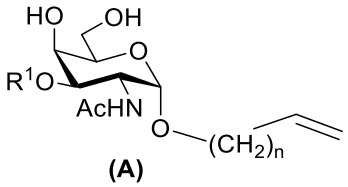
CLAIMS

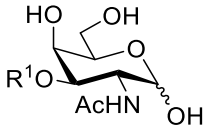
1. A process for synthesizing a reactive carbohydrate of Formula (A)



(A)

where R^1 is H and n is an integer from 1 to 5,

comprising ~~reacting, under heating,~~adding a compound of Formula (A_0)



(A_0)

~~with HO-$(CH_2)_n$-CH=CH_2 in the presence of an acid capable of liberating a proton, resulting in a reaction mixture comprising the compound of Formula (A), and~~to a solution comprising HO-$(CH_2)_n$-CH=CH_2 and acetyl chloride at a mixing temperature from about 0 °C to about 25 °C resulting in an intermediate reaction mixture at low temperature comprising the compound of Formula (A_0), HO-$(CH_2)_n$-CH=CH_2 and HCl,

heating the intermediate reaction mixture with a heat source at a temperature of from about 60 °C to about 80 °C, and

cooling the reaction mixture to obtain a cooled mixture comprising the compound of Formula (A).

~~2. The process of claim 1, wherein the acid comprises acetyl chloride, acetic acid, an acidic cation exchange resin, camphorsulfonic acid, p-toluenesulfonic acid monohydrate, HCl or any mixture thereof.~~

~~3. The process of claim 1 or 2, wherein the acid comprises acetyl chloride.~~

~~4. The process of any one of claims 1 to 3, wherein reacting the compound of Formula (A_0) comprises adding the compound of Formula (A_0) to a solution comprising HO-$(CH_2)_n$-CH=CH_2 and acetyl chloride at a mixing temperature from about 0 °C to about 25 °C resulting in an~~

~~intermediate reaction mixture at low temperature comprising the compound of Formula (A_0), $HO-(CH_2)_n-CH=CH_2$ and HCl.~~

~~5.~~2. The process of claim ~~4~~1, wherein the mixing temperature is ~~about 0 °C, or about 0 °C to about 10 °C, or about 0 °C to about 20 °C, or about 10 °C to about 20 °C,~~ about 10 °C to about 25 °C.

3. The process of claim 1, wherein the mixing temperature is about 10 °C to about 20 °C.

~~6.~~4. The process of any one of claim~~s 4 1 or 5~~to 3, wherein the solution comprising $HO-(CH_2)_n-CH=CH_2$ and acetyl chloride is prepared at a temperature of about 0 °C under inert atmosphere.

~~7. The process of any one of claims 4 to 6, wherein reacting the compound of Formula (A_0) comprises contacting the intermediate reaction mixture with a heat source at a temperature of from about 40 °C to about 80 °C.~~

~~8.~~5. The process of any one of claims 1 to ~~7~~4, wherein the heating is performed at a reaction temperature from about ~~40~~ 60 °C to about 80 °C for a reaction time of from about 30 minutes to 5 hours.

~~9. The process of claim 8, wherein the reaction temperature is from about 60 °C to about 80 °C.~~

~~10.~~6. The process of claim ~~8 or 9~~5, wherein the reaction temperature is about 70 °C.

~~11.~~7. The process of ~~any one of~~ claim~~s 8 to 10~~5 or 6, wherein the reaction time is from about 30 min to about 1 hour.

~~12.~~8. The process of any one of claims ~~8~~ 5 to ~~11~~7, wherein the reaction time is from about 30 min to about 45 min.

~~13.~~9. The process of any one of claims ~~8~~ 5 to ~~12~~8, wherein the reaction time is about 30 min.

~~14. The process of claim 1 or 2, wherein the acid comprises acetic acid, an acidic cation exchange resin, camphorsulfonic acid, p-toluenesulfonic acid monohydrate, HCl or any mixture thereof.~~

~~15. The process of claim 14, wherein reacting the compound of Formula (A_0) with HO-(CH_2)$_n$-CH=CH_2 comprises heating a solution comprising the compound of Formula (A_0), HO-(CH_2)$_n$-CH=CH_2 and the acid.~~

~~16. The process of claim 15, wherein the solution further comprises a solvent selected from the group consisting of dichoromethane, chloroform, 1,3-dioxolane, diethoxymethane, dimethoxymethane, 2,5,7,10-tetraoxaundecane, dipropoxymethane and any combination thereof.~~

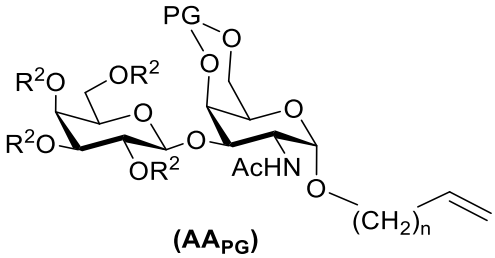
~~17. The process of claim 15 or 16, wherein the reaction is performed at a temperature of from about 30 °C to about 70 °C.~~

~~18. The process of any one of claims 15 to 17, wherein the reaction is performed for a reaction time of about 0.5 hour to about 15 hours, or from about 0.5 hour to about 10 hours, or from about 0.5 hour to about 5 hours, or from about 0.5 hour to about 2 hours.~~

~~19.~~10. The process of any one of claims 1 to ~~18~~9, further comprising neutralizing the cooled mixture.

~~20.~~11. The process of any one of claims 1 to ~~19~~10, further comprising isolating the compound of Formula (A).

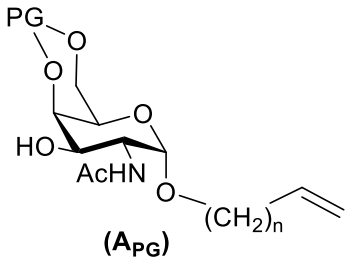
~~21.~~12. A process for synthesizing a reactive carbohydrate of Formula (AA_{PG})



(AA_{PG})

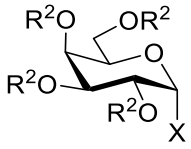
where R^2 is a monovalent protecting group, PG is a divalent protecting group and n is an integer from 1 to 5,

comprising reacting, in the presence of a metal-containing zeolite, a compound of Formula (A_{PG})



(A_{PG})

with a compound of Formula (A_1)



(A_1)

where X is -I, -Br, -Cl, -CN, -OTf (Triflate), -OMs (Mesylate), -OTs (Tosylate), methylsulfate, or trichloroacetimidate.

~~22. The process of claim 21, wherein the metal in the metal-containing zeolite comprises Ag, Al, Cd, Co, Cu, Fe, Ga, In, Mo, Pd, Pt, Sn, Sb, V, Zr or any mixture thereof.~~

~~23. The process of claim 21, wherein the metal-containing zeolite comprises a zeolite selected from the group consisting of Sn-Beta, Zr-Beta, Al-Beta(OH), Al-Beta(F), Pt@MCM-22, K-PtSn/MFI, 0.3Pt/0.5Sn-Si-Beta, Pt/Sn 2.0-Beta, 0.5CoSi-Beta, V-Beta, H-[Fe]ZSM-5, Fe-BEA, Ga-Beta, Ga-Beta-200, Mo/HZSM-5, or any mixture thereof.~~

~~24. The process of claim 21, wherein the metal-containing zeolite comprises a silver-containing zeolite.~~

~~25. The process of any one of claims 21 to 24, wherein the reaction is performed in an organic solvent selected from the group consisting of toluene, dichorometane-toluene mixture, DMSO-toluene mixture, and N-methylpyrrolidone-toluene mixture.~~

~~26. The process of any one of claims 21 to 25, wherein the reaction is performed in toluene.~~

~~27. The process of any one of claims 21 to 26, wherein the reaction is performed in the presence of a molecular sieve.~~

28. The process of any one of claims 21 to 27, wherein the reaction is performed in the presence of a molecular sieve of type 3Å, type 4Å, type 5Å, type 13X or any mixture thereof.

29. The process of any one of claims 21 to 28, wherein the reaction is performed at a temperature of from about 20°C to about 80°C.

30. The process of any one of claims 21 to 29, wherein the reaction is performed at a temperature of from about 20°C to about 50°C.

31. The process of any one of claims 21 to 30, wherein the reaction is performed at a temperature of from about 20°C to about 30°C.

32. The process of any one of claims 21 to 31, wherein the reaction is performed for about 5 hours to about 50 hours.

33. The process of any one of claims 21 to 32, wherein the reaction is performed for about 5 hours to about 30 hours.

34. The process of any one of claims 21 to 31, wherein the reaction is performed at about 60 to about 80 °C for about 15 hours to about 20 hours.

35. The process of any one of claims 21 to 31, wherein the reaction is performed at about 20 °C to about 25°C for about 20 hours to about 30 hours.

36. The process of any one of claims 21 to 35, wherein R^2 is selected from the group consisting of Ac, Bz, allyl, benzoate, methoxymethyl (MOM), tetrahydropropyranyl (THP), t-butyl, pivalate, t-butyldimethylsilyl (TBDMS) and t-butyldiphenylsilyl (TBDPS).

37. The process of any one of claims 21 to 36, wherein R^2 is Ac or Bz.

38. The process of any one of claims 21 to 37, wherein PG is selected from the group consisting of PhCH, Me_2C, O=C, Me_2Si and 2,6-bis(trifluoromethyl)phenyl-B.

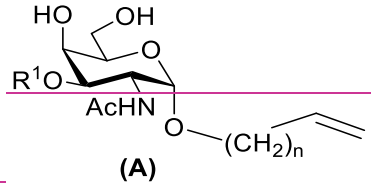
39. The process of any one of claims 21 to 38, wherein PG is PhCH.

~~40. The process of any one of claims 21 to 39, wherein X is Br.~~

~~41. The process of any one of claims 21 to 40, wherein the reaction is performed under inert atmosphere.~~

~~42. The process of any one of claims 21 to 41, further comprising isolating the compound of Formula (AA_{PG}).~~

~~43. The process of any one of claims 21 to 42, wherein the compound of Formula (A_{PG}) is formed by protecting a compound of Formula (A)~~



(A)

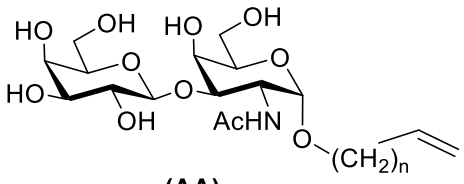
~~where R^1 is H, with the protecting group PG.~~

~~44. The process of claim 43, wherein protecting the compound of Formula (A) is performed by reaction with a compound selected from the group consisting of $PhCH(OMe)_2$, triphosgene, Me_2SiCl_2, $Me_2C(OMe)_2$, 2-methoxypropene and 2,6-bis(trifluoromethyl)phenylboronic ester.~~

~~45. The process of claim 43 or 44, wherein protecting the compound of Formula (A) is performed in an organic solvent selected from the group consisting of DMF, Dimethyl acetamide (DMAC), DMSO, THF, Dioxane, 1-3 Dioxolane, acetonitrile, 2,5-dimethyl tetrahydrofuran (DMTHF), Gamma-vaterolactone (GVL), Dihydrolevoglucoserone (Cyrene), methyl levulinate (ML), Ethyl levulinate (EL), Ethyl levulinate propyleneglycol ketal (ELPK), Dimethyl glutarate (DMG), Dimethylpropylene urea (DMPU), Poly(propyleneglycol) (PPG), Glycofurol (THFP), 1-Ethyl-3-methylimidazolium acetate ([emim][OAc]) and any combination thereof.~~

~~46. The process of any one of claims 43 to 45, wherein the compound of Formula (A) is obtained by the process of any one of claims 1 to 20.~~

~~47.~~13. A process for synthesizing a reactive carbohydrate of Formula (AA)



(AA)

where n is an integer from 1 to 5,

comprising deprotecting the compound of Formula (AA_{PG}) obtained by the process of ~~any one of~~ claim~~s 21 to 46~~12.

~~48. The process of claim 47, wherein deprotecting comprises reacting the compound of Formula (AA_{PG}) with a basic solution to form an intermediate product, and then treating the intermediate product with an acidic solution.~~

~~49. The process of claim 48, wherein the basic solution comprises a base is selected from the group consisting of a methoxide, ethoxide and 2-methylpropan-2-olate, preferably the base is sodium methoxide.~~

~~50. The process of claim 48 or 49, wherein the basic solution comprises a solvent selected from the group consisting of methanol, ethanol and isopropanol, preferably the solvent is methanol.~~

~~51. The process of any one of claims 48 to 50, wherein the acidic solution comprises an acetic acid-water mixture or an ethanolic acid-water mixture, preferably the acidic solution is an aqueous acetic acid solution.~~

~~52. The process of any one of claims 48 to 51, wherein the reaction with the basic solution is performed at a temperature of from about 0°C to about 50°C, preferably at room temperature.~~

~~53. The process any one of claims 48 to 52, wherein the reaction with the basic solution is performed for a period of about 0.5 hour to about 5 hours, preferably about 1 hour to about 2 hours.~~

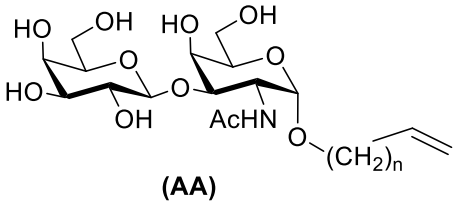
~~54. The process of any one of claims 48 to 53, wherein treating with the acidic solution is performed at a temperature of from about 50 °C to about 70 °C, preferably at about 60 °C.~~

~~55. The process of any one of claims 48 to 54, wherein treating with the acidic solution is performed for a period of about 1 hour to about 5 hours, preferably about 1 hour to about 2 hours.~~

~~56. The process of any one of claims 48 to 55, further comprising neutralizing the basic solution after reacting with the compound of Formula (AA_{PG}) and evaporating any liquid to afford the intermediate product in crude form.~~

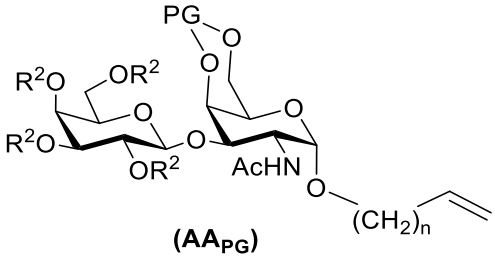
~~57. The process of any one of claims 48 to 56, wherein the intermediate product is crude when treated with the acidic solution.~~

~~58.~~14. A process for synthesizing a reactive carbohydrate of Formula (AA)



(AA)

comprising a deprotection a compound of Formula (AA_{PG})



(AA_{PG})

where n is an integer from 1 to 5, R^2 is a monovalent protecting group, and PG is a divalent protecting group,

the deprotection comprising reacting the compound of Formula (AA_{PG}) with a basic solution to form an intermediate crude product, and then treating the intermediate crude product with an acidic solution.

~~59. The process of claim 58, wherein the basic solution comprises a base selected from the group consisting of a methoxide, ethoxide and 2-methylpropan-2-olate, preferably the base is sodium methoxide.~~

~~60. The process of claim 58 or 59, wherein the basic solution comprises a solvent selected from the group consisting of methanol, ethanol and isopropanol, preferably the solvent is methanol.~~

~~61. The process of any one of claims 58 to 60, wherein the acidic solution comprises an acetic acid-water mixture or an ethanolic acid-water mixture, preferably the acidic solution is an aqueous acetic acid solution.~~

~~62. The process any one of claims 58 to 61, wherein the reaction with the basic solution is performed at a temperature of from about 0 °C to about 50 °C, preferably at room temperature.~~

~~63. The process any one of claims 58 to 62, wherein the reaction with the basic solution is performed for a period of about 0.5 hour to about 5 hours, preferably about 1 hour to about 2 hours.~~

~~64. The process of any one of claims 58 to 63, wherein treating with the acidic solution is performed at a temperature of from about 50 °C to about 70 °C, preferably at about 60 °C.~~

~~65. The process of any one of claims 58 to 64, wherein treating with the acidic solution is performed for a period of about 1 hour to about 5 hours, preferably about 1 hour to about 2 hours.~~

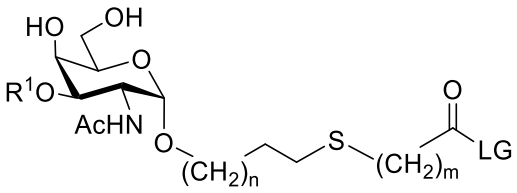
~~66. The process of any one of claims 58 to 65, further comprising neutralizing the basic solution after reacting with the compound of Formula (AA_{PG}) and evaporating any liquid to afford the intermediate crude product.~~

~~67. The process of any one of claims 58 to 66, wherein R^2 is Ac or Bz, preferably Bz.~~

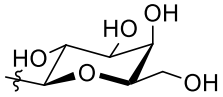
~~68. The process of any one of claims 58 to 67, wherein PG is selected from the group consisting of PhCH, Me_2C, O=C, Me_2Si and 2,6-bis(trifluoromethyl)phenyl-B.~~

~~69. The process of any one of claims 58 to 68, wherein PG is PhCH.~~

~~70.~~15. A process for synthesizing a reactive carbohydrate of Formula (B) or Formula (BB)

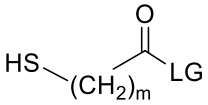


(B): R^1 is H

(BB): R^1 is 

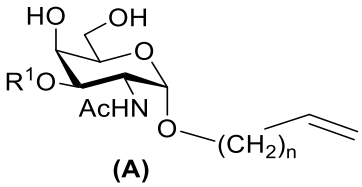
where n is an integer from 1 to 5, m is an integer from 1 to 5 and LG is a leaving group enabling an amido bond formation when the compound of Formula (B) or (BB) is reacted with an amino group,

comprising reacting a compound of Formula (C)



(C)

with a compound of Formula (A)

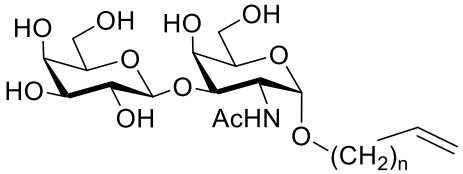


(A)

where R^1 is H, to form the compound of Formula (B)

or

with a compound of Formula (AA)



(AA)

to form the compound of Formula (BB).

~~71. The process of claim 70, wherein reacting the compound of Formula (C) with the compound of Formula (A) or (AA) is performed in the presence of a photoinitiator.~~

72. The process of claim 71, wherein the photoinitiator is selected from the group consisting of a free radical-generating azo compound, lithium phenyl-2,4,6-trimethylbenzoylphosphinate (LAP), metals or metal ions-based photoinitiator, peroxides, ammonium persulfate, 2,2-dimethoxy-2-phenylacetophenone (DMPA), and any combination thereof.

73. The process of claim 72, wherein the free radical-generating azo compound is selected from the group consisting of azobisisobutyronitrile (AIBN); 2,2′-azobis(2-methylpropionitrile); 4,4′-azobis(4-cyanopentanoic acid) (ACVA); 1,1′-azobis(cyanocyclohexane) (ACHN); diazenedicarboxylic acid bis(N,N-dimethylamide) (TMAD); azodicarboxylic acid dipiperidide (ADD); 2,2’-azobis[2-(2-imidazolin-2-yl)propane]dihydrochloride; 2,2’-azobis(2-amidinopropane) dihydrochloride (AAPH); 2,2′-azobis(2-methylpropionitrile); 4,4'-(diazene-1,2-diyl)bis(4-cyanopentanoic acid); 2,2'-azodi(2-methylbutyronitrile); and any combination thereof.

74. The process of claim 72 or 73, wherein the peroxide is selected from the group consisting of tert-butyl peroxyisobutyrate, tert-butyl hydroperoxide, benzoyl peroxide and any combination thereof.

75. The process of any one of claims 70 to 74, wherein reacting the compound of Formula (C) with the compound of Formula (A) or (AA) is performed in water or an organic solvent.

76. The process of any one of claims 70 to 75, wherein reacting the compound of Formula (C) with the compound of Formula (A) or (AA) is performed in a solvent selected from the group consisting of water, dioxane, acetonitrile, tetrahydrofuran (THF), diisopropyl ether, isopropanol, chlorobenzene, methyl-tert-butyl ether, methanol, ethanol, tert-butanol, chloroform and any combination thereof.

77. The process of any one of claims 70 to 76, wherein reacting the compound of Formula (C) with the compound of Formula (A) or (AA) is performed at a temperature ranging from about 40 °C to about 110 °C.

78. The process of any one of claims 70 to 77, wherein reacting the compound of Formula (C) with the compound of Formula (A) or (AA) is performed for a period of about 1 hour to about 10 hours.

79. The process of claim 70, wherein reacting the compound of Formula (C) with the compound of Formula (A) or (AA) is performed under visible light in the presence of a visible light absorbing transition metal photocatalyst.

80. The process of claim 70, wherein reacting the compound of Formula (C) with the compound of Formula (A) or (AA) is performed under ultraviolet light irradiation.

81. The process of claim 70, wherein reacting the compound of Formula (C) with the compound of Formula (A) or (AA) is performed under ultraviolet light irradiation in the presence of a photoinitiator.

82. The process of claim 81, wherein the photoinitiator is selected from the group consisting of 2,2'-azidobis[2-imidazolin-2-yl)propane]dihydrochloride; 2,2-dimethoxy-2-phenylacetophenone (DMPA); and combination thereof.

83. The process of any one of claims 80 to 82, wherein reacting the compound of Formula (C) with the compound of Formula (A) or (AA) is performed in an alcoholic solvent such as methanol, ethanol, isopropanol or any combination thereof.

84. The process of any one of claims 80 to 83, wherein reacting the compound of Formula (C) with the compound of Formula (A) or (AA) is performed at a temperature ranging from about 20 °C to about 30 °C.

85. The process of any one of claims 80 to 84, wherein reacting the compound of Formula (C) with the compound of Formula (A) or (AA) is performed for a period of about 1 hour to about 24 hours.

86. The process of any one of claims 80 to 85, wherein the ultraviolet light irradiation is short-wave, medium-wave or long-wave ultraviolet light irradiation.

87. The process of any one of claims 70 to 86, wherein m is an integer from 1 to 3.

88. The process of any one of claims 70 to 87, wherein m is 2.

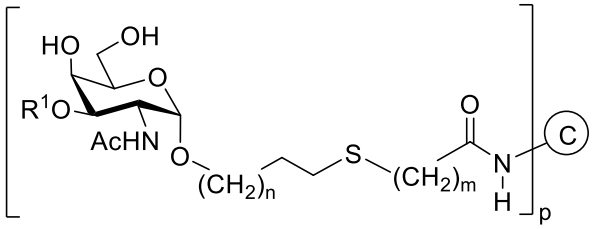
~~89. The process of any one of claims 70 to 88, wherein LG is an O-fluorophenyl group such as $OPhF_5$ or $OPhF_4$(para SO_3Na), or an O (*N*-succinimidyl) group.~~

~~90. The process of any one of claims 70 to 89, wherein LG is an O (*N*-succinimidyl) group.~~

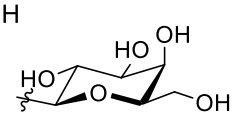
~~91.~~16. The process of ~~any one of~~ claim~~s 70 to 90~~15, wherein the compound of Formula (A) is obtained by the process of any one of claims 1 to ~~20~~11 and the compound of Formula (AA) is obtained by the process of claim 12.

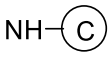
~~92. The process of any one of claims 70 to 90, wherein the compound of Formula (AA) is obtained by the process of any one of claims 47 to 69.~~

~~93.~~17. A process for preparing a glycoconjugate of Formula (I) or (II)



(I): R^1 = H

(II): R^1 = 

where n is an integer from 1 to 5, m is an integer from 1 to 5, p is an integer from 1 to 50 and 

is a carrier material containing at least one amino group available for conjugation, comprising conjugating at least one free amino group of the carrier material with a compound of Formula (B) to form the glycoconjugate of Formula (I) or with a compound of Formula (BB) to form the glycoconjugate of Formula (I), wherein the compounds of Formula (B) and (BB) are obtained by the process of ~~any one of~~ claim~~s~~ 15 or 16~~ 70 to 92~~.

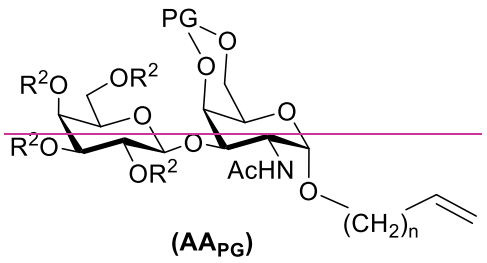
~~94.~~18. The process of claim ~~93~~17, wherein the carrier material comprises a protein, polypeptide or peptide.

~~95.~~19. The process of any one of claims 1 to ~~94~~18, wherein n is an integer from 1 to 3.

~~96. The process of any one of claims 1 to 95, wherein n is 1 or 2.~~

~~97.~~20. The process of any one of claims 1 to ~~96~~19, wherein n is 1.

~~98. A compound of Formula (AA_{PG})~~



(AA_{PG})

~~where n is an integer from 1 to 5, R^2 is Ac and PG is a divalent protecting group selected from PhCH, Me_2C, O=C, Me_2Si and 2,6-bis(trifluoromethyl)phenyl-B.~~

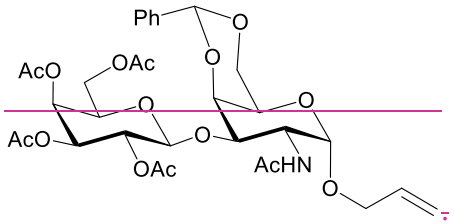
~~99. The compound of claim 98, wherein PG is PhCH.~~

~~100. The compound of claim 98 or 99, wherein n is an integer from 1 to 3.~~

~~101. The compound of any one of claims 98 to 100, wherein n is 1 or 2.~~

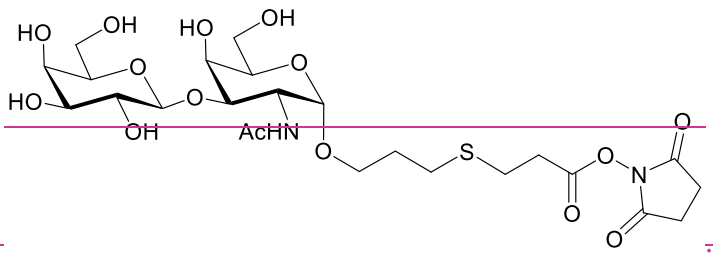
~~102. The compound of any one of claims 98 to 101, wherein n is 1.~~

~~103. The compound of claim 98, having the formula:~~



~~.~~

~~104. A compound of formula:~~


HO
OH
HO
OH
O
O
HO
O
OH
AcHN
O
S
O
O
N
O
O