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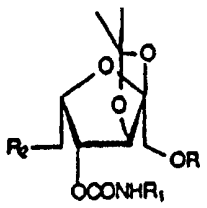

(I)

(57) Abstract

This invention relates generally to compounds and processes for synthesizing derivatives of 2–3–O– isopropylidene–α –L–xylo–2–hexulofuranosonic acid, of formula (I) compounds of this invention are useful, inter–alia, for the inhibition and prevention of cell adhesion and cell adhesion–mediated pathologies, including inflammatory and autoimmune diseases, such as bronchial asthma, rheumatoid arthritis, type I diabetes, multiple sclerosis, allograft rejection and psoriasis. This invention also relates to pharmacological compositions containing derivatives of 2–3–O– isopropylidene–α –L–xylo–2– hexulofuranosonic acid and the methods of treating such pathologies as listed above.

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2,3-O-ISOPROYLIDENE DERIVATIVES OF MONOSACCHARIDES AS CELL ADHESION INHIBITORS

FIELD OF THE INVENTION

This invention relates generally to compounds and processes for synthesizing derivatives of 2-3-O-isopropylidene-α-L-xylo-2-hexulofuranosonic acid. The compounds of this invention are useful, inter-alia, for the inhibition and prevention of cell adhesion and cell adhesion-mediated pathologies, including inflammatory and autoimmune diseases, such as bronchial asthma, rheumatoid arthritis, type I diabetes, multiple sclerosis, allograft rejection and psoriasis. This invention also relates to pharmacological compositions containing derivatives of 2-3-O-isopropylidene-α-L-xylo-2-hexulofuranosonic acid and the methods of treating such pathologies as listed above.

BACKGROUND OF THE INVENTION

Cell adhesion is a process by which cells associate with each other and migrate towards a specific target localized within the extracellular matrix. Specialized molecules, called cell adhesion molecules (CAMs), mediate these reactions. CAMs have been demonstrated to participate in various cell-cell, cell-extracellular matrix, and platelet-platelet interactions. CAMs influence the leukocytes' adhesion to the vascular endothelium, their transendothelial

migration, retention at extravascular sites, and activation of T cells and eosinophils. These processes are central to the pathogenesis of inflammatory and autoimmune diseases. Therefore, CAMs are considered potential targets for treating such disorders.

CAMs can be classified into three groups: integrins, selectins, and the immunoglobulin superfamily. Of these, integrins are the key mediators in the adhesive interactions between hemopoietic cells and their microenvironment. They are comprised of alpha-beta heterodimers and integrate signals from the outside to the inside of cells, and vice versa. Integrins can be classified on the basis of the beta subunits they contain. For example, the beta-1 subfamily contains beta-1 subunit noncovalently linked to one of the 10 different alpha subunits.

The alpha-4 beta-1 integrin, also known as VLA_4 (very late activation antigen 4), is a member of the beta-1 integrin family and comprises alpha-4 and beta-1 subunits. VLA_4 interacts with two specific ligands—the vascular cell adhesion molecule (VCAM-1) and the CS1 region of the protein fibronectin. Adhesion mediated by VLA_4 is central to the process of transendothelial migration of leukocytes. Ligation of VLA_4 is followed by gross rearrangement of the cytoskeleton, leading to flattening of cells along the blood vessel wall, followed by expression of specific molecules that digest the endothelial cell wall and diapedesis. Once in the extraluminal region, the interactions of VLA_4 with extracellular fibronectin play a crucial role in the migration of leukocytes to the site of inflammation, T cell proliferation,

expression of cytokines and inflammatory mediators. Additionally, VLA_4 ligation provides co-stimulatory signals to the leukocytes, resulting in enhanced immunoreactivity. Thus, appropriate VLA_4 antagonists would, in theory, ameliorate the immune response through a twofold action—inhibition of T cell recruitment at the site of inflammation and inhibition of co-stimulatory activation of immune cells.

In this respect, inhibitors of VLA_4 interactions have been demonstrated to exhibit beneficial therapeutic effects in several animal models of inflammatory and allergic diseases, including sheep allergic asthma (Abraham et al, J. Clin. Invest. 1994;93:776); arthritis (Wahl et al, J. Clin. Invest. 1994;94:655); experimental allergic encephalomyelitis (Yednock et al, Nature (Lond), 1992;356:63 and Baron et al, J. Exp. Med. 1993;177:57); contact hypersensitivity (Chisolm et al, Eur J. Immunol. 1993;23:682); type I diabetes (Yang et al, Proc. Natl. Acad. Sci. (USA) 1993;90:10494); and inflammatory bowel disease (Podolsky et al, J. Clin. Invest. 1993;92:372).

The CS1 moiety region of fibronectin involved in the interaction with VLA_4 was identified as the tripeptide Leu-Asp-Val (LDV) (Komoriya et al, J. Biol. Chem. 1991;266:15075). Several peptides containing the LDV sequence were synthesized and shown to inhibit the *in vivo* interaction of VLA_4 to its ligands (Ferguson et al, Proc. Natl. Acad. Sci. (USA) 1991;88:8072; Wahl et al, J. Clin. Invest. 1994;94:655; Nowlin et al, J. Biol. Chem. 1993;268(27):20352; and PCT publication WO91/4862).

Despite these advances a need for small and specific inhibitors of VLA_4-dependent cell adhesion molecules remains. Ideally, such inhibitors are water soluble with oral efficacy. Such compounds would provide useful agents for the treatment, prevention or suppression of various inflammatory pathologies mediated by VLA_4 binding.

It is generally known that isopropylidene and benzylidene groups are the most commonly used protective groups in carbohydrate chemistry. Although both groups are introduced into a molecule under similar conditions, the location of the protection can be quite different, and this difference is directly related to the stability of each protected molecule. Since protection normally occurs under conditions that allow reversibility, the reaction proceeds until equilibrium is reached. The distribution of products at equilibrium is determined by their relative thermodynamic stabilities. In other words, these reactions are thermodynamically controlled. Benzylidene groups prefer to be part of 6-membered ring acetals, while the ketals resulting from acetonation generally are 5-membered rings. The difference is attributed to the effect of the methyl and phenyl substituents on the stability of the particular ring systems. These blocking methods are described in the U.S. Pat. Nos. 2,715,121, 4,056,322, 4,735,934, 4,996,195 and 5,010,058, the disclosures of which are incorporated herein by reference. Other blocking methods are also described in J. Carbohydr. Chem. 1985;4:227 and 1984;3:331; Methods in Carbohydr. Chem. 1962;1:107 and 1962;1:191; Can J. Chem. 1984;62:2728, 1969;47:1195, 1455, and 1970;48:1754, all incorporated herein by reference. The prior art reveals that D-glucose is blocked at the 1,2;5,6-positions with

either the isopropylidene or cyclohexylidene blocking group, leaving the 3-position open to undergo derivatization. The therapeutic activity of hexoses and their derivatives are also disclosed in some of the above-cited prior art.

The compounds of the present invention were screened for inhibitory activity in VLA_4-mediated cell adhesion assay and the classical murine hypersensitivity assay in mice. Several compounds exhibited significant inhibitory activity in both tests. The salts of these compounds could be easily solubilized in water and used in the treatment of chronic, cell adhesion-mediated, allergic, autoimmune and inflammatory disorders, such as bronchial asthma and rheumatoid arthritis. Some of the prior art describes development of peptide derivatives as cell adhesion antagonists for treatment of these diseases. However, because treatment of chronic diseases requires prolonged (mid-term to long-term) administration of drugs, the development of specific, orally available cell adhesion inhibitors would be very beneficial.

There is no example available in the prior art wherein the compounds, containing a sugar nucleus coupled with carbamate moiety, of the present invention are used as therapy for the inhibition, prevention and suppression of VLA_4-mediated cell adhesion and pathologies associated with that adhesion.

SUMMARY OF THE INVENTION

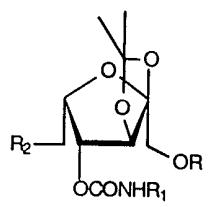
An object of the present invention is to provide a process for synthesizing a new class of compounds that exhibit significant activity as VLA_4 antagonists.

Most of the compounds described in U.S. Pat. No. 5,637,570 have shown significant anti-cancer activities and were devoid of any anti-cell adhesion activities. Therefore, the compounds of the present invention were designed and synthesized so as to enhance their anti-cell adhesion properties. It was discovered that, for a compound to be active as a cell adhesion inhibitor, it is best if the sugar has a carbamate moiety along with other functionalities.

It is a further object of this invention to provide a process for the preparation of novel carbohydrate-based water-soluble compounds that exhibit significant activity to be used as cell adhesion antagonists.

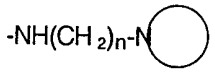
Other objects and advantages of the present invention will be set forth in the description that follows, will be in part apparent from the description, or may be learned by the practice of the invention. The objects and advantages of this invention may be realized and obtained by means of the mechanisms and combinations pointed out in the appended claims.

In order to achieve the above-mentioned objects and in accordance with one aspect of the present invention, there is provided a process for the synthesis of monosaccharide derivatives and the derivatives themselves, having the structure of Formula I:



FORMULA I

wherein R is C_1 to C_{15} alkyl, alkene, alkyne (straight chain or branched), aryl, substituted aryl or alkylaryl, R_1 is phenyl , o,- m- or p-chlorophenyl, tolyl, methoxyphenyl or nitrophenyl and R_2 is H, pyrrolidinyl, piperidinyl, morphilinyl or hexamethyleneimino or a radical of the formula - NHR_3 wherein R_3 is C_1 to C_{15} alkyl, alkene or alkyne (straight chain or branched) or a radical of Formula III:



FORMULA III

wherein n is a whole number up to 5 and

is a five-, six- or seven-membered heterocyclic ring containing one or more heteroatoms, and wherein preferably

is pyrrolidinyl, piperidinyl, morpholinyl or hexamethyleneimino moieties.

Preferred compounds are those wherein R_1 and R_2 are not H at the same time. Acid addition salts of the above compounds are also included in the invention.

In accordance with another aspect of the present invention there is provided a list of compounds as shown below in the description of the invention section.

In accordance with another aspect of the present invention there are provided methods of preventing, inhibiting or suppressing cell adhesion in an animal (the term animal as used herein includes humans or mammals), comprising administering to said animal, the compounds described above.

In accordance with another aspect of the present invention there is provided a method for treating an animal suffering from bronchial asthma, rheumatoid arthritis, multiple sclerosis, type I diabetes, psoriasis, allograft rejection, and other inflammatory and/or autoimmune disorders, comprising administering to said animal, the compounds described above.

In accordance with yet another aspect of the present invention there is provided a method for preventing, inhibiting or suppressing cell adhesion-associated inflammation with compounds described above.

In accordance with a further aspect of the present invention there is provided a method for preventing, inhibiting or suppressing a cell adhesion-associated immune or autoimmune response with the compounds described above.

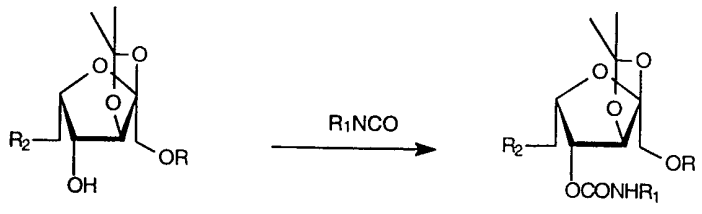
In accordance with another aspect of the present invention there is provided a method for treating or preventing a disease selected from the group consisting of asthma, arthritis, psoriasis, allograft rejection, multiple sclerosis, diabetes and inflammatory bowel disease, with the compounds as described above.

The compounds of the present invention are novel and exhibit significant potency in terms of their activity, which was determined by *in vitro* VLA_4-mediated cell adhesion assay and *in vivo* mouse ear swelling test. The compounds that were found active in *in vitro* assay were tested *in vivo*. Some of the compounds of the present invention were found to be potent VLA_4 antagonists. Therefore, the present invention provides the pharmaceutical compositions for the possible treatment of bronchial asthma and other inflammatory and autoimmune disorders. In addition, the compounds of the above invention can be administered orally or parenterally.

DETAILED DESCRIPTION OF THE INVENTION

The compounds of the present invention may be prepared by techniques well-known in the art and familiar to the average synthetic organic chemist. In addition, the compounds of the present invention may be prepared by the following novel and inventive reaction sequence, which also show preferred R, R_1 and R_2 groups.

SCHEME I



FORMULA II FORMULA I

2,3-0-Isopropyl-1-0-alkyl or arylalkyl-6-deoxy-6-aminosubstituted-L-xylo-2-hexulofuranose compounds of Formula II, as shown in Scheme I, are prepared according to the method described in U.S. Pat. No. 5,637,570 and are the intermediates for the synthesis of the compounds of Formula I of the present invention. Thus, the following intermediates were prepared following the process as described in U.S. Pat. No. 5,637,570:

2,3-O-isopropylidene-6-deoxy-6-hexamethyleneimino-1-O-dodecyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-6-deoxy-6-hexamethyleneimino-1-O-decyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-6-deoxy-6-hexamethyleneimino-1-O-heptyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-6-deoxy-6-pyrrolidinyl-1-O-dodecyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-6-deoxy-6-pyrrolidinyl-1-O-decyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-6-deoxy-6-pyrrolidinyl-1-O-heptyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-6-deoxy-6-morphilinyl-1-O-dodecyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-6-deoxy-6-morphilinyl-1-O-decyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-6-deoxy-6-morphilinyl-1-O-heptyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-6-deoxy-6-piperidinyl-1-O-dodecyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-6-deoxy-6-piperidinyl-1-O-decyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-6-deoxy-6-piperidinyl-1-O-heptyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-6-deoxy-6-ethylpyrrolidinyl-1-O-dodecyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-6-deoxy-6-ethylpyrrolidinyl-1-O-decyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-6-deoxy-6-ethylpyrrolidinyl-1-O-heptyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-6-deoxy-6-ethylmorpholinyl-1-O-dodecyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-6-deoxy-6-ethylmorpholinyl-1-O-decyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-6-deoxy-6-ethylmorpholinyl-1-O-heptyl-α-L-xylo-2-hexulofuranose.

Thus, the compound of Formula II is treated with an appropriate isocyanate in a suitable solvent at low temperature, preferably at 0–10° C to afford the compounds of Formula I of the present invention. An illustrative list of particular compounds according to the invention and capable of being produced by Scheme I include:

Compound No.	Chemical Name
01.	2,3-O-Isopropylidene-1-O-decyl-4-(methylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose
02.	2,3-O-Isopropylidene-1-O-dodecyl-4-(methylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose
03.	2,3-O-Isopropylidene-1-O-dodecyl-4-(phenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose
04.	2,3-O-Isopropylidene-1-O-dodecyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose
05.	2,3-O-Isopropylidene-1-O-dodecyl-4-(p-tolylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose
06.	2,3-O-Isopropylidene-1-O-dodecyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L- xylo-2-hexulofuranose
07.	2,3-O-Isopropylidene-1-O-dodecyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose
08.	2,3-O-Isopropylidene-1-O-decyl-4-(phenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose
09.	2,3-O-Isopropylidene-1-O-decyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose
10.	2,3-O-Isopropylidene-1-O-decyl-4-(p-tolylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose
11.	2,3-O-Isopropylidene-1-O-decyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

12. 2,3-O-Isopropylidene-1-O-decyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

13. 2,3-O-Isopropylidene-1-O-heptyl-4-(phenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

14. 2,3-O-Isopropylidene-1-O-heptyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

15. 2,3-O-Isopropylidene-1-O-heptyl-4-(p-tolylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

16. 2,3-O-Isopropylidene-1-O-heptyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

17. 2,3-O-Isopropylidene-1-O-heptyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

18. 2,3-O-Isopropylidene-1-O-dodecyl-4-(phenylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

19. 2,3-O-Isopropylidene-1-O-dodecyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

20. 2,3-O-Isopropylidene-1-O-dodecyl-4-(p-tolylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

21. 2,3-O-Isopropylidene-1-O-dodecyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

22. 2,3-O-Isopropylidene-1-O-dodecyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

23. 2,3-O-Isopropylidene-1-O-decyl-4-(phenylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

24. 2,3-O-Isopropylidene-1-O-decyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

25. 2,3-O-Isopropylidene-1-O-decyl-4-(p-tolylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

26. 2,3-O-Isopropylidene-1-O-decyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

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28. 2,3-O-Isopropylidene-1-O-heptyl-4-(phenylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

29. 2,3-O-Isopropylidene-1-O-heptyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

30. 2,3-O-Isopropylidene-1-O-heptyl-4-(p-tolylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

31. 2,3-O-Isopropylidene-1-O-heptyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

32. 2,3-O-Isopropylidene-1-O-heptyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

33. 2,3-O-Isopropylidene-1-O-dodecyl-4-(phenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

34. 2,3-O-Isopropylidene-1-O-dodecyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

35. 2,3-O-Isopropylidene-1-O-dodecyl-4-(p-tolylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

36. 2,3-O-Isopropylidene-1-O-dodecyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-piperidinyl-α-L-axylo-2-hexulofuranose

37. 2,3-O-Isopropylidene-1-O-dodecyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

38. 2,3-O-Isopropylidene-1-O-decyl-4-(phenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

39. 2,3-O-Isopropylidene-1-O-decyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

40. 2,3-O-Isopropylidene-1-O-decyl-4-(p-tolylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

41. 2,3-O-Isopropylidene-1-O-decyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

42. 2,3-O-Isopropylidene-1-O-decyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

43. 2,3-O-Isopropylidene-1-O-heptyl-4-(phenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

44. 2,3-O-Isopropylidene-1-O-heptyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

45. 2,3-O-Isopropylidene-1-O-heptyl-4-(p-tolylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

46. 2,3-O-Isopropylidene-1-O-heptyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

47. 2,3-O-Isopropylidene-1-O-heptyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

48. 2,3-O-Isopropylidene-1-O-dodecyl-4-(phenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

49. 2,3-O-Isopropylidene-1-O-dodecyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

50. 2,3-O-Isopropylidene-1-O-dodecyl-4-(p-tolylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

51. 2,3-O-Isopropylidene-1-O-dodecyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

52. 2,3-O-Isopropylidene-1-O-dodecyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

53. 2,3-O-Isopropylidene-1-O-decyl-4-(phenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

54. 2,3-O-Isopropylidene-1-O-decyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

55. 2,3-O-Isopropylidene-1-O-decyl-4-(p-tolylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

56. 2,3-O-Isopropylidene-1-O-decyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

57. 2,3-O-Isopropylidene-1-O-decyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

58. 2,3-O-Isopropylidene-1-O-heptyl-4-(phenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

59. 2,3-O-Isopropylidene-1-O-heptyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

60. 2,3-O-Isopropylidene-1-O-heptyl-4-(p-tolylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

61. 2,3-O-Isopropylidene-1-O-heptyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

62. 2,3-O-Isopropylidene-1-O-heptyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

63. 2,3-O-Isopropylidene-1-O-dodecyl-4-(phenylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose

64. 2,3-O-Isopropylidene-1-O-dodecyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose

65. 2,3-O-Isopropylidene-1-O-dodecyl-4-(p-tolylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose

66. 2,3-O-Isopropylidene-1-O-dodecyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose

67. 2,3-O-Isopropylidene-1-O-dodecyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose

68. 2,3-O-Isopropylidene-1-O-decyl-4-(phenylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose

69. 2,3-O-Isopropylidene-1-O-decyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose

70. 2,3-O-Isopropylidene-1-O-decyl-4-(p-tolylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose

71. 2,3-O-Isopropylidene-1-O-decyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose

72. 2,3-O-Isopropylidene-1-O-decyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose

73. 2,3-O-Isopropylidene-1-O-heptyl-4-(phenylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose

74. 2,3-O-Isopropylidene-1-O-heptyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose

75. 2,3-O-Isopropylidene-1-O-heptyl-4-(p-tolylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose

76. 2,3-O-Isopropylidene-1-O-heptyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose

77. 2,3-O-Isopropylidene-1-O-heptyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose

78. 2,3-O-Isopropylidene-1-O-dodecyl-4-(phenylcarbamate)-6-deoxy-6-(2-ethylpiperidinyl)-α-L-xylo-2-hexulofuranose

79. 2,3-O-Isopropylidene-1-O-dodecyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-(2-ethylpiperidinyl)-α-L-xylo-2-hexulofuranose

80. 2,3-O-Isopropylidene-1-O-dodecyl-4-(p-tolylcarbamate)-6-deoxy-6-(2-ethylpiperidinyl)-α-L-xylo-2-hexulofuranose

81. 2,3-O-Isopropylidene-1-O-dodecyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-(2-ethylpiperidinyl)-α-L-xylo-2-hexulofuranose

82. 2,3-O-Isopropylidene-1-O-dodecyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-(2-ethylpiperidinyl)-α-L-xylo-2-hexulofuranose

83. 2,3-O-Isopropylidene-1-O-decyl-4-(phenylcarbamate)-6-deoxy-6-(2-ethylpiperidinyl)-α-L-xylo-2-hexulofuranose

84. 2,3-O-Isopropylidene-1-O-decyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-(2-ethylpiperidinyl)-α-L-xylo-2-hexulofuranose

85. 2,3-O-Isopropylidene-1-O-decyl-4-(p-tolylcarbamate)-6-deoxy-6-(2-ethylpiperidinyl)-α-L-xylo-2-hexulofuranose

86. 2,3-O-Isopropylidene-1-O-decyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-(2-ethylpiperidinyl)-α-L-xylo-2-hexulofuranose

87. 2,3-O-Isopropylidene-1-O-decyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-(2-ethylpiperidinyl)-α-L-xylo-2-hexulofuranose

88. 2,3-O-Isopropylidene-1-O-heptyl-4-(phenylcarbamate)-6-deoxy-6-(2-ethylpiperidinyl)-α-L-xylo-2-hexulofuranose

89. 2,3-O-Isopropylidene-1-O-heptyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-(2-ethylpiperidinyl)-α-L-xylo-2-hexulofuranose

90. 2,3-O-Isopropylidene-1-O-heptyl-4-(p-tolylcarbamate)-6-deoxy-6-(2-ethylpiperidinyl)-α-L-xylo-2-hexulofuranose

91. 2,3-O-Isopropylidene-1-O-heptyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-(2-ethylpiperidinyl)-α-L-xylo-2-hexulofuranose

92. 2,3-O-Isopropylidene-1-O-heptyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-(2-ethylpiperidinyl)-α-L-xylo-2-hexulofuranose

93. 2,3-O-Isopropylidene-1-O-dodecyl-4-(phenylcarbamate)-6-deoxy-6-(2-ethylmorphilinyl)-α-L-xylo-2-hexulofuranose

94. 2,3-O-Isopropylidene-1-O-dodecyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-(2-ethylmorphilinyl)-α-L-xylo-2-hexulofuranose

95. 2,3-O-Isopropylidene-1-O-dodecyl-4-(p-tolylcarbamate)-6-deoxy-6-(2-ethylmorphilinyl)-α-L-xylo-2-hexulofuranose

96. 2,3-O-Isopropylidene-1-O-dodecyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-(2-ethylmorphilinyl)-α-L-xylo-2-hexulofuranose

97. 2,3-O-Isopropylidene-1-O-dodecyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-(2-ethylmorphilinyl)-α-L-xylo-2-hexulofuranose

98. 2,3-O-Isopropylidene-1-O-decyl-4-(phenylcarbamate)-6-deoxy-6-(2-ethylmorphilinyl)-α-L-xylo-2-hexulofuranose

99. 2,3-O-Isopropylidene-1-O-decyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-(2-ethylmorphilinyl)-α-L-xylo-2-hexulofuranose

100. 2,3-O-Isopropylidene-1-O-decyl-4-(p-tolylcarbamate)-6-deoxy-6-(2-ethylmorphilinyl)-α-L-xylo-2-hexulofuranose

101. 2,3-O-Isopropylidene-1-O-decyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-(2-ethylmorphilinyl)-α-L-xylo-2-hexulofuranose

102. 2,3-O-Isopropylidene-1-O-dodecyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-(2-ethylmorphilinyl)-α-L-xylo-2-hexulofuranose

103. 2,3-O-Isopropylidene-1-O-heptyl-4-(phenylcarbamate)-6-deoxy-6-(2-ethylmorphilinyl)-α-L-xylo-2-hexulofuranose

104. 2,3-O-Isopropylidene-1-O-heptyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-(2-ethylmorphilinyl)-α-L-xylo-2-hexulofuranose

105. 2,3-O-Isopropylidene-1-O-heptyl-4-(p-tolylcarbamate)-6-deoxy-6-(2-ethylmorphilinyl)-α-L-xylo-2-hexulofuranose

106. 2,3-O-Isopropylidene-1-O-heptyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-(2-ethylmorphilinyl)-α-L-xylo-2-hexulofuranose

107. 2,3-O-Isopropylidene-1-O-heptyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-(2-ethylmorphilinyl)-α-L-xylo-2-hexulofuranose

108. 2,3-O-Isopropylidene-1-O-dodecyl-4-(methylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

109. 2,3-O-Isopropylidene-1-O-dodecyl-4-(methylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

110. 2,3-O-Isopropylidene-1-O-dodecyl-4-(methylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

111. 2,3-O-Isopropylidene-1-O-dodecyl-4-(methylcarbamate)-6-deoxy-6-(2-ethylpyrroldinyl)-α-L-xylo-2-hexulofuranose

112. 2,3-O-Isopropylidene-1-O-dodecyl-4-(methylcarbamate)-6-deoxy-6-(2-ethylmorpholinyl)-α-L-xylo-2-hexulofuranose

113. 2,3-O-Isopropylidene-1-O-decyl-4-(methylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

114. 2,3-O-Isopropylidene-1-O-decyl-4-(methylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

115. 2,3-O-Isopropylidene-1-O-decyl-4-(methylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

116. 2,3-O-Isopropylidene-1-O-decyl-4-(methylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose

117. 2,3-O-Isopropylidene-1-O-decyl-4-(methylcarbamate)-6-deoxy-6-(2-ethylmorpholinyl)-α-L-xylo-2-hexulofuranose

118. 2,3-O-Isopropylidene-1-O-heptyl-4-(methylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

119. 2,3-O-Isopropylidene-1-O-heptyl-4-(methylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

120. 2,3-O-Isopropylidene-1-O-heptyl-4-(methylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

121. 2,3-O-Isopropylidene-1-O-heptyl-4-(methylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

122. 2,3-O-Isopropylidene-1-O-heptyl-4-(methylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose

123. 2,3-O-Isopropylidene-1-O-heptyl-4-(methylcarbamate)-6-deoxy-6-(2-ethylmorpholinyl)-α-L-xylo-2-hexulofuranose.

The sugar derivatives of the present invention exhibit various pharmacological properties and are useful for treating animals, the term animal as defined herein includes human or mammal, with various inflammatory and autoimmune disorders, such as bronchial asthma, rheumatoid arthritis, type I diabetes, multiple sclerosis, allograft rejection and psoriasis.

The free amino compounds of the present invention are basic and form organic and inorganic acid salts. The resulting salts are useful by themselves and in the therapeutic composition and method of use. These salts may be prepared by the usual prior art techniques, such as suspending the compound in water and then adding one equivalent of the desired organic or mineral acid. Examples of preferred acids include hydrochloric, sulphuric, nitric, maleic, benzoic, tartaric, acetic, p-aminobenzoic, oxalic, succinic and glucoronic acid.

The neutral solution of the resulting salt is subjected to rotary evaporation under diminished pressure to the volume necessary to ensure precipitation of the salt upon cooling, which is then filtered and dried. The salts of the present invention may also be prepared strictly under non-aqueous conditions. For example, dissolving the free amine in a suitable organic solvent, adding exactly one equivalent of the desired acid to the same solvent and stirring the solution at 0–5° C causes precipitation of the amine salt, which is then filtered, washed with solvent and dried. The amine salts are often preferred for use in formulating the therapeutic compositions as they are crystalline and relatively more stable and non-hydroscopic. The amine salts are also better adapted for intramuscular injection than are the free amines.

Because of their valuable pharmacological properties, the compounds of the present invention may be administered to an animal for treatment orally, topically, rectally, internasally or by parenteral route. When the therapeutic composition is to be administered orally, it is preferred that the compounds of the present invention are admixed with a filler and/or binder, such as starch and a disintegrator. The admixture may be pressed into a tablet conveniently sized for oral administration. Capsules may also be filled with the powdered therapeutic composition for oral administration. Alternatively, a water solution of the amine salt or suspension of the therapeutic composition may be admixed with a flavored syrup and administered orally. A salt of the free acid is usually preferred when the compound is administered by parenteral route.

The pharmaceutical compositions of the present invention are preferably produced and administered in dosage units, with each unit containing a certain amount of at least one compound of the invention and/or at least one physiologically acceptable base salt addition thereof. The dosage may be varied over extremely wide limits, as the compounds are effective at low dosage levels and relatively free of toxicity. The compounds may be administered in the low micromolar concentration, which is therapeutically effective, and the dosage may be increased as desired up to the maximum dosage tolerated by the patient.

The present invention also includes within its scope prodrugs of the compounds of Formula I. In general, such prodrugs will be functional derivatives of these compounds which are readily converted *in vivo* into the defined compounds. Conventional procedures for the selection and preparation of suitable prodrugs are known.

The present invention also includes the enantiomers, diastereomers, N-oxides, polymorphs and pharmaceutically acceptable salts of these compounds as well as metabolites having the same type of activity. This invention further includes pharmaceutical compositions comprising the molecules of Formula I or prodrugs, metabolite enantiomers, diastereomers, N-oxides, polymorphs or pharmaceutically acceptable salts thereof, in combination with pharmaceutically acceptable carriers and optionally included excipients.

The examples mentioned below demonstrate the general synthetic procedure as well as the specific preparation of the preferred compounds. The examples are provided to illustrate the details of the invention and should not be considered to limit the scope of the present invention.

EXPERIMENTAL DETAILS

Various solvents, such as acetone, methanol, pyridine, ether, tetrahydrofuran, hexane and dichloromethane, were dried using various drying agents according to the procedure described in the literature. Wet solvents gave poor yields of the products and intermediates. IR spectra were recorded as nujol mulls or a thin neat film on a Perkin Elmer Paragon instrument. Nuclear Magnetic Resonance (NMR) data (H, C) were recorded using a Varian XL-300 MHz instrument using tetramethylsilane as an internal standard. Chemical Ionization Mass Spectra (CIMS) were obtained using a Finnigan MAT-4510 mass spectrometer equipped with an INCOS data system. Generally, a direct exposure probe and methane as the reagent gas (0.33 mmHg, 120° C source temperature) were used.

EXAMPLE 1

Preparation of 2,3-O-isopropylidene-1-O-dodecyl-4-(phenylcarbamate)-6-deoxy-6-hexa-methyleneimino-α-L-xylo-2-hexulofuranose.

2,3-O-Isopropylidene-1-O-dodecyl-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose (prepared according to the method described in U.S. Pat. No. 5,637,570) (2.0 gm) was dissolved in dry methylene chloride (20 ml). To this solution was added phenyl isocyanate (0.64 gm) dropwise at 0–10° C

and the reaction mixture was stirred at the same temperature for 2 hours. It was then washed with water (2 times 5 ml) and brine (2 times 5 ml). The organic layer was dried and the solvent was removed. The crude product so obtained was purified by column chromatography and eluted with 50% ethylacetate in hexane. Pure product yield: 61%.

The following compounds were synthesized similarly by reacting 2,3-O-isopropylidene-1-O-dodecyl-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose with a suitable isocyanate:

2,3-O-isopropylidene-1-O-dodecyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-dodecyl-4-(p-tolylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-dodecyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-dodecyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-dodecyl-4-(methylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose.

EXAMPLE 2

Preparation of 2,3-O-isopropylidene-1-O-decyl-4-(phenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose.

2,3-O-isopropylidene-1-O-dodecyl-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose (prepared as described in Example 1 by replacing the

hexamethyleneimino group with pyrrolidine at position 6) (1.9 gm) was dissolved in methylene chloride (20 ml). To this solution was added phenyl isocyanate (0.56 gm) dropwise at 0–10° C and the reaction mixture was stirred at the same temperature for 2 hours. The organic layer was washed with water (2 times 10 ml), followed by saturated solution of sodium chloride (2 times 10 ml), dried over anhydrous sodium sulfate and filtered. The solvent was removed with rotary evaporation. The crude product so obtained was purified by flash chromatography using silica gel and eluted with 30% ethylacetate in hexane. Pure product yield: 53.80% (1.0 gm).

The following compounds were synthesized similarly by reacting 2,3-O-isopropylidene-1-O-dodecyl-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose with a suitable isocyanate:

2,3-O-isopropylidene-1-O-dodecyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-dodecyl-4-(p-tolylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-dodecyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-dodecyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-dodecyl-4-(methylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose.

EXAMPLE 3

Preparation of 2,3-O-isopropylidene-1-O-decyl-4-(phenylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose.

2,3-O-Isopropylidene-1-O-dodecyl-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose (prepared as described in Example 1 by replacing the hexamethyleneimino group with the morpholine group at position 6) (2.0 gm) was dissolved in methylene chloride (20 ml). To this solution was added phenyl isocyanate (1.0 ml) dropwise at 0–10° C and the reaction mixture was stirred at the same temperature for 2 hours. The organic layer was washed with water (2 times 10 ml), followed by saturated solution of sodium chloride (2 times 10 ml), dried over anhydrous sodium sulfate and filtered. The solvent was removed with rotary evaporation. The crude product so obtained was purified by flash chromatography using silica gel and eluted with 30% ethylacetate in hexane. Pure product yield: 54.6% (1.20 gm).

The following compounds were synthesized similarly by reacting 2,3-O-isopropylidene-1-O-dodecyl-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose with a suitable isocyanate:

2,3-O-isopropylidene-1-O-dodecyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-dodecyl-4-(p-tolylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-dodecyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-dodecyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-dodecyl-4-(methylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose.

EXAMPLE 4

Preparation of 2,3-O-isopropylidene-1-O-dodecyl-4-(phenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose.

2,3-O-Isopropylidene-1-O-dodecyl-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose (prepared as described in Example 1 by replacing the hexamethyleneimino group with the piperidino group at position 6) (2.0 gm) was dissolved in methylene chloride (20 ml). To this solution was added phenyl isocyanate (0.58 gm) dropwise at 0–10° C and the reaction mixture was stirred at the same temperature for 2 hours. The reaction was monitored with thin layer chromatography (TLC). The organic layer was washed with water (2 times 10 ml), followed by saturated solution of sodium chloride (2 times 10 ml), dried over anhydrous sodium sulfate and filtered. The solvent was removed with rotary evaporation. The crude product so obtained was purified by flash chromatography using silica gel and eluted with 30% ethylacetate in hexane. Pure product yield: 35.1% (0.90 gm).

The following compounds were synthesized similarly by reacting 2,3-O-isopropylidene-1-O-dodecyl-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose with a suitable isocyanate:

2,3-O-isopropylidene-1-O-dodecyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-dodecyl-4-(p-tolylcarbamate)-6-deoxy-6-piperidinol-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-dodecyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-dodecyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-dodecyl-4-(methylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose.

EXAMPLE 5

Preparation of 2,3-O-isopropylidene-1-O-decyl-4-(phenylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose.

2,3-O-Isopropylidene-1-O-dodecyl-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose (prepared as described in Example 1 by replacing the hexamethyleneimino group with the 2-ethylpyrrolidinyl group at position 6) (1.5 gm) was dissolved in methylene chloride (20 ml). To this solution was added phenyl isocyanate (1.0 ml) dropwise at 0–10° C and the reaction mixture was stirred at the same temperature for 2 hours. The reaction was monitored with TLC. The organic layer was washed with water (2 times 10 ml), followed by saturated solution of sodium chloride (2 times 10 ml), dried over anhydrous sodium sulfate and filtered. The solvent was removed with rotary evaporation. The crude product so obtained was purified by flash

chromatography using silica gel and eluted with 30% ethylacetate in hexane. Pure product yield: 60.2% (1.1 gm).

The following compounds were synthesized similarly by reacting 2,3-O-isopropylidene-1-O-dodecyl-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose with a suitable isocyanate:

2,3-O-isopropylidene-1-O-dodecyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-dodecyl-4-(p-tolylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-dodecyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-dodecyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-dodecyl-4-(methylcarbamate)-6-deoxy-6-(2-ethylpyrroldinyl)-α-L-xylo-2-hexulofuranose.

EXAMPLE 6

Preparation of 2,3,O-isopropylidene-1-O-dodecyl-4-(phenylcarbamate)-6-deoxy-6-(2-ethylmorpholinyl)-α-L-xylo-2-hexulofuranose.

2,3-O-Isopropylidene-1-O-dodecyl-6-deoxy-6-(2-ethylmorpholinyl)-α-L-xylo-2-hexulofuranose (prepared as described in Example 1 by replacing the hexamethyleneimino group with the 2-ethylmorpholino group at position 6) (2.0 gm) was dissolved in methylene chloride (20 ml). To this solution was added phenyl isocyanate (0.56 gm) dropwise at 0–10° C and the reaction

mixture was stirred at the same temperature for 2 hours. The reaction was monitored with TLC. The organic layer was washed with water (2 times 10 ml), followed by saturated solution of sodium chloride (2 times 10 ml), dried over anhydrous sodium sulfate and filtered. The solvent was removed with rotary evaporation. The crude product so obtained was purified by flash chromatography using silica gel and eluted with 30% ethylacetate in hexane. Pure product yield: 30.4% (0.75 gm).

The following compounds were synthesized similarly by reacting 2,3-O-isopropylidene-1-O-dodecyl-6-deoxy-6-(2-ethylmorpholinyl)-α-L-xylo-2-hexulofuranose with a suitable isocyanate:

2,3-O-isopropylidene-1-O-dodecyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-(2-ethylmorpholinyl)-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-dodecyl-4-(p-tolylcarbamate)-6-deoxy-6-(2-ethylmorpholinyl)-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-dodecyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-(2-ethylmorpholinyl)-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-dodecyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-(2-ethylmorpholinyl)-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-dodecyl-4-(methylcarbamate)-6-deoxy-6-(2-ethylmorpholinyl)-α-L-xylo-2-hexulofuranose.

EXAMPLE 7

Preparation of 2,3,O-isopropylidene-1-O-decyl-4-(phenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose.

This compound was prepared according to method described in Example 2 by reacting 2,3-O-isopropylidene-1-O-decyl-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose with phenyl isocyanate at 0–10° C. Pure product yield: 58%.

The following compounds were synthesized similarly by reacting 2,3-O-isopropylidene-1-O-decyl-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose with the desired isocyanate:

2,3-O-isopropylidene-1-O-dodecyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-dodecyl-4-(p-tolylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-dodecyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-dodecyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-dodecyl-4-(methylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose.

EXAMPLE 8

Preparation of 2,3,O-isopropylidene-1-O-decyl-4-(phenylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose.

This compound was prepared according to the method described in Example 3 by reacting 2,3-O-isopropylidene-1-O-decyl-6-deoxy-6-

morpholinyl-α-L-xylo-2-hexulofuranose with phenyl isocyanate at 0–10° C. Pure product yield: 61%.

The following compounds were synthesized similarly by reacting 2,3-O-isopropylidene-1-O-decyl-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose with the desired isocyanate:

2,3-O-isopropylidene-1-O-decyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-decyl-4-(p-tolylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-decyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-decyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-decyl-4-(methylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose.

EXAMPLE 9

Preparation of 2,3-O-isopropylidene-1-O-decyl-4-(phenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose.

This compound was prepared according to the method described in Example 1 by reacting 2,3-O-isopropylidene-1-O-decyl-6-deoxy-6 examethyleneimino-α-L-xylo-2-hexulofuranose with phenyl isocyanate at 0–10° C. Pure product yield: 69%.

The following compounds were synthesized similarly by reacting 2,3-O-isopropylidene-1-O-decyl-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose with the desired isocyanate:

2,3-O-isopropylidene-1-O-decyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-decyl-4-(p-tolylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-decyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-decyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-decyl-4-(methylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose.

EXAMPLE 10

Preparation of 2,3-O-isopropylidene-1-O-decyl-4-(phenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose.

This compound was prepared according to the method described in Example 3 by reacting 2,3-O-isopropylidene-1-O-decyl-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose with phenyl isocyanate at 0–10° C. Pure product yield: 74%.

The following compounds were synthesized similarly by reacting 2,3-O-isopropylidene-1-O-decyl-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose with the desired isocyanate:

2,3-O-isopropylidene-1-O-decyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-decyl-4-(p-tolylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-decyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-decyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-decyl-4-(methylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose.

EXAMPLE 11

Preparation of 2,3-O-isopropylidene-1-O-decyl-4-(phenylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose.

This compound was prepared according to the method described in Example 3 by reacting 2,3-O-isopro-pylidene-1-O-decyl-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose with phenyl isocyanate at 0–10° C. Pure product yield: 74%.

The following compounds were synthesized similarly by reacting 2,3-O-isopropylidene-1-O-decyl-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose with the desired isocyanate:

2,3-O-isopropylidene-1-O-decyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-decyl-4-(p-tolylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-decyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-decyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-decyl-4-(methylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose.

EXAMPLE 12

Preparation of 2,3-O-isopropylidene-1-O-decyl-4-(phenylcarbamate)-6-deoxy-6-(2-ethylmorpholinyl)-α-L-xylo-2-hexulofuranose.

This compound was prepared according to the method described in Example 3 by reacting 2,3-O-isopropylidene-1-O-decyl-6-deoxy-6-(2-ethylmorpholinyl)-α-L-xylo-2-hexulofuranose with phenyl isocyanate at 0–10° C. Pure product yield: 72%.

The following compounds were synthesized similarly by reacting 2,3-O-isopropylidene-1-O-decyl-6-deoxy-6-(2-ethylmorpholinyl)-α-L-xylo-2-hexulofuranose with the desired isocyanate:

2,3-O-isopropylidene-1-O-decyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-(2-ethylmorpholinyl)-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-decyl-4-(p-tolylcarbamate)-6-deoxy-6-(2-ethylmorpholinyl)-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-decyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-(2-ethylmorpholinyl)-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-decyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-(2-ethylmorpholinyl)-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-decyl-4-(methylcarbamate)-6-deoxy-6-(2-ethylmorpholinyl)-α-L-xylo-2-hexulofuranose.

EXAMPLE 13

Preparation of 2,3-O-isopropylidene-1-O-heptyl-4-(phenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose.

This compound was prepared according to the method described in Example 2 by reacting 2,3-O-isopropylidene-1-O-heptyl-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose with phenyl isocyanate at 0–10° C. Pure product yield: 85.4%

The following compounds were synthesized similarly by reacting 2,3-O-isopropylidene-1-O-heptyl-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose with the desired isocyanate:

2,3-O-isopropylidene-1-O-heptyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-heptyl-4-(p-tolylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-heptyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-heptyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-heptyl-4-(methylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose.

EXAMPLE 14

Preparation of 2,3-O-isopropylidene-1-O-heptyl-4-(phenylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose.

This compound was prepared according to the method described in Example 3 by reacting 2,3-O-isopropylidene-1-O-heptyl-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose with phenyl isocyanate at 0–10° C. Pure product yield: 79%.

The following compounds were synthesized similarly by reacting 2,3-O-isopropylidene-1-O-decyl-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose with the desired isocyanate:

2,3-O-isopropylidene-1-O-heptyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-heptyl-4-(p-tolylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-heptyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-heptyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-heptyl-4-(methylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose.

EXAMPLE 15

Preparation of 2,3-O-isopropylidene-1-O-heptyl-4-(phenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose.

This compound was prepared according to the method described in Example 3 by reacting 2,3-O-isopropylidene-1-O-heptyl-6-deoxy-6-hexamethylene-imino-α-L-xylo-2-hexulofuranose with phenyl isocyanate at 0–10° C. Pure product yield: 91%.

The following compounds were synthesized similarly by reacting 2,3-O-isopropylidene-1-O-heptyl-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose with the desired isocyanate:

2,3-O-isopropylidene-1-O-heptyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-heptyl-4-(p-tolylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-heptyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-heptyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-heptyl-4-(methylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose.

EXAMPLE 16

Preparation of 2,3-O-isopropylidene-1-O-heptyl-4-(phenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose.

This compound was prepared according to the method described in Example 3 by reacting 2,3-O-isopropylidene-1-O-heptyl-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose with phenyl isocyanate at 0–10° C. Pure product yield: 47.6%.

The following compounds were synthesized similarly by reacting 2,3-O-isopropylidene-1-O-heptyl-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose with the desired isocyanate:

2,3-O-isopropylidene-1-O-heptyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-heptyl-4-(p-tolylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-heptyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-heptyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-heptyl-4-(methylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose.

EXAMPLE 17

Preparation of 2,3-O-isopropylidene-1-O-heptyl-4-(phenylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose.

This compound was prepared according to the method described in Example 3 by reacting 2,3-O-isopropylidene-1-O-heptyl-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose with phenyl isocyanate at 0–10° C. Pure product yield: 68%.

The following compounds were synthesized similarly by reacting 2,3-O-isopropylidene-1-O-heptyl-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose with the desired isocyanate:

2,3-O-isopropylidene-1-O-heptyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-heptyl-4-(p-tolylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-heptyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-heptyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-heptyl-4-(methylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose.

EXAMPLE 18

Preparation of 2,3-O-isopropylidene-1-O-heptyl-4-(phenylcarbamate)-6-deoxy-6-(2-ethylmorpholinyl)-α-L-xylo-2-hexulofuranose.

This compound was prepared similarly according to the method described in Example 3 by reacting 2,3-O-isopropylidene-1-O-heptyl-6-deoxy-

6-(2-ethylmorpholinyl)-α-L-xylo-2-hexulofuranose with phenyl isocyanate at 0–10° C. Pure product yield: 75.8%.

The following compounds were synthesized similarly by reacting the 2,3-O-isopropylidene-1-O-heptyl-6-deoxy-6-(2-ethylmorpholinyl)-α-L-xylo-2-hexulofuranose with the desired isocyanate:

2,3-O-isopropylidene-1-O-heptyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-(2-ethylmorpholinyl)-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-heptyl-4-(p-tolylcarbamate)-6-deoxy-6-(2-ethylmorpholinyl)-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-heptyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-(2-ethylmorpholinyl)-α-L-xylo-2-hexulofuranose

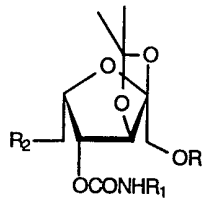
2,3-O-isopropylidene-1-O-heptyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-(2-ethylmorpholinyl)-α-L-xylo-2-hexulofuranose

2,3-O-isopropylidene-1-O-heptyl-4-(methylcarbamate)-6-deoxy-6-(2-ethylmorpholinyl)-α-L-xylo-2-hexulofuranose.

While the present invention has been described in terms of its specific embodiments, certain modifications and equivalents will be apparent to those skilled in the art and are intended to be included within the scope of this invention, which is to be limited only by the scope of the appended claims.

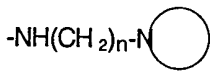
CLAIMS

1. Compounds having the structure of Formula I:



FORMULA I

and their pharmaceutically acceptable salts, esters, enantiomers, diastereomers, N-oxides, amides, prodrugs, metabolites or polymorphs, wherein R is C_1 to C_{15} alkyl, alkene, alkyne (straight chain or branched), aryl, substituted aryl or alkylaryl and R_1 is phenyl o-, m- or p-chlorophenyl, tolyl, methoxyphenyl or nitrophenyl and R_2 is H, pyrrolidinyl, piperidinyl, morpholinyl or hexamethyleneimino or a radical of the formula NHR_3, wherein R_3 is C_1 to C_{15} alkyl, alkene or alkyne (straight chain or branched) or a radical of Formula III:



FORMULA III

wherein n is a whole number up to 5 and

is a five-, six- or seven-membered heterocyclic ring containing one or more heteroatoms.

2. The compounds of claim 1, wherein 

is pyrrolidinyl, piperidinyl, morpholinyl or hexamethyleneimino.

3. Compounds according to claim 1 selected from the group consisting of:

2,3-O-Isopropylidene-1-O-decyl-4-(methylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(methylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(phenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(p-tolylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(phenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(p-tolylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(phenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(p-tolylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(phenylcarbamate)-6-deoxy-6-morphilinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-morphilinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(p-tolylcarbamate)-6-deoxy-6-morphilinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-morphilinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-morphilinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(phenylcarbamate)-6-deoxy-6-morphilinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-morphilinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(p-tolylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(phenylcarbamate)-6-deoxy-6-morphilinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-morphilinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(p-tolylcarbamate)-6-deoxy-6-morphilinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-morphilinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-morphilinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(phenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(p-tolylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(phenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(p-tolylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(phenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose)

2,3-O-Isopropylidene-1-O-heptyl-4-(p-tolylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(phenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(p-tolylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(phenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(p-tolylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(phenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(p-tolylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(phenylcarbamate)-6-deoxy-6-ethylpyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-ethylpyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(p-tolylcarbamate)-6-deoxy-6-ethylpyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-ethylpyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-ethylpyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(phenylcarbamate)-6-deoxy-6-ethylpyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-ethylpyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(p-tolylcarbamate)-6-deoxy-6-ethylpyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-ethylpyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-ethylpyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(phenylcarbamate)-6-deoxy-6-ethylpyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-ethylpyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(p-tolylcarbamate)-6-deoxy-6-ethylpyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-ethylpyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-ethylpyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(phenylcarbamate)-6-deoxy-6-ethylpiperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-ethylpiperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(p-tolylcarbamate)-6-deoxy-6-ethylpiperidinyl-α-L-xylo-2-hexulofuranose

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2,3-O-Isopropylidene-1-O-dodecyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-ethylpiperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(phenylcarbamate)-6-deoxy-6-ethylpiperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-ethylpiperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(p-tolylcarbamate)-6-deoxy-6-ethylpiperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-ethylpiperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-ethylpiperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(phenylcarbamate)-6-deoxy-6-ethylpiperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-ethylpiperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(p-tolylcarbamate)-6-deoxy-6-ethylpiperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-ethylpiperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-ethylpiperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(phenylcarbamate)-6-deoxy-6-ethylmorphilinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-ethylmorphilinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(p-tolylcarbamate)-6-deoxy-6-ethylmorphilinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-ethylmorphilinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-ethylmorphilinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(phenylcarbamate)-6-deoxy-6-ethylmorphilinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-ethylmorphilinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(p-tolylcarbamate)-6-deoxy-6-ethylmorphilinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(p-methoxyphenylcarbamate)-6deoxy-6-ethylmorphilinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-ethylmorphilinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(phenylcarbamate)-6-deoxy-6-ethylmorphilinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(p-chlorophenylcarbamate)-6-deoxy-6-ethylmorphilinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(p-tolylcarbamate)-6-deoxy-6-ethylmorphilinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(p-methoxyphenylcarbamate)-6-deoxy-6-ethylmorphilinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(p-nitrophenylcarbamate)-6-deoxy-6-ethylmorphilinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(methylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(methylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(methylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(methylcarbamate)-6-deoxy-6-(2-ethylpyrroldinyl)-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-dodecyl-4-(methylcarbamate)-6-deoxy-6-(2-ethylmorpholinyl)-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(methylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(methylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(methylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(methylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-decyl-4-(methylcarbamate)-6-deoxy-6-(2-ethylmorpholinyl)-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(methylcarbamate)-6-deoxy-6-pyrrolidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(methylcarbamate)-6-deoxy-6-morpholinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(methylcarbamate)-6-deoxy-6-hexamethyleneimino-α-L-xylo-2-hexulofuranose

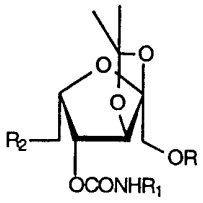
2,3-O-Isopropylidene-1-O-heptyl-4-(methylcarbamate)-6-deoxy-6-piperidinyl-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(methylcarbamate)-6-deoxy-6-(2-ethylpyrrolidinyl)-α-L-xylo-2-hexulofuranose

2,3-O-Isopropylidene-1-O-heptyl-4-(methylcarbamate)-6-deoxy-6-(2-ethylmorpholinyl)-α-L-xylo-2-hexulofuranose.

4. A pharmaceutical composition comprising a pharmaceutically effective amount of a compound as defined in claims 1, 2 or 3 and a pharmaceutically acceptable carrier.

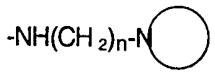
5. A process, according to claim 1, for preparing compounds of Formula I:



FORMULA I

and their pharmaceutically acceptable salts, esters, enantiomers, diastereomers, N-oxides, amides, prodrugs, metabolites or polymorphs, wherein R is C_1 to C_{15} alkyl, alkene, alkyne (straight chain or branched), aryl, substituted aryl or alkylaryl and R_1 is phenyl o-, m- or p-chlorophenyl, tolyl, methoxyphenyl or nitrophenyl and R_2 is H,

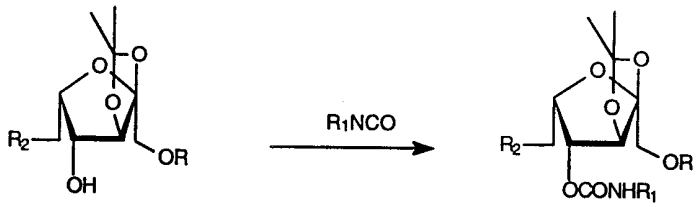
pyrrolidinyl, piperidinyl, morpholinyl or hexamethyleneimino or a radical of the formula NHR_3, wherein R_3 is C_1 to C_{15} alkyl, alkene or alkyne (straight chain or branched) or a radical of Formula III:



FORMULA III

wherein n is a whole number up to 5 and

is a five-, six- or seven-membered heterocyclic ring containing one or more heteroatoms, by treating the compound of Formula II with a suitable isocyanate and in a suitable solvent at low temperature as follows:

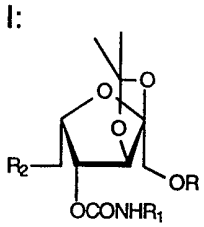


FORMULA II FORMULA I

6. A process according to claim 5, wherein

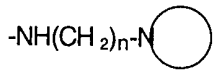
is pyrrolidinyl, piperidinyl, morpholinyl or hexamethyleneimino.

7. The method of preventing, inhibiting or suppressing cell adhesion in an animal comprising administering to said animal, a compound having the structure of Formula I:



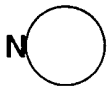
FORMULA I

and its pharmaceutically acceptable salts, esters, enantiomers, diastereomers, N-oxides, amides, prodrugs, metabolites, or polymorphs, wherein R is C_1 to C_{15} alkyl, alkene, alkyne (straight chain or branched), aryl, substituted aryl or alkylaryl and R_1 is phenyl, o,- m- or p-chlorophenyl, tolyl, methoxyphenyl or nitrophenyl and R_2 is H, pyrrolidinyl, piperidinyl, morphilinyl or hexamethyleneimino or a radical of the formula NHR_3, wherein R_3 is C_1 to C_{15} alkyl, alkene or alkyne (straight chain or branched) or a radical of Formula III:



FORMULA III

in which n is a whole number up to 5 and

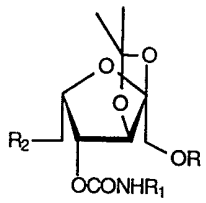


is a five-, six- or seven-membered heterocyclic ring containing one or more heteroatoms.

8. The method of claim 7, wherein

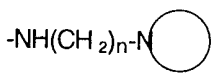
is pyrrolidinyl, piperidinyl, morpholinyl or hexamethyleneimino moieties.

9. A method for treating an animal suffering from bronchial asthma, rheumatoid arthritis, multiple sclerosis, type I diabetes, psoriasis, allograft rejection, and other inflammatory and/or autoimmune disorders in an animal comprising administering to said animal a compound of the structure of Formula I:



FORMULA I

wherein R is C_1 to C_{15} alkyl, alkene, alkyne (straight chain or branched), aryl, substituted aryl or alkylaryl and R_1 is phenyl, o,- m- or p-chlorophenyl, tolyl, methoxyphenyl or nitrophenyl and R_2 is H, pyrrolidinyl, piperidinyl, morphilinyl or hexamethyleneimino or a radical of formula NHR_3,wherein R_3 is C_1 to C_{15} alkyl, alkene or alkyne (straight chain or branched) or a radical of Formula III:



FORMULA III

in which n is a whole number up to 5 and

is a five-, six- or seven-membered heterocyclic ring containing one or more heteroatoms.

10. The method of claim 9, wherein

is pyrrolidinyl, piperidinyl, morpholinyl or hexamethyleneimino.

11. The method of preventing, inhibiting or suppressing cell adhesion in an animal comprising the step of administering to said animal the pharmaceutical composition according to claim 4.

12. The method according to claim 7 wherein said method is used for preventing, inhibiting or suppressing cell adhesion-associated inflammation.

13. The method according to claim 7 wherein said method is used for preventing, inhibiting or suppressing a cell adhesion-associated immune or autoimmune response.

14. The method according to claim 7 or 9 wherein said method is used to treat or prevent a disease selected from the group consisting of asthma, arthritis, psoriasis, allograft rejection, multiple sclerosis, diabetes and inflammatory bowel disease.

INTERNATIONAL SEARCH REPORT

national Application No
PCT/IB 00/00022

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07H9/04 A61K31/70

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07H A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 379 397 A (GREENWICH PHARMA) 25 July 1990 (1990-07-25) abstract page 4, line 1 - line 16	1,4,5, 7-14
A	EP 0 404 136 A (GREENWICH PHARMA) 27 December 1990 (1990-12-27) claims 1-21	1,4,5, 7-14
A	WO 94 11381 A (GREENWICH PHARMA) 26 May 1994 (1994-05-26) abstract	1,4,5, 7-14

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
25 May 2000	13/06/2000
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Authorized officer Scott, J

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB 00/00022

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

national Application No
PCT/IB 00/00022

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