, 2C, C-5/C-5'), 70.3 (d, $^3J_{\text{C4-F2}} = 7.2$ Hz, 1C, C-4), 69.6 (s, 1C, C-4'), 68.5 (s, 1C, C-2'), 68.3 (s, 1C, C-3'), 66.4 (d, $^2J_{\text{C3-F2}} = 17.2$ Hz, 1C, C-3), 62.2 (s, 1C, C-6'), 62.1 (s, 1C, C-6); ^{19}F NMR (470 MHz, acetone) δ -136.1 (dd, $J = 19.7, 8.9$ Hz, 2F, Ar), -136.2 (dd, $J = 20.3, 8.3$ Hz, 2F, Ar), -164.3 (tt, $J = 20.3, 7.2$ Hz, 1F, Ar), -164.7 (tt, $J = 20.3, 6.6$ Hz, 1F, Ar), -197.1 (ddt, $^2J_{\text{F2-H2}} = 49.0$ Hz, $^3J_{\text{F2-H3}} = 12.0$, $^3J_{\text{F2-H1}} = 2.9$ Hz, $^4J_{\text{F2-H4}} = 2.5$ Hz, 1F, F-2); HRMS calcd for $\text{C}_{30}\text{H}_{33}\text{O}_{12}\text{N}_6\text{F}_4\text{S}^+$ $[\text{M} + \text{H}]^+$ 777.1808, found 777.1835.

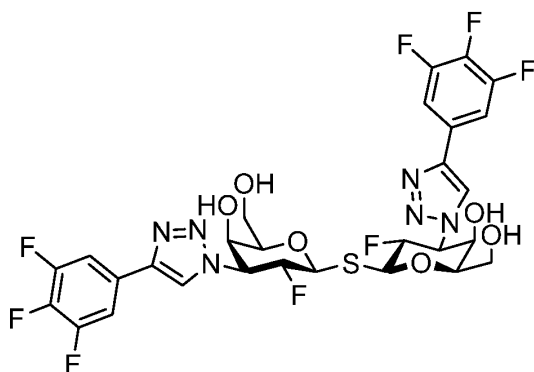
[0065] Bis-(4,6-di-*O*-acetyl-2,3-di-deoxy-2-fluoro-3-[4-(3,4,5-trifluorophenyl)-1*H*-1,2,3-triazol-1-yl]- β -D-galactopyranosyl)sulfane (**14OAc**):



[0066] To a stirred solution of compound **11** (49 mg, 0.1000 mmol) in dry DCM (2 mL) was added HBr/AcOH 33% wt (1 mL, half of DCM). The reaction was capped and stirred at room temperature overnight. The reaction was diluted with DCM (20 mL) and washed with water (10 mL), a saturated aqueous NaHCO_3 solution (10 mL) and brine (10 mL). The organic phase was dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The crude bromo **13** was used without any further purification. To a stirred solution of bromo **13** in dry MeCN (previously

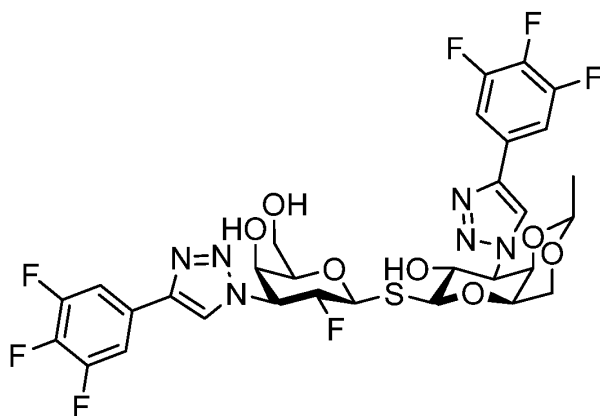
nitrogen gas purged for 10 mins) (2 mL) was added compound **12** (59.6 mg, 0.09617 mmol). To the mixture was added cesium fluoride (CsF) (16.1 mg, 0.1058 mmol, 1.1 equiv.) and the reaction was stirred at room temperature for 1h. Another batch of CsF (16.1 mg, 0.1058 mmol, 1.1 equiv.) was added and the reaction was stirred at room temperature another 2h. The reaction was concentrated under reduced pressure and purified by flash chromatography (silica gel, EtOAc/Hexanes, 2:3 to 3:2) to give **14OAc** as a white amorphous solid (32.5 mg, 0.03643 mmol, 38% yield). R_f : 0.20 (EtOAc/Hexanes, 3:2); $[\alpha]_D^{25} = 5.7$ (c 0.7, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 8.00 (s, 2H, triazole), 7.53 – 7.44 (m, 4H, Ar), 5.71 (t, $^3J_{H4-H3} = ^4J_{H4-F2} = 3.1$ Hz, 2H, H-4), 5.44 (dt, $^2J_{H2-F2} = 49.0$ Hz, $^3J_{H2-H3} = ^3J_{H2-H1} = 9.9$ Hz, 2H, H-2), 5.14 (dd, $^3J_{H1-H2} = 9.5$ Hz, $^3J_{H1-F2} = 2.3$ Hz, 2H, H-1), 5.09 (td, $^3J_{H3-H2} = ^3J_{H3-F2} = 10.3$ Hz, $^3J_{H3-H4} = 3.3$ Hz, 2H, H-3), 4.35 (dd, $^2J_{H6a-H6b} = 11.4$ Hz, $^3J_{H6a-H5} = 6.4$ Hz, 2H, H-6a), 4.21 (t, $^3J_{H5-H6a} = ^3J_{H5-H6b} = 6.5$ Hz, 2H, H-5), 4.13 (dd, $^2J_{H6b-H6a} = 11.4$ Hz, $^3J_{H6b-H5} = 6.7$ Hz, 2H, H-6b), 2.08 (s, 6H, OAc-6), 2.05 (s, 6H, OAc-4); ^{13}C NMR (126 MHz, CDCl_3) δ 170.8 (s, 2C, OAc-6), 169.2 (s, 2C, OAc-4), 151.8 (ddd, $J = 250.3, 10.3, 4.3$ Hz, 4C, Ar), 145.7 (q, $J = 2.4$ Hz, 2C, triazole), 139.9 (dt, $J = 253.2, 15.7$ Hz, 2C, Ar), 126.2 (td, $J = 8.5, 4.8$ Hz, 2C, Ar), 120.2 (s, 2C, triazole), 110.1 (dd, $J = 17.4, 6.0$ Hz, 4C, Ar), 85.9 (d, $^1J_{C2-F2} = 190.7$ Hz, 2C, C-2), 81.0 (d, $^2J_{C1-F2} = 23.8$ Hz, 2C, C-1), 76.1 (s, 2C, C-5), 68.9 (d, $^3J_{C4-F2} = 7.2$ Hz, 2C, C-4), 63.7 (d, $^2J_{C3-F2} = 19.1$ Hz, 2C, C-3), 61.4 (s, 2C, C-6), 20.8 (s, 2C, OAc-6), 20.5 (s, 2C, OAc-4); ^{19}F NMR (470 MHz, CDCl_3) δ -133.3 (dd, $J = 20.3, 7.2$ Hz, 4F, Ar), -160.0 (ddt, $J = 20.3, 13.1, 6.6$ Hz, 2F, Ar), -195.2 (ddt, $^2J_{F2-H2} = 48.9$ Hz, $^3J_{F2-H3} = 10.7$ Hz, $^3J_{F2-H1} = ^4J_{F2-H4} = 3.0$ Hz, 2F, F-2); HRMS calcd for $\text{C}_{36}\text{H}_{33}\text{O}_{10}\text{N}_6\text{F}_8\text{S}^+$ $[M + H]^+$ 893.1846, found 893.1824.

[0067] Bis-(2,3-di-deoxy-2-fluoro-3-[4-(3,4,5-trifluorophenyl)-1*H*-1,2,3-triazol-1-yl]- β -D-galactopyranosyl)sulfane (**14**):



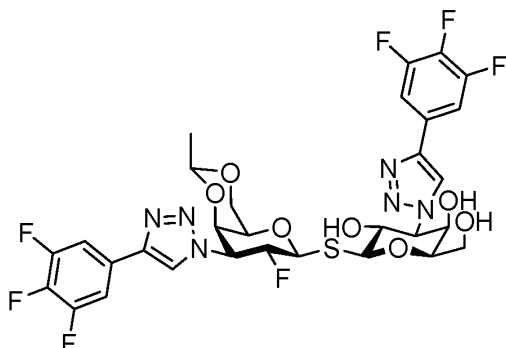
[0068] To a stirred solution of **14OAc** in MeOH (500 μ L) and DCM (1 mL) was added a 1.7 M solution of NaOMe in MeOH (2 drops, $\sim$ pH 9-10). The resulting solution was stirred 16h and neutralized to pH $\approx$ 7 with acidic resin. The mixture was filtered and concentrated under reduced pressure. The product was purified by flash column chromatography (MeOH/DCM, 19:1 to 17:3) to give **14** as a white amorphous solid (21.0 mg, 0.02898 mmol, 80% yield). R_f : 0.56 (MeOH/DCM, 3:17); $[\alpha]_D^{25} = 39$ (c 0.5, MeOH); $^1\text{H NMR}$ (500 MHz, acetone) δ 8.80 (s, 2H, triazole), 7.77 – 7.67 (m, 4H, Ar), 5.43 (dt, $^2J_{H2-F2} = 50.6$ Hz, $^3J_{H2-H1} = ^3J_{H2-H3} = 10.0$ Hz, 2H, H-2), 5.41 (d, $^3J_{H1-H2} = 9.2$ Hz, 2H, H-1), 5.38 – 5.31 (m, 2H, H-3), 5.10 (d, $^3J_{OH4-H4} = 5.9$ Hz, 2H, OH-4), 4.45 (dtd, $^3J_{H4-OH4} = 5.7$ Hz, $^3J_{H4-H3} = 2.9$ Hz, $^4J_{H4-F2} = 2.5$ Hz, $^3J_{H4-H5} = 1.3$ Hz, 2H, H-4), 4.23 (br, 2H, OH-6), 4.09 (td, $^3J_{H5-H6a} = ^3J_{H5-H6b} = 5.8$ Hz, $^3J_{H5-H4} = 1.1$ Hz, 2H, H-5), 3.88 (dt, $^2J_{H6a-H6b} = 11.3$ Hz, $^3J_{H6a-H5} = 6.1$ Hz, $^3J_{H6a-OH6} = 5.7$ Hz, 2H, H-6a), 3.83 (dt, $^2J_{H6b-H6a} = 11.4$ Hz, $^3J_{H6b-H5} = ^3J_{H6b-OH6} = 5.7$ Hz, 2H, H-6b); $^{13}\text{C NMR}$ (126 MHz, acetone) δ 152.3 (ddd, $J = 247.0, 10.0, 4.1$ Hz, 4C, Ar), 145.1 (q, $J = 2.4$ Hz, 2C, triazole), 139.8 (dt, $J = 249.4, 15.5$ Hz, 2C, Ar), 129.1 (td, $J = 8.8, 5.1$ Hz, 2C, Ar), 122.2 (s, 2C, triazole), 110.4 (dd, $J = 17.7, 5.0$ Hz, 4C, Ar), 88.1 (d, $^1J_{C2-F2} = 186.9$ Hz, 2C, C-2), 81.2 (d, $^2J_{C1-F2} = 23.4$ Hz, 2C, C-1), 80.5 (s, 2C, C-5), 70.2 (dd, $^3J_{C4-F2} = 7.4$ Hz, 4.5 Hz, 2C, C-4), 66.3 (d, $^2J_{C3-F2} = 17.2$ Hz, 2C, C-3), 61.9 (d, $^5J_{C6-F2} = 5.2$ Hz, 2C, C-6); $^{19}\text{F NMR}$ (470 MHz, acetone) δ -136.1 (dd, $J = 20.3, 8.3$ Hz, 4F, Ar), -164.4 (tt, $J = 20.3, 6.6$ Hz, 2F, Ar), -197.7 (ddd, $^2J_{F2-H2} = 51.3$ Hz, $^3J_{F2-H3} = 12.5$ Hz, $^4J_{F2-H4} = 3.6$ Hz, 2F, F-2); HRMS calcd for $\text{C}_{28}\text{H}_{25}\text{O}_{10}\text{N}_6\text{F}_8\text{S}^+$ $[\text{M} + \text{H}]^+$ 725.1423, found 725.1400.

[0069] 4',6'-O-ethylidene-2,3, 3'-tri-deoxy-2-fluoro-1,1'-sulfanediyl-3,3'-[4-(3,4,5-trifluorophenyl)-1*H*-1,2,3-triazol-1-yl]-di- β -D-galactopyranoside (**18**):



[0070] To a stirred solution of **17** (36.7 mg, 0.05079 mmol) in MeCN (2 mL) was added 1,1-diethoxyethane (7.2 μ L, 0.0508 mmol, 1 equiv.) and *p*-TsOH (1.9 mg, 0.0102 mmol, 0.2 equiv). The reaction was stirred at room temperature overnight. The reaction was quenched with Et₃N (15 μ L, 0.11 mmol, 1.5 equiv) and concentrated under reduced pressure. The crude mixture was purified by flash chromatography (silica gel, MeOH/DCM, 1:19 to 3:17) to give **18** as a white amorphous solid (10.5 mg, 0.0140 mmol, 28% yield) and **19** as a white amorphous solid (6.7 mg, 0.00896 mmol, 18% yield). Analytical data for **18**: *R*_f = 0.45 (MeOH/DCM, 1:9); ¹H NMR (500 MHz, acetone) δ 8.78 (s, 1H, triazole), 8.53 (s, 1H, triazole), 7.81 – 7.61 (m, 4H, Ar/Ar'), 5.71 (ddd, ²*J*_{H2-F2} = 49.3 Hz, ³*J*_{H2-H3} = 10.4 Hz, ³*J*_{H2-H1} = 9.5 Hz, 1H, H-2), 5.32 (ddd, ³*J*_{H3-F2} = 11.1 Hz, ³*J*_{H3-H2} = 10.6 Hz, ³*J*_{H3-H4} = 2.9 Hz, 1H, H-3), 5.29 (dd, ³*J*_{H1-H2} = 9.4 Hz, ³*J*_{H1-F2} = 2.9 Hz, 1H, H-1), 5.17 (d, ³*J*_{OH4-H4} = 5.5 Hz, 1H, OH-4), 5.10 (dd, ³*J*_{H3-H2} = 10.6 Hz, ³*J*_{H3-H4} = 3.5 Hz, 1H, H-3'), 5.08 (d, ³*J*_{H1-H2} = 9.4 Hz, 1H, H-1'), 4.77 (q, *J* = 5.1 Hz, 1H, CHCH₃'), 4.75 (ddd, ³*J*_{H2-H3} = 10.6 Hz, ³*J*_{H2-H1} = 9.4 Hz, ³*J*_{H2-OH2} = 5.3 Hz, 1H, H-2'), 4.53 (d, ³*J*_{OH2-H2} = 5.4 Hz, 1H, OH-2'), 4.52 (dtd, ³*J*_{H4-OH4} = 5.4 Hz, ³*J*_{H4-H3} = ⁴*J*_{H4-F2} = 3.1 Hz, ³*J*_{H4-H5} = 1.1 Hz, 1H, H-4), 4.38 (dd, ³*J*_{H4-H3} = 3.5 Hz, ³*J*_{H4-H5} = 1.3 Hz, 1H, H-4'), 4.28 (br dd, ³*J*_{OH6-H6b} = 6.5 Hz, ³*J*_{OH6-H6a} = 4.7 Hz, 1H, OH-6), 4.21 (dd, ²*J*_{H6a-H6b} = 12.6 Hz, ³*J*_{H6a-H5} = 1.5 Hz, 1H, H-6a'), 4.09 (ddd, ³*J*_{H5-H6a} = 6.2 Hz, ³*J*_{H5-H6b} = 5.3 Hz, ³*J*_{H5-H4} = 1.1 Hz, 1H, H-5), 4.05 (dd, ²*J*_{H6b-H6a} = 12.7 Hz, ³*J*_{H6b-H6a} = 1.9 Hz, 1H, H-6b'), 3.95 (q, ³*J*_{H5-H6a} = ³*J*_{H5-H6b} = ³*J*_{H5-H4} = 1.7 Hz, 1H, H-5'), 3.89 (ddd, ²*J*_{H6a-H6b} = 11.0 Hz, ³*J*_{H6a-H5} = 6.2 Hz, ³*J*_{H6a-OH6} = 4.8 Hz, 1H, H-6a), 3.83 (ddd, ²*J*_{H6b-H6a} = 11.5 Hz, ³*J*_{H6b-OH6} = 6.6 Hz, ³*J*_{H6b-H5} = 5.3 Hz, 1H, H-6b), 1.23 (d, *J* = 5.0 Hz, 3H, CHCH₃); ¹³C NMR (126 MHz, acetone) δ 152.33 (dt, *J* = 245.7, 10.2, 4.1 Hz, 2C, Ar/Ar'), 152.29 (ddd, *J* = 246.2, 10.2, 3.8 Hz, 2C, Ar/Ar'), 144.9 (q, *J* = 2.4 Hz, 1C, triazole), 144.7 (q, *J* = 2.4 Hz, triazole), 139.7 (dt, *J* = 248.3, 16.5 Hz, 2C, Ar/Ar'), 129.2 (td, *J* = 9.8, 4.6 Hz, 2C, Ar/Ar'), 122.5 (s, 2C, triazole), 110.34 (dd, *J* = 17.4, 5.7 Hz, 2C, Ar/Ar'), 110.27 (dd, *J* = 16.8, 5.7 Hz, 2C, Ar/Ar'), 99.7 (s, 1C, CHCH₃), 87.8 (d, ¹*J*_{C2-F2} = 186.0 Hz, 1C, C-2), 85.9 (s, 1C, C-1'), 81.9 (d, ²*J*_{C1-F2} = 23.8 Hz, 1C, C-1), 80.6 (s, 1C, C-5), 75.3 (s, 1C, C-4'), 71.2 (s, 1C, C-5'), 70.4 (d, ³*J*_{C4-F2} = 7.6 Hz, 1C, C-4), 69.5 (s, 1C, C-6'), 68.3 (s, 1C, C-2'), 66.30 (s, 1C, C-3'), 66.28 (d, ²*J*_{C3-F2} = 17.6 Hz, 1C, C-3), 62.2 (s, 1C, C-6), 20.9 (s, 1C, CHCH₃); ¹⁹F NMR (470 MHz, acetone) δ -136.1 (dd, *J* = 19.9, 8.3 Hz, 2F, Ar/Ar'), -136.2 (dd, *J* = 19.9, 8.3 Hz, 2F, Ar/Ar'), -164.4 (tt, *J* = 19.9, 6.6 Hz, 1F, Ar/Ar'), -164.6 (ddd, *J* = 26.5, 19.9, 6.6 Hz, 1F, Ar/Ar'), -197.3 (ddt, ²*J*_{F2-H2} = 50.6 Hz, ³*J*_{F2-H3} = 11.4 Hz, ³*J*_{F2-H1} = ⁴*J*_{F2-H4} = 3.1 Hz, 1F, F-2); HRMS calcd for C₃₀H₂₈O₇N₆F₇S⁺ [M + H]⁺ 749.1623, found 749.1595.

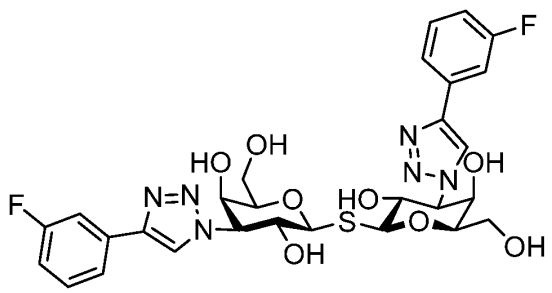
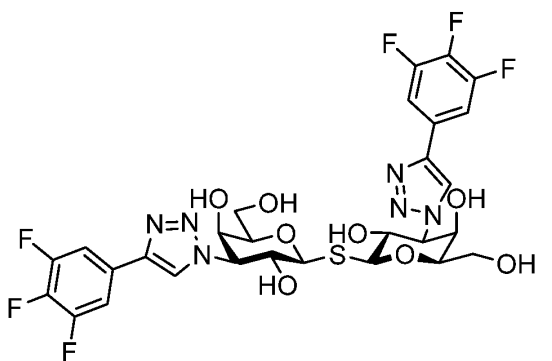
[0071] 4',6'-O-ethylidene-2',3, 3'-tri-deoxy-2-fluoro-1,1'-sulfanediyl-3,3'-[4-(3,4,5-trifluorophenyl)-1*H*-1,2,3-triazol-1-yl]-di- β -D-galactopyranoside (**19**):

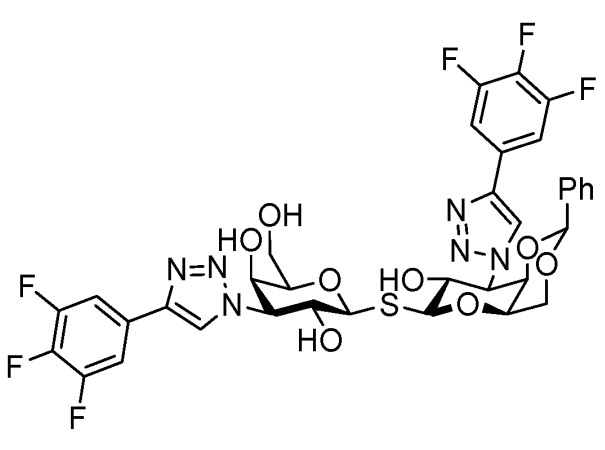
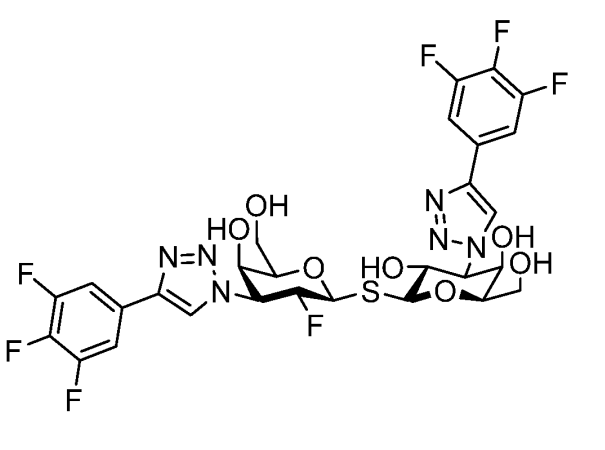


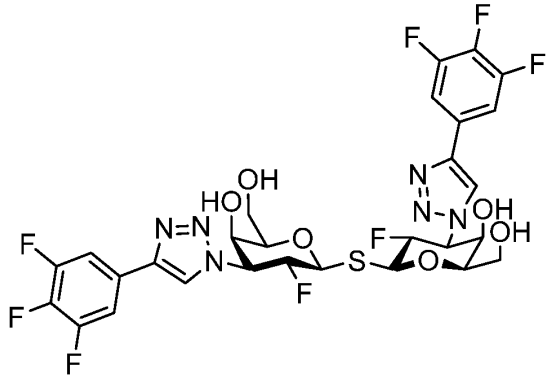
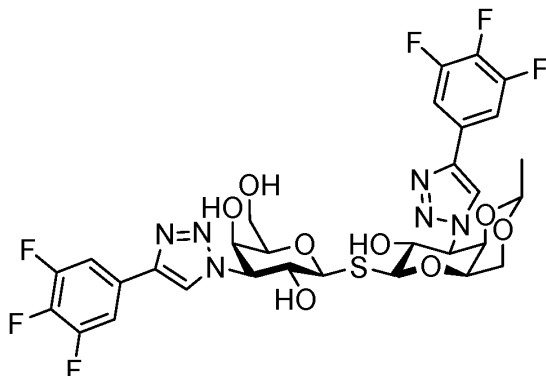
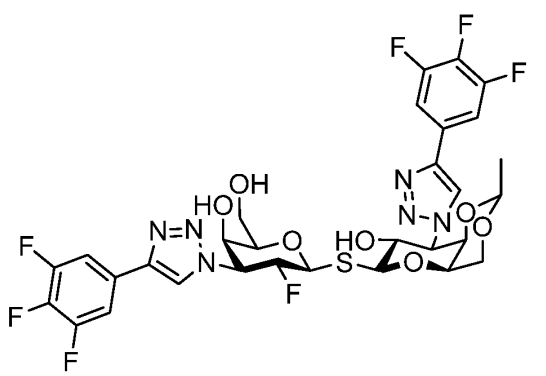
[0072] Analytical data for **19**: R_f = 0.38 (MeOH/DCM, 1:9); ^1H NMR (500 MHz, acetone) δ 8.71 (s, 1H, triazole), 8.68 (s, 1H, triazole), 7.80 – 7.68 (m, 4H, Ar/Ar'), 5.48 (td, $^3J_{H3-F2}$ = 11.8 Hz, $^3J_{H3-H2}$ = 10.8 Hz, $^3J_{H3-H4}$ = 2.9 Hz, 1H, H-3), 5.44 (ddd, $^2J_{H2-F2}$ = 51.2 Hz, $^3J_{H2-H3}$ = 10.8 Hz, $^3J_{H2-H1}$ = 9.2 Hz, 1H, H-2), 5.42 (dd, $^3J_{H1-H2}$ = 8.8 Hz, $^3J_{H1-F2}$ = 1.9 Hz, 1H, H-1), 5.06 (d, $^3J_{H1-H2}$ = 9.2 Hz, 1H, H-1'), 4.94 (dd, $^3J_{H3-H2}$ = 10.3 Hz, $^3J_{H3-H4}$ = 2.9 Hz, 1H, H-3'), 4.86 (d, $^3J_{OH4-H4}$ = 5.7 Hz, 1H, OH-4'), 4.80 (q, J = 5.1 Hz, 1H, CHCH₃), 4.70 (ddd, $^3J_{H2-H3}$ = 10.1 Hz, $^3J_{H2-H1}$ = 9.3 Hz, $^3J_{H2-OH2}$ = 6.2 Hz, 1H, H-2'), 4.67 (d, $^3J_{OH2-H2}$ = 6.0 Hz, 1H, OH-2'), 4.52 (ddd, $^3J_{H4-H3}$ = 3.4 Hz, $^4J_{H4-F2}$ = 2.2 Hz, $^3J_{H4-H5}$ = 1.0 Hz, 1H, H-4), 4.36 (ddd, $^3J_{H4-OH4}$ = 5.6 Hz, $^3J_{H4-H3}$ = 2.9 Hz, $^3J_{H4-H5}$ = 1.2 Hz, 1H, H-4'), 4.22 (dd, $^2J_{H6a-H6b}$ = 13.6 Hz, $^3J_{H6a-H5}$ = 2.3 Hz, 1H, H-6a), 4.16 (dd, $^3J_{OH6-H6b}$ = 6.3 Hz, $^3J_{OH6-H6a}$ = 5.5 Hz, 1H, OH-6'), 4.05 (dd, $^2J_{H6b-H6a}$ = 13.2 Hz, $^3J_{H6b-H5}$ = 1.8 Hz, 1H, H-6b), 4.04 (td, $^3J_{H5-H6a}$ = $^3J_{H5-H6b}$ = 1.9 Hz, $^3J_{H5-H4}$ = 1.0 Hz, 1H, H-5), 3.96 (td, $^3J_{H5-H6a}$ = $^3J_{H5-H6b}$ = 5.7 Hz, $^3J_{H5-H4}$ = 1.2 Hz, 1H, H-5'), 3.86 (dt, $^2J_{H6a-H6b}$ = 10.9 Hz, $^3J_{H6a-H5}$ = 5.8 Hz, $^3J_{H6a-OH6}$ = 4.7 Hz, 1H, H-6a'), 3.82 (dt, $^2J_{H6b-H6a}$ = 11.4 Hz, $^3J_{H6b-H5}$ = $^3J_{H6b-OH6}$ = 5.9 Hz, 1H, H-6b'), 1.27 (d, J = 5.1 Hz, 3H, CHCH₃); ^{13}C NMR (126 MHz, acetone) δ 152.3 (dt, J = 248.9, 10.1, 4.8 Hz, 4C, Ar/Ar'), 145.3 (q, J = 2.4 Hz, triazole), 144.5 (q, J = 2.4 Hz, triazole), 139.8 (dt, J = 249.9, 18.2, 16.9 Hz, 2C, Ar/Ar'), 129.5 (td, J = 9.8, 4.6 Hz, 2C, Ar/Ar'), 122.8 (s, 1C, triazole), 122.5 (s, 1C, triazole), 110.5 (dd, J = 17.4, 5.5 Hz, 2C, Ar/Ar'), 110.1 (dd, J = 17.8, 6.3 Hz, 2C, Ar/Ar'), 99.8 (s, 1C, CHCH₃), 87.4 (d, $^1J_{C2-F2}$ = 187.4 Hz, 1C, C-2), 85.5 (s, 1C, C-1'), 81.4 (d, $^2J_{C1-F2}$ = 22.9 Hz, 1C, C-1), 80.4 (s, 1C, C-5'), 75.8 (d, $^3J_{C4-F2}$ = 7.2 Hz, 1C, C-4), 71.0 (s, 1C, C-5), 69.8 (s, 1C, C-4'), 69.0 (s, 1C, C-6), 68.5 (s, 1C, C-3'), 68.4 (s, 1C, C-2'), 64.5 (d, $^2J_{C3-F2}$ = 19.1 Hz, 1C, C-3), 62.3 (s, 1C, C-6'), 20.9 (s, 1C, CHCH₃); ^{19}F NMR (470 MHz, acetone) δ -136.1 (dd, J = 19.7, 8.9 Hz, 2F, Ar/Ar'), -136.3 (dd, J = 20.3, 8.3 Hz, 2F, Ar/Ar'), -164.3 (tt, J = 20.3, 6.6 Hz, 1F, Ar/Ar'), -164.8 (tt, J = 20.3, 7.1 Hz, 1F, Ar/Ar'), -195.8 (ddt, $^2J_{F2-H2}$ = 50.7 Hz, $^3J_{F2-H3}$ = 12.5 Hz, $^3J_{F2-H1}$ = $^4J_{F2-H4}$ = 2.5 Hz, 1F, F-2); HRMS calcd for C₃₀H₂₈O₇N₆F₇S⁺ [M + H]⁺ 749.1623, found 749.1594.

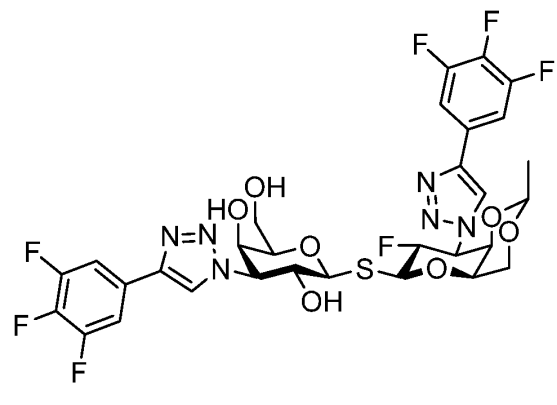
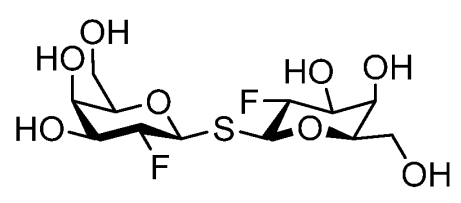
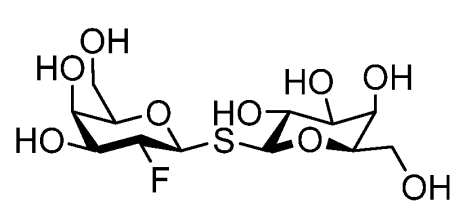
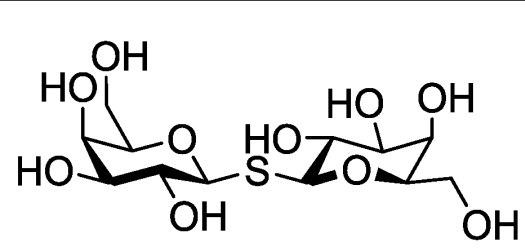
[0073] The compounds selected for further analysis are presented in Table 2.

Table 2. Molecular weight (MW) of the compounds

Name	Structure	MW
GB0139		648.64
1		720.60

2a		808.71
17		722.59

14		724.58
6		746.16
18		748.16

19		748.16
772a (Prior art)		362.34
774a (Prior art)		360.35
TDG (Prior art)		390.36

[0074] The biochemical evaluation of the compounds of Table 2 was performed by an *in vitro* hemagglutination assay. The compounds were solubilized in dimethyl sulfoxide (DMSO) to

achieve a final concentration of 100 mM. The DMSO was then mixed in an aqueous phase with methanol (2% MeOH and 0.1% DMSO). Galectin-1 and galectin-3 were then added at 1 μ M concentration and hemagglutination was observed with red blood cells. In the presence of a galectin inhibitor the hemagglutination of red blood cells occurs even in the presence of galectin 3. The results are presented in Table 3 below. The compounds **2a** and **18** demonstrated the best selectivity for galectin-3 while compound **6** also demonstrated some selectivity towards galectin-3.

[0075] The hemagglutinin assay demonstrated the ability of the compounds to inhibit galectin-mediated cross-linking. Some compounds were found to be more specific for galectin-3 (including compound **2a**) than others. Although selective galectin-3 inhibitors are preferred in some cases, on the other hand, in other situations, broad-spectrum inhibitors are preferable. In that sense it should be noted that compound **1** and **17** had similar or greater inhibitory potency than TD139.

Table 3. Inhibition results

Cmpd	Gal	Inhibitor concentration (μ M)											
		100	50	25	12.5	6.25	3.125	1.563	0.781	0.391	0.195	0.098	0
772a	1	+	+	+	+	+	+	+	+	+	+	+	+
	3	+	+	+	+	+	+	+	+	+	+	+	+
774a	1	-	$\pm$	$\pm$	+	+	+	+	+	+	+	+	+
	3	+	+	+	+	+	+	+	+	+	+	+	+
GB0139	1	-	-	-	-	-	-	-	$\pm$	$\pm$	+	+	+
	3	-	-	-	-	-	-	-	$\pm$	+	+	+	+

Cmpd	Gal	Inhibitor concentration (μM)												
		100	50	25	12.5	6.25	3.125	1.563	0.781	0.391	0.195	0.098	0	
1	1	-	-	-	-	-	-	-	-	±	±	+	+	+
	3	-	-	-	-	-	-	-	-	-	±	+	+	+
2a	1	+	+	+	+	+	+	+	+	+	+	+	+	+
	3	-	-	-	-	-	-	-	-	-	±	+	+	+
17	1	-	-	-	-	-	-	-	±	±	+	+	+	+
	3	-	-	-	-	-	-	-	-	-	-	±	+	+
14	1	±	±	+	+	+	+	+	+	+	+	+	+	+
	3	-	±	+	+	+	+	+	+	+	+	+	+	+
6	1	-	-	-	-	-	-	±	+	+	+	+	+	+
	3	-	-	-	-	-	-	-	-	-	-	±	±	+
18	1	-	-	-	-	-	-	±	+	+	+	+	+	+
	3	-	-	-	-	-	-	-	-	-	±	+	+	+
19	1	+	±	±	+	+	+	+	+	+	+	+	+	+

Cmpd	Gal	Inhibitor concentration (μ M)											
		100	50	25	12.5	6.25	3.125	1.563	0.781	0.391	0.195	0.098	0
	3	+	+	-	-	-	$\pm$	+	+	+	+	+	+
TDG	1	$\pm$	$\pm$	+	+	+	+	+	+	+	+	+	+
	3	+	+	+	+	+	+	+	+	+	+	+	+

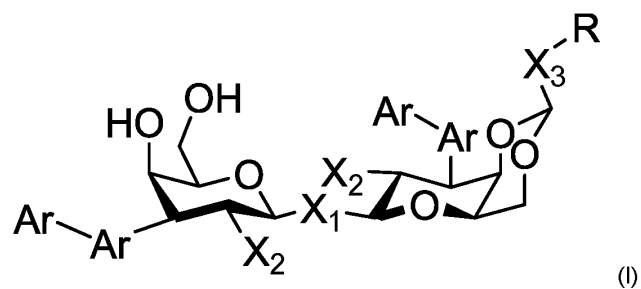
+ means that the test compound does not inhibit galectin binding to red blood cells

- means that the compound is inhibiting galectin binding to red blood cells

$\pm$ means inconclusive results

WHAT IS CLAIMED IS:

1. A compound of formula I



X_1 is O or S,

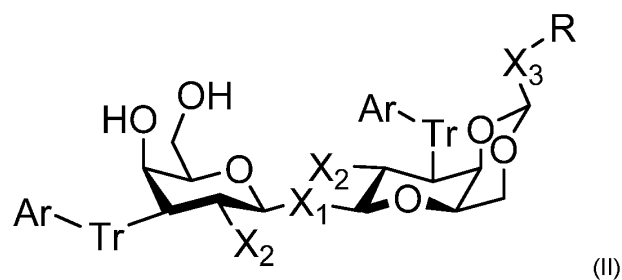
X_2 is OH or a halogen,

X_3 is O, S, N(J) or is absent, wherein J is H or R,

R is a branched or linear alkyl, a cycloalkyl, an aryl or a heteroaryl that is optionally substituted with one or more of a halogen, an alkyl, -O-alkyl, or -NH-alkyl, and

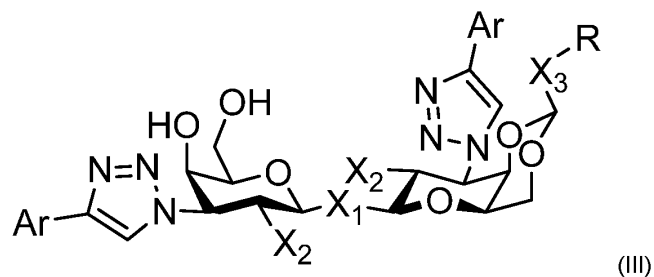
Ar are each independently an aryl or a heteroaryl that is optionally substituted with one or more of a halogen, an alkyl, -O-alkyl, or -NH-alkyl.

2. The compound of claim 1, wherein the compound of formula I is of formula II



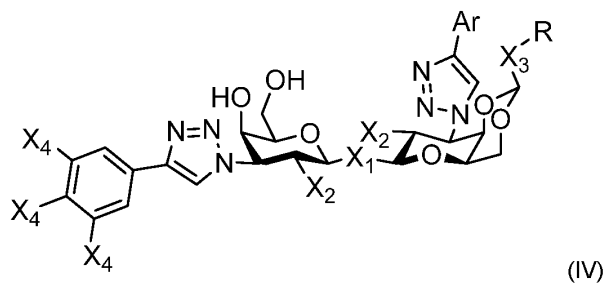
wherein X_1 , X_2 , X_3 , R and Ar are as defined in claim 1 and wherein Tr is a triazole that is optionally substituted with one or more of a halogen, an alkyl, -O-alkyl, or -NH-alkyl.

3. The compound of claim 1, wherein the compound of formula I is of formula III



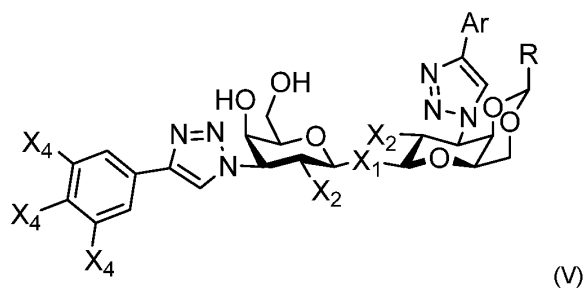
wherein X_1 , X_2 , X_3 , Ar and R are as defined in claim 1.

4. The compound of claim 1, wherein the compound of formula I is of formula IV



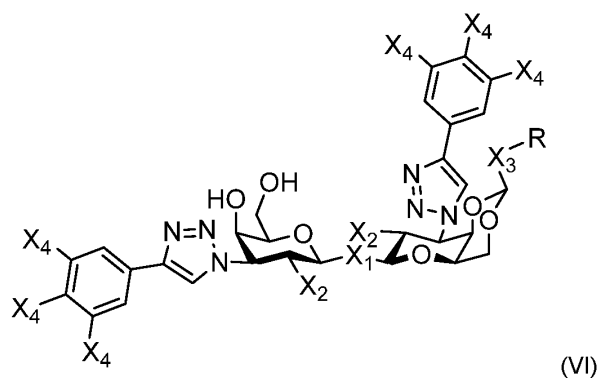
wherein X_1 , X_2 , X_3 , Ar and R are as defined in claim 1, and wherein each of X_4 is independently a halogen or a hydrogen.

5. The compound of claim 1, wherein the compound of formula I is of formula V



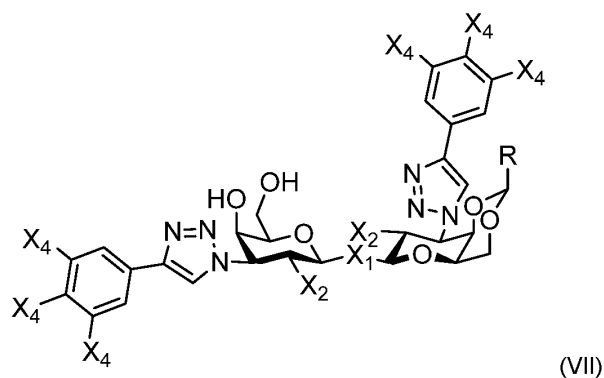
wherein X_1 , X_2 , Ar and R are as defined in claim 1, and wherein each of X_4 is independently a halogen or a hydrogen.

6. The compound of claim 1, wherein the compound of formula I is of formula VI



wherein X_1 , X_2 , X_3 , and R are as defined in claim 1, and wherein each of X_4 is independently a halogen or a hydrogen.

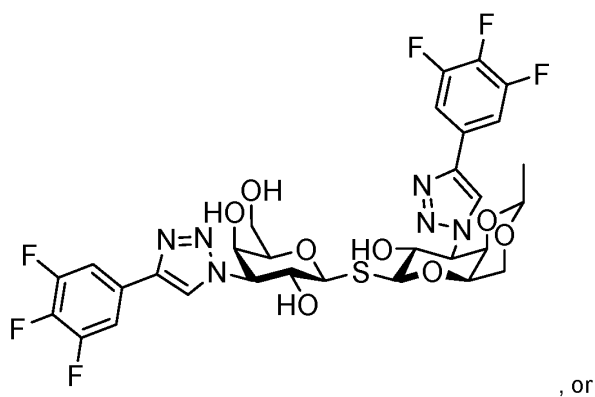
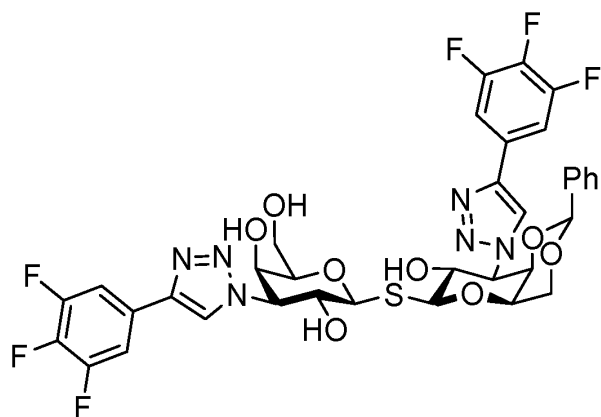
7. The compound of claim 1, wherein the compound of formula I is of formula VII

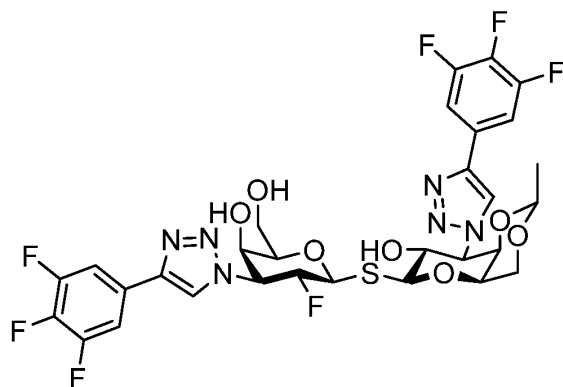


wherein X_1 , X_2 , and R are as defined in claim 1, and wherein each of X_4 is independently a halogen or a hydrogen.

8. The compound of any one of claims 1 to 7, wherein the halogen is F, Br or Cl.
9. The compound of any one of claims 1 to 8, wherein for R the branched or linear alkyl is a C_1 - C_6 .
10. The compound of any one of claims 1 to 9, wherein X_1 is S.

11. The compound of any one of claims 1 to 10, wherein the cycloalkyl is a C₃-C₆ cycloalkyl.
12. The compound of any one of claims 2 to 11, wherein the aryl is phenyl.
13. The compound of any one of claims 1 to 12, wherein the heteroaryl is pyridine or pyrimidine.
14. The compound of any one of claims 1 to 7, wherein R is methyl or phenyl.
15. The compound of any one of claims 1 to 14, wherein the alkyl of the alkyl or -O-alkyl substituents is a C1-C7 branched or linear alkyl.
16. The compound of claim 1, wherein the compound is





17. A method for treating fibrosis or cancer in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of the compound as defined in any one of claims 1 to 16.
18. The method of claim 17, wherein the cancer is selected from lymphoma, glioblastoma, pulmonary metastasis in breast or colon cancer, lung carcinoma, lung adenocarcinoma, breast cancer, prostate cancer, bladder cancer, melanoma, thyroid cancer colon cancer, ovarian cancer, pancreatic carcinoma, gastric cancer, hepatocellular carcinoma, or oral squamous cell carcinoma.
19. Use of the compound as defined in any one of claims 1 to 16, for treating fibrosis or cancer in a subject in need thereof.
20. The use of claim 19, wherein the cancer is selected from lymphoma, glioblastoma, pulmonary metastasis in breast or colon cancer, lung carcinoma, lung adenocarcinoma, breast cancer, prostate cancer, bladder cancer, melanoma, thyroid cancer colon cancer, ovarian cancer, pancreatic carcinoma, gastric cancer, hepatocellular carcinoma, or oral squamous cell carcinoma.