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(54) Title: MONOSACCHARIDE DERIVATIVES

(57) Abstract: The present invention relates to monosaccharide derivatives as anti-inflammatory agents. The compounds disclosed herein can be useful for inhibition and prevention of inflammation and associated pathologies, including inflammatory and autoimmune diseases such as bronchial asthma, rheumatoid arthritis, type I diabetes, multiple sclerosis, allograft rejection, psoriasis, inflammatory bowel disease, ulcerative colitis, acne, atherosclerosis, cancer, pruritis or allergic rhinitis. Pharmacological compositions containing the compounds of the present invention and the methods of treating bronchial asthma, chronic obstructive pulmonary disease, rheumatoid arthritis, multiple sclerosis, type I diabetes, psoriasis, allograft rejection, inflammatory bowel disease, ulcerative colitis, acne, atherosclerosis, cancer, pruritis or allergic rhinitis and other inflammatory and/or autoimmune disorders, using the compounds are also provided.

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MONOSACCHARIDE DERIVATIVES

Field of the Invention

The present invention relates to monosaccharide derivatives as anti-inflammatory agents. The compounds provided herein can be useful for inhibition and prevention of inflammation and associated pathologies, including inflammatory and autoimmune diseases such as bronchial asthma, rheumatoid arthritis, type I diabetes, multiple sclerosis, allograft rejection, psoriasis, inflammatory bowel disease, ulcerative colitis, acne, atherosclerosis, cancer, pruritis or allergic rhinitis. Pharmacological compositions containing the compounds of the present invention and the methods of treating bronchial asthma, chronic obstructive pulmonary disease, rheumatoid arthritis, multiple sclerosis, type I diabetes, psoriasis, allograft rejection, inflammatory bowel disease, ulcerative colitis, acne, atherosclerosis, cancer, pruritis or allergic rhinitis and other inflammatory and/or autoimmune disorders, using the compounds are also provided.

Background of the Invention

Inflammation is a key defense mechanism of the body that is activated as a result of tissue injury. The inflammatory process is self-containing, however, under certain pathophysiological conditions, the inflammatory process tends to perpetuate itself, giving rise to chronic inflammatory diseases like bronchial asthma, rheumatoid arthritis etc.

Although the exact cellular and molecular bases of most chronic inflammatory disease remain unclear, it has become apparent that several inflammatory cells act in concert towards initiation and perpertuation of an inflammatory response by releasing a wide range of chemokine, cytokine, proteolytic enzymes and other bioactive molecules. A case in point is mast cells primed by lymphocytes interact with environmental allergens and release mediators like histamine, prostaglandin, leukotrienes, etc. (*Clin. Exp. Allergy*, 32, 1682, 2002) to initiate an early inflammatory response. This is followed by a delayed inflammatory response due to release of cytokines (IL-4, IL-5, IL-6, IL-8, IL-13, GM-CSF and TNFalpha), chemokines and proteolytic enzymes (chymase, tryptase) (*Chest* 112, 523, 1997; *Lancet* 350, 59, 1997) that not only bring about tissue damage, but attract other inflammatory cells and initiate tissue fibrosis, and the cycle continues. Eosinophils infiltrate inflamed tissue following allergen - mast cell interaction in bronchial asthma and allergic rhinitis. Evidence is emerging that mast cells also interact with bacterial endotoxins leading to generation of cytokines like TNFalpha, that encourage neutrophil

influx into the site of inflammation (*Br. J. Pharmacol* 123, 31 (1998); *Br. J. Pharmacol* 128, 700, (1999); *Br. J. Pharmacol* 136, 111, (2002); *J. Clin. Invest.*, 109, 1351, 2002). Involvement of mast cells in the inflammatory response of chronic obstructive pulmonary disease (*New Eng. J. Med.*, 347, 1040, 2002; *Thorax* 57, 649, 2002), inflammatory bowel disease (*Gut,* 45 Suppl II6, 1999) as well as rheumatoid arthritis (*Science,* 297, 1626, 2002), pathologies with prominent neutrophilic inflammation, has been proposed.

U.S. Patent No. 6,329,344B1 discloses several monosaccharide derivatives described as cell adhesion inhibitors. It generally relates to substituted pentose and hexose monosaccharide derivatives, which are said to exhibit cell adhesion inhibitory and anti-inflammatory activities. U.S. Patent No. 6,590,085B1 discloses several monosaccharide derivatives described as inhibitors of cell adhesion and cell adhesion mediated pathologies, including inflammatory and autoimmune diseases. U.S. Patent Application US 2002/0173632 A1 discloses furanose and amino furanose compounds said to be useful for rheumatoid, arthritis, immunomodulatory diseases inflammatory and proliferative diseases. U.S. Patent No. 5,298,494 discloses derivatives of monosaccharides, which allegedly exhibit anti-proliferative and/or anti-inflammatory activity and are described as useful for treating mammals having inflammatory disorders and/or autoimmune disorders. U.S. Patent No. 5,367,062 discloses derivatives of disubstituted and deoxydisubstituted α,D-lyxofuranosides which reportedly exhibit significant anti-inflammatory and antiproliferative activity and are said to be useful for treating inflammatory and/or autoimmune disorders. U.S. Patent No. 5,360,794 discloses deoxydisubstituted or dideoxy disubstituted derivatives of α-D-mannofuranoside and β-L-gulofuranosides, which are said to exhibit anti-inflammatory and antiproliferative activity. U.S Patent 4,996,195 discloses derivatives of α,D-glucofuranose and α,D-allofuranose described as useful for treating animals and mammals with inflammatory and/or autoimmune disorders. U.S. Patent No. 5,010,058 discloses derivatives of 1,2-O-iso-propylidene-α-D-glucofuranose described as useful for treating animals and mammals with inflammatory and/or autoimmune disorders.

WO 93/13117 and U.S. Patent No. 5,360,792 discloses 5- or 6-deoxy hexose monosaccharides having a saturated nitrogen containing heterocycle described as useful as anti-proliferative and anti-inflammatory compounds. WO 94/28910 discloses 5,6-dideoxy-5-amino derivatives of idose and 6-deoxy–6-amino derivatives of glucose, which are said to exhibit immunomodulatory, anti-inflammatory and anti-proliferative activity.

WO 94/11381 discloses derivatives of pentose monosaccharides described as anti-proliferative and anti inflammatory compound.

Summary of the Invention

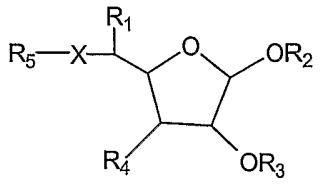
Monosaccharide derivatives, which can be used for the for inhibition and prevention of inflammation and associated pathologies including inflammatory and autoimmune diseases such as bronchial asthma, rheumatoid arthritis, type I diabetes, multiple sclerosis, allograft rejection or psoriasis are provided.

Pharmaceutically acceptable salts, pharmaceutically acceptable solvates, enantiomers, diastereomers or N-oxides of these compounds having the same type of activity are also provided.

Pharmaceutical compositions containing the compounds, and which may also contain pharmaceutically acceptable carriers or diluents, which may be used for the treatment of inflammatory and autoimmune diseases such as bronchial asthma, rheumatoid arthritis, type I diabetes, multiple sclerosis, allograft rejection, psoriasis, inflammatory bowel disease, ulcerative colitis, acne, atherosclerosis, cancer, pruritis and allergic rhinitis.

Other aspects will be set forth in accompanying description which follows and in part will be apparent from the description or may be learnt by the practice of the invention.

In accordance with one aspect, there are provided compounds having the structure of Formula I



Formula I

X can be

$(CH_2)_pNR_j$ or $(CH_2)_pO$ (wherein p is an integer 0 or 1 and R_j is selected from hydrogen, lower (C_1-C_6) alkyl, lower (C_2-C_6) alkenyl, lower (C_2-C_6) alkynyl, lower (C_3-C_8) cycloalkyl, aryl, heteroaryl, lower (C_1-C_6) aralkyl, lower (C_1-C_6) heteroarylalkyl, and lower 3-6 ring membered heterocyclylalkyl).

R_1 can be

A) hydrogen,

B) lower (C_1-C_6) alkyl [wherein alkyl is optionally substituted with hydroxyl, -OR_x (wherein R_x is alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, or heterocyclylalkyl), acyloxy, cycloalkyl, aryl, substituted amino, -C(=O)QR_z (wherein Q is O or NH and R_z is selected from hydrogen, alkyl, aralkyl, aryl, and heteroarylalkyl), heteroaryl, and heterocyclyl],

C) lower (C_2-C_6) alkenyl,

D) lower (C_2-C_6) alkynyl,

E) aryl,

F) heterocyclyl (with the proviso that when p=0, the heterocyclyl cannot be linked through a heteroatom),

G) heteroaryl (with the proviso that when p=0, the heteroaryl cannot be linked through a heteroatom),

H) -OR_x (wherein R_x is as defined above except that when p=0 and X is a derivative of a heteroatom such as O or N, then R_1 cannot be OR_x), and

I) -C(=O)QR_z (wherein Q and R_z is the same as defined above).

R_2 and R_3 together can form a five membered acetal wherein the carbon joining the oxygens is substituted with R_L and R_m, [wherein R_L and R_m are independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, and aralkyl; or R_L and R_m can together join to form a 3- to 8-membered ring, wherein the ring may optionally contain one or more heteroatoms selected from O, N or S, and the ring may be optionally substituted with one or more of alkyl, alkenyl, alkynyl, acyl, substituted amino, cycloalkyl, -C(=O)QR_7 (wherein Q is same as defined earlier and R_7 is selected from alkyl, alkenyl, alkynyl, aryl, aralkyl, cycloalkyl, and heteroarylalkyl), carboxy, oxo, hydroxyl, alkoxy, aryloxy, halogen (FCl, Br, I), aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, or heterocyclylalkyl; or R_L and R_m together join to form an oxo linkage].

R_4 can be hydrogen, or OR_c (wherein R_c is selected from alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, and heterocyclylalkyl) and, when R_4 is OR_c, then R_3 and R_c may together form an acetal (wherein the acetal is the same as defined earlier) and R_2 can be alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, heterocyclylalkyl.

Further, R_2 and R_3, instead of forming an acetal, may optionally and independently be selected from lower (C_1-C_4) alkyl, $(CH_2)_k$-aryl wherein k is an integer from 1-4, -$C(=R_y)NHR_x$ wherein R_y is O or S and R_x is the same as defined earlier, and acyl; with R_4 defined as earlier.

Also, when R_4=OR_c, R_3 and R_c, instead of forming an acetal, may optionally and independently be selected from lower (C_1-C_4) alkyl, $(CH_2)_k$-aryl wherein k is an integer from 1-4, -$C(=R_y)NHR_x$ wherein R_y is O or S and R_x is the same as defined earlier, and acyl; with R_2 defined as earlier.

R_5 can be

A) -$(CH_2)_nG_1$ [(wherein n is an integer 2-4 and one or more carbon(s) in the linker may optionally and independently be substituted with alkyl, aryl, aralkyl, hydroxyl, carboxy, alkoxy, aryloxy, cycloalkyloxy, -$C(=O)QR_z$ wherein Q and R_z are the same as defined earlier, or substituted amino); except that the carbons directly linked to X and G_1 are optionally and independently substituted with alkyl, carboxy, aryl, aralkyl, or -$C(=O)QR_z$ wherein Q and R_z is same as defined earlier]; and

G_1 can be

1) OR_e {wherein R_e is selected from acyl, -$C(=O)NR_fR_q$ [wherein R_f and R_q can be independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heteroaryl, heteroarylalkyl, hetrocyclylalkyl, and $S(O)_2R_6$ (wherein R_6 is selected from alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heterocyclylalkyl, heteroarylalkyl, and substituted amino); and also R_f and R_q can together form a ring]};

2) -$NR_jC(=O)OR_s$ (wherein R_j is same as described earlier and R_s is selected from alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heterocyclylalkyl, and hetroarylalkyl);

3) -NHYR_d (wherein Y can be -C(=O), -C(=S) or SO_2, and R_d can be alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl and heterocyclylalkyl);

4) -$NR_jC(=T)NR_tR_x$ [wherein R_t is OH or R_x (and T is O, S, -N(CN), -$N(NO_2)$, or -$CH(NO_2)$) and R_x is the same as defined earlier]; or

5) heterocyclyl, wherein the heterocyclic ring, which may or may not be benzofused, is always substituted.

R_5 can also be

B) $-(CH_2)_wG_2$, (wherein w ranges from 1-5, and one or more carbon(s) in the linker may be optionally and independently be substituted with lower (C_1-C_6) alkyl, lower (C_1-C_4) aralkyl, or aryl); and

G_2 can be

1) $-(C=O)OR_z$ when R_z is same as defined earlier; or

2) $-(C=O)NR_aR_b$ (wherein R_a and R_b are independently selected from hydrogen, or R_d, wherein R_d is same as defined earlier); and R_a and R_b, together with the nitrogen atom carrying them, can be the N-terminus of an aminoacid or di-tetrapeptide.

Also, when X is $(CH_2)_pNR_j$, and R_1 is not hydrogen, then R_5 can be alkyl, alkenyl, alkynyl, aryl, aralkyl, heteroaryl, heterocylyl, heteroarylalkyl, or heterocyclylalkyl; except that

(1) if R_3 and R_c form an isopropylidene radical and R_2 is hydrogen, C_5-C_{15} alkyl, n-C_5-C_{15}-alkoxy-C_2-C_4-alkyl, or phenypropyl and X is NR_j where R_j is hydrogen and R_1 is H and R_5 is alkyl, then this alkyl must be C_1-C_4 alkyl;

(2) if either R_2 and R_3 or R_3 and R_c form an isopropylidene radical and R_c and R_2 are C_5-C_{15} alkyl respectively, and R_1 is H and X is NR_j where R_j is H, then R_5 cannot be C_3-C_8 alkyl, C_3-C_8 hydroxyalkyl, cyclohexyl- C_1-C_5-alkyl, phenyl- C_2-C_5-alkyl or pyridinyl- C_1-C_5-alkyl; and

(3) if R_3 and R_c form an isopropylidene radical, R_2 is nonyloxypropyl, phenylpropyl, 4-(1-pyrolidinyl)butyl, 2-octyne, or C_7-C_{15} alkyl and X is NR_j where R_j is hydrogen and R_1 is CH_3, CH_2OH, CH_2-pyrrolidinyl, CH_2-piperidinyl, CH_2-morpholinyl, CH_2-hexamethyleneimino, CH_2-aminoethylmorpholinyl, CH_2-aminoethylpiperidinyl, CH_2-aminoethylpyrrolidinyl, CH_2-amino C_7-C_{15} alkyl or C_7-C_{15} alkyl and R_5 is alkyl, then this alkyl must be C_1-C_6 lower alkyl.

For example X-R_5 can be aminoaryl, aminoalkyl, aminoalkaryl, aminoalkyl-oxy-carbonyl-aminoaryl, aminoaryl-urea-aryl, aminoalkyl-carboxyl, aminoheterocyclyl, oxy-alkyl-heterocyclyl, amino-heterocyclyl, or amino acid

The following definitions apply to terms as used herein. The term "alkyl", unless otherwise specified, refers to a monoradical branched or unbranched saturated hydrocarbon chain having from 1 to 20 carbon atoms. This term can be exemplified by groups such as methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, t-butyl, n-hexyl, n-decyl, tetradecyl, and the like. Alkyl may further be substituted with one or more

substituents selected from alkenyl, alkynyl, alkoxy, cycloalkyl, cycloalkenyl, acyl, acylamino, acyloxy, alkoxycarbonylamino, azido, cyano, halogen, hydroxy, oxo, thiocarbonyl, carboxy, arylthio, thiol, alkylthio, aryloxy, aminosulfonyl, aminocarbonylamino, -$COOR_x$ (wherein R_x is the same as defined earlier), -$NHC(=O)R_x$, -NR_aR_b, -$C(=O)NR_aR_b$, -$NHC(=O)NR_xR_t$, -$N(OH)C(=O)NR_xR_t$, -C(=O)heteroaryl, C(=O)heterocyclyl, -O-$C(=O)NR_aR_b$ wherein R_x, R_t, R_a and R_b are the same as defined earlier, nitro, -$S(O)_mR_6$ wherein m is an integer from 0-2 and R_6 is the same as defined earlier. Unless otherwise constrained by the definition, all such alkyl substituents may be further substituted by 1-3 substituents chosen from alkyl, carboxy, -NR_aR_b, -$C(=O)NR_aR_b$, -O-$C(=O)NR_aR_b$, -$NHC(=O)NR_aR_b$ wherein R_a and R_b are the same as defined earlier, hydroxy, alkoxy, halogen, CF_3, cyano, and –$S(O)_mR_6$, where R_6 and m are the same as defined earlier; or an alkyl group as defined above may also be interrupted by 1-5 atoms of groups independently chosen from oxygen, sulfur and -NR_a-, where R_a is chosen from hydrogen, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, acyl, aralkyl,-$C(=O)OR_s$ wherein R_s is the same as defined earlier, $S(O)_2R_6$ where R_6 is as defined earlier, -$C(=O)NR_aR_b$ wherein R_a and R_b are as defined earlier.

The term "alkenyl," unless otherwise specified, refers to a monoradical of a branched or unbranched unsaturated hydrocarbon group preferably having from 2 to 20 carbon atoms with cis or trans geometry. In the event that alkenyl is attached to the heteroatom, the double bond cannot be alpha to the heteroatom. Alkenyl groups may further be substituted with one or more substituents selected from alkyl, alkynyl, alkoxy, cycloalkyl, cycloalkenyl, acyl, acylamino, acyloxy, -$COOR_x$ (wherein R_x is the same as defined earlier), -$NHC(=O)R_x$, -NR_aR_b, -$C(=O)NR_aR_b$, -$NHC(=O)NR_xR_t$, -$N(OH)C(=O)NR_xR_t$, -O-$C(=O)NR_aR_b$ (wherein R_a and R_b are the same as defined earlier), alkoxycarbonylamino, azido, cyano, halogen, hydroxy, oxo, thiocarbonyl, carboxy, arylthio, thiol, alkylthio, aryl, aralkyl, aryloxy, heterocyclyl, heteroaryl, heterocyclyl alkyl, heteroaryl alkyl, aminosulfonyl, aminocarbonylamino, alkoxyamino, nitro, $S(O)_mR_6$ wherein R_6 and m are the same as defined earlier. Unless otherwise constrained by the definition, all such alkenyl substituents may optionally be further substituted by 1-3 substituents chosen from alkyl, carboxy, hydroxy, alkoxy, halogen,-CF_3, cyano, -NR_aR_b, -$C(=O)NR_aR_b$, -O-$C(=O)NR_aR_b$ wherein R_a and R_b are the same as defined earlier and -$S(O)_mR_6$, where R_6 and m are the same as defined earlier.

The term "alkynyl," unless otherwise specified, refers to a monoradical of an unsaturated hydrocarbon, preferably having from 2 to 20 carbon atoms. In the event that alkynyl is attached to the heteroatom, the triple bond cannot be alpha to the heteroatom. Alkynyl substituents may further be substituted with one or more substituents selected from alkyl, alkenyl, alkoxy, cycloalkyl, cycloalkenyl, acyl, acylamino, acyloxy, alkoxycarbonylamino, azido, cyano, halogen, hydroxy, oxo, thiocarbonyl, carboxy, arylthio, thiol, alkylthio, aryl, aralkyl, aryloxy, aminosulfonyl, aminocarbonylamino, nitro, heterocyclyl, heteroaryl, heterocyclyl alkyl, heteroarylalkyl, $-COOR_x$ (wherein R_x is the same as defined earlier), $-NHC(=O)R_x$, $-NR_aR_b$, $-NHC(=O)NR_xR_t$, $-N(OH)C(=O)NR_xR_t$, $-C(=O)NR_aR_b$, $-O-C(=O)NR_aR_b$ (wherein R_x, R_t, R_a and R_b are the same as defined earlier), and $-S(O)_mR_6$ (wherein R_6 and m are the same as defined earlier). Unless otherwise constrained by the definition, all substituents may optionally be further substituted by 1-3 substituents chosen from alkyl, carboxy, carboxyalkyl, hydroxy, alkoxy, halogen, CF_3, $-NR_aR_b$, $-C(=O)NR_aR_b$, $-NHC(=O)NR_xR_t$, $-C(=O)NR_aR_b$ wherein R_x, R_t, R_a and R_b are the same as defined earlier cyano, and $-S(O)_mR_6$, where R_6 and m are the same as defined earlier.

The term "cycloalkyl" refers to cyclic alkyl groups of from 3 to 20 carbon atoms having a single cyclic ring or multiple condensed rings, which may optionally contain one or more olefinic bonds, unless or otherwise constrained by the definition. Such cycloalkyl groups include, by way of example, single ring structures such as cyclopropyl, cyclobutyl, cyclooctyl, cyclopentenyl, and the like, or multiple ring structures such as adamantanyl, and bicyclo [2.2.1]heptane, or cyclic alkyl groups to which is fused an aryl group, for example indane, and the like. Cycloalkyl groups may further be substituted with one or more substituents selected from alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, cycloalkenyl, acyl, acylamino, acyloxy, alkoxycarbonylamino, azido, cyano, halogen, hydroxy, oxo, thiocarbonyl, carboxy, carboxyalkyl, arylthio, thiol, alkylthio, aryl, aralkyl, aryloxy, aminosulfonyl, aminocarbonylamino, $-COOR_x$ (wherein R_x is the same as defined earlier), $-NR_aR_b$, $-NHC(=O)NR_xR_t$, $-NHC(=O)R_x$, $-N(OH)C(=O)NR_xR_t$, $-C(=O)NR_aR_b$, $-O-C(=O)NR_aR_b$ (wherein R_x, R_t, R_a and R_b are the same as defined earlier), nitro, heterocyclyl, heteroaryl, heterocyclylalkyl, heteroarylalkyl, and $S(O)_m-R_6$ (wherein R_6 and m are the same as defined earlier). Unless otherwise constrained by the definition, all such cycloalkyl substituents may optionally be further substituted by 1-3 substituents chosen from alkyl, carboxy, hydroxy, alkoxy, halogen, CF_3, $-NR_aR_b$, $-C(=O)NR_aR_b$, -

$NHC(=O)NR_xR_t$, -O-$C(=O)NR_aR_b$ wherein R_x, R_t, R_a and R_b are the same as defined earlier cyano, and $-S(O)_mR_6$, where R_6 and m are the same as defined earlier.

The term "alkoxy" denotes the group O-alkyl wherein alkyl is the same as defined above.

The term "aralkyl" refers to alkyl-aryl linked through alkyl (wherein alkyl is the same as defined above) portion and the said alkyl portion contains carbon atoms from 1-6 and aryl is as defined below. Examples of aralkyl groups can include benzyl and the like.

The term "aryl" herein refers to a carbacyclic aromatic group, for example phenyl, biphenyl or naphthyl ring and the like optionally substituted with 1 to 3 substituents selected from $-(CH_2)_wC(=O)R_g$ wherein w is an integer from 1-4 and R_g is hydroxy, OR_z, NR_aR_b, -$NHOR_z$ or –NHOH, halogen (F, Cl, Br, I), hydroxy, alkyl, alkenyl, alkynyl, cycloalkyl, alkoxy, acyl, aryloxy, cyano, nitro, -$COOR_x$ (wherein R_x is the same as defined earlier), $NHC(=O)R_x$, -NR_aR_b, -$N(OH)C(=O)NR_xR_t$, -$C(=O)NR_aR_b$, -$NHC(=O)NR_xR_t$, -$(SO_2)_mR_6$ (wherein R_6, R_x, R_a, R_b, R_z and R_t and m are the same as defined earlier), carboxy, heterocyclyl, heteroaryl, heterocyclylalkyl, and heteroarylalkyl. The aryl group may optionally be fused with cycloalkyl group, wherein the cycloalkyl group may optionally contain heteroatoms selected from O, N, S.

The term "aryloxy" denotes the group O-aryl wherein aryl is the same as defined above.

The term "carboxy" as defined herein refers to –C(=O)OH.

The term "heteroaryl," unless otherwise specified, refers to an aromatic ring structures containing 5 or 6 atoms, or a bicyclic aromatic group having 8 to 10 atoms, with one or more heteroatom(s) independently selected from N, O and S optionally substituted with 1 to 3 substituent(s) selected from halogen (F, Cl, Br, I), hydroxy, alkyl, alkenyl, alkynyl, cycloalkyl, acyl, carboxy, aryl, alkoxy, aralkyl, cyano, nitro, -$COOR_x$ (wherein R_x is the same as defined earlier), -NR_aR_b, $-(CH_2)_wC(=O)R_g$ wherein w is an integer from 1-4 and R_g is hydroxy, OR_z, NR_aR_b, -$NHOR_z$ or –NHOH, -$N(OH)C(=O)NR_xR_t$, -$C(=O)NR_aR_b$ and $-NHC(=O)NR_xR_t$, -SO_2R_6, -O-$C(=O)NR_aR_b$ wherein R_6, R_z, R_t, R_x, R_a and R_b are the same as defined earlier. Unless otherwise constrained by the definition, the heteroaryl substituents are attached to the ring atom, be it carbon or heteroatom. Examples of heteroaryl groups can include pyridinyl, pyridazinyl, pyrimidinyl, pyrrolyl,

oxazolyl, thiazolyl, thienyl, isoxazolyl, triazinyl, furanyl, benzofuranyl, indolyl, benzothiazolyl, benzoxazolyl, and the like.

The term "heterocyclyl," unless otherwise specified, refers to a non-aromatic monocyclic or bicyclic cycloalkyl group having 5 to 10 atoms in which 1 to 3 carbon atoms in a ring are replaced by heteroatoms selected from O, S or N, and are optionally benzofused or fused heteroaryl of 5-6 ring members and/or are optionally substituted wherein the substituents are selected from halogen (F, Cl, Br, I), hydroxy, alkyl, alkenyl, alkynyl, cycloalkyl, acyl, aryl, alkoxy, alkaryl, cyano, nitro, oxo, carboxy, -$COOR_x$ (wherein R_x is the same as defined earlier), -$C(=O)NR_aR_b$, SO_2R_6,-$O-C(=O)NR_aR_b$, -$NHC(=O)NR_xR_t$, -$N(OH)C(=O)NR_xR_t$, and -NR_aR_b (wherein R_x, R_t, R_a and R_b are the same as defined earlier). Unless otherwise constrained by the definition, the heterocyclyl substituents are attached to the ring atom, be it carbon or heteroatom. Also unless otherwise constrained by the definition, the heterocyclyl ring may optionally contain one or more olefinic bond(s). Examples of heterocyclyl groups can include tetrahydrofuranyl, dihydrofuranyl, dihydropyridinyl, dihydrobenzofuryl, azabicyclohexyl, dihydroindolyl, piperidinyl or piperazinyl.

"Heteroarylalkyl" refers to alkyl-heteroaryl group linked through alkyl portion, wherein the alkyl and heteroaryl are the same as defined earlier.

"Heterocyclylalkyl" refers to alkyl-heterocyclyl group linked through alkyl portion, wherein the alkyl and heterocyclyl are the same as defined earlier.

"Acyl" refers to –C(=O)R'' wherein R'' is selected from the group alkyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl or heterocyclylalkyl.

"Substituted amino," unless otherwise specified, refers to $-N(R_k)_2$ wherein each R_k is independently selected from hydrogen (provided that both R_k groups are not hydrogen, defined as "amino"), alkyl, alkenyl, alkynyl, aralkyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, heterocyclylalkyl, heteroarylalkyl, acyl, $S(O)_mR_6$ (wherein m and R_6 are the same as defined above), -$C(=R_y)NR_aR_b$ (wherein R_y, R_a and R_b are the same as defined earlier) or $NHC(=R_y)NR_tR_x$ (wherein R_y, R_t and R_x are the same as defined earlier). Unless otherwise constrained by the definition, all amino substituents may optionally be further substituted by 1-3 substituents chosen from alkyl, aralkyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, carboxy, carboxyalkyl, hydroxy, alkoxy, halogen, CF_3, cyano, -

$C(=R_y)NR_aR_b$, $-O(C=O)NR_aR_b$ (wherein R_a, R_b and R_y are the same as defined earlier) and $-OC(=R_y)NR_aR_b$,, and-$S(O)_mR_6$, where R_6 is the same as defined above and m is 0, 1 or 2.

The term "leaving group" generally refers to groups that exhibit the properties of being labile under the defined synthetic conditions and also, of being readily separated from synthetic products under defined conditions. Examples of such leaving groups include but are not limited to, halogen (F, Cl, Br, I), triflates, tosylate, mesylates, alkoxy, thioalkoxy, hydroxy radicals and the like.

The term "activated derivative of a carboxylic acid," for example, that of a suitable protected amino acid, aliphatic acid or an aromatic acid refer to the corresponding acyl halide (e.g., acid fluoride, acid chloride and acid bromide), corresponding activated esters (e.g. nitro phenyl ester, the ester of 1- hydroxybenzotriazole or the ester of hydroxysuccinimide, HOSu) or a mixed anhydride for example anhydride with ethyl chloroformate and other conventional derivatives within the skill of the art.

The term "protecting groups" is used herein to refer to moieties which have the property of preventing specific chemical reactions at a site on the molecule undergoing chemical modification intended to be left unaffected by the particular chemical modification. Also the term protecting group, unless otherwise specified, may be used with groups such as hydroxy, amino, carboxy and examples of such groups are found in T.W. Greene and P.G.M. Wuts, "Protective Groups in Organic Synthesis", 2nd Ed, John Wiley and Sons, New York, N.Y., which is incorporated herein by reference. The species of the carboxylic protecting groups, amino protecting groups or hydroxy protecting group employed are not critical, so long as the derivatised moieties/moiety is/are stable to conditions of subsequent reactions and can be removed at the appropriate point without disrupting the remainder of the molecule.

"Amino acid" refers to both natural and unnatural amino acids. The term "natural amino acid", as used herein is intended to represent the twenty two naturally occurring amino acids glycine, alanine, valine, leucine, isoleucine, serine, methionine, threonine, phenylalanine , tyrosine, trytophan, cysteine, proline, proline, histidine, aspartic acid, asparagines, glutamic acid, glutamine, γ-carboxyglutamic acid, arginine, ornithine and lysine in their L form. The term "unnatural amino acid", as used herein, is intended to represent the 'D' form of the twenty two naturally occurring amino acids described above. It is futher understood that the term unnatural amino acid includes homologues of the

natural amino acids, and synthetically modified form of the natural amino acids commonly utilized by those in the peptide chemistry arts when preparing synthetic analogues of naturally occurring peptides, including D and L forms. The synthetically modified forms include amino acids having alkylene chains shortened or lengthened by up to two carbon atoms, amino acids comprising optionally substituted aryl groups, and amino acids comprised halogenated groups preferably halogenated alkyl and aryl groups. The term "unnatural amino acids," as used herein, is also intended to represent beta amino acids.

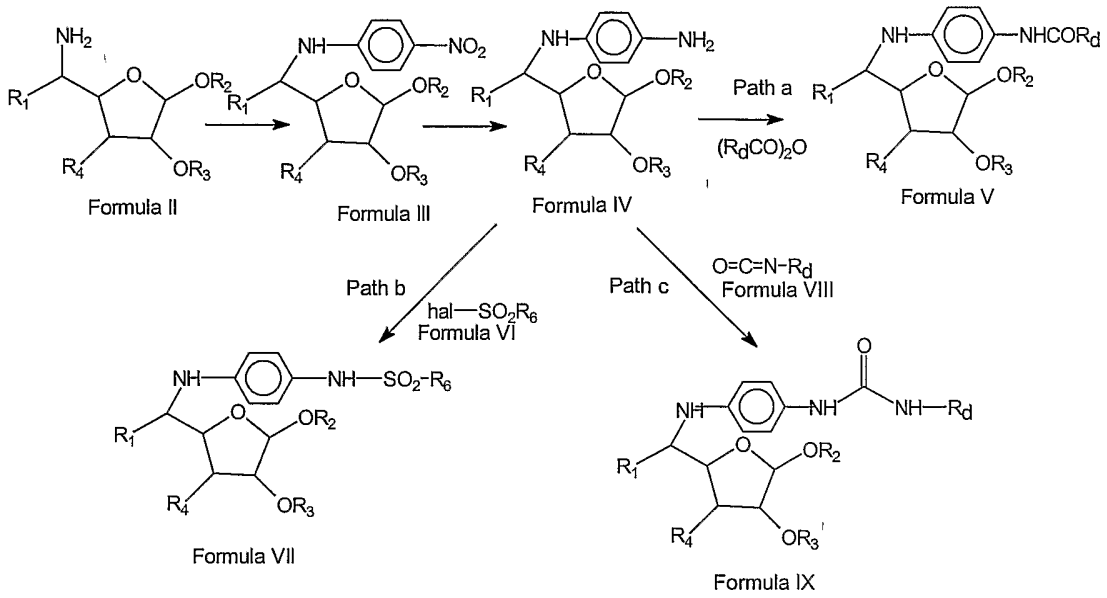
The term "peptide" refers to a molecule comprising a series of amino acids linked through amide linkages. Dipeptide comprises 2 amino acids, tripeptide refers to a peptide having 3 amino acids and tetrapeptide refers to one having four amino acids, wherein the term amino acid is as defined earlier. "LDVP" refers to a tetrapeptide leucyl-aspartyl-valyl-prolyl. "DVP" refers to a tripeptide aspartyl-valyl-prolyl. "VP" refers to a dipeptide valyl-prolyl.

The compounds disclosed herein generally contain one or more asymmetric carbon atoms and thus can occur as racemates and racemic mixtures, single enantiomers, diastereomeric mixtures and individual diastereomers. All such isomeric forms of these compounds are expressly included herein. Each stereogenic carbon may be of the R or S configuration. Although the specific compounds exemplified in this application may be depicted in a particular stereochemical configuration, compounds having either the opposite stereochemistry at any given chiral center or mixtures thereof are envisioned. Although amino acids and amino acid side chains may be depicted in a particular configuration, both natural and unnatural forms are envisioned.

Detailed Description of the Invention

Compounds disclosed herein may be prepared by techniques well known in the art and familiar to synthetic organic chemist of ordinary skill. In addition, the compounds of the present invention may be prepared by following the reaction scheme as depicted below.

Scheme I



Compounds of Formula V, VII and IX can be prepared following Scheme I, thus a compound of Formula II is reacted with 4-nitrofluorobenzene to form a compound of Formula III, which on hydrogenation yields a compound of Formula IV(wherein R_1,R_2, R_3 and R_4 are same as defined earlier).

Path a: The compound of Formula IV can be reacted with $(R_dCO)_2O$, for example, acetic anhydride, to form a compound of Formula V (wherein R_d, R_1, R_2, R_3 & R_4 are same as defined earlier).

Path b: The compound of Formula IV can be reacted with a compound of Formula VI (wherein *hal* is halogen and R_6 is as defined earlier) to yield a compound of Formula VII (wherein R_6, R_1, R_2, R_3 and R_4 are same as defined earlier).

Path c: The compound of Formula IV can be reacted with a compound of Formula VIII to form a compound of Formula IX. (Wherein R_d, R_1, R_2, R_3 and R_4 are same as defined earlier).

The compound of Formula II can be reacted with *p*-nitrofluorobenzene to form a compound of Formula III in an organic solvent, for example, acetonitrile, dimethylsulphoxide or ethyl acetate, in the presence of a organic base, for example, diisopropylethylamine, pyridine or triethylamine.

The catalytic hydrogenation of compound of Formula III can be carried out to form a compound of Formula IV in an organic solvent, for example, methanol, ethanol,

propanol, isopropyl alcohol, tetrahydrofuran or ethyl acetate, under hydrogen atmosphere utilizing, for example, catalytic palladium on carbon. Alternatively, a person skilled in the art of this invention can utilize a palladium-catalyzed coupling reaction of an amine with aryl halides (which are exemplified by reactions known as Buchwald-Hartwig coupling reactions) for the synthesis of analogous compounds of Formula III, V, VII or IX with various aryl subsitutents.

The reaction of compound of Formula IV with an anhydride (*Path a*), for example, acetic anhydride to form a compound of Formula V can be carried out in an organic solvent, for example, dichloromethane, dichloroethane, chloroform or carbon tetrachloride, in the presence of a organic base triethylamine, diisopropylethylamine or pyridine. Alternatively, compounds of Formula IV can react with an acid halide to provide compounds of Formula V in the presence of a base, such as triethylamine, diisopropylethylamine, pyridine, or with an activated derivative of a carboxylic acid, as defined earlier.

The reaction of compound of Formula IV with a compound of Formula VI to form a compound of Formula VII (*Path b*) can be carried out in an organic solvent, such as dichloromethane, dichloroethane, chloroform or carbon tetrachloride, and in the presence of a base, such as triethylamine, diisopropylethylamine or pyridine.

The reaction of compounds of Formula IV with a compound of Formula VIII to yield a compound of Formula IX (*path c*) can be carried out in an organic solvent, for example, dichloromethane, dichloroethane, chloroform or carbon tetrachloride. Alternatively, a compound of Formula IV may react with an amine in the presence of carbonyldiimidazole (CDI) to yield a compound of Formula IX or may react with a carbamate such as phenyl or p-nitrophenyl carbamate of an amine to yield a compound of Formula IX.

Compounds prepared following Scheme I, are:

1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-{4-nitro-phenyl}-amino-β-L-gulofuranoside (Compound No. 1)

Path a

1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-{4-amino-phenyl}-amino-β-L-gulofuranoside (Compound No. 2)

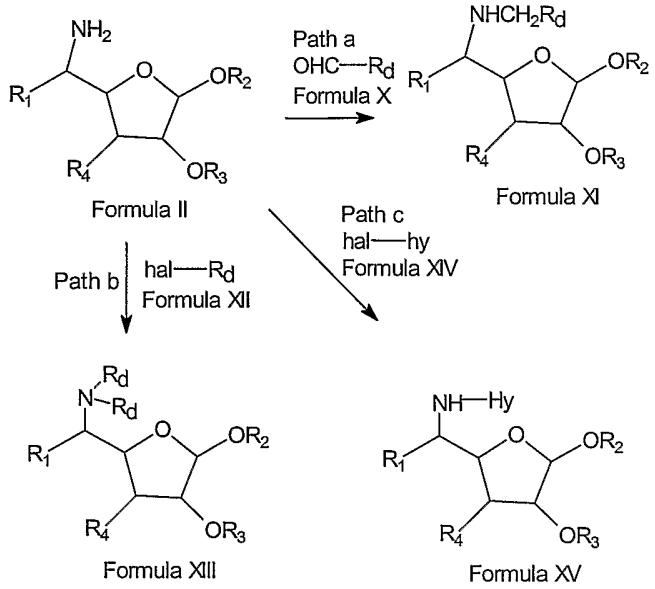
Path b

1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-{[4-(4-methyl-phenyl-sulphonyl)-amino]-phenyl}-amino-β-L-gulofuranoside (Compound No. 3)

Path c

1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-{4-[3-(2-methyl-phenyl)-ureido]-phenyl}-amino-β-L-gulofuranoside (Compound No. 4)

Scheme II



The compounds of Formula XI, XIII and XV can be prepared following Scheme II.

Path a: A compound of Formula II can be reacted with a compound of Formula X to form a compound of Formula XI (wherein R_1, R_2, R_3, R_4 and R_d is same as defined earlier).

Path b: The compound of Formula II can be reacted with compound of Formula XII (wherein *hal* is a halogen and R_d is same as defined earlier) to yield a compound of Formula XIII (wherein R_1, R_2, R_3, R_4& R_d are as described before).

Path c: The compound of Formula II can be reacted with a compound of Formula XIV (wherein *hal* is a halogen and *Hy* is heterocyclyl or heteroaryl) to yield a compound of Formula XV.

The compound of Formula II can be reacted with compound of Formula X to yield a compound of Formula XI in an organic solvent, for example, methanol or ethanol, using a reducing agent, for example, sodium triacetoxyborohydride, sodium cyanoborohydride, sodium borohydride, borane in pyridine or H_2/Pd catalyst, and when desired, the reaction

can be carried out in the presence of catalytic amount of an acid, for example, acetic acid or propionic acid.

The compound of Formula II can be reacted with a compound of Formula XII to provide a compound of Formula XIII and the reaction can be carried out in an organic solvent, for example, acetone, acetonitrile, tetrahydrofuran or dimethylformamide, in the presence of a base, for example, potassium carbonate, sodium carbonate, triethylamine or pyridine.

The compound of Formula II can be reacted with a compound of Formula XIV to form a compound of Formula XV and the reaction can be carried out in an organic solvent, for example, tetrahydrofuran or dimethylformamide, in the presence of a base, for example, pyridine, triethylamine or diisopropylethylamine.

Also, an alternative synthetic route to produce compounds of Formula XV is presented in Scheme IV.

Compounds prepared following Scheme II are:

Path a

1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-{2-methyl-butyl}-amino-β-L-gulofuranoside (Compound No. 5)

1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-{3-phenyl-propyl}-amino-β-L-gulofuranoside (Compound No. 6)

1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-{2-phenyl-propyl}-amino-β-L-gulofuranoside (Compound No. 7)

1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-{4-fluoro-benzyl}-amino-β-L-gulofuranoside (Compound No. 8)

1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-(2,2-dimethyl-propyl)-amino-β-L-gulofuranoside (Compound No. 9)

1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-(2-carboxyethyl)-amino-β-L-gulofuranoside (Compound No. 10)

1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-{2,6-dichloro-benzyl}-amino-β-L-gulofuranoside (Compound No. 26)

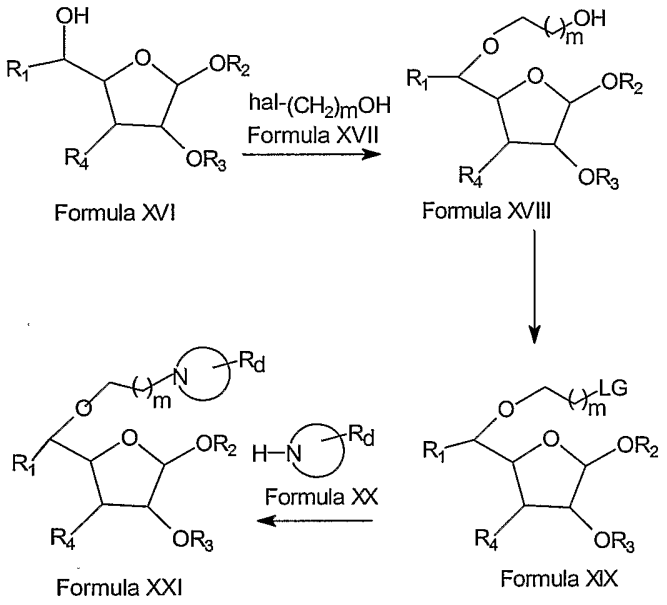
Path b

1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-dibenzyl-amino-β-L-gulofuranoside (Compound No. 11)

Path c

1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-(benzoxazol-2-yl)-amino-β-L-gulofuranoside (Compound No. 12)

Scheme III



The compound of Formula XXI can be prepared following Scheme III. Thus a compound of Formula XVI can be reacted with a compound of Formula XVII (wherein m is an integer from 1-3 and *hal* is halogen) to yield a compound of Formula XVIII, the hydroxy group of which can be converted to a leaving group in a compound of Formula XIX (wherein LG is a leaving group and R_1, R_2, R_3, R_4 are same as defined earlier), which on further reaction with a compound of Formula XX can form a compound of Formula XXI (wherein m, R_d, R_1, R_2, R_3, R_4 are same as defined before).

The compound of Formula XVI can be reacted with 3-chloropropanol to form a compound of Formula XVIII in the presence of a base, for example, sodium hydroxide, potassium hydroxide, sodium hydride or potassium tert-butoxide.

The hydroxy group in compound of Formula XVIII can be converted to a leaving group, for example, tosyl, mesyl or triflyl. Thus, for example, Formula XVIII can be

tosylated with p-tosyl chloride to form a compound of Formula XIX in the presence of a base, for example, pyridine, triethylamine or diisopropylethylamine.

The reaction of compound of Formula XIX with a compound of Formula XX to provide a compound of Formula XXI can be facilitated in the presence of a base, such as triethylamine, diisopropylethylamine or pyridine, in a solvent such as acetone, acetonitrile, tetrahydrofuran or dimethylformamide.

Compounds prepared following Scheme III, are:

1,2-O-Isopropylidene-3-O-decyl-5-O-[1-(4-{4-methoxy-phenyl})-piperazinyl]-propyl}-α-D-xylofuranoside (Compound No. 13)

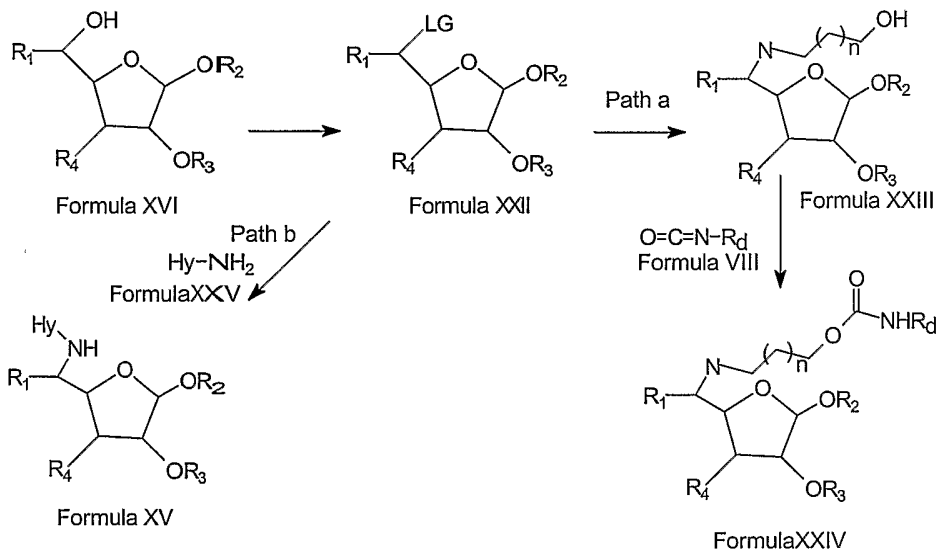
1,2-O-Isopropylidene-3-O-decyl-5-O-[3-(1-{4-benzyl}-piperazinyl)-propyl]-α-D-xylofuranoside (Compound No. 14)

1,2-O-Isopropylidene-3-O-decyl-5-O-[3-(1-{4-[2-methoxy-phenyl]}-piperazinyl)-propyl]-α-D-xylofuranoside (Compound No. 15)

1,2-O-Isopropylidene-3-O-heptyl-5-O-(N-phthalimido-ethyl)-α-D-xylofuranoside (Compound No. 21)

1,2-O-Isopropylidene-3-O-dodecyl-5-O-{3-[4-({[4-(2-methoxy-2-oxoethyl)phenyl] amino}carbonyl)-piperazinyl]-propyl}-α-D-xylofuranoside (Compound No. 27)

Scheme IV



The compounds of Formula XXIV and XV can be prepared according to Scheme IV. Thus, a compound of Formula XVI can be reacted with a leaving group to form a compound of Formula XXII.

Path a: A compound of Formula XXII on reaction with aminoalkylalcohol, such as 3-aminopropanol can form a compound of Formula XXIII (wherein n is an integer 0-2), which on reaction with a compound of Formula VIII can form a compound of Formula XXIV (wherein n, R_d, R_1, R_2, R_3, R_4 are same as described earlier).

Path b: The compound of Formula XXII on reaction with a compound of Formula XXV can yield a compound of Formula XV (wherein *Hy* is heterocyclyl or heteroaryl and R_1, R_2, R_3, R_4 are same as described earlier).

The hydroxy group in compound of Formula XVI can be converted to a leaving group, for example tosyl, mesyl or triflyl. Thus, for example, Formula XVI can be tosylated with p-tosyl chloride to form a compound of Formula XXII in the presence of a base, for example, pyridine, triethylamine or diisopropylethylamine.

The reaction of compound of Formula XXIII with a compound of Formula VIII to give a compound of Formula XXIV can be carried out in the presence of a solvent, for example, dichloromethane, dichloroethane, chloroform or carbon tetrachloride.

The reaction of compound of Formula XXII with a compound of Formula XXV to yield a compound of Formula XV can be carried out in an organic solvent, for example, tetrahydrofuran or dimethylformamide in the presence of a base, for example, sodium hydride or potassium tert-butoxide.

Compounds prepared following Scheme IV are:

Path a

1-O-Methyl-2,3-O-isopropylidene-5-deoxy-5-[{3-[(4-{2-hydroxy-2-oxo-ethyl}-phenyl)-amino]-carbonyloxy}-propyl]-amino-α-D-lyxofuranoside (Compound No. 16)

Path b

1,2-O-Isopropylidene-3-O-decyl-5-deoxy-5-[2-(4-phenylthiazolyl)-amino]-α-D-xylofuranoside (Compound No. 17)

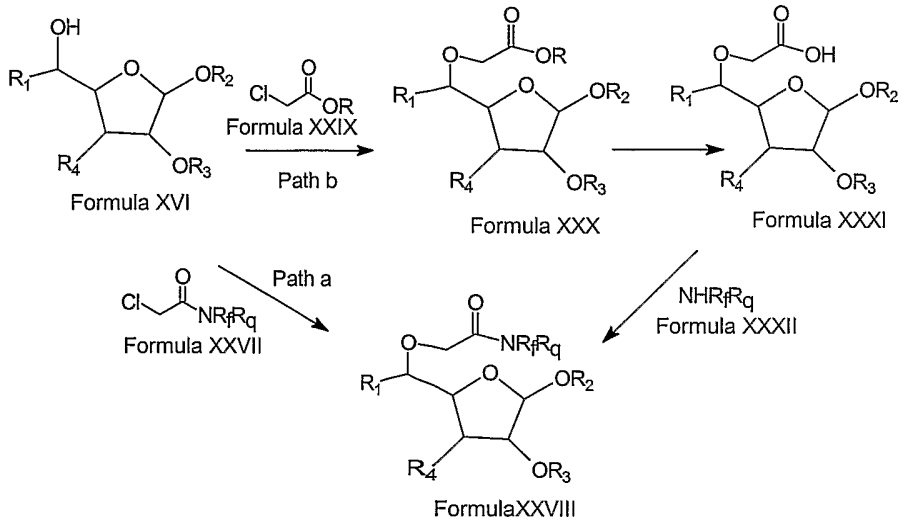
1,2-O-Isopropylidene-3-O-dodecyl-5-deoxy-5-{2-thiazolyl-amino}-α-D-xylofuranoside (Compound No. 18)

1,2-O-Isopropylidene-3-O-dodecyl-5-deoxy-5-{2-(benzimidazolyl)-amino}-α-D-xylofuranoside (Compound No. 19)

1,2-O-Isopropylidene-3-O-hexyl-5-deoxy-5-[2-(5-benzoyl-1*H*-benzimidazolyl)-amino]-α-D-xylofuranoside (Compound No. 20)

1,2-O-Isopropylidene-3-O-dodecyl-5-deoxy-5-[(4-methyl-1,3-thiazolyl)-amino]-α-D-xylofuranoside (Compound No. 28)

SchemeV



A compound of Formula XXVIII can be prepared following either *Path a* or *Path b* of Scheme V.

Path a: A compound of Formula XVI can be reacted with a compound of Formula XXVII to yield a compound of Formula XXVIII (wherein R_f, R_q, R_1, R_2, R_3 and R_4 are same as defined earlier).

Path b: A compound of Formula XVI can be reacted with a compound of Formula XXIX (wherein R is alkyl or aralkyl), for example, ester of chloroacetic acid to form a compound of Formula XXX, which on hydrolysis can yield a compound of Formula XXXI. The compound of Formula XXXI on reaction with a compound of Formula XXXII can yield a compound of Formula XXVIII (wherein R_f, R_q, R_1, R_2, R_3 and R_4 are same as defined earlier).

Following *Path a,* the reaction of a compound of Formula XVI with a compound of Formula XXVII to yield a compound of Formula XXVIII can be facilitated in an organic solvent such as tetrahydrofuran or dimethylformamide, in the presence of a base, for example, sodium hydride or potassium tert-butoxide.

Alternatively, a compound of Formula XXVIII may also be formed by following *Path b.* Thus, the reaction of a compound of Formula XVI with a compound of Formula XXIX to form a compound of Formula XXX can be facilitated in an organic solvent, for example, tetrahydrofuran or dimethylformamide, in the presence of a base, for example, sodium hydride or potassium tert-butoxide.

Hydrolysis of a compound of Formula XXX to yield a compound of Formula XXXI can be carried out in a solvent, for example, methanol in water, ethanol, propanol, tetrahydrofuran or isopropyl alcohol, in the presence of a base, for example, sodium hydroxide, lithium hydroxide or potassium hydroxide.

The coupling of compound of Formula XXXI with a compound of Formula XXXII to yield a compound of Formula XXVIII can be carried out in a solvent, for example, dimethylformamide or tetrahydrofuran, in the presence of a condensing agent, for example, 1-ethyl- (3-dimethylamino propyl)-3-carbodimide, in the presence of 1-hydroxybenzotriazole and a base, for example, N-methylmorpholine or alternatively, through a mixed anhydride by reaction of Formula XXXI with a chloroformate, for example, ethyl chloroformate or isobutyl chloroformate.

Compounds prepared following Scheme V are:

1,2-O-Isopropylidene-3-O-decyl-5-O-{(4S, 7S, 10S)-3,6,9-triaza-11-[1-(2S-carboxy)-pyrrolidinyl]-7-(2-hydroxy-2-oxo-ethyl)-10-isopropyl-4-(2-methylpropyl)-2,5,8,11-tetraoxo-undecyl}-α-D-xylofuranoside (Compound No. 22)

1,2-O-Isopropylidene-3-O-decyl-5-O-{(4S, 7S)-3,6-diaza-8-[1-(2S-carboxy)-pyrrolidinyl]-4-(2-hydroxy-2-oxo-ethyl)-7-isopropyl-2, 5,8-trioxo-octyl}-α-D-xylofuranoside (Compound No. 23)

1,2-O-Isopropylidene-3-O-decyl-5-O-{(4S, 7S, 10S)-3,6,9-triaza-11-[1-(2S-benzyloxycarbonyl)-pyrrolidinyl]-7-[2-benzyloxy-2-oxo-ethyl]-10-isopropyl-4-(2-methylpropyl)-2,5,8,11-tetraoxo-undecyl}-α-D-xylofuranoside (Compound No. 24)

1,2-O-Isopropylidene-3-O-decyl-5-O-[2-{1-(2S-carboxy)-pyrrolidinyl}-2-oxo-ethyl]-α-D-xylofuranoside (Compound No. 25)

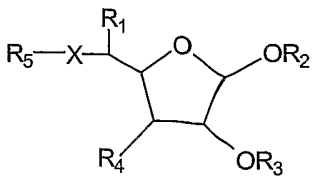
Also, in all the above representative examples, wherever esters are specified one skilled in the art could optionally hydrolyze them to their respective acids, for example, hydrolysis of alkyl esters (such as ethyl, methyl or benzyl ester) to their corresponding

acids can be carried out in the presence of a base for example lithium hydroxide, sodium hydroxide or potassium hydroxide. Alternatively hydrolysis of benzyl ester can be carried out hydrogenatically using catalysts for example palladium on carbon or platinum on carbon. Esters such as tert-butyl can be hydrolyzed to their corresponding acids in the presence of acid for example trifluoroacetic acid or hydrochloric acid.

In the above schemes, where specific bases, acids, solvents, condensing agents, hydrolyzing agents, etc., are mentioned, it is to be understood that other acids, bases, solvents, condensing agents, hydrolyzing agents, etc., known to those skilled in the art may also be used. Similarly, the reaction temperature and duration of the reactions may be adjusted according to the desired needs.

Particular compounds described herein being produced by Schemes I-V are listed below in the Table I and Table II

Table I



Formula I

When R_3 & R_c (when R_4 is OR_c) are together forming isopropylidene radical

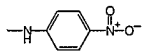
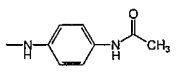
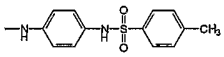
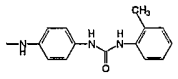
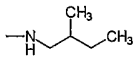
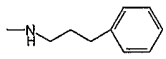
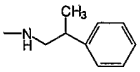
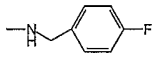
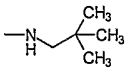
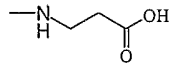
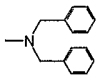
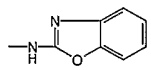
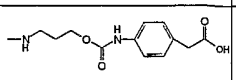
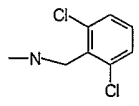
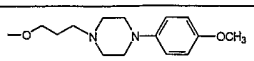
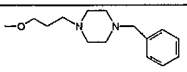
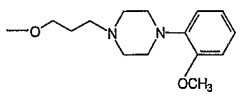
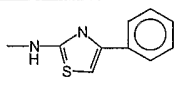
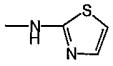
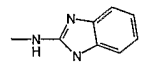
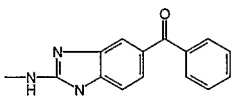
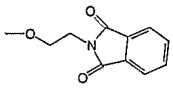
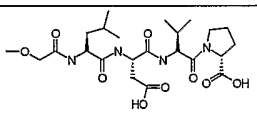
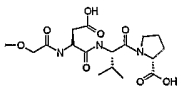
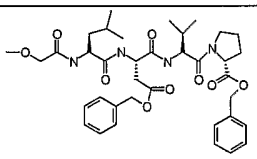
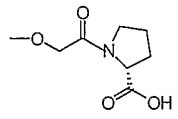
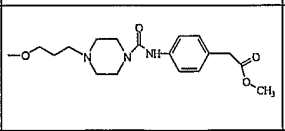
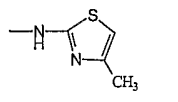
Compound No.	R_2	R_1	$-XR_5$	Compound No.	R_2	R_1	$-XR_5$
1	$C_{12}H_{25}$	CH_3		2	$C_{12}H_{25}$	CH_3	
3	$C_{12}H_{25}$	CH_3		4	$C_{12}H_{25}$	CH_3	
5	$C_{12}H_{25}$	CH_3		6	$C_{12}H_{25}$	CH_3	
7	$C_{12}H_{25}$	CH_3		8	$C_{12}H_{25}$	CH_3	
9	$C_{12}H_{25}$	CH_3		10	$C_{12}H_{25}$	CH_3	
11	$C_{12}H_{25}$	CH_3		12	$C_{12}H_{25}$	CH_3	
16 **	O-CH_3	H		26	$C_{12}H_{25}$	CH_3	

Table II

When R_2 & R_3 are together forming an isopropylidene radical

Compound No.	R_4	R_1	XR_5	Compound No.	R_4	R_1	$-XR_5$
13	$OC_{10}H_{21}$	H		14	$OC_{10}H_{21}$	H	
15	$OC_{10}H_{21}$	H		17	$OC_{10}H_{21}$	H	
18	$OC_{12}H_{25}$	H		19	$OC_{12}H_{25}$	H	
20	OC_6H_{13}	H		21	OC_7H_{15}	H	
22	$OC_{10}H_{21}$	H		23	$OC_{10}H_{21}$	H	
24	$OC_{10}H_{21}$	H		25	$OC_{10}H_{21}$	H	
27	$OC_{12}H_{25}$	H		28	$OC_{12}H_{25}$	H	

Examples set forth below demonstrate the general synthetic procedure for the preparation of representative compounds. The examples are provided to illustrate particular aspect of the disclosure and should not be constrained to limit the scope of the present invention.

EXAMPLES

Example A: Synthesis of 1-O-dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-amino-β-L-gulofuranoside

Step a: Synthesis of 1-O-dodecyl-2,3-O-isopropylidene-5,6–dideoxy-5-O-methane sulphonyl-α ,D-mannofuranoside

A solution of 1-O-dodecyl-2,3-O-isopropylidene-6-deoxy-*α-D*-mannofuranoside (synthesized following the procedure as described in United States Patent No. 6,329,344) (11.5g) in dichloromethane (50 ml) was cooled at -5°C. To the reaction mixture was added triethylamine (3.75g) followed by slow addition of methanesulphonyl chloride (4.25g) over a period of 30 minutes with stirring. The reaction mixture was diluted with water. The layers were separated and aqueous layer was extracted with dichloromethane. The combined organic layer was washed with water and brine and dried over anhydrous sodium sulphate. The solvent was evaporated off under vacuum to obtain the title compound (12g).

Step b: Synthesis of 2,3-O-isopropylidene-1-O-dodecyl-5,6–dideoxy-5-benzylamino-β-L-gulofuranoside

To a compound obtained from step *a* above (10.1g), was added benzyl amine (30 ml), and the mixture was stirred at 120°C for 5-6 hours. Benzyl amine was removed by distillation under vacuum and the reaction mixture was diluted with water and stirred for 30-40 minutes. The aqueous layer was extracted with ethyl acetate. The combined hexane layer was washed with water. The combined organic layer was washed with brine and dried over anhydrous sodium sulphate. The solvent was evaporated off and the residue was purified by column chromatography to obtain the title compound (9.2g).

Step c: Synthesis of 1-O-dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-amino-β-L-gulofuranoside

To a solution of the compound obtained from step *b* above (9.2 g) in methanol (200 ml), was added 10% palladium on carbon (4g). The reaction mixture was shaken for 7 hours under hydrogen atmosphere at 55 psi. The reaction mixture was filtered through celite pad. The filtrate was concentrated under reduced pressure. The residue was purified by column chromatography using 2% triethylamine in ethyl acetate as eluent to furnish the title compound (5.7 g).

Example B: Synthesis of methyl {4-[(piperazin-1-yl-carbonyl)-amino]-phenyl}-acetate

Step a: Synthesis of methyl (4-{[(4-benzylpiperazin-1-yl)-carbonyl]-amino}-phenyl)-acetate

To a solution of 1-benzylpiperazine (0.5g) in dry tetrahydrofuran (10ml) was added triethylamine (0.47ml) and methyl {4-[(phenoxycarbonyl)-amino]-phenyl}-acetate (obtained by the reaction of methyl 4-aminophenylacetate and phenyl chloroformate) (0.808g) and stirred overnight. Reaction mixture was taken in distilled water and extracted with ethyl acetate. Organic layer was washed with distilled water and brine and dried over anhydrous sodium sulphate. Solvent was evaporated and residue was purified by silica gel column using 70% ethyl acetate - hexane as eluent to get the title compound (0.985g).

Step b: Synthesis of methyl {4-[(piperazin-1-yl-carbonyl)-amino]-phenyl}-acetate

To a solution of the compound (0.98g) obtained form *step a* above in methanol (15ml) was added 10% palladium/carbon (0.5g) and dry ammonium formate (0.338g). Reaction mixture was refluxed at 70°C for about 3 hr. Reaction mixture was filtered through celite and filtrate was concentrated. Residue was taken in water and extracted with ethyl acetate. The organic layer was washed with water and brine, and dried over anhydrous sodium sulphate. The solvents were evaporated under reduced pressure to obtain the title compound (0.06g).

SCHEME I

Example 1: Synthesis of 1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-{4-nitro-phenyl}-amino-β-L-gulofuranoside (Compound No. 1)

To a solution of 1-O-dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-amino-β-L-gulofuranoside (from Example A 1 gm) in acetonitrile (5ml) was added 4-nitro-fluoro-benzene (0.37gm) and diisopropylethylamine (0.52 ml) and the reaction mixture refluxed overnight. The reaction mixture was cooled, poured into water and extracted with ethyl acetate. The combined organic extracts were washed with water and brine and dried over anhydrous sodium sulphate. The solvent was evaporated followed by purification of the crude residue over a silica gel column using 7.5% ethyl acetate-hexane as eluent to furnish the title compound (0.43 gm).

^{1}H NMR ($CDCl_3$, 300 MHz):δ 8.07 (2H, d, J=9Hz) & 6.58 (2H, d, J=9Hz) [aromatic], 5.00 (1H, s, H-1), 4.72 (1H, dd, J=6 and 3Hz, H-3), 4.65 (1H, d, NH), 4.60 (1H, d, J=6Hz,

H-2), 3.98 (1H, q, J=6Hz, CH-N), 3.87 (1H, dd, J=6 and 3Hz, H-4), 3.59 (1H, dt, J=6.6 and 3Hz) & 3.38 (1H, dt, J=6 and 3Hz) [OCH_2], 1.54 (2H, m, OCH_2CH_2), 1.34 (3H, s, CCH_3), 1.32 (3H, d, J=6Hz, CH_3CH), 1.31 (s) & 1.26 (bs) [21H, CCH_3 and CH_2×9] and 0.88 (3H, t, J=6Hz terminal CH_3).

LCMS (m/e): 493.6 (M+1, 100%)

SCHEME I, Path a

Example 2: Synthesis of 1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-{4-acetamido-phenyl}-amino-β-L-gulofuranoside (Compound No. 2)

Step a: Synthesis of 1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-{4-amino-phenyl}-amino-β-L-gulofuranoside

To a solution of 1-O-dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-{4-nitro-phenyl}-amino-β-L-gulofuranoside (0.43 gm) taken in methanol (20 ml) was added 50 mg of 10% Pd/C and the reaction mixture was shaken under hydrogen atmosphere at 50-55 psi using a Parr shaker for 4 hours. The insoluble were filtered through a bed of celite and the filtrate concentrated, the crude product was purified using column chromatography to furnish the title compound (230 mg)

Step b: Synthesis of 1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-{4-acetamido-phenyl}-amino-β-L-gulofuranoside (Compound No. 2)

The compound 1-O-dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-{4-amino-phenyl}-amino-β-L-gulofuranoside (150 mg) obtained from *step a* was taken in dry dichloromethane (10 ml) and was cooled to 0°C, to it was added acetic anhydride (0.03 ml) and triethylamine (0.14 ml). The reaction mixture was stirred for 2 hours, poured into water and extracted with dichloromethane. The combined organic extracts were washed with brine and dried over anhydrous sodium sulphate and concentrated. The crude residue was purified over a silica gel column using 70% ethyl acetate-hexane as eluent to furnish the title compound (156 mg).

^{1}H NMR ($CDCl_3$, 300 MHz):δ 7.24 (2H, d, J=8.1Hz) & 6.64 (2H, d, J=8.4Hz) [aromatic], 6.94 (1H, d, NH), 4.99 (1H, s, H-1), 4.72 (1H, dd, J=5.7 and 3Hz, H-3), 4.58 (1H, d, J=6Hz, H-2), 3.81 (2H, m, H-4 and CH-N), 3.62 (1H, dt, J=6.6 and 3Hz) & 3.75 (1H, dt, J=6.6 and 3Hz) [OCH_2], 2.04 (3H, s, $COCH_3$), 1.54 (2H, m, OCH_2CH_2), 1.47 (3H, s,

CCH_3), 1.31 (s) & 1.26 (bs) [24H, CH_2×9, CCH_3 and CH_3CH] and 0.88 (3H, t, J=6Hz, terminal CH_3).

LCMS (m/e): 505.8 (M+1, 100%)

SCHEME I, Path b

Example 3: Synthesis of 1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-{[4-(4-methyl-phenyl-sulphonyl)-amino]-phenyl}-amino-β-L-gulofuranoside (Compound No. 3)

To a solution of 1-O-dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-{4-amino-phenyl}-amino-β-L-gulofuranoside (150 mg) obtained from *step a* of Example 2, in dry dichloromethane (5 ml) at 0°C, was added p–toluenesulphonyl-chloride (61 mg) and triethylamine (0.05 ml) and stirred for 2 hours. The reaction mixture was poured into water and extracted with dichloromethane. The combined organic extracts were washed with brine and dried over anhydrous sodium sulphate. The solvent was evaporated under reduced pressure, followed by purification of the residue over a silica gel column using 20% ethyl acetate-hexane as eluent to furnish the title compound (153 mg).

^1H NMR ($CDCl_3$, 300 MHz):δ 7.56 (2H, d, J=8.07Hz), 7.21 (2H, d, J=8.01Hz), 6.82 (2H, d, J=8.61Hz) & 6.52 (2H, d, J=8.61Hz) [aromatic], 6.03 (1H, s, NH), 4.99 (1H, s, H-1), 4.71 (1H, dd, J=5.97 and 2.97Hz, H-3), 4.58 (1H, d, J=5.85Hz, H-2), 3.75-3.85 (2H, m, H-4 and CH-N), 3.62 (1H, dt, J=9.69 and 2.76Hz) & 3.38 (1H, dt, J=9.69 and 3.06Hz) [OCH_2], 2.39 (3H, s, $ArCH_3$), 1.54 (2H, m, OCH_2CH_2), 1.46 (3H, s, CCH_3), 1.31 (s) & 1.26 (bs) [24H, CH_2×9, CCH_3 and CH_3CH) and 0.88 (3H, t, J=5.52Hz, terminal CH_3)

LCMS (m/e): 617.6 (M+1, 100%).

SCHEME I, Path c

Example 4: Synthesis of 1-O-dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-{4-[3-(2-methyl-phenyl)-ureido]-phenyl}-amino-β-L-gulofuranoside (Compound No. 4)

To a solution of 1-O-dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-{4-amino-phenyl}-amino-β-L-gulofuranoside ((150 mg) obtained in *step a* of Example 2, in dry dichloromethane (5 ml) at room temperature was added O-tolyl isocyanate (43 mg) and stirred for 1 hour. The reaction mixture was concentrated and the crude residue was chromatographed over silica gel column using 20% ethyl acetate-hexane as eluent to furnish the title compound (95 mg).

^{1}H NMR ($CDCl_3$, 300 MHz):δ 7.70 (1H, d, J=9Hz), 7.00-7.26 (5H, m) & 6.68 (2H, d, J=9Hz), [aromatic] 6.31 (1H, s, NH), 6.25 (1H, s, NH), 5.00 (1H, s, H-1), 4.72 (1H, dd, J=6 and 3Hz, H-3), 4.59 (1H, d, J=6Hz, H-2), 3.84 (2H, bs, CH-N and H-4), 3.62 (1H, dt, J=9 and 3Hz) & 3.39 (1H, dt, J=9 and 3Hz) [OCH_2], 2.13 (3H, s, $ArCH_3$), (2H, t, J=6Hz, OCH_2CH_2), 1.48 (3H, s, CCH_3), 1.32 (s) & 2.6(bs) [24H, CCH_3, CH_3CH and CH_2×9] and 0.88 (3H, t, J=6Hz, terminal CH_3)

LCMS (m/e): 596.8 (M+1, 100%)

SCHEME II *Path a*

Example 5: Synthesis of 1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-{2-methyl-butyl}-amino-β-L-gulofuranoside (Compound No. 5)

To a solution of 1-O-dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-amino-β-L-gulofuranoside (500 mg) in methanol (10 ml) was added acetic acid (0.5 ml) and 2-methylbutyraldehyde (0.15 ml, 1.35 mmol). The reaction mixture was stirred at room temperature for 30 minutes and then cooled to 0°C. Sodium triacetoxyborohydride (428 mg) was added and the reaction mixture stirred overnight. The volatiles were evaporated under reduced pressure and the residue chromatographed over silica gel using 5% methanol-dichloromethane as eluent to furnish the title compound. (180 mg).

^{1}H NMR ($CDCl_3$, 300 MHz):δ 4.97 (1H, s, H-1), 4.67 (1H, dd, J=5.7 and 3.7Hz, H-3), 4.56 (1H, d, J=6Hz, H-2), 3.84 (1H, dd, J=9 and 6Hz, H-4), 3.64 (1H, dt, J=9.6Hz) & 3.36 (1H, dt, J=6.6 and 3.6Hz) [OCH_2], 3.14 (1H, m, CH–N), 2.4-2.60 (2H, m, NCH_2), 1.53 (1H, m, $CHCH_3$), 1.45 (2H, m, OCH_2CH_2), 1.41 (3H, s, CH_3), 1.30 (3H, s, CH_3), 1.26 (23H, CH_2×10 and CH_3), 0.94 (3H, d, J=6.3Hz, CH_3CH), 0.89 (3H, t, J=7.5Hz, CH_3) and 0.88 (3H, t, J=7.5Hz, terminal CH_3)

LCMS (m/e): 443.5 (M+2, 100%)

Analogues of 1-O-Dodecyl-2, 3-O-isopropylidene-5, 6-dideoxy-5- {2 methylbutyl}-amino-β-L-gulofuranoside (Compound No. 5) described below were prepared by analogously replacing the appropriate aldehyde in place of 2-methylbutyraldehyde, as applicable in each case.

1-O-Dodecyl-2, 3-O-isopropylidene-5, 6-dideoxy-5- {3-phenyl-propyl}-amino-β-L-gulofuranoside (Compound No. 6)

1-O-Dodecyl-2, 3-O-isopropylidene-5, 6-dideoxy-5- {2-phenyl-propyl}-amino-β-L-gulofuranoside (Compound No. 7)

1-O-Dodecyl-2, 3-O-isopropylidene-5, 6-dideoxy-5- {4-fluoro-benzyl}-amino-β-L-gulofuranoside (Compound No. 8)

1-O-Dodecyl-2, 3-O-isopropylidene-5, 6-dideoxy-5- (2,2-dimethyl-propyl)-amino-β-L-gulofuranoside (Compound No. 9)

1-O-Dodecyl-2, 3-O-isopropylidene-5, 6-dideoxy-5- (3-hydroxy-3-oxo-propyl)-amino-β-L-gulofuranoside (Compound No. 10)

1-O-Dodecyl-2, 3-O-isopropylidene-5, 6-dideoxy-5- {2,6-dichloro-benzyl}-amino-β-L-gulofuranoside (Compound No. 26)

SCHEME II, *Path b*

Example 6: Synthesis of 1-O-dodecyl-2, 3-O-isopropylidene-5, 6-dideoxy-5-dibenzyl-amino-β-L-gulofuranoside (Compound No. 11)

To a solution of 1-O-dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-amino-β-L-gulofuranoside (0.5 gm) in dry acetone (7 ml) was added benzyl bromide (0.32 ml) and potassium carbonate (0.46 gm) and stirred at room temperature overnight. The solids were filtered and, the filtrate concentrated and taken into water and extracted with ethyl acetate. The combined organic extracts were washed with brine and dried over anhydrous sodium sulphate and concentrated. The crude residue was purified over a silica gel column using 30% ethyl acetate-hexane as eluent to furnish the title compound. (130 mg)

^{1}H NMR ($CDCl_3$, 300 MHz):δ 7.43 (4H, d, J=7.2Hz), 7.27 (4H, t, J=7.5Hz) & 7.18 (2H, q, J=7.2Hz) [aromatic], 5.05 (1H, s, H-1), 4.58 (1H, dd, J=5.7 and 2.4Hz, H-3), 4.53 (1H, d, J=6Hz, H-2), 4.02 (1H, dd, J=9.9 and 3.3Hz, H-4), 3.82 and 3.73 (4H, ABq, J=13.5Hz, $NC\underline{H}_2Ar\times2$), 3.75 (1H, m, C$\underline{H}$-N), 3.48 (1H, dt, J=9.6Hz) & 3.27 (1H, dt, J=3.3Hz) [$OC\underline{H}_2$], 1.56 (2H, t, J=7.2Hz, $OCH_2C\underline{H}_2$), 1.25 (24H, bs, $C\underline{H}_2\times9$ and $CC\underline{H}_3\times2$), 1.07 (3H, d, J=6.9Hz, $C\underline{H}_3CH$) and 0.88 (3H, t, J=6.3Hz, terminal $C\underline{H}_3$).

LCMS (m/e): 552.5 (M+1, 100%)

SCHEME II, *Path c*

Example 7: Synthesis of 1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-(benzoxazol-2-yl)-amino-β-L-gulofuranoside (Compound No. 12)

To a solution of 1-O-dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-amino-β-L-gulofuranoside (500 mg) in dry tetrahydrofuran (10 ml) was added 2-chlorobenzoxazole (0.15 ml) and pyridine (0.3 ml). The reaction mixture was refluxed for 3 hour cooled, poured into water (20 ml) and extracted with ethyl acetate. The combined organic extracts were washed with brine and dried over anhydrous sodium sulphate. The solvent was evaporated followed by purification of the residue over a silica gel column using 2.5% methanol-dichloromethane as eluent to furnish the title compound. (220 mg).

^{1}H NMR ($CDCl_3$, 300 MHz):δ 8.6 (1H, bs, NH), 7.15-7.45 (4H, m, aromatic), 4.78 (1H, s, H-1), 4.74 (1H, dd, J=5.7 and 3.9Hz, H-3), 4.61 (1H, d, J=5.7Hz, H-2), 4.37 (1H, m, CH-N), 4.00 (1H, dd, J=8.4 and 3.6Hz, H-4), 3.65 (1H, dt, J=9.6 and and 3Hz) & 3.32 (1H, dt, J=6.9 and 3Hz) [OCH_2], 1.49 (3H, d, J=7.8Hz, CH_3CH), 1.48 (5H, bs, OCH_2CH_2 and CCH_3), 1.29 (3H, s, CCH_3), 1.25 (18H, bs, CH_2×9) and 0.88 (3H, t, J=6.9Hz, terminal CH_3).

LCMS (m/e): 489.5 (M+1, 100%)

SCHEME III

Example 8: Synthesis of 1,2-O–Isopropylidene-3-O-decyl-5-O-{3-[1-(4-{4-methoxyphenyl})-piperazinyl]-propyl}-α-D-xylofuranoside (Compound No. 13)

Step a: Synthesis of 1,2-O–Isopropylidene-3-O-decyl-5-O-{3-hydroxypropyl}-α-D-xylofuranoside

A mixture of 1,2-O-isopropylidene-3-O-decyl-α-D-xylofuranoside (3.5 gm) (prepared following the procedure described in U.S.Patent 6,329,344), 3-chloropropanol (1.202 g) and sodium hydroxide (1.27 g) in dimethyl sulphoxide (20 ml) was stirred at 110-120°C for 24 hours. Reaction mixture was cooled and extracted with ethyl acetate followed by washing with water and brine. It was then dried over anhydrous sodium sulphate and solvent evaporated under reduced pressure. The crude product was purified by column chromatography using 30% ethyl acetate/hexane as eluent furnish the title compound (2.0 g).

Step b: - Synthesis of 1,2-O–Isopropylidene-3-O-decyl-5-O-[3-(p-toluenesulphonyl)–oxypropyl]-α-D-xylofuranoside

To a solution of the compound (2.0g) obtained from *step a* in pyridine, a solution of p- tosyl chloride (1.0g) in pyridine (10ml) was added dropwise with continuous stirring at 0-5^{0}C. After 5 hours, water was added to the reaction mixture and then the solvents were removed at reduced pressure. The product was extracted with ethyl acetate followed by washing with water and brine and dried over anhydrous sodium sulphate. The solvent was evaporated under reduced pressure and the residue thus obtained was purified by column chromatography to furnish the title compound (1.5g).

Step c: Synthesis of 1,2-O–Isopropylidene-3-O-decyl-5-O-{3-[1-(4-{4-methoxyphenyl})-piperazinyl]-propyl}-α-D-xylofuranoside (Compound No. 13)

To a solution of the compound (0.25 g) obtained from *step b* in dimethylformamide (5 ml) was added 1-(4-methoxy-phenyl)-piperazine (0.11 g) and the reaction mixture was stirred at 60-70°C for 8 hours. The reaction mixture was diluted with ethyl acetate followed by washing with saturated sodium bicarbonate, water and brine. It was then dried over anhydrous sodium sulphate, filtered and the solvent evaporated under reduced pressure. The crude residue was purified by column chromatography using 50% ethyl acetate/hexane as eluent to furnish the title compound. (120 mg).

Analogues of 1,2-O–Isopropylidene-3-O-decyl-5-O-{3-[1-(4-{4-methoxyphenyl})-piperazinyl]-propyl}-α-D-xylofuranoside (Compound No. 13) described below were prepared by replacing the appropriate piperazine in place of 1-(4-methoxy-phenyl)-piperazine, as applicable in each case.

1,2-O-Isopropylidene-3-O-decyl-5-O-[3-(1-{4-benzyl}-piperazinyl)-propyl]-α-D-xylofuranoside (Compound No. 14)

1,2-O-Isopropylidene-3-O-decyl-5-O-[3-(1-{4-[2-methoxy-phenyl]}-piperazinyl)-propyl]-α-D-xylofuranoside (Compound No. 15)

1,2-O-Isopropylidene-3-O-heptyl-5-O-(N-phthalimido-ethyl)-α-D-xylofuranoside (Compound No. 21)

Example 8a: Synthesis of 1,2-O-Isopropylidene-3-O-dodecyl-5-O-{3-[4-({[4-(2-methoxy-2-oxoethyl)phenyl]amino}carbonyl)-piperazinyl]-propyl}-α-D-xylofuranoside (Compound No. 27)

Step a: Synthesis of 1,2-O–Isopropylidene-3-O-dodecyl-5-O-{3-hydroxypropyl}-α-D-x xylofuranoside

To a solution of 1,2-O-isopropylidene-3-O-dodecyl-α-D-xylofuranoside (0.5g) (prepared following the procedure described in U.S.Patent 6,329,344), in dry dimethylsulphoxide (5ml) was added 3-chloropropanol (0.160g) and sodium hydroxide(0.167g) stirred at 110°C – 120°C for overnight. The reaction mixture was quenched with dilute sodium hydrogen sulphate solution and extracted with ethyl acetate, the organic layer was washed with water and brine and dried over anhydrous sodium sulphate and the solvent was evaporated, residue was purified by silica gel column using 15% ethyl acetate -hexane as eluent to get the title compound (0.170g).

Step b: - Synthesis of 1,2-O–Isopropylidene-3-O-dodecyl-5-O-[3-(p-methylsulphonyl) -oxypropyl]-α-D-xylofuranoside

To a solution of compound obtained from the *step a* above (0.170g) in dichloromethane (5ml) at 0°C was added triethylamine (0.085ml) and reaction mixture was stirred for 15 minutes followed by the addition of methansulphonyl chloride (0.047ml) and further stirred for 2hrs from 0°C to room temperature. The reaction mixture was taken in distilled water and extracted with dichloromethane, the organic layer was washed with water and brine and dried over anhydrous sodium sulphate and the solvent was evaporated to get the title compound (250g).

Step c: - Synthesis of 1,2-O-Isopropylidene-3-O-dodecyl-5-O-{3-[4-({[4-(2-methoxy-2-oxoethyl)phenyl]amino}carbonyl)-piperazinyl]-propyl}-α-D-xylofuranoside

To a solution of methyl {4-[(piperazin-1-yl-carbonyl)-amino]-phenyl}-acetate (0.26g) in dry dimethylformamide (5ml) was added dry potassium carbonate (0.209g) at 0°C and reaction mixture was stirred for 15 minutes followed by the addition of solution of compound obtained from the *step b* above (0.25g) in dry dimethylformamide (2ml) and further stirred for overnight at room temperature. The reaction mixture was taken in water, extracted with ethyl acetate and the organic layer was washed with distilled water and brine and dried over anhydrous sodium sulphate, the solvent was evaporated and

residue was purified by silica gel column using 70% ethyl acetate - hexane as eluent to furnish the title compound (0.035g).

1H NMR (CDCl3) , 300MHz:-7.377(2H, d, 8.1Hz) 7.099(2H, d, 8.4Hz) 6.871(1H, d, 2.1Hz) 5.858-5.803(1H, m) 4.563(1H, d, 3.9Hz) 4.141-4.011(2H, m) 3.755-3.372(15H, m) 2.35(bs, 4H) 2.20-2.00(2H, m), 1.8-1.5(2H, m) 1.460-1.161(26H, m) 0.854-0.846(3H, bs).

LCMS (m/z):-676(M+1).

SCHEME IV, Path a

Example 9: Synthesis of Tris salt of 1-O-Methyl-2,3-O-isopropylidene-5-deoxy-5-[{3-[(4-{2-hydroxy-2-oxo-ethyl}-phenyl)-amino]-carbonyloxy}-propyl]-amino-α-D-lyxofuranoside (Compound No. 16)

Step a: Synthesis of 1-O-Methyl-2,3-O-isopropylidene-5-deoxy-5-[3-hydroxypropyl]-amino-α-D-lyxofuranoside

A mixture of 1-O-methyl-2,3-O-isopropylidene-5-tosyl-α-D-lyxofuranoside (prepared as described in U.S. Patent No. 6,329,344) (5.0gm) and 3-aminopropanol (2.0gm) were heated up to 60-70°C for 16 hours. Reaction mixture was diluted with hexane (100ml), the solid obtained was filtered off and the compound extracted with ethyl acetate. The organic extract was washed with water and brine and dried over anhydrous sodium sulphate. Solvent was evaporated under reduced pressure and the crude compound thus obtained was purified by column chromatography using ethyl acetate as eluent to furnish the title compound (257 mg).

Step b: Synthesis of 1-O-Methyl-2,3-O-isopropylidene-5-deoxy-5-[{3-[(4-{2-methoxy-2-oxo-ethyl}-phenyl)-amino]-carbonyloxy}-propyl]-amino-α-D-lyxofuranoside

To a solution of the compound obtained from *step a* (115mg) in dichloromethane (2ml) cooled to 0°C was added methyl 4-isocynatophenyl acetate (84 mg) and stirred for one hour. It was then diluted with dichloromethane (5ml), washed with water and brine and dried over anhydrous sodium sulphate and concentrated. The crude product was purified by column chromatography to furnish the title compound. (130 mg).

Step c: Synthesis of 1-O-Methyl-2,3-O-isopropylidene-5-deoxy-5-[{3-[(4-{2-hydroxy-2-oxo-ethyl}-phenyl)-amino]-carbonyloxy}-propyl]-amino-α-D-lyxofuranoside

To a solution of the compound obtained in *step 2* (130mg) in methanol (3 ml) was added 10 ml 2 N solution of sodium hydroxide. The reaction mixture was heated upto 50-60°C for 3 hours. The reaction mixture was cooled and acidified with 10% HCl solution. The aqueous layer was extracted with ethyl acetate and the organic extracts washed with water and brine and dried over anhydrous sodium sulphate and concentrated. The crude product was purified by column chromatography to furnish the title compound. (110 mg).

^{1}H NMR (DMSO, 300 MHz): δ 7.36 (2H, d, 8.1Hz), 7.14 (2H, d, 8.1Hz), 4.89 (1H, s), 4.79 (1H, bs), 4.53 (1H, d, 5.7Hz), 4.27-4.15 (4H, m), 3.47-3.15 (8H, m), 2.07 (2H, m), 1.36 (3H, s), 1.23 (3H, s).

Step d: Synthesis of Tris salt of 1-O-Methyl-2,3-O-isopropylidene-5-deoxy-5-[{3-[(4-{2-hydroxy-2-oxo-ethyl}-phenyl)-amino]-carbonyloxy}-propyl]-amino-α-D-lyxofuranoside (Compound No. 16)

The compound obtained in *step c* (100mg) was dissolved is ethanol (1 ml) and equivalent amount of tris (hydroxymethyl) aminomethane (27.65mg) was added to it. The reaction mixture stirred for 2 hours and the solvent was removed to get yellowish semi-solid as the title compound. (80 mg)

SCHEME IV, Path b

Example 10: Synthesis of 1,2-O-Isopropylidene-3-O-decyl-5-deoxy-5-[2-(4-phenyl-thiazolyl)-amino]-α-D-xylofuranoside (Compound No. 17)

Step a: Synthesis of 1,2-O-Isopropylidene-3-O-decyl-5-deoxy-5-bromo-α-D-xylofuranoside

Lithium bromide (1.25 g) was added to a solution of 1,2-O-Isopropylidene-3-O-decyl-5-tosyl-α-D-xylofuranoside (2.5 g), in dry dimethylformamide (25 ml) at room temperature with stirring. After complete addition, the temperature of the reaction mixture was raised up to 70-80°C and stirred for 36 hours. After the completion of reaction dimethylformamide was removed at reduced pressure and extracted with ethyl acetate followed by washing with saturated sodium bicarbonate, water and brine and then dried over anhydrous sodium sulphate. Evaporated the solvent under reduced pressure to obtain

crude residue, which was then purified by column chromatography to furnish the title compound. (500 mg)

Step b: Synthesis of 1,2-O-Isopropylidene-3-O-decyl-5-deoxy-5-[2-(4-phenyl-thiazolyl)-amino]-α-D-xylofuranoside

To a suspension of sodium hydride (1.0 gm) in dry tetrahydrofuran (10 ml) added dropwise 4-phenyl-thiazolyl-amine (166 mg) taken in dry tetrahydrofuran (5 ml) and allowed the reaction to proceed at 5-10°C. After 2 hour, the compound (200 mg) obtained from *step a* in dry tetrahydrofuran (5 ml) was added through a dropping funnel and allowed the reaction to proceed at 70-80°C. After 10 hour the solvent was evaporated under reduced pressure and extracted with ethyl acetate followed by washing with water, sodium carbonate and brine and dried over anhydrous sodium sulphate. Evaporated the solvent and the crude residue thus obtained was purified by column chromatography using hexane as eluent to furnish the title compound. (100 mg)

Analogues of 1,2-O-Isopropylidene-3-O-decyl-5-deoxy-5-[2-(4-phenyl-thiazolyl)-amino]-α-D-xylofuranoside (Compound No.17) described below were prepared by replacing the appropriate heterocyclyl groups in place of 4-phenyl-thiazol-2-yl-amine, as applicable in each case.

1,2-O-Isopropylidene-3-O-dodecyl-5-deoxy-5-{2-thiazolyl-amino}-α-D-xylofuranoside (Compound No. 18)

1,2-O-Isopropylidene-3-O-dodecyl-5-deoxy-5-{2-(benzimidazolyl)-amino}-α-D-xylofuranoside (Compound No. 19)

1,2-O-Isopropylidene-3-O-hexyl-5-deoxy-5-[2-(5-benzoyl-1H-benzimidazolyl)-amino]-α-D-xylofuranoside (Compound No. 20)

Example 10a: Synthesis1,2-O-Isopropylidene-3-O-dodecyl-5-deoxy-5-[(4-methyl-1,3-thiazolyl)-amino]-α-D-xylofuranoside (Compound No. 28)

Step a: Synthesis of 1,2-O-Isopropylidene-3-O-dodecyl-5-O-methanesulfonyl-α-D-xylofuranoside

To a solution of 1,2-O-isopropylidene-3-O-dodecyl-α-D-xylofuranoside (0.23g) in dry dichloromethane (2ml) was added triethylamine 0.13ml) at 0°C and stirred for 15 min followed by addition of methansulphonyl chloride (0.074ml). The reaction mixture

wasfurther stirred for 2hrs allowing the temperature to raise from 0°C to room temperature. The reaction mixture was taken in distilled water and extracted with dichloromethane, the organic layer was washed with distilled water and brine and dried over anhydrous sodium sulphate and the solvent was evaporated to get the title compound (0.266g)

Step b :Synthesis of 1,2-O-Isopropylidene-3-O-dodecyl-5-deoxy-5-[(4-methyl-1,3-thiazolyl)-amino]-α-D-xylofuranoside

To a solution of compound obtained from the *step a* above (0.26g) in dry dimethylformamide (3ml) was added sodium hydride (0.057g 50%) at 0°C and stirred for 30 minutes. To the reaction mixture was added a solution of 2-amino-4-methyl thiazole (0.136g) in dry dimethylformamide (2ml) and stirred for 3 hrs at room temperature and then at 60°C for overnight followed by heating to 100°C for about 4hrs. The reaction mixture was taken in distilled water and extracted with ethyl acetate, the organic layer was washed with distilled water and brine and dried over anhydrous sodium sulphate.Solvent was evaporated under reduced pressure and the residue thus obtained was purified by silica gel column using 8% ethyl acetate-hexane as eluent to furnish the title compound (0.070g).

^{1}H NMR ($CDCl_3$) , 300MHz:-5.975(1H, d, 3Hz) 5.2-5.0(1H, bs) 4.565(1H, d, 3Hz) 4.29-4.27(1H, m) 3.95-3.91(3H, m) 3.65-3.42(2H, m) 1.68-1.42(8H, m) 1.13-1.11(21H, m) 0.95-0.86(3H, m).

LCMS (m/z):-445(M+1).

Example 11: Pharmacological activity

The compounds disclosed herein were tested in one or both of the assays described herein. Standard assays were used to evaluate activity of compounds on inflammatory cells. Attenuation of agonist induced release of lipid mediators of neutrophil chemotaxis, leukotriene B4 (LTB4), was used to evaluate inhibitory effect on neutrophils.

A23187 induced LTB_4 release

Venous blood was collected from healthy human donors using heparin as an anti-coagulant. Neutrophils were isolated from freshly drawn blood after dextran sedimentation and ficoll separation (*Eur J Biochem.* **169**, 175, 1987). 180 µl of the of neutrophil suspension ($0.2x10^6$ cells/ml) was taken and added 19µL of Hank's Buffer salt solution

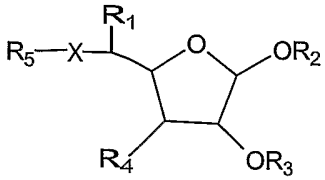
along with 1μL of the test drug (200 times concentrated) in a 24 well plate and incubated at 37°C for 1hour. 3 minutes before the end of test compound incubation, 0.25 mM Ca^{++}/Mg^{++} were added. Then, 0.3 μg/ml A23187 (Sigma Chem, USA) was added and incubated for further 10 min at 37°C. The reaction was stopped by adding 80 μL of cold methanol and centrifuged to remove cell debris (J Pharmacol Exp Ther. 297:267, 2001). The samples were analysed for LTB_4 release using LTB_4 ELISA kits (Assay Design Inc., USA). The amount of LTB_4 released was quantified and percent inhibition of LTB_4 release was calculated with respect to the difference between the A23187 stimulated and negative control cells, to compute IC_{50} values. *In vitro* data obtained on compounds numbered 1-7, 9-12 and 26-28 showed that several compounds were active with IC_{50} values of < 30 μM (for example, from about 6 μM to about 30μM, or from about 6 μM to about 23μM, or from about 6 μM to about 10μM) and others were more moderately active compounds, with IC_{50} values of >30μM.

Assay for 5-Lipoxygenase Activity

In a 96 well UV-plate, 100 μl of phosphate buffer saline (PBS) containing DTT (200 μM), ATP (100 μM) and calcium chloride (100 μM) was added. To each well 0.5 μl of test drug (200 times concentrated) or vehicle was added, followed by 4 μl of recombinant 5-Lox (3 units/μl) and was incubated at 37°C for 5 min. The reaction was initiated by adding 1 μl of 1mM freshly prepared arachidonic acid and increase in absorbance was monitored at 236 nm for 10 min. (*J Biol. Chem.* 261:11512, 1986) A plot of absorbance verses time curve was prepared and area under curve (AUC) was computed for each well. Percent inhibition of AUC for different treatments was calculated with respect to the difference between the Arachidonic acid stimulated and negative control values, to compute IC_{50} values. Particular compound numbers 1, 8, 10, 16, and 27 were examined, showing activity from about 1.9 μM to about 8 μM, or from about 1.9 μM to about 3 μM.

We Claim:

1. A compound of structure of Formula I



Formula I

wherein

X is $(CH_2)_pNR_j$ or $(CH_2)_pO$ (wherein p is an integer 0 or 1 and R_j is selected from hydrogen, lower (C_1-C_6) alkyl, lower (C_2-C_6) alkenyl, lower (C_2-C_6) alkynyl, lower (C_3-C_8) cycloalkyl, aryl, heteroaryl, lower (C_1-C_6) aralkyl, lower (C_1-C_6) heteroarylalkyl, and lower 3-6 ring membered heterocyclylalkyl);

R_1 is hydrogen, lower (C_1-C_6) alkyl [wherein alkyl is optionally substituted with hydroxyl, $-OR_x$ (wherein R_x is alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, or heterocyclylalkyl), acyloxy, cycloalkyl, aryl, substituted amino, $-C(=O)QR_z$ (wherein Q is O or NH and R_z is selected from hydrogen, alkyl, aralkyl, aryl, and heteroarylalkyl), heteroaryl, and heterocyclyl], lower (C_2-C_6) alkenyl, lower (C_2-C_6) alkynyl, aryl, heterocyclyl (with the proviso that when p=0, the heterocyclyl cannot be linked through a heteroatom), heteroaryl (with the proviso that when p=0, the heteroaryl cannot be linked through a heteroatom), $-OR_x$ (wherein R_x is as defined above except that when p=0 and X is a derivative of a heteroatom such as O or N, then R_1 cannot be OR_x), or $-C(=O)QR_z$ (wherein Q and R_z is the same as defined above);

R_2 and R_3 together form a five membered acetal wherein the carbon joining the oxygens is substituted with R_L and R_m, [wherein R_L and R_m are independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, and aralkyl; or R_L and R_m can together join to form a 3- to 8-membered ring, wherein the ring may optionally contain one or more heteroatoms selected from O, N or S, and the ring may be optionally substituted with one or more of alkyl, alkenyl, alkynyl, acyl, substituted amino, cycloalkyl, $-C(=O)QR_7$ (wherein Q is same as defined earlier and R_7 is selected from alkyl, alkenyl, alkynyl, aryl, aralkyl, cycloalkyl, and heteroarylalkyl), carboxy, oxo, hydroxyl, alkoxy, aryloxy, halogen (FCl, Br, I), aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, or heterocyclylalkyl; or R_L and R_m together join to form an oxo linkage];

R_4 is hydrogen, or OR_c (wherein R_c is selected from alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, and heterocyclylalkyl) and, when R_4 is OR_c, then R_3 and R_c may together form an acetal (wherein the acetal is the same as defined earlier) and R_2 can be alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, heterocyclylalkyl, further, R_2 and R_3, instead of forming an acetal, may optionally and independently be selected from lower (C_1-C_4) alkyl, $(CH_2)_k$-aryl wherein k is an integer from 1-4, $-C(=R_y)NHR_x$ wherein R_y is O or S and R_x is the same as defined earlier, and acyl; with R_4 defined as earlier, also, when R_4=OR_c, R_3 and R_c, instead of forming an acetal, may optionally and independently be selected from lower (C_1-C_4) alkyl, $(CH_2)_k$-aryl wherein k is an integer from 1-4, $-C(=R_y)NHR_x$ wherein R_y is O or S and R_x is the same as defined earlier, and acyl; with R_2 defined as earlier;

R_5 is

A) $-(CH_2)_nG_1$ [(wherein n is an integer 2-4 and one or more carbon(s) in the linker may optionally and independently be substituted with alkyl, aryl, aralkyl, hydroxyl, carboxy, alkoxy, aryloxy, cycloalkyloxy, $-C(=O)QR_z$ wherein Q and R_z are the same as defined earlier, or substituted amino); except that the carbons directly linked to X and G_1 are optionally and independently substituted with alkyl, carboxy, aryl, aralkyl, or $-C(=O)QR_z$ wherein Q and R_z is same as defined earlier]; and

G_1 is

1) OR_e {wherein R_e is selected from acyl, $-C(=O)NR_fR_q$ [wherein R_f and R_q can be independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heteroaryl, heteroarylalkyl, hetrocyclylalkyl, and $S(O)_2R_6$ (wherein R_6 is selected from alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heterocyclylalkyl, and heteroarylalkyl, and substituted amino); and also R_f and R_q can together form a ring]};

2) $-NR_jC(=O)OR_s$ (wherein R_j is same as described earlier and R_s is selected from alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heterocyclylalkyl, and hetroarylalkyl);

3) $-NHYR_d$ (wherein Y can be -C(=O), -C(=S) or SO_2, and R_d can be alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl and heterocyclylalkyl);

4) $-NR_jC(=T)NR_tR_x$ [wherein R_t is OH or R_x (and T is O, S, -N(CN), $-N(NO_2)$, or $-CH(NO_2)$) and R_x is the same as defined earlier]; or

5) heterocyclyl, wherein the heterocyclic ring, which may or may not be benzofused, is always substituted,

or R_5 is

B) $-(CH_2)_wG_2$, (wherein w ranges from 1-5, and one or more carbon(s) in the linker may be optionally and independently be substituted with lower (C_1-C_6) alkyl, lower (C_1-C_4) aralkyl, or aryl); and

G_2 is

1) $-(C=O)OR_z$ when R_z is same as defined earlier; or

2) $-(C=O)NR_aR_b$ (wherein R_a and R_b are independently selected from hydrogen, or R_d, wherein R_d is same as defined earlier); and R_a and R_b, together with the nitrogen atom carrying them, can be the N-terminus of an aminoacid or di-tetrapeptide,

also, when X is $(CH_2)_pNR_j$, and R_1 is not hydrogen, then R_5 can be alkyl, alkenyl, alkynyl, aryl, aralkyl, heteroaryl, heterocylyl, heteroarylalkyl, or heterocyclylalkyl; except that

1) if R_3 and R_c form an isopropylidene radical and R_2 is hydrogen, C_5-C_{15} alkyl, n-C_5-C_{15}-alkoxy-C_2-C_4-alkyl, or phenypropyl and X is NR_j where R_j is hydrogen and R_1 is H and R_5 is alkyl, then this alkyl must be C_1-C_4 alkyl;

2) if either R_2 and R_3 or R_3 and R_c form an isopropylidene radical and R_c and R_2 are C_5-C_{15} alkyl respectively, and R_1 is H and X is NR_j where R_j is H, then R_5 cannot be C_3-C_8 alkyl, C_3-C_8 hydroxyalkyl, cyclohexyl- C_1-C_5– alkyl, phenyl- C_2-C_5-alkyl or pyridinyl- C_1-C_5-alkyl; and

3) if R_3 and R_c form an isopropylidene radical, R_2 is nonyloxypropyl, phenylpropyl, 4-(1-pyrolidinyl)butyl, 2-octyne, or C_7-C_{15} alkyl and X is NR_j where R_j is hydrogen and R_1 is CH_3, CH_2OH, CH_2-pyrrolidinyl, CH_2-piperidinyl, CH_2-morpholinyl, CH_2-hexamethyleneimino, CH_2-aminoethylmorpholinyl, CH_2-aminoethylpiperidinyl, CH_2-aminoethylpyrrolidinyl, CH_2-amino C_7-C_{15} alkyl or C_7-C_{15} alkyl and R_5 is alkyl, then this alkyl must be C_1-C_6 lower alkyl.

2. The compound of claim 1, wherein

R_1 is hydrogen, lower (C_1-C_6) alkyl [wherein alkyl is optionally substituted with hydroxyl, $-OR_x$ (wherein R_x is alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, or heterocyclylalkyl), acyloxy, cycloalkyl, aryl, substituted amino, $-C(=O)QR_z$ (wherein Q is O or NH and R_z is selected from hydrogen, alkyl,

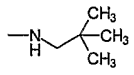
aralkyl, aryl, and heteroarylalkyl), heteroaryl, and heterocyclyl];

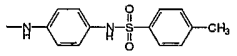
R_2 is alkyl;

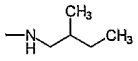
R_3 and R_4 (as OR_c) form an isopropylidene radical; and

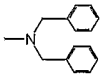
$X\text{-}R_5$ is amino aryl, aminoalkyl, aminoalkaryl, aminoalkyl -oxy carbonyl-amino - aryl, amino–aryl-urea-aryl, aminoalkyl-carboxyl, or aminoheterocyclyl.

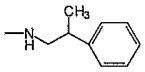
3. The compound of claim 2, wherein $X\text{-}R_5$ is

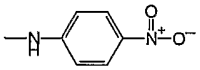


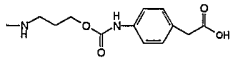


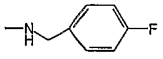


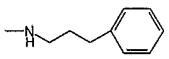


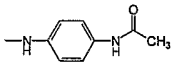


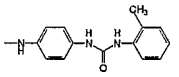












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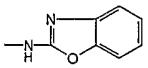
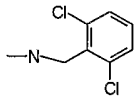
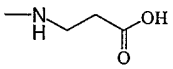






4. The compound of claim 1, wherein

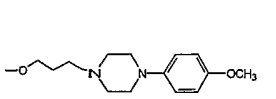
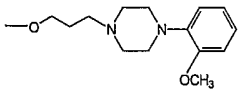
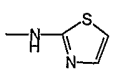
R_1 is hydrogen, lower (C_1-C_6) alkyl [wherein alkyl is optionally substituted with hydroxyl, $-OR_x$ (wherein R_x is alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, or heterocyclylalkyl), acyloxy, cycloalkyl, aryl, substituted amino, $-C(=O)QR_z$ (wherein Q is O or NH and R_z is selected from hydrogen, alkyl, aralkyl, aryl, and heteroarylalkyl), heteroaryl, and heterocyclyl];

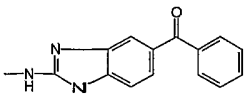
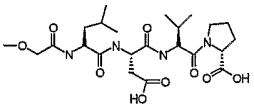
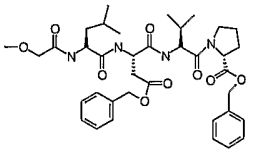
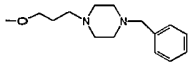
R_2 and R_3 form an isopropylidene group;

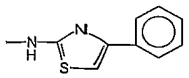
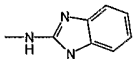
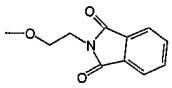
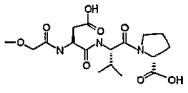
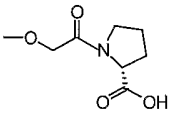
R_4 is hydrogen, or OR_c (wherein R_c is selected from alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, and heterocyclylalkyl); and

$X\text{-}R_5$ is oxyalkylheterocyclyl, amino-heterocyclyl, or amino acid.

5. The compound of claim 4, wherein X-R_5 is

 ,  ,  ,

 ,  ,  ,  ,

 ,  ,  ,  , and  .

6. A compound selected from:

1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-{4-nitro-phenyl}-amino-β-L-gulofuranoside (Compound No. 1)

1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-{4-amino-phenyl}-amino-β-L-gulofuranoside (Compound No. 2)

1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-{[4-(4-methyl-phenyl-sulphonyl)-amino]-phenyl}-amino-β-L-gulofuranoside (Compound No. 3)

1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-{4-[3-(2-methyl-phenyl)-ureido]-phenyl}-amino-β-L-gulofuranoside (Compound No. 4)

1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-{2-methyl-butyl}-amino-β-L-gulofuranoside (Compound No. 5)

1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-{3-phenyl-propyl}-amino-β-L-gulofuranoside (Compound No. 6)

1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-{2-phenyl-propyl}-amino-β-L-gulofuranoside (Compound No. 7)

1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-{4-fluoro-benzyl}-amino-β-L-gulofuranoside (Compound No. 8)

1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-(2,2-dimethyl-propyl)-amino-β-L-gulofuranoside (Compound No. 9)

1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-(2-carboxyethyl)-amino-β-L-gulofuranoside (Compound No. 10)

1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-dibenzyl-amino-β-L-gulofuranoside (Compound No. 11)

1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-(benzoxazol-2-yl)-amino-β-L-gulofuranoside (Compound No. 12)

1,2-O-Isopropylidene-3-O-decyl-5-O-[1-(4-{4-methoxy-phenyl})-piperazinyl]-propyl}-α-D-xylofuranoside (Compound No. 13)

1,2-O-Isopropylidene-3-O-decyl-5-O-[3-(1-{4-benzyl}-piperazinyl)-propyl]-α-D-xylofuranoside (Compound No. 14)

1,2-O-Isopropylidene-3-O-decyl-5-O-[3-(1-{4-[2-methoxy-phenyl]}-piperazinyl)-propyl]-α-D-xylofuranoside (Compound No. 15)

1-O-Methyl-2,3-O-isopropylidene-5-deoxy-5-[{3-[(4-{2-hydroxy-2-oxo-ethyl}-phenyl)-amino]-carbonyloxy}-propyl]-amino-α-D-lyxofuranoside (Compound No. 16)

1,2-O-Isopropylidene-3-O-decyl-5-deoxy-5-[2-(4-phenylthiazolyl)-amino]-α-D-xylofuranoside (Compound No. 17)

1,2-O-Isopropylidene-3-O-dodecyl-5-deoxy-5-{2-thiazolyl-amino}-α-D-xylofuranoside (Compound No. 18)

1,2-O-Isopropylidene-3-O-dodecyl-5-deoxy-5-{2-(benzimidazolyl)-amino}-α-D-xylofuranoside (Compound No. 19)

1,2-O-Isopropylidene-3-O-hexyl-5-deoxy-5-[2-(5-benzoyl-1*H*-benzimidazolyl)-amino]-α-D-xylofuranoside (Compound No. 20)

1,2-O-Isopropylidene-3-O-heptyl-5-O-(N-phthalimido-ethyl)-α-D-xylofuranoside (Compound No. 21)

1,2-O-Isopropylidene-3-O-decyl-5-O-{(4S, 7S, 10S)-3,6,9-triaza-11-[1-(2S-carboxy)-pyrrolidinyl]-7-(2-hydroxy-2-oxo-ethyl)-10-isopropyl-4-(2-methylpropyl)-2,5,8,11-tetraoxo-undecyl}-α-D-xylofuranoside (Compound No. 22)

1,2-O-Isopropylidene-3-O-decyl-5-O-{(4S, 7S)-3,6-diaza-8-[1-(2S-carboxy)-pyrrolidinyl]-4-(2-hydroxy-2-oxo-ethyl)-7-isopropyl-2, 5,8-trioxo-octyl}-α-D-xylofuranoside (Compound No. 23)

1,2-O-Isopropylidene-3-O-decyl-5-O-{(4S, 7S, 10S)-3,6,9-triaza-11-[1-(2S-benzyloxycarbonyl)-pyrrolidinyl]-7-[2-benzyloxy-2-oxo-ethyl]-10-isopropyl-4-(2-methylpropyl)-2,5,8,11-tetraoxo-undecyl}-α-D-xylofuranoside (Compound No. 24)

1,2-O-Isopropylidene-3-O-decyl-5-O-[2-{1-(2S-carboxy)-pyrrolidinyl}-2-oxo-ethyl]-α-D-xylofuranoside (Compound No. 25)

1-O-Dodecyl-2,3-O-isopropylidene-5,6-dideoxy-5-{2,6-dichloro-benzyl}-amino-β-L-gulofuranoside (Compound No. 26)

1,2-O-Isopropylidene-3-O-dodecyl-5-O-{3-[4-({[4-(2-methoxy-2-oxoethyl)phenyl] amino}carbonyl)-piperazinyl]-propyl}-α-D-xylofuranoside (Compound No. 27)

1,2-O-Isopropylidene-3-O-dodecyl-5-deoxy-5-[(4-methyl-1,3-thiazolyl)-amino]-α-D-xylofuranoside (Compound No. 28).

7. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 1 and at least one pharmaceutically acceptable excipient.

8. A method of inhibiting or preventing inflammation, comprising administering a therapeutically effective amount of the pharmaceutical composition of claim 7 to a patient in need thereof.

9. A method of inhibiting or preventing autoimmune disease, comprising administering a therapeutically effective amount of the pharmaceutical composition of claim 7 to a patient in need thereof.

10. A method of treating bronchial asthma, comprising administering a therapeutically effective amount of the pharmaceutical composition of claim 7 to a patient in need thereof.

11. A method of treating chronic obstructive pulmonary disorder, comprising administering the pharmaceutical composition of claim 7 to a patient in need thereof.

12. A method of treating rheumatoid arthritis, comprising administering a therapeutically effective amount of the pharmaceutical composition of claim 7 to a patient in need thereof.

13. A method of treating type I diabetes, comprising administering a therapeutically effective amount of the pharmaceutical composition of claim 7to a patient in need thereof.

14. A method of treating multiple sclerosis, comprising administering a therapeutically effective amount of the pharmaceutical composition of claim 7 to a patient in need thereof.

15. A method of treating allograft rejection, comprising administering a therapeutically effective amount of the pharmaceutical composition of claim 7 to a patient in need thereof.

16. A method of treating psoriasis, comprising administering a therapeutically effective amount of the pharmaceutical composition of claim 7 to a patient in need thereof.

17. A method of treating inflammatory bowel disease, comprising administering the pharmaceutical composition of claim 7 to a patient in need thereof.

18. A method of treating ulcerative colitis, comprising administering the pharmaceutical composition of claim 7 to a patient in need thereof.

19. A method of treating acne, comprising administering the pharmaceutical composition of claim 7 to a patient in need thereof.

20. A method of treating atherosclerosis, comprising administering the pharmaceutical composition of claim 7 to a patient in need thereof.

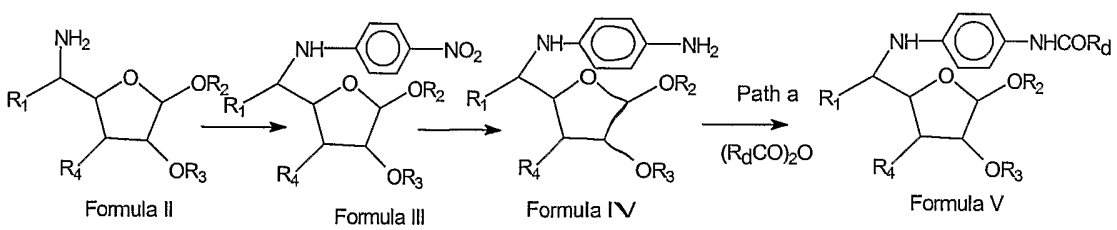
21. A method of treating cancer, comprising administering the pharmaceutical composition of claim 7 to a patient in need thereof.

22. A method of treating pruritis, comprising administering the pharmaceutical composition of claim 7 to a patient in need thereof.

23. A method of treating allergic rhinitis, comprising administering the pharmaceutical composition of claim 7 to a patient in need thereof.

24. A method of making a compound of Formula V

Scheme I



wherein

R_1 is hydrogen, lower (C_1-C_6) alkyl [wherein alkyl is optionally substituted with hydroxyl, -OR_x (wherein R_x is alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, or heterocyclylalkyl), acyloxy, cycloalkyl, aryl, substituted amino, -C(=O)QR_z (wherein Q is O or NH and R_z is selected from hydrogen, alkyl, aralkyl, aryl, and heteroarylalkyl), heteroaryl, and heterocyclyl], lower (C_2-C_6) alkenyl, lower (C_2-C_6) alkynyl, aryl, heterocyclyl (with the proviso that when p=0, the heterocyclyl cannot be linked through a heteroatom), heteroaryl (with the proviso that when p=0, the heteroaryl cannot be linked through a heteroatom), -OR_x (wherein R_x is as defined above except that when p=0 and X is a derivative of a heteroatom such as O or N, then R_1 cannot be OR_x), or -C(=O)QR_z (wherein Q and R_z is the same as defined above);

R_2 and R_3 together form a five membered acetal wherein the carbon joining the oxygens is substituted with R_L and R_m, [wherein R_L and R_m are independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, and aralkyl; or R_L and R_m can together join to form a 3- to 8-membered ring, wherein the ring may optionally contain one or more heteroatoms selected from O, N or S, and the ring may be optionally substituted with one or more of alkyl, alkenyl, alkynyl, acyl, substituted amino, cycloalkyl, -C(=O)QR_7 (wherein Q is same as defined earlier and R_7 is selected from alkyl, alkenyl, alkynyl, aryl, aralkyl, cycloalkyl, and heteroarylalkyl), carboxy, oxo, hydroxyl, alkoxy, aryloxy, halogen (FCl, Br, I), aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, or heterocyclylalkyl; or R_L and R_m together join to form an oxo linkage];

R_4 is hydrogen, or OR_c (wherein R_c is selected from alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, and heterocyclylalkyl) and, when R_4 is OR_c, then R_3 and R_c may together form an acetal (wherein the acetal is the same as defined earlier) and R_2 can be alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, heterocyclylalkyl, further, R_2 and R_3, instead of forming an acetal, may optionally and independently be selected from lower (C_1-C_4) alkyl, $(CH_2)_k$-aryl wherein k is an integer from 1-4, -C(=R_y)NHR_x wherein R_y is O or S and R_x is the same as defined earlier, and acyl; with R_4 defined as earlier, also, when R4 is OR_c, R_3 and R_c, instead of forming an acetal, may optionally and independently be selected from lower (C_1-C_4) alkyl, $(CH_2)_k$-aryl wherein k is an integer from 1-4, -C(=R_y)NHR_x wherein R_y is O or S and R_x is the same as defined earlier, and acyl; with R_2 defined as earlier,

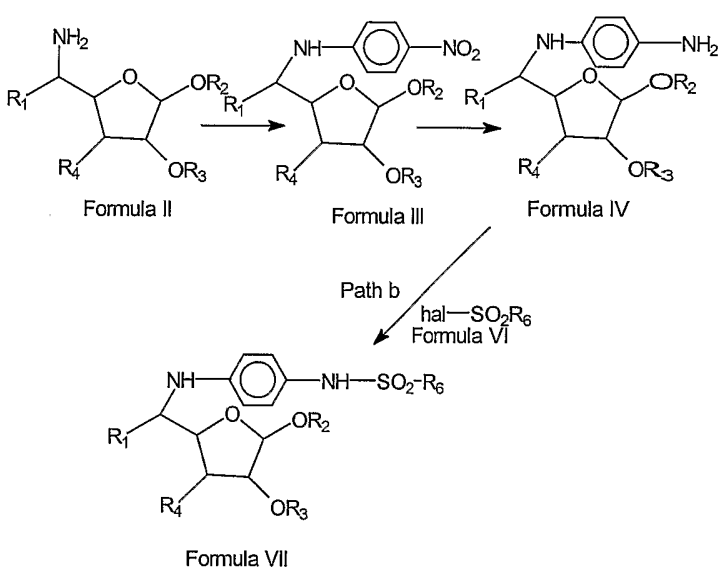
the method comprising

reacting a compound of Formula II with 4-nitrofluorobenzene to form a compound of Formula III;

hydrogenating the compound of Formula III to form a compound of Formula IV; and

reacting the compound of Formula IV with $(R_dCO)_2O$ (wherein Rd is alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl and heterocyclylalkyl) to form a compound of Formula V.

25. A method of making a compound of Formula VII



wherein

R_1 is hydrogen, lower (C_1-C_6) alkyl [wherein alkyl is optionally substituted with hydroxyl, $-OR_x$ (wherein R_x is alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, or heterocyclylalkyl), acyloxy, cycloalkyl, aryl, substituted amino, $-C(=O)QR_z$ (wherein Q is O or NH and R_z is selected from hydrogen, alkyl, aralkyl, aryl, and heteroarylalkyl), heteroaryl, and heterocyclyl], lower (C_2-C_6) alkenyl, lower (C_2-C_6) alkynyl, aryl, heterocyclyl (with the proviso that when p=0, the heterocyclyl cannot be linked through a heteroatom), heteroaryl (with the proviso that when p=0, the heteroaryl cannot be linked through a heteroatom), $-OR_x$ (wherein R_x is as defined above except that when p=0 and X is a derivative of a heteroatom such as O or N, then R_1 cannot be OR_x), or $-C(=O)QR_z$ (wherein Q and R_z is the same as defined above);

R_2 and R_3 together form a five membered acetal wherein the carbon joining the oxygens is substituted with R_L and R_m, [wherein R_L and R_m are independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, and aralkyl; or R_L and R_m can together join to form a 3- to 8-membered ring, wherein the ring may optionally contain one or more heteroatoms selected from O, N or S, and the ring may be optionally substituted with one or more of alkyl, alkenyl, alkynyl, acyl, substituted amino, cycloalkyl, $-C(=O)QR_7$ (wherein Q is same as defined earlier and R_7 is selected from alkyl, alkenyl, alkynyl, aryl, aralkyl, cycloalkyl, and heteroarylalkyl), carboxy, oxo, hydroxyl, alkoxy, aryloxy, halogen (FCl, Br, I), aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, or heterocyclylalkyl; or R_L and R_m together join to form an oxo linkage];

R_4 is hydrogen, or OR_c (wherein R_c is selected from alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, and heterocyclylalkyl) and, when R_4 is OR_c, then R_3 and R_c may together form an acetal (wherein the acetal is the same as defined earlier) and R_2 can be alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, heterocyclylalkyl, further, R_2 and R_3, instead of forming an acetal, may optionally and independently be selected from lower (C_1-C_4) alkyl, $(CH_2)_k$-aryl wherein k is an integer from 1-4, $-C(=R_y)NHR_x$ wherein R_y is O or S and R_x is the same as defined earlier, and acyl; with R_4 defined as earlier, also, when R4 is OR_c, R_3 and R_c, instead of forming an acetal, may optionally and independently be selected from lower (C_1-C_4) alkyl, $(CH_2)_k$-aryl wherein k is an integer from 1-4, $-C(=R_y)NHR_x$ wherein R_y is O or S and R_x is the same as defined earlier, and acyl; with R_2 defined as earlier,

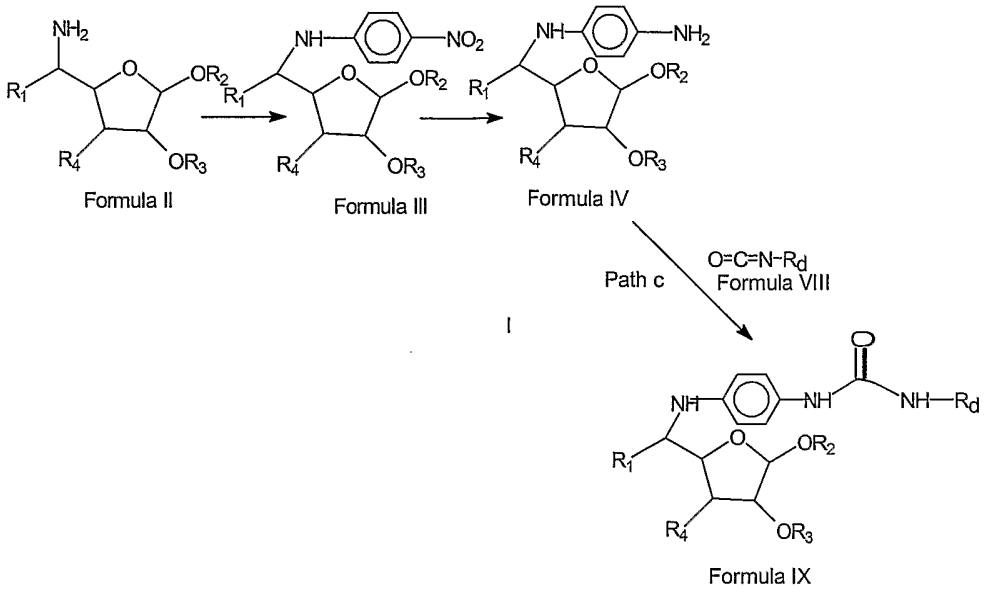
the method comprising

reacting a compound of Formula II with 4-nitrofluorobenzene to form a compound of Formula III;

hydrogenating the compound of Formula III to form a compound of Formula IV; and

reacting the compound of Formula IV with a compound of Formula VI (wherein hal is halogen and R_6 is alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heterocyclylalkyl, heteroarylalkyl, and substituted amino) to form a compound of Formula VII.

26. A method of making a compound of Formula IX



wherein

R_1 is hydrogen, lower (C_1-C_6) alkyl [wherein alkyl is optionally substituted with hydroxyl, -OR_x (wherein R_x is alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, or heterocyclylalkyl), acyloxy, cycloalkyl, aryl, substituted amino, -C(=O)QR_z (wherein Q is O or NH and R_z is selected from hydrogen, alkyl, aralkyl, aryl, and heteroarylalkyl), heteroaryl, and heterocyclyl], lower (C_2-C_6) alkenyl, lower (C_2-C_6) alkynyl, aryl, heterocyclyl (with the proviso that when p=0, the heterocyclyl cannot be linked through a heteroatom), heteroaryl (with the proviso that when p=0, the heteroaryl cannot be linked through a heteroatom), -OR_x (wherein R_x is as defined above except that when p=0 and X is a derivative of a heteroatom such as O or N, then R_1 cannot be OR_x), or -C(=O)QR_z (wherein Q and R_z is the same as defined above);

R_2 and R_3 together form a five membered acetal wherein the carbon joining the oxygens is substituted with R_L and R_m, [wherein R_L and R_m are independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, and aralkyl; or R_L and R_m can together join to form a 3- to 8-membered ring, wherein the ring may optionally contain one or more heteroatoms selected from O, N or S, and the ring may be optionally substituted with one or more of alkyl, alkenyl, alkynyl, acyl, substituted amino, cycloalkyl, -C(=O)QR_7

(wherein Q is same as defined earlier and R_7 is selected from alkyl, alkenyl, alkynyl, aryl, aralkyl, cycloalkyl, and heteroarylalkyl), carboxy, oxo, hydroxyl, alkoxy, aryloxy, halogen (FCl, Br, I), aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, or heterocyclylalkyl; or R_L and R_m together join to form an oxo linkage];

R_4 is hydrogen, or OR_c (wherein R_c is selected from alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, and heterocyclylalkyl) and, when R_4 is OR_c, then R_3 and R_c may together form an acetal (wherein the acetal is the same as defined earlier) and R_2 can be alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, heterocyclylalkyl, further, R_2 and R_3, instead of forming an acetal, may optionally and independently be selected from lower (C_1-C_4) alkyl, $(CH_2)_k$-aryl wherein k is an integer from 1-4, $-C(=R_y)NHR_x$ wherein R_y is O or S and R_x is the same as defined earlier, and acyl; with R_4 defined as earlier, also, when R_4 is OR_c, R_3 and R_c, instead of forming an acetal, may optionally and independently be selected from lower (C_1-C_4) alkyl, $(CH_2)_k$-aryl wherein k is an integer from 1-4, $-C(=R_y)NHR_x$ wherein R_y is O or S and R_x is the same as defined earlier, and acyl; with R_2 defined as earlier,

the method comprising

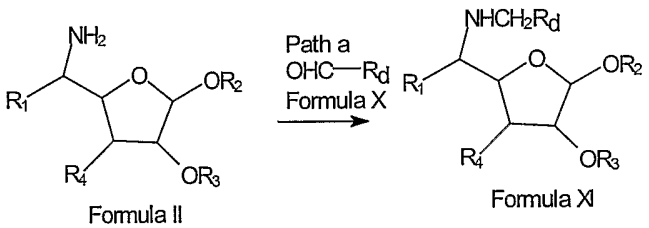
reacting a compound of Formula II with 4-nitrofluorobenzene to form a compound of Formula III;

hydrogenating the compound of Formula III to form a compound of Formula IV; and

reacting the compound of Formula IV with a compound of Formula VIII (wherein R_d is alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl and heterocyclylalkyl) to form a compound of Formula IX.

27. A method for making a compound of Formula XI

Scheme II



Formula II Formula XI

wherein

R_1 is hydrogen, lower (C_1-C_6) alkyl [wherein alkyl is optionally substituted with hydroxyl, -OR_x (wherein R_x is alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, or heterocyclylalkyl), acyloxy, cycloalkyl, aryl, substituted amino, -C(=O)QR_z (wherein Q is O or NH and R_z is selected from hydrogen, alkyl, aralkyl, aryl, and heteroarylalkyl), heteroaryl, and heterocyclyl], lower (C_2-C_6) alkenyl, lower (C_2-C_6) alkynyl, aryl, heterocyclyl (with the proviso that when p=0, the heterocyclyl cannot be linked through a heteroatom), heteroaryl (with the proviso that when p=0, the heteroaryl cannot be linked through a heteroatom), -OR_x (wherein R_x is as defined above except that when p=0 and X is a derivative of a heteroatom such as O or N, then R_1 cannot be OR_x), or -C(=O)QR_z (wherein Q and R_z is the same as defined above);

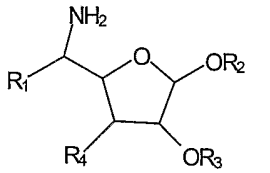
R_2 and R_3 together form a five membered acetal wherein the carbon joining the oxygens is substituted with R_L and R_m, [wherein R_L and R_m are independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, and aralkyl; or R_L and R_m can together join to form a 3- to 8-membered ring, wherein the ring may optionally contain one or more heteroatoms selected from O, N or S, and the ring may be optionally substituted with one or more of alkyl, alkenyl, alkynyl, acyl, substituted amino, cycloalkyl, -C(=O)QR_7 (wherein Q is same as defined earlier and R_7 is selected from alkyl, alkenyl, alkynyl, aryl, aralkyl, cycloalkyl, and heteroarylalkyl), carboxy, oxo, hydroxyl, alkoxy, aryloxy, halogen (FCl, Br, I), aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, or heterocyclylalkyl; or R_L and R_m together join to form an oxo linkage];

R_4 is hydrogen, or OR_c (wherein R_c is selected from alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, and heterocyclylalkyl) and, when R_4 is OR_c, then R_3 and R_c may together form an acetal (wherein the acetal is the same as defined earlier) and R_2 can be alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, heterocyclylalkyl, further, R_2 and R_3, instead of forming an acetal, may optionally and independently be selected from lower (C_1-C_4) alkyl, $(CH_2)_k$-aryl wherein k is an integer from 1-4, -C(=R_y)NHR_x wherein R_y is O or S and R_x is the same as defined earlier, and acyl; with R_4 defined as earlier, also, when R4 is OR_c, R_3 and R_c, instead of forming an acetal, may optionally and independently be selected from lower (C_1-C_4) alkyl, $(CH_2)_k$-aryl wherein k is an integer from 1-4, -C(=R_y)NHR_x wherein R_y is O or S and R_x is the same as defined earlier, and acyl; with R_2 defined as earlier,

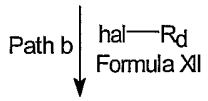
the method comprising

reacting a compound of Formula II with a compound of Formula X to form a compound of Formula XI (wherein R_d is alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl and heterocyclylalkyl).

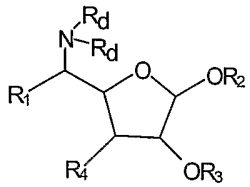
28. A method of making a compound of Formula XIII.



Formula II



Formula XI



Formula XIII

wherein

R_1 is hydrogen, lower (C_1-C_6) alkyl [wherein alkyl is optionally substituted with hydroxyl, -OR_x (wherein R_x is alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, or heterocyclylalkyl), acyloxy, cycloalkyl, aryl, substituted amino, -C(=O)QR_z (wherein Q is O or NH and R_z is selected from hydrogen, alkyl, aralkyl, aryl, and heteroarylalkyl), heteroaryl, and heterocyclyl], lower (C_2-C_6) alkenyl, lower (C_2-C_6) alkynyl, aryl, heterocyclyl (with the proviso that when p=0, the heterocyclyl cannot be linked through a heteroatom), heteroaryl (with the proviso that when p=0, the heteroaryl cannot be linked through a heteroatom), -OR_x (wherein R_x is as defined above except that when p=0 and X is a derivative of a heteroatom such as O or N, then R_1 cannot be OR_x), or -C(=O)QR_z (wherein Q and R_z is the same as defined above);

R_2 and R_3 together form a five membered acetal wherein the carbon joining the oxygens is substituted with R_L and R_m, [wherein R_L and R_m are independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, and aralkyl; or R_L and R_m can together join to form a 3- to 8-membered ring, wherein the ring may optionally contain one or more heteroatoms selected from O, N or S, and the ring may be optionally substituted with one

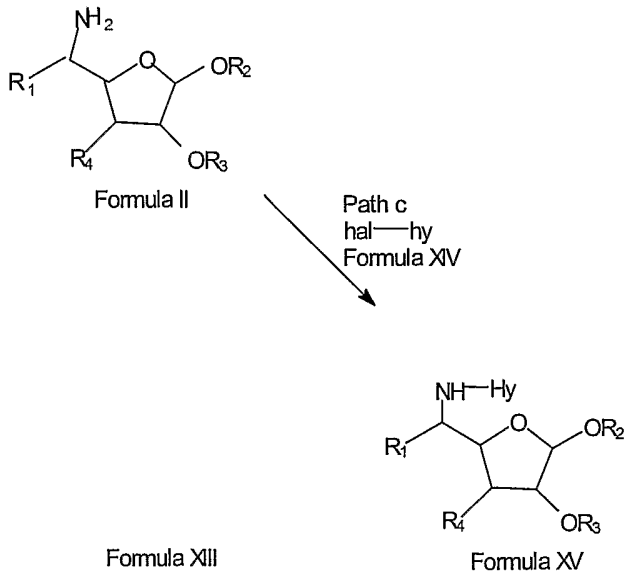
or more of alkyl, alkenyl, alkynyl, acyl, substituted amino, cycloalkyl, -C(=O)QR_7 (wherein Q is same as defined earlier and R_7 is selected from alkyl, alkenyl, alkynyl, aryl, aralkyl, cycloalkyl, and heteroarylalkyl), carboxy, oxo, hydroxyl, alkoxy, aryloxy, halogen (FCl, Br, I), aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, or heterocyclylalkyl; or R_L and R_m together join to form an oxo linkage];

R_4 is hydrogen, or OR_c (wherein R_c is selected from alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, and heterocyclylalkyl) and, when R_4 is OR_c, then R_3 and R_c may together form an acetal (wherein the acetal is the same as defined earlier) and R_2 can be alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, heterocyclylalkyl, further, R_2 and R_3, instead of forming an acetal, may optionally and independently be selected from lower (C_1-C_4) alkyl, $(CH_2)_k$-aryl wherein k is an integer from 1-4, -C(=R_y)NHR_x wherein R_y is O or S and R_x is the same as defined earlier, and acyl; with R_4 defined as earlier, also, when R4 is OR_c, R_3 and R_c, instead of forming an acetal, may optionally and independently be selected from lower (C_1-C_4) alkyl, $(CH_2)_k$-aryl wherein k is an integer from 1-4, -C(=R_y)NHR_x wherein R_y is O or S and R_x is the same as defined earlier, and acyl; with R_2 defined as earlier,

the method comprising

reacting a compound of Formula II with a compound of Formula XII to form a compound of Formula XIII (wherein hal is halogen, and R_d is alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl and heterocyclylalkyl).

29. A method of making a compound of Formula XV



wherein

R_1 is hydrogen, lower (C_1-C_6) alkyl [wherein alkyl is optionally substituted with hydroxyl, -OR_x (wherein R_x is alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, or heterocyclylalkyl), acyloxy, cycloalkyl, aryl, substituted amino, -C(=O)QR_z (wherein Q is O or NH and R_z is selected from hydrogen, alkyl, aralkyl, aryl, and heteroarylalkyl), heteroaryl, and heterocyclyl], lower (C_2-C_6) alkenyl, lower (C_2-C_6) alkynyl, aryl, heterocyclyl (with the proviso that when p=0, the heterocyclyl cannot be linked through a heteroatom), heteroaryl (with the proviso that when p=0, the heteroaryl cannot be linked through a heteroatom), -OR_x (wherein R_x is as defined above except that when p=0 and X is a derivative of a heteroatom such as O or N, then R_1 cannot be OR_x), or -C(=O)QR_z (wherein Q and R_z is the same as defined above);

R_2 and R_3 together form a five membered acetal wherein the carbon joining the oxygens is substituted with R_L and R_m, [wherein R_L and R_m are independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, and aralkyl; or R_L and R_m can together join to form a 3- to 8-membered ring, wherein the ring may optionally contain one or more heteroatoms selected from O, N or S, and the ring may be optionally substituted with one or more of alkyl, alkenyl, alkynyl, acyl, substituted amino, cycloalkyl, -C(=O)QR_7 (wherein Q is same as defined earlier and R_7 is selected from alkyl, alkenyl, alkynyl, aryl, aralkyl, cycloalkyl, and heteroarylalkyl), carboxy, oxo, hydroxyl, alkoxy, aryloxy, halogen (FCl, Br, I), aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, or heterocyclylalkyl; or R_L and R_m together join to form an oxo linkage];

R_4 is hydrogen, or OR_c (wherein R_c is selected from alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, and heterocyclylalkyl) and, when R_4 is OR_c, then R_3 and R_c may together form an acetal (wherein the acetal is the same as defined earlier) and R_2 can be alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, heterocyclylalkyl, further, R_2 and R_3, instead of forming an acetal, may optionally and independently be selected from lower (C_1-C_4) alkyl, $(CH_2)_k$-aryl wherein k is an integer from 1-4, -C(=R_y)NHR_x wherein R_y is O or S and R_x is the same as defined earlier, and acyl; with R_4 defined as earlier, also, when R4 is OR_c, R_3 and R_c, instead of forming an acetal, may optionally and independently be selected from lower (C_1-C_4) alkyl, $(CH_2)_k$-aryl wherein k is an integer from 1-4, -C(=R_y)NHR_x wherein R_y is O or S and R_x is the same as defined earlier, and acyl; with R_2

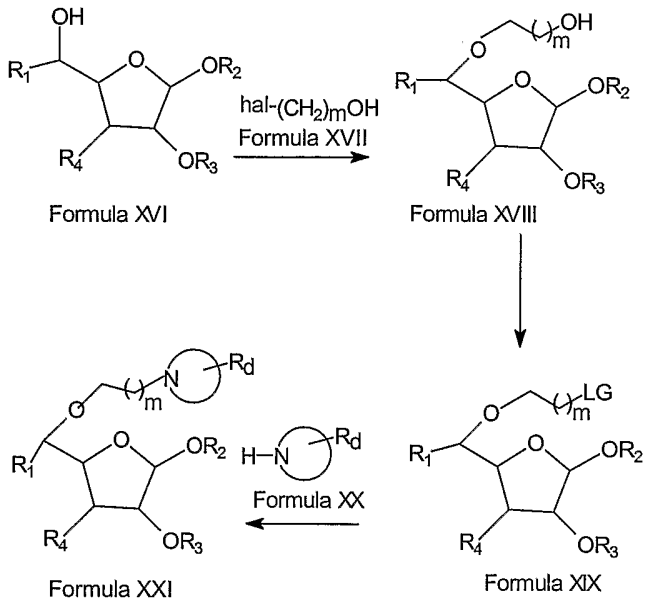
defined as earlier,

the method comprising

reacting a compound of Formula II with a compound of Formula XIV (wherein *hal* is a halogen and *Hy* is heterocyclyl or heteroaryl) to yield a compound of Formula XV.

30. A method of making compounds of Formula XXI

Scheme III



wherein

R_1 is hydrogen, lower (C_1-C_6) alkyl [wherein alkyl is optionally substituted with hydroxyl, -OR_x (wherein R_x is alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, or heterocyclylalkyl), acyloxy, cycloalkyl, aryl, substituted amino, -C(=O)QR_z (wherein Q is O or NH and R_z is selected from hydrogen, alkyl, aralkyl, aryl, and heteroarylalkyl), heteroaryl, and heterocyclyl], lower (C_2-C_6) alkenyl, lower (C_2-C_6) alkynyl, aryl, heterocyclyl (with the proviso that when p=0, the heterocyclyl cannot be linked through a heteroatom), heteroaryl (with the proviso that when p=0, the heteroaryl cannot be linked through a heteroatom), -OR_x (wherein R_x is as defined above except that when p=0 and X is a derivative of a heteroatom such as O or N, then R_1 cannot be OR_x), or -C(=O)QR_z (wherein Q and R_z is the same as defined above);

R_2 and R_3 together form a five membered acetal wherein the carbon joining the oxygens is substituted with R_L and R_m, [wherein R_L and R_m are independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, and aralkyl; or R_L and R_m can together

join to form a 3- to 8-membered ring, wherein the ring may optionally contain one or more heteroatoms selected from O, N or S, and the ring may be optionally substituted with one or more of alkyl, alkenyl, alkynyl, acyl, substituted amino, cycloalkyl, $-C(=O)QR_7$ (wherein Q is same as defined earlier and R_7 is selected from alkyl, alkenyl, alkynyl, aryl, aralkyl, cycloalkyl, and heteroarylalkyl), carboxy, oxo, hydroxyl, alkoxy, aryloxy, halogen (FCl, Br, I), aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, or heterocyclylalkyl; or R_L and R_m together join to form an oxo linkage];

R_4 is hydrogen, or OR_c (wherein R_c is selected from alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, and heterocyclylalkyl) and, when R_4 is OR_c, then R_3 and R_c may together form an acetal (wherein the acetal is the same as defined earlier) and R_2 can be alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, heterocyclylalkyl, further, R_2 and R_3, instead of forming an acetal, may optionally and independently be selected from lower (C_1-C_4) alkyl, $(CH_2)_k$-aryl wherein k is an integer from 1-4, $-C(=R_y)NHR_x$ wherein R_y is O or S and R_x is the same as defined earlier, and acyl; with R_4 defined as earlier, also, when R4 is OR_c, R_3 and R_c, instead of forming an acetal, may optionally and independently be selected from lower (C_1-C_4) alkyl, $(CH_2)_k$-aryl wherein k is an integer from 1-4, $-C(=R_y)NHR_x$ wherein R_y is O or S and R_x is the same as defined earlier, and acyl; with R_2 defined as earlier,

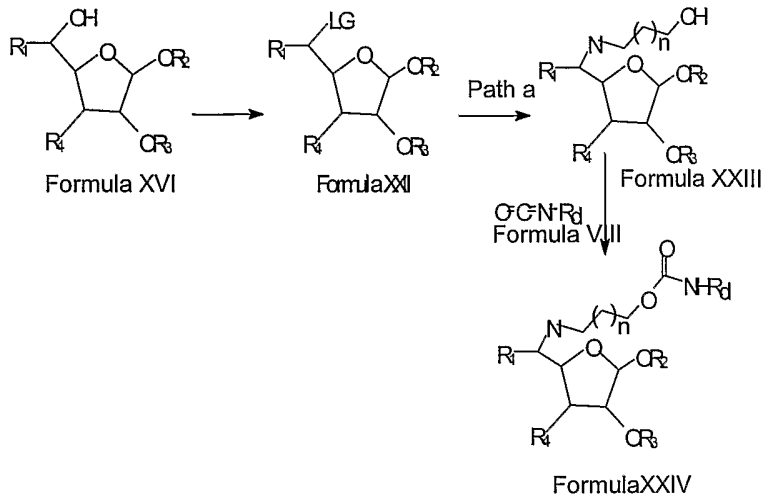
the method comprising

reacting a compound of Formula XVI with a compound of Formula XVII (wherein m is an integer from 1-3 and *hal* is halogen) to yield a compound of Formula XVIII;

converting the compound of Formula XVIII to the compound of Formula XIX (wherein LG is a leaving group); and

reacting the compound of Formula XIX with a compound of Formula XX (wherein R_d is alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl and heterocyclylalkyl) to give a compound of Formula XXI.

31. A method of making a compound of Formula XXIV



wherein

R_1 is hydrogen, lower (C_1-C_6) alkyl [wherein alkyl is optionally substituted with hydroxyl, -OR_x (wherein R_x is alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, or heterocyclylalkyl), acyloxy, cycloalkyl, aryl, substituted amino, -C(=O)QR_z (wherein Q is O or NH and R_z is selected from hydrogen, alkyl, aralkyl, aryl, and heteroarylalkyl), heteroaryl, and heterocyclyl], lower (C_2-C_6) alkenyl, lower (C_2-C_6) alkynyl, aryl, heterocyclyl (with the proviso that when p=0, the heterocyclyl cannot be linked through a heteroatom), heteroaryl (with the proviso that when p=0, the heteroaryl cannot be linked through a heteroatom), -OR_x (wherein R_x is as defined above except that when p=0 and X is a derivative of a heteroatom such as O or N, then R_1 cannot be OR_x), or -C(=O)QR_z (wherein Q and R_z is the same as defined above);

R_2 and R_3 together form a five membered acetal wherein the carbon joining the oxygens is substituted with R_L and R_m, [wherein R_L and R_m are independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, and aralkyl; or R_L and R_m can together join to form a 3- to 8-membered ring, wherein the ring may optionally contain one or more heteroatoms selected from O, N or S, and the ring may be optionally substituted with one or more of alkyl, alkenyl, alkynyl, acyl, substituted amino, cycloalkyl, -C(=O)QR_7 (wherein Q is same as defined earlier and R_7 is selected from alkyl, alkenyl, alkynyl, aryl, aralkyl, cycloalkyl, and heteroarylalkyl), carboxy, oxo, hydroxyl, alkoxy, aryloxy, halogen

(FCl, Br, I), aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, or heterocyclylalkyl; or R_L and R_m together join to form an oxo linkage];

R_4 is hydrogen, or OR_c (wherein R_c is selected from alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, and heterocyclylalkyl) and, when R_4 is OR_c, then R_3 and R_c may together form an acetal (wherein the acetal is the same as defined earlier) and R_2 can be alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, heterocyclylalkyl, further, R_2 and R_3, instead of forming an acetal, may optionally and independently be selected from lower (C_1-C_4) alkyl, $(CH_2)_k$-aryl wherein k is an integer from 1-4, $-C(=R_y)NHR_x$ wherein R_y is O or S and R_x is the same as defined earlier, and acyl; with R_4 defined as earlier, also, when R4 is OR_c, R_3 and R_c, instead of forming an acetal, may optionally and independently be selected from lower (C_1-C_4) alkyl, $(CH_2)_k$-aryl wherein k is an integer from 1-4, $-C(=R_y)NHR_x$ wherein R_y is O or S and R_x is the same as defined earlier, and acyl; with R_2 defined as earlier,

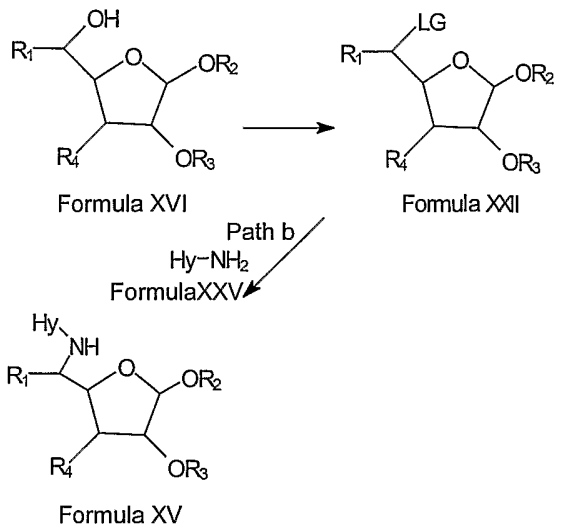
the method comprising

reacting a compound of Formula XVI with a leaving group to give a compound of Formula XXII;

reacting the compound of Formula XXII with an aminoalkylalcohol to give a compound of Formula XXIII (wherein n is an integer 0-2); and

reacting the compound of Formula XXIII with a compound of Formula VIII to give a compound of Formula XXIV (wherein R_d is alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl and heterocyclylalkyl).

32. A method of making a compound of Formula XV



wherein

R_1 is hydrogen, lower (C_1-C_6) alkyl [wherein alkyl is optionally substituted with hydroxyl, -OR_x (wherein R_x is alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, or heterocyclylalkyl), acyloxy, cycloalkyl, aryl, substituted amino, -C(=O)QR_z (wherein Q is O or NH and R_z is selected from hydrogen, alkyl, aralkyl, aryl, and heteroarylalkyl), heteroaryl, and heterocyclyl], lower (C_2-C_6) alkenyl, lower (C_2-C_6) alkynyl, aryl, heterocyclyl (with the proviso that when p=0, the heterocyclyl cannot be linked through a heteroatom), heteroaryl (with the proviso that when p=0, the heteroaryl cannot be linked through a heteroatom), -OR_x (wherein R_x is as defined above except that when p=0 and X is a derivative of a heteroatom such as O or N, then R_1 cannot be OR_x), or -C(=O)QR_z (wherein Q and R_z is the same as defined above);

R_2 and R_3 together form a five membered acetal wherein the carbon joining the oxygens is substituted with R_l and R_m, [wherein R_L and R_m are independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, and aralkyl; or R_L and R_m can together join to form a 3- to 8-membered ring, wherein the ring may optionally contain one or more heteroatoms selected from O, N or S, and the ring may be optionally substituted with one or more of alkyl, alkenyl, alkynyl, acyl, substituted amino, cycloalkyl, -C(=O)QR_7 (wherein Q is same as defined earlier and R_7 is selected from alkyl, alkenyl, alkynyl, aryl, aralkyl, cycloalkyl, and heteroarylalkyl), carboxy, oxo, hydroxyl, alkoxy, aryloxy, halogen (FCl, Br, I), aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, or heterocyclylalkyl; or R_l and R_m together join to form an oxo linkage];

R_4 is hydrogen, or OR_c (wherein R_c is selected from alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, and heterocyclylalkyl) and, when R_4 is OR_c, then R_3 and R_c may together form an acetal (wherein the acetal is the same as defined earlier) and R_2 can be alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, heterocyclylalkyl, further, R_2 and R_3, instead of forming an acetal, may optionally and independently be selected from lower (C_1-C_4) alkyl, $(CH_2)_k$-aryl wherein k is an integer from 1-4, -C(=R_y)NHR_x wherein R_y is O or S and R_x is the same as defined earlier, and acyl; with R_4 defined as earlier, also, when R4 is OR_c, R_3 and R_c, instead of forming an acetal, may optionally and independently be selected from lower (C_1-C_4) alkyl, $(CH_2)_k$-aryl wherein k is an integer from 1-4, -

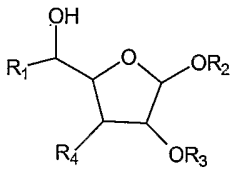
$C(=R_y)NHR_x$ wherein R_y is O or S and R_x is the same as defined earlier, and acyl; with R_2 defined as earlier,

the method comprising

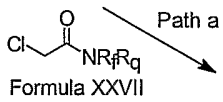
reacting a compound of Formula XVI with a leaving group to give a compound of Formula XXII;

reacting the compound of Formula XXII with a compound of Formula XXV (wherein *Hy* is heterocyclyl or heteroaryl) to give a compound of Formula XV.

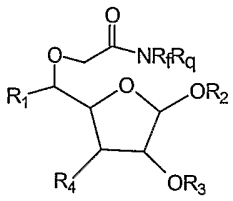
33. A method of making a compound of Formula XXVIII



Formula XVI



Formula XXVII



FormulaXXVIII

wherein

R_1 is hydrogen, lower (C_1-C_6) alkyl [wherein alkyl is optionally substituted with hydroxyl, $-OR_x$ (wherein R_x is alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, or heterocyclylalkyl), acyloxy, cycloalkyl, aryl, substituted amino, $-C(=O)QR_z$ (wherein Q is O or NH and R_z is selected from hydrogen, alkyl, aralkyl, aryl, and heteroarylalkyl), heteroaryl, and heterocyclyl], lower (C_2-C_6) alkenyl, lower (C_2-C_6) alkynyl, aryl, heterocyclyl (with the proviso that when p=0, the heterocyclyl cannot be linked through a heteroatom), heteroaryl (with the proviso that when p=0, the heteroaryl cannot be linked through a heteroatom), $-OR_x$ (wherein R_x is as defined above except that when p=0 and X is a derivative of a heteroatom such as O or N, then R_1 cannot be OR_x), or $-C(=O)QR_z$ (wherein Q and R_z is the same as defined above);

R_2 and R_3 together form a five membered acetal wherein the carbon joining the oxygens is substituted with R_L and R_m, [wherein R_L and R_m are independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, and aralkyl; or R_L and R_m can together join to form a 3- to 8-membered ring, wherein the ring may optionally contain one or more

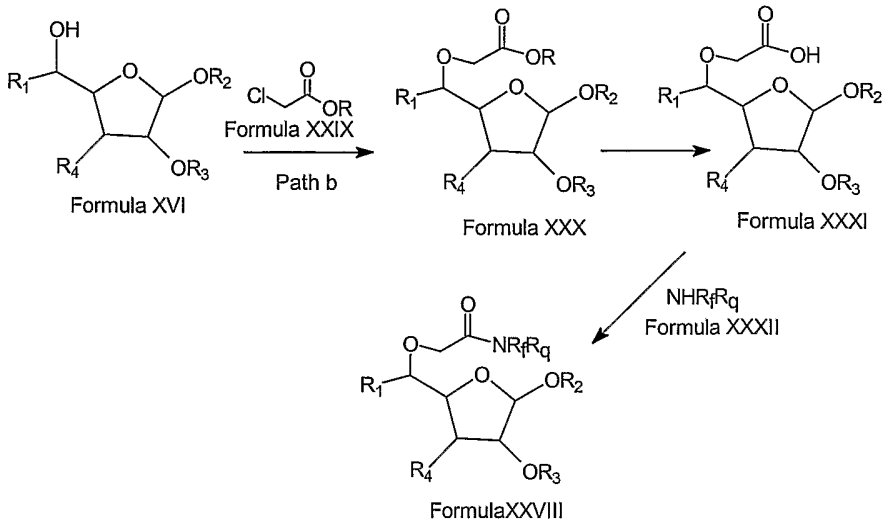
heteroatoms selected from O, N or S, and the ring may be optionally substituted with one or more of alkyl, alkenyl, alkynyl, acyl, substituted amino, cycloalkyl, -C(=O)QR_7 (wherein Q is same as defined earlier and R_7 is selected from alkyl, alkenyl, alkynyl, aryl, aralkyl, cycloalkyl, and heteroarylalkyl), carboxy, oxo, hydroxyl, alkoxy, aryloxy, halogen (FCl, Br, I), aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, or heterocyclylalkyl; or R_l and R_m together join to form an oxo linkage];

R_4 is hydrogen, or OR_c (wherein R_c is selected from alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, and heterocyclylalkyl) and, when R_4 is OR_c, then R_3 and R_c may together form an acetal (wherein the acetal is the same as defined earlier) and R_2 can be alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, heterocyclylalkyl, further, R_2 and R_3, instead of forming an acetal, may optionally and independently be selected from lower (C_1-C_4) alkyl, $(CH_2)_k$-aryl wherein k is an integer from 1-4, -$C(=R_y)NHR_x$ wherein R_y is O or S and R_x is the same as defined earlier, and acyl; with R_4 defined as earlier, also, when R4 is OR_c, R_3 and R_c, instead of forming an acetal, may optionally and independently be selected from lower (C_1-C_4) alkyl, $(CH_2)_k$-aryl wherein k is an integer from 1-4, -$C(=R_y)NHR_x$ wherein R_y is O or S and R_x is the same as defined earlier, and acyl; with R_2 defined as earlier,

the method comprising

reacting a compound of Formula XVI with a compound of Formula XXVII (wherein R_f and R_q can be independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heteroaryl, heteroarylalkyl, hetrocyclylalkyl, and $S(O)_2R_6$ (wherein R_6 is selected from alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heterocyclylalkyl, heteroarylalkyl, and substituted amino); and also R_f and R_q can together form a ring) to give a compound of Formula XXVIII.

34. A method of making a compound of Formula XXVIII



wherein

R_1 is hydrogen, lower (C_1-C_6) alkyl [wherein alkyl is optionally substituted with hydroxyl, -OR_x (wherein R_x is alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, or heterocyclylalkyl), acyloxy, cycloalkyl, aryl, substituted amino, -C(=O)QR_z (wherein Q is O or NH and R_z is selected from hydrogen, alkyl, aralkyl, aryl, and heteroarylalkyl), heteroaryl, and heterocyclyl], lower (C_2-C_6) alkenyl, lower (C_2-C_6) alkynyl, aryl, heterocyclyl (with the proviso that when p=0, the heterocyclyl cannot be linked through a heteroatom), heteroaryl (with the proviso that when p=0, the heteroaryl cannot be linked through a heteroatom), -OR_x (wherein R_x is as defined above except that when p=0 and X is a derivative of a heteroatom such as O or N, then R_1 cannot be OR_x), or -C(=O)QR_z (wherein Q and R_z is the same as defined above);

R_2 and R_3 together form a five membered acetal wherein the carbon joining the oxygens is substituted with R_l and R_m, [wherein R_l and R_m are independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, and aralkyl; or R_l and R_m can together join to form a 3- to 8-membered ring, wherein the ring may optionally contain one or more heteroatoms selected from O, N or S, and the ring may be optionally substituted with one or more of alkyl, alkenyl, alkynyl, acyl, substituted amino, cycloalkyl, -C(=O)QR_7 (wherein Q is same as defined earlier and R_7 is selected from alkyl, alkenyl, alkynyl, aryl, aralkyl, cycloalkyl, and heteroarylalkyl), carboxy, oxo, hydroxyl, alkoxy, aryloxy, halogen (FCl, Br, I), aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, or heterocyclylalkyl; or R_l and R_m together join to form an oxo linkage];

R_4 is hydrogen, or OR_c (wherein R_c is selected from alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, and heterocyclylalkyl) and, when R_4 is OR_c, then R_3 and R_c may together form an acetal (wherein the acetal is the same as defined earlier) and R_2 can be alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, heterocyclylalkyl, further, R_2 and R_3, instead of forming an acetal, may optionally and independently be selected from lower (C_1-C_4) alkyl, $(CH_2)_k$-aryl wherein k is an integer from 1-4, $-C(=R_y)NHR_x$ wherein R_y is O or S and R_x is the same as defined earlier, and acyl; with R_4 defined as earlier, also, when R_4 is OR_c, R_3 and R_c, instead of forming an acetal, may optionally and independently be selected from lower (C_1-C_4) alkyl, $(CH_2)_k$-aryl wherein k is an integer from 1-4, $-C(=R_y)NHR_x$ wherein R_y is O or S and R_x is the same as defined earlier, and acyl; with R_2 defined as earlier,

the method comprising

reacting a compound of Formula XVI with a compound of Formula XXIX (wherein R is alkyl or aralkyl) to give a compound of Formula XXXI;

reacting the compound of Formula XXXI with a compound of Formula XXXII (wherein R_f and R_q can be independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heteroaryl, heteroarylalkyl, hetrocyclylalkyl, and $S(O)_2R_6$ (wherein R_6 is selected from alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heterocyclylalkyl, heteroarylalkyl, and substituted amino); and also R_f and R_q can together form a ring) to give a compound of Formula XXVIII.