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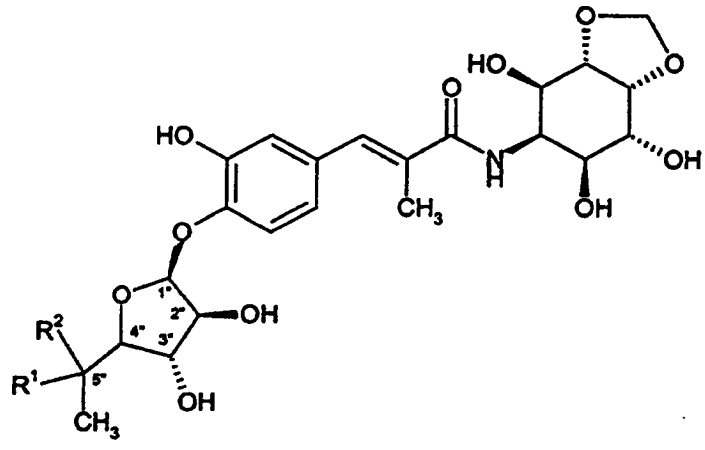
(54) **Title:** HYGROMYCIN A DERIVATIVES

(57) **Abstract**

The invention relates to compounds of formula (1) and to pharmaceutically acceptable salts, prodrugs and solvates thereof, wherein R^1 and R^2 are as defined herein. The compounds of formula (1) are antibacterial and antiprotozoal agents that may be used to treat various bacterial and protozoal infections and disorders related to such infections. The invention also relates to pharmaceutical compositions containing the compounds of formula (1) and the methods of treating bacterial and protozoal infections by administering the compounds of formula (1).



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HYGROMYCIN A DERIVATIVES

Background Of The Invention

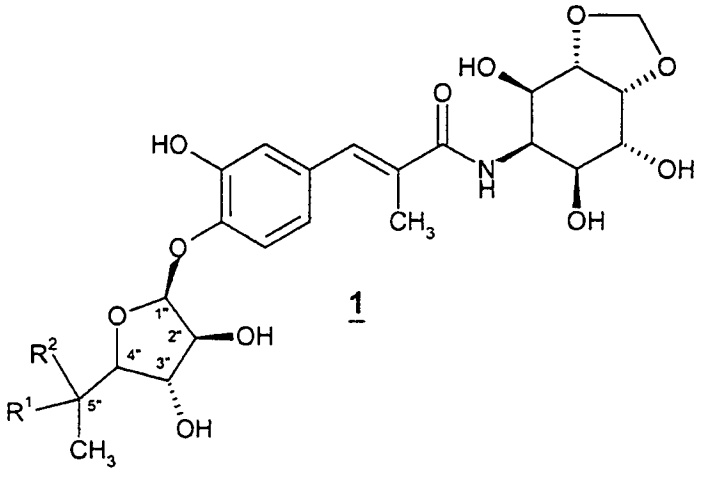
This invention relates to novel hygromycin A derivatives that are useful as antibacterial and antiprotozoal agents in mammals, including man, as well as in fish and birds. This invention also relates to pharmaceutical compositions containing the novel compounds and to methods of treating bacterial and protozoal infections in mammals, fish and birds by administering the novel compounds to mammals, fish and birds requiring such treatment.

Hygromycin A is a fermentation-derived natural product first isolated from *Streptomyces hygroscopicus* in 1953. As an antibiotic, hygromycin A possesses activity against human pathogens and is reported to possess potent *in vitro* activity against *Serpulina (Treponema) hyodysenteriae* which causes swine dysentery. Several references refer to semisynthetic modifications of hygromycin A, including the following: derivatization of the 5" ketone of hygromycin A to the 2,4-dinitrophenylhydrazone is referred to in K. Isono *et al.*, *J. Antibiotics* **1957**, 10, 21, and R.L. Mann and D.O. Woolf, *J. Amer Chem. Soc.* **1957**, 79, 120. K. Isono *et al.*, ibid., also refer to the thiosemicarbazone at 5"; reduction of the 5" ketone of hygromycin A to the 5" alcohol is referred to in R.L. Mann and D.O. Woolf, ibid., as well as in S.J. Hecker *et al.*, *Bioorg. Med. Chem. Lett.* **1992**, 2, 533 and S.J. Hecker *et al.*, *Bioorg. Med. Chem. Lett.* **1993**, 3, 295; furanose analogues are referred to in B.H. Jaynes et al., *Bioorg. Med. Chem. Lett.* **1993**, 3, 1531, and B.H. Jaynes et al., *J. Antibiot.* **1992**, 45, 1705; aromatic ring analogues are referred to in S.J. Hecker et al., *Bioorg. Med. Chem. Lett.* **1993**, 3, 289, and C.B. Cooper et al., *Bioorg. Med. Chem. Lett.* **1997**, 7, 1747; enamide analogues are referred to in S.J. Hecker et al., *Bioorg. Med. Chem. Lett.* **1992**, 2, 533; aminocyclitol analogues are referred to in S.J. Hecker et al., *Bioorg. Med. Chem. Lett.* **1992**, 2, 1015, and in S.J. Hecker et al., *Bioorg. Med. Chem. Lett.* **1992**, 2, 1043. The hygromycin A derivatives of the present invention possess activity against both gram-negative and gram-positive bacteria and protozoa.

Filed concurrently with the present application, United States provisional patent application no. 60/084058, filed May 4, 1998, entitled "2"-Deoxy Hygromycin Derivatives", (Attorney docket number PC 10186), with named inventor R. G. Linde II, also refers to hygromycin analogues and is incorporated herein by reference in its entirety.

Summary of the Invention

The present invention relates to compounds of the formula



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and to pharmaceutically acceptable salts, prodrugs and solvates thereof wherein:

R^1 is H and R^2 is $-NR^3R^4$, $-NR^4C(O)R^3$, $-OC(O)NR^3R^4$ or $-OR^3$;

or R^1 and R^2 are taken together to form $=N-OR^3$, $=CR^4R^3$, $=CR^4C(O)R^3$, $=CR^4C(O)OR^3$, or $=CR^4C(O)NR^3R^4$;

each R^3 is independently selected from H, C_1-C_{10} alkyl, C_2-C_{10} alkenyl, $-(CH_2)_t(C_3$-C_{10} cycloalkyl), $-(CH_2)_t(C_6$-C_{10} aryl), and $-(CH_2)_t$(4-10 membered heterocyclic), wherein t is an integer ranging from 0 to 5, said alkyl group optionally contains 1 or 2 hetero moieties selected from O, $-S(O)_j-$ wherein j is an integer ranging from 0 to 2, and $-N(R^7)-$ with the proviso that two O atoms, two S atoms, or an O and S atom are not attached directly to each other; said cycloalkyl, aryl and heterocyclic R^3 groups are optionally fused to a benzene ring, a C_5-C_8 saturated cyclic group, or a 4-10 membered heterocyclic group; the $-(CH_2)_t-$ moieties of the foregoing R^3 groups optionally include a carbon-carbon double or triple bond where t is an integer between 2 and 5; and the foregoing R^3 groups, except H but including any optional fused rings referred to above, are optionally substituted by 1 to 5 R^5 groups, with the proviso that R^3 is not H, methyl or ethyl where R^1 is H and R^2 is $-OR^3$;

each R^4 is independently H or C_1-C_{10} alkyl;

each R^5 is independently selected from C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, halo, cyano, nitro, trifluoromethyl, difluoromethoxy, trifluoromethoxy, azido, $-OR^6$, $-C(O)R^6$, $-C(O)OR^6$, $-NR^7C(O)OR^9$, $-OC(O)R^6$, $-NR^7SO_2R^9$, $-SO_2NR^6R^7$, $-NR^7C(O)R^6$, $-C(O)NR^6R^7$, $-NR^6R^7$, $-S(O)_j(CH_2)_m(C_6$-C_{10} aryl), $-S(O)_j(C_1$-C_6 alkyl), wherein j is an integer ranging from 0 to 2, $-(CH_2)_m(C_6$-C_{10} aryl), $-O(CH_2)_m(C_6$-C_{10} aryl), $-NR^7(CH_2)_m(C_6$-C_{10} aryl), and $-(CH_2)_m$(4-10 membered heterocyclic), wherein m is an integer ranging from 0 to 4; said alkyl group

optionally contains 1 or 2 hetero moieties selected from O, -S(O)$_j$- wherein j is an integer ranging from 0 to 2, and -N(R^7)- with the proviso that two O atoms, two S atoms, or an O and S atom are not attached directly to each other; said cycloalkyl, aryl and heterocyclic R^5 groups are optionally fused to a C_6-C_{10} aryl group, a C_5-C_8 saturated cyclic group, or a 4-10 membered heterocyclic group; and said alkyl, cycloalkyl, aryl and heterocyclic R^5 groups are optionally substituted by 1 to 5 substituents independently selected from halo, cyano, nitro, trifluoromethyl, difluoromethoxy, trifluoromethoxy, azido, -$NR^7SO_2R^9$, -$SO_2NR^6R^7$, -$C(O)R^6$, -$C(O)OR^6$, -$OC(O)R^6$, -$NR^7C(O)OR^9$, -$NR^7C(O)R^6$, -$C(O)NR^6R^7$, -NR^6R^7, -OR^6, C_1-C_{10} alkyl, -$(CH_2)_m$(C_6-C_{10} aryl), and -$(CH_2)_m$(4-10 membered heterocyclic), wherein m is an integer ranging from 0 to 4;

each R^6 is independently selected from H, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, -$(CH_2)_m$(C_6-C_{10} aryl), and -$(CH_2)_m$(4-10 membered heterocyclic), wherein m is an integer ranging from 0 to 4; said alkyl group optionally includes 1 or 2 hetero moieties selected from O, -S(O)$_j$- wherein j is an integer ranging from 0 to 2, and -N(R^7)- with the proviso that two O atoms, two S atoms, or an O and S atom are not attached directly to each other; said cycloalkyl, aryl and heterocyclic R^6 groups are optionally fused to a C_6-C_{10} aryl group, a C_5-C_8 saturated cyclic group, or a 4-10 membered heterocyclic group; and the foregoing R^6 substituents, except H, are optionally substituted by 1 to 5 substituents independently selected from halo, cyano, nitro, trifluoromethyl, difluoromethoxy, trifluoromethoxy, azido, -$C(O)R^7$, -$C(O)OR^7$, -$OC(O)R^7$, -$NR^7C(O)R^8$, -$C(O)NR^7R^8$, -NR^7R^8, hydroxy, C_1-C_6 alkyl, and C_1-C_6 alkoxy;

each R^7 and R^8 is independently H or C_1-C_6 alkyl; and,

R^9 is selected from the substituents provided in the definition of R^6 except H.

Preferred compounds of formula 1 include those wherein R^1 and R^2 are taken together to form =N-OR^3, and R^3 is C_1-C_4 alkyl, C_2-C_4 alkenyl, -$(CH_2)_t$(C_6-C_{10} aryl) or -$(CH_2)_t$(4-10 membered heterocyclic), wherein t is an integer ranging from 0 to 3, the heterocyclic group is optionally fused to a benzene ring, the aryl group is optionally fused to a 5 or 6 membered heterocyclic group, and the foregoing R^3 groups, including said optionally fused moieties, are optionally substituted by 1 to 5 substituents independently selected from nitro, halo, C_1-C_3 alkoxy, C_1-C_4 alkyl, trifluoromethyl, acetamido, *tert*-butoxycarbonylamino, *tert*-butoxycarbonylaminomethyl, *tert*-butoxycarbonyl, -NR^6R^7, phenyl, cyclohexyl, carboxy, aminomethyl, difluoromethoxy, trifluoromethoxy, cyano, piperidinyl, morpholino, phenoxy, and phenylthio.

Other preferred compounds of formula 1 include those wherein R^1 and R^2 are taken together to form =N-OR^3, and R^3 is -$(CH_2)_t$(C_6-C_{10} aryl) or -$(CH_2)_t$(4-10 membered heterocyclic), wherein t is an integer ranging from 0 to 3, the heterocyclic group is optionally

fused to a benzene ring, the aryl group is optionally fused to a 5 or 6 membered heterocyclic group, and the foregoing R^3 groups, including said optionally fused moieties, are optionally substituted by 1 to 5 substituents independently selected from nitro, halo, C_1-C_3 alkoxy, C_1-C_4 alkyl, trifluoromethyl, acetamido, *tert*-butoxycarbonyl. *tert*-butoxycarbonylamino, $-NR^6R^7$, phenyl, cyclohexyl, carboxy, *tert*-butoxycarbonylaminomethyl, aminomethyl, difluoromethoxy, trifluoromethoxy, cyano, piperidinyl, morpholino, phenoxy, and phenylthio.

Other preferred compounds of formula 1 include those wherein R^1 is H, R^2 is $-NR^3R^4$, R^4 is H or methyl, and R^3 is $-(CH_2)_t(C_6$-C_{10} aryl) or $-(CH_2)_t$(4-10 membered heterocyclic), wherein t is an integer ranging from 0 to 2, and the R^3 group is optionally substituted by 1 to 5 substituents independently selected from halo, C_1-C_3 alkoxy, C_1-C_4 alkyl, and trifluoromethyl.

Other preferred compounds of formula 1 include those wherein R^1 is H, R^2 is $-NR^4C(O)R^3$, R^4 is H, and R^3 is C_3-C_6 cycloalkyl, $-(CH_2)_t(C_6$-C_{10} aryl) or $-(CH_2)_t$(4-10 membered heterocyclic), wherein t is an integer ranging from 0 to 2. the aryl group is optionally fused to a 5 or 6 membered heterocyclic group, the heterocyclic group is optionally fused to a benzene ring, and the foregoing R^3 groups, including said optionally fused moieties, are optionally substituted by 1 to 5 substituents independently selected from halo, C_1-C_3 alkoxy, C_1-C_4 alkyl, and trifluoromethyl.

Other preferred compounds of formula 1 include those wherein R^1 and R^2 are taken together to form $=CR^4C(O)OR^3$ or $=CR^4C(O)NR^3R^4$, R^4 is H, and R^3 is H, C_1-C_6 alkyl, C_3-C_5 cycloalkyl, $-(CH_2)_t$(4-10 membered heterocyclic), or $-(CH_2)_t(C_6$-C_{10} aryl) wherein t is an integer ranging from 0 to 2, the aryl group is optionally fused to a 5 or 6 membered heterocyclic group, the heterocyclic group is optionally fused to a benzene ring, and the foregoing R^3 groups, except H but including said optionally fused moieties, are optionally substituted by 1 to 5 substituents independently selected from halo, C_1-C_3 alkoxy, C_1-C_4 alkyl, $-NR^6R^7$ and trifluoromethyl.

Other preferred compounds of formula 1 include those wherein R^1 is H, R^2 is $-OR^3$, and R^3 is C_1-C_4 alkyl, $-(CH_2)_t$(4-10 membered heterocyclic), or $-(CH_2)_t(C_6$-C_{10} aryl) wherein t is an integer ranging from 1 to 2, the aryl group is optionally fused to a 5 or 6 membered heterocyclic group, the heterocyclic group is optionally fused to a benzene ring, and the foregoing R^3 groups, including said optionally fused moieties, are optionally substituted by 1 to 5 substituents independently selected from halo, C_1-C_3 alkoxy, C_1-C_4 alkyl, cyclohexyl, cyano, trifluoromethyl, benzyloxy and trifluoromethyl.

Other preferred compounds of formula 1 include those wherein R^1 is H, R^2 is $-OC(O)NR^3R^4$, R^4 is H, and R^3 is $-(CH_2)_t(C_6$-C_{10} aryl) wherein t is an integer ranging from 0 to

2, and the R^3 group is optionally substituted by 1 to 5 substituents independently selected from halo, C_1-C_3 alkoxy, C_1-C_4 alkyl, and trifluoromethyl.

Specific preferred compounds of formula 1 include those selected from the group consisting of:

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(benzofuran-2-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(benzofuran-2-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-phenylmethyloxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-phenylmethyloxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(4-chlorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3,4-dichlorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3,4-dichlorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(4-pyridinyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(4-(4-morpholinyl)phenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[cyclohexylmethyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(4-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-b-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(2,4-dichlorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3,4-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(furan-3-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(furan-3-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(1,3-benzodioxol-5-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(1,3-benzodioxol-5-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3-chlorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(4-cyclohexylphenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3-aminophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[[(4-aminomethyl)phenyl]methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[3-(4-chlorophenyl)propyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[3-(4-chlorophenyl)propyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3-(trifluoromethoxy)phenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(4-(1-piperidinyl)phenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(2-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[2-(phenylthio)ethyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(benzofuran-5-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(benzofuran-5-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(2-phenylpyrimidin-5-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3-fluoro-4-methoxyphenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3,4-dihydro-2H-1-benzopyran-4-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(5,6-dideoxy-5-(methyl(phenylmethyl)amino-α-L-*galacto*-furanos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol;

5-Deoxy-5-[[3-[4-[(5,6-dideoxy-5-phenylamino-α-L-*galacto*-furanos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol;

5-Deoxy-5-[[3-[4-[(6-deoxy-5-*O*-[(3,4-dichlorophenyl)methyl]-β-D-*altro*-furanos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(furan-2-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(5-methyl-β-D-*arabino*-hept-5-(*E*)-enofuranuron-1-ylic acid)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, ethyl ester;

5-Deoxy-5-[[3-[4-[[N-(furan-2-yl)methyl]-(5-methyl-β-D-*arabino*-hept-5-(*E*)-enofuranuron-1-yl-amide)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[3-(phenyl)propyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(2-propen-1-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-(2-propen-1-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(4-methylphenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(4-methoxyphenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3-(trifluoromethyl)phenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-5-*O*-[(4-chlorophenyl)methyl]-β-D-*altro*-furanos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[diphenylmethyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-5-phenylcarbamate-β-D-*altro*-furanos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol;

5-Deoxy-5-[[3-[4-[(6-deoxy-5-[(3,4-dichlorophenyl)methyl]carbamate-β-D-*altro*-furanos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3-chlorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3-chloro-2-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3-chloro-2-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3-chloro-4-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3-chloro-4-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3-chloro-5-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3-chloro-5-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-*(E)*-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(5-chloro-2-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-*(E)*-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, *(E)*-*O*-[(5-chloro-2-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3,5-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3,5-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(4-chloro-3-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(4-chloro-3-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(4-chloro-1,3-benzodioxol-6-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(4-chloro-1,3-benzodioxol-6-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(5-chloro-1,3-benzodioxol-6-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(5-chloro-1,3-benzodioxol-6-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(4-chloro-1,3-benzodioxol-5-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(4-chloro-1,3-benzodioxol-5-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-*(E)*-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, *(E)*-*O*-[(2,3-dihydrobenzofuran-6-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-*(E)*-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(2,3-dihydrobenzofuran-6-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(2,3-dihydrobenzofuran-5-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(2,3-dihydrobenzofuran-5-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-(1,2,3,4-tetrahydronaphthalen-1-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(1,2,3,4-tetrahydronaphthalen-1-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-(7-chloro-1,2,3,4-tetrahydronaphthalen-1-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(7-chloro-1,2,3,4-tetrahydronaphthalen-1-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-(7-fluoro-1,2,3,4-tetrahydronaphthalen-1-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(7-fluoro-1,2,3,4-tetrahydronaphthalen-1-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-(8-chloro-3,4-dihydro-2*H*-1-benzopyran-4-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(8-chloro-3,4-dihydro-2*H*-1-benzopyran-4-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-(6-chloro-3,4-dihydro-2*H*-1-benzopyran-4-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(6-chloro-3,4-dihydro-2*H*-1-benzopyran-4-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-(8-fluoro-3,4-dihydro-2*H*-1-benzopyran-4-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(8-fluoro-3,4-dihydro-2*H*-1-benzopyran-4-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-(6-fluoro-3,4-dihydro-2*H*-1-benzopyran-4-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(6-fluoro-3,4-dihydro-2*H*-1-benzopyran-4-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(quinolin-2-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(quinolin-2-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(quinolin-3-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(quinolin-3-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[4-(phenylmethyl)phenylmethyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[4-(phenylmethyl)phenylmethyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[4-(phenoxy)phenylmethyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[4-(phenoxy)phenylmethyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3,5-dichlorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3,5-dichlorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(phenyl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-(phenyl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(3-chloro-4-fluorophenyl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-(3-chloro-4-fluorophenyl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(4-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(4-chlorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3,4-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(2,4-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(2,4-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(2,1,3-benzoxadiazol-5-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(2,1,3-benzoxadiazol-5-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(2,3,5,6-tetrafluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(2,3,5,6-tetrafluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(2,3-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(2,3-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(4-phenyl-furan-3-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(4-phenyl-furan-3-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(4-phenyl-furan-2-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(4-phenyl-furan-2-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(2,3-difluoro-6-methoxyphenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(2,3-difluoro-6-methoxyphenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3-chloro-thiophen-2-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3-chloro-thiophen-2-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(5-chloro-thiophen-2-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(5-chloro-thiophen-2-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3-chloro-2,6-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3-chloro-2,6-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(2-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[1-(3-chlorophenyl)ethyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(3-difluoromethoxy-phenyl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-(3-difluoromethoxy-phenyl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(4-difluoromethoxy-phenyl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-(4-difluoromethoxy-phenyl)oxime;

and the pharmaceutically acceptable salts and solvates of said compounds.

In a more specific embodiment, the present invention includes the following compounds:

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(1,3-benzodioxol-5-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3-chlorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3-chlorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(benzofuran-2-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3,5-dichlorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3,5-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3,5-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3-chloro-2-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3-chloro-2-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3-chloro-4-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3-chloro-4-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(4-chloro-3-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(4-chloro-3-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(4-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(4-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(4-chlorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(4-chlorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(4-phenyl-furan-2-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3-chloro-5-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3,4-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3,4-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(2,3-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(2,4-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(2,4-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(2,3,5,6-tetrafluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(3-chloro-4-fluorophenyl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-(3-chloro-4-fluorophenyl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(5-chloro-thiophen-2-yl)methyl]oxime;

and the pharmaceutically acceptable salts and solvates of said compounds.

The invention also relates to a pharmaceutical composition for the treatment of a disorder selected from a bacterial infection, a protozoal infection, and disorders related to bacterial infections or protozoal infections, in a mammal, fish, or bird which comprises a therapeutically effective amount of a compound of formula 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

The invention also relates to a method of treating a disorder selected from a bacterial infection, a protozoal infection, and disorders related to bacterial infections or protozoal infections, in a mammal, fish, or bird which comprises administering to said mammal, fish or bird a therapeutically effective amount of a compound of formula 1 or a pharmaceutically acceptable salt thereof.

The invention also relates to a method of preparing a composition containing hygromycin A and *epi*-hygromycin, wherein the ratio of hygromycin A to *epi*-hygromycin is at least 10:1, which comprises fermenting *Streptomyces hygroscopicus* in media having a pH less than 6.9 at a temperature ranging from 25°C to 35°C. In a preferred embodiment of said method said *Streptomyces hygroscopicus* is *Streptomyces hygroscopicus* NRRL2388 or a mutant thereof, said pH ranges from 6.2 to 6.7, said temperature is about 29°C, and the ratio of hygromycin A to *epi*-hygromycin is at least 14:1. In a further aspect of the above method, said composition is maintained at a pH of 6.0 to 6.4, preferably about 6.0, and the temperature of said composition is maintained at a temperature ranging from 25°C to 35°C during purification of said hygromycin A to an oil.

The term "treating", as used herein, unless otherwise indicated, means reversing, alleviating, inhibiting the progress of, or preventing the disorder or condition to which such term applies, or one or more symptoms of such disorder or condition. The term "treatment", as used herein, refers to the act of treating, as "treating" is defined immediately above.

As used herein, unless otherwise indicated, the terms or phrases "bacterial infection(s)", "protozoal infection(s)", and "disorders related to bacterial infections or protozoal infections" include the following: pneumonia, otitis media, sinusitus, bronchitis, tonsillitis, and mastoiditis related to infection by *Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis, Staphylococcus aureus, Enterococcus faecalis, E. faecium, E. casselflavus, S. epidermidis, S. haemolyticus,* or *Peptostreptococcus* spp.; pharyngitis, rheumatic fever, and glomerulonephritis related to infection by *Streptococcus pyogenes,* Groups C and G streptococci, *Corynebacterium diphtheriae,* or *Actinobacillus haemolyticum;* respiratory tract infections related to infection by *Mycoplasma pneumoniae, Legionella pneumophila, Streptococcus pneumoniae, Haemophilus influenzae,* or *Chlamydia pneumoniae;* blood and tissue infections, including endocarditis and osteomyelitis, caused by *S. aureus, S. haemolyticus, E. faecalis, E. faecium, E. durans,* including strains resistant to known antibacterials such as, but not limited to, beta-lactams, vancomycin, aminoglycosides, quinolones, chloramphenicol, tetracylines and macrolides; uncomplicated skin and soft tissue infections and abscesses, and puerperal fever related to infection by *Staphylococcus aureus,* coagulase-negative staphylococci (i.e., *S. epidermidis, S. hemolyticus,* etc.), *Streptococcus*

pyogenes , *Streptococcus agalactiae,* Streptococcal groups C-F (minute-colony streptococci), viridans streptococci, *Corynebacterium minutissimum, Clostridium* spp., or *Bartonella henselae;* uncomplicated acute urinary tract infections related to infection by *Staphylococcus aureus,* coagulase-negative staphylococcal species, or *Enterococcus* spp.; urethritis and cervicitis; sexually transmitted diseases related to infection by *Chlamydia trachomatis, Haemophilus ducreyi, Treponema pallidum, Ureaplasma urealyticum,* or *Neiserria gonorrheae;* toxin diseases related to infection by *S. aureus* (food poisoning and toxic shock syndrome), or Groups A, B, and C streptococci; ulcers related to infection by *Helicobacter pylori;* systemic febrile syndromes related to infection by *Borrelia recurrentis;* Lyme disease related to infection by *Borrelia burgdorferi;* conjunctivitis, keratitis, and dacrocystitis related to infection by *Chlamydia trachomatis, Neisseria gonorrhoeae, S. aureus, S. pneumoniae, S. pyogenes, H. influenzae,* or *Listeria* spp.; disseminated *Mycobacterium avium* complex (MAC) disease related to infection by *Mycobacterium avium,* or *Mycobacterium intracellulare;* infections caused by *Mycobacterium tuberculosis, M. leprae, M. paratuberculosis, M. kansasii,* or *M. chelonei;* gastroenteritis related to infection by *Campylobacter jejuni;* intestinal protozoa related to infection by *Cryptosporidium* spp.; odontogenic infection related to infection by viridans streptococci; persistent cough related to infection by *Bordetella pertussis;* gas gangrene related to infection by *Clostridium perfringens* or *Bacteroides* spp.; and atherosclerosis or cardiovascular disease related to infection by *Helicobacter pylori* or *Chlamydia pneumoniae.* Bacterial infections and protozoal infections, and disorders related to such infections, which may be treated or prevented in animals include the following: bovine respiratory disease related to infection by *P. haemolytica, P. multocida, Mycoplasma bovis,* or *Bordetella* spp.; cow enteric disease related to infection by protozoa (i.e., coccidia, cryptosporidia, etc.); dairy cow mastitis related to infection by *S. aureus, Strep. uberis, Streptococcus agalactiae, Streptococcus dysgalactiae, Corynebacterium,* or *Enterococcus* spp.; swine respiratory disease related to infection by *A. pleuro., P. multocida,* or *Mycoplasma* spp.; swine enteric disease related to infection by *Lawsonia intracellularis, Salmonella,* or *Serpulina hyodysinteriae*; cow footrot related to infection by *Fusobacterium* spp.; cow hairy warts related to infection by *Fusobacterium necrophorum* or *Bacteroides nodosus;* cow pink-eye related to infection by *Moraxella bovis*; cow premature abortion related to infection by protozoa (i.e. neosporium); skin and soft tissue infections in dogs and cats related to infection by *S. epidermidis, S. intermedius,* coagulase neg. *Staphylococcus* or *P. multocida;* and dental or mouth infections in dogs and cats related to infection by *Alcaligenes* spp., *Bacteroides* spp., *Clostridium* spp., *Enterobacter* spp., *Eubacterium, Peptostreptococcus, Porphyromonas,* or *Prevotella.* Other bacterial infections and protozoal infections, and disorders related to such

infections, which may be treated or prevented in accord with the method of the present invention are referred to in J. P. Sanford et al., "The Sanford Guide To Antimicrobial Therapy," 26th Edition, (Antimicrobial Therapy, Inc., 1996).

The term "halo", as used herein, unless otherwise indicated, includes fluoro, chloro, bromo or iodo. Preferred halo groups are fluoro, chloro and bromo.

The term "alkyl", as used herein, unless otherwise indicated, includes saturated monovalent hydrocarbon radicals having straight or branched moieties. Said alkyl group may include one or two double or triple bonds. It is understood that for said alkyl group to include a carbon-carbon double or triple bond at least two carbon atoms are required in said alkyl group.

The term "aryl", as used herein, unless otherwise indicated, includes an organic radical derived from an aromatic hydrocarbon by removal of one hydrogen, such as phenyl or naphthyl.

The term "4-10 membered heterocyclic", as used herein, unless otherwise indicated, includes aromatic and non-aromatic heterocyclic groups containing one or more heteroatoms each selected from O, S and N, wherein each heterocyclic group has from 4-10 atoms in its ring system. Non-aromatic heterocyclic groups include groups having only 4 atoms in their ring system, but aromatic heterocyclic groups must have at least 5 atoms in their ring system. The heterocyclic groups include benzo-fused ring systems and ring systems substituted with one or more oxo moieties. An example of a 4 membered heterocyclic group is azetidinyl (derived from azetidine). An example of a 5 membered heterocyclic group is thiazolyl and an example of a 10 membered heterocyclic group is quinolinyl. Examples of non-aromatic heterocyclic groups are pyrrolidinyl, tetrahydrofuranyl, tetrahydrothienyl, tetrahydropyranyl, tetrahydrothiopyranyl, piperidino, morpholino, thiomorpholino, thioxanyl, piperazinyl, azetidinyl, oxetanyl, thietanyl, homopiperidinyl, oxepanyl, thiepanyl, oxazepinyl, diazepinyl, thiazepinyl, 1,2,3,6-tetrahydropyridinyl, 2-pyrrolinyl, 3-pyrrolinyl, indolinyl, 2H-pyranyl, 4H-pyranyl, dioxanyl, 1,3-dioxolanyl, pyrazolinyl, dithianyl, dithiolanyl, dihydropyranyl, dihydrothienyl, dihydrofuranyl, pyrazolidinyl, imidazolinyl, imidazolidinyl, 3-azabicyclo[3.1.0]hexanyl, 3-azabicyclo[4.1.0]heptanyl, 3H-indolyl and quinolizinyl. Examples of aromatic heterocyclic groups are pyridinyl, imidazolyl, pyrimidinyl, pyrazolyl, triazolyl, pyrazinyl, tetrazolyl, furyl, thienyl, isoxazolyl, thiazolyl, oxazolyl, isothiazolyl, pyrrolyl, quinolinyl, isoquinolinyl, indolyl, benzimidazolyl, benzofuranyl, cinnolinyl, indazolyl, indolizinyl, phthalazinyl, pyridazinyl, triazinyl, isoindolyl, pteridinyl, purinyl, oxadiazolyl, thiadiazolyl, furazanyl, benzofurazanyl, benzothiophenyl, benzothiazolyl, benzoxazolyl, quinazolinyl, quinoxalinyl, naphthyridinyl, and furopyridinyl. The foregoing groups, as derived from the compounds listed above, may be C-attached or N-attached where such is possible. For instance, a group derived from pyrrole may be pyrrol-1-yl (N-attached) or pyrrol-3-yl (C-attached).

The phrase "pharmaceutically acceptable salt(s)", as used herein, unless otherwise indicated, includes salts of acidic or basic groups which may be present in the compounds of the present invention. The compounds of the present invention that are basic in nature are capable of forming a wide variety of salts with various inorganic and organic acids. The acids that may be used to prepare pharmaceutically acceptable acid addition salts of such basic compounds of are those that form non-toxic acid addition salts, i.e., salts containing pharmacologically acceptable anions, such as the hydrochloride, hydrobromide, hydroiodide, nitrate, sulfate, bisulfate, phosphate, acid phosphate, isonicotinate, acetate, lactate, salicylate, citrate, acid citrate, tartrate, pantothenate, bitartrate, ascorbate, succinate, maleate, gentisinate, fumarate, gluconate, glucuronate, saccharate, formate, benzoate, glutamate, methanesulfonate, ethanesulfonate, benzenesulfonate, p-toluenesulfonate and pamoate [i.e., 1,1'-methylene-bis-(2-hydroxy-3-naphthoate)] salts. The compounds of the present invention that include a basic moiety, such as an amino group, may form pharmaceutically acceptable salts with various amino acids, in addition to the acids mentioned above.

Those compounds of the present invention that are acidic in nature are capable of forming base salts with various pharmacologically acceptable cations. Examples of such salts include the alkali metal or alkaline earth metal salts and, particularly, the calcium, magnesium, sodium and potassium salts of the compounds of the present invention.

The compounds of the present invention have asymmetric centers and therefore exist in different enantiomeric and diastereomeric forms. This invention relates to the use of all optical isomers and stereoisomers of the compounds of the present invention, and mixtures thereof, and to all pharmaceutical compositions and methods of treatment that may employ or contain them. In this regard, the invention includes both the E and Z configurations of the $-OR^3$ group connected to the nitrogen where R^1 and R^2 are taken together as an oxime moiety of the formula $=N-OR^3$. The compounds of formula 1 may also exist as tautomers. This invention relates to the use of all such tautomers and mixtures thereof.

The subject invention also includes isotopically-labelled compounds, and the pharmaceutically acceptable salts thereof, which are identical to those recited in Formula 1, but for the fact that one or more atoms are replaced by an atom having an atomic mass or mass number different from the atomic mass or mass number usually found in nature. Examples of isotopes that can be incorporated into compounds of the invention include isotopes of hydrogen, carbon, nitrogen, oxygen, phosphorous, fluorine and chlorine, such as ^{2}H, ^{3}H, ^{13}C, ^{14}C, ^{15}N, ^{18}O, ^{17}O, ^{35}S, ^{18}F, and ^{36}Cl, respectively. Compounds of the present invention, prodrugs thereof, and pharmaceutically acceptable salts of said compounds or of said prodrugs which contain the aforementioned isotopes and/or other isotopes of other atoms are

within the scope of this invention. Certain isotopically-labelled compounds of the present invention, for example those into which radioactive isotopes such as ^{3}H and ^{14}C are incorporated, are useful in drug and/or substrate tissue distribution assays. Tritiated, i.e., ^{3}H, and carbon-14, i.e., ^{14}C, isotopes are particularly preferred for their ease of preparation and detectability. Further, substitution with heavier isotopes such as deuterium, i.e., ^{2}H, can afford certain therapeutic advantages resulting from greater metabolic stability, for example increased *in vivo* half-life or reduced dosage requirements and, hence, may be preferred in some circumstances. Isotopically labelled compounds of Formula 1 of this invention and prodrugs thereof can generally be prepared by carrying out the procedures disclosed in the Schemes and/or in the Examples and Preparations below, by substituting a readily available isotopically labelled reagent for a non-isotopically labelled reagent.

This invention also encompasses pharmaceutical compositions containing and methods of treating bacterial infections through administering prodrugs of compounds of the formula 1. Compounds of formula 1 having free amino, amido, hydroxy or carboxylic groups can be converted into prodrugs. Prodrugs include compounds wherein an amino acid residue, or a polypeptide chain of two or more (e.g., two, three or four) amino acid residues is covalently joined through an amide or ester bond to a free amino, hydroxy or carboxylic acid group of compounds of formula 1. The amino acid residues include but are not limited to the 20 naturally occurring amino acids commonly designated by three letter symbols and also includes 4-hydroxyproline, hydroxylysine, demosine, isodemosine, 3-methylhistidine, norvalin, beta-alanine, gamma-aminobutyric acid, citrulline homocysteine, homoserine, ornithine and methionine sulfone.

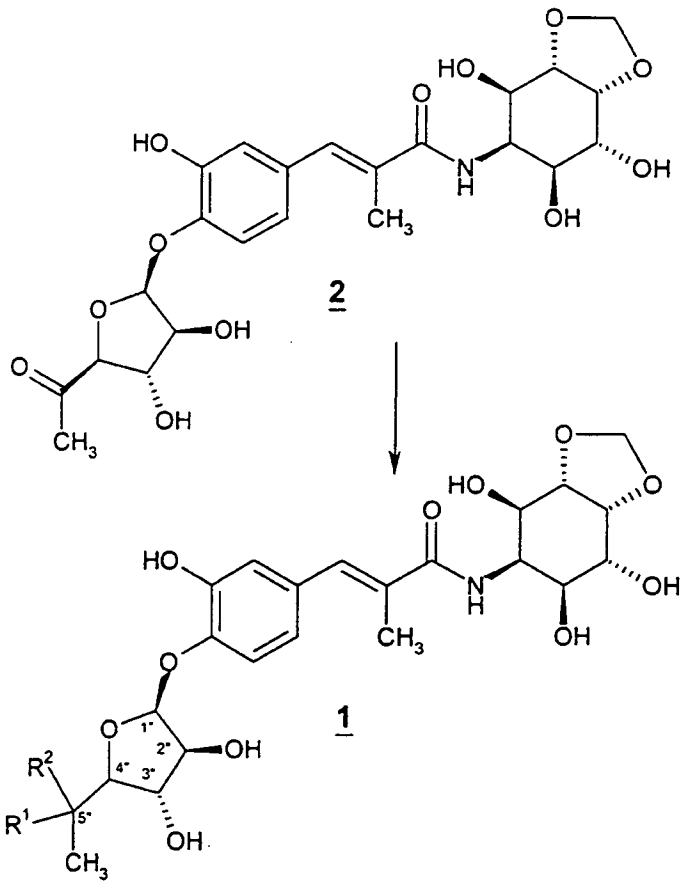
Additional types of prodrugs are also encompassed. For instance, free carboxyl groups can be derivatized as amides or alkyl esters. The amide and ester moieties may incorporate groups including but not limited to ether, amine and carboxylic acid functionalities. Free hydroxy groups may be derivatized using groups including but not limited to hemisuccinates, phosphate esters, dimethylaminoacetates, and phosphoryloxymethyloxycarbonyls, as outlined in D. Fleisher, R. Bong, B.H. Stewart, Advanced Drug Delivery Reviews (1996) 19, 115. Carbamate prodrugs of hydroxy and amino groups are also included, as are carbonate prodrugs and sulfate esters of hydroxy groups. Derivatization of hydroxy groups as (acyloxy)methyl and (acyloxy)ethyl ethers wherein the acyl group may be an alkyl ester, optionally substituted with groups including but not limited to ether, amine and carboxylic acid functionalities, or where the acyl group is an amino acid ester as described above, are also encompassed. Prodrugs of this type are described in R.P. Robinson et al., J. Medicinal Chemistry (1996) 39, 10.

Selective introduction of prodrug side chains can be carried out on the hydroxy groups of the hygromycin A core molecule. For instance, exhaustive silylation of the six hydroxy groups of hygromycin A can be carried out, for instance with tert-butyl dimethylsilyl chloride. Subjection of the hexasilyl derivative to the action of potassium carbonate in methanol at room temperature selectively removes the phenolic silyl group, allowing further selective modification at that position. In another example, incomplete silylation of hygromycin A (see PC 10186, R. Linde, 2"-deoxy hygromycin A derivatives, U.S. provisional patent application no. 60/084,058, filed May 4, 1998) provides the pentasilyl derivative in which the C-2" hydroxy group is free. Selective acylation, alkylation, etc. can be carried out on this derivative to provide prodrug attachment at C-2".

Detailed Description of the Invention

The preparation of the compounds of the present invention is illustrated in the following Scheme.

Scheme



The compounds of the present invention are readily prepared. With reference to the Scheme illustrated above, the starting compound of formula 2 is hygromycin A which may be prepared according to procedures known to those skilled in the art, such as by fermentation of *Streptomyces hygroscopicus* NRRL 2388. The methyl ketone at 4" on the furanose sugar of the hygromycin A molecule can exist in the S configuration (hygromycin A) or R configuration (*epi*-hygromycin) on the furanose sugar. When published protocols are used as a model for fermentation and recovery of hygromycin A (U.S. Patent 3,100,176; Antibiotic Chemotherapy (1953)3:1268-1278, 1279-1282), the hygromycin product is an approximately 3:1 mixture of hygromycin A (the 4"-(S) epimer), with the beta-oriented methyl ketone on the furanose sugar, as drawn, and *epi*-hygromycin. It is known in the literature (Journal of Antibiotics 33(7), 695-704, 1980) that pure hygromycin A will convert to *epi*-hygromycin in alkaline solutions. By carefully controlling the pH below 6.9 during the fermentation, and the pH, temperature and solvent exposure during the purification process, the final recovered product may be improved to at least a 14:1 ratio of hygromycin A : *epi*-hygromycin. Using this material, substantially single isomers derived from the 4"-(S) hygromycin may be prepared for use as templates for further synthetic modification.

Hygromycin A enriched for the 4"-(S) epimer is produced by fermentation of *Streptomyces hygroscopicus* NRRL2388, or mutants thereof, in media with pH controlled at less than 6.9, preferably 6.2 to 6.7, throughout the process. The medium contains assimilable sources of carbon, nitrogen and trace elements, as known to those skilled in the art. The fermentation is run at a temperature of about 25-35°C, preferably about 29°C. The fermentation is monitored, for example by high pressure liquid chromatography. Incubation is continued until the yield of the compound reaches a maximum, generally for a period of about 3 to 10 days, preferably about 4 to 6 days.

The formation of *epi*-hygromycin is minimized during the purification process by using an aqueous buffer (rather than unbuffered water) and controlling the pH of the active streams to near 6.0. *Epi*-hygromycin formation is also minimized by minimizing the time the recovered material is subject to higher temperatures. Thus, where it is necessary to reduce solvent concentrations, it is preferred to dilute active streams with the aqueous buffer and avoid use of rotary evaporation at elevated temperatures. Also, as means of avoiding higher temperatures, a resin column may be used to concentrate the active solution prior to the final purification step in order to reduce the volume of solution that must be boiled. The final purification step in the process is the concentration of the active cuts to solids using vacuum and a bath temperature of about 35-50°C. The period in which the solution is subject to elevated temperatures may be minimized by boiling in stages.

The compounds of formula 1 wherein R^1 and R^2 are taken together to form an oxime of the formula $=NOR^3$, wherein R^3 is as defined above, may be prepared by treating hygromycin A (the compound of formula 2) with a hydroxylamine of the formula R^3ONH_2, using the free base or salt of the hydroxylamine, preferably the free base of the hydroxylamine. The reaction is carried out in an inert solvent, such as methanol, ethanol or pyridine, with addition of base, such as Na_2CO_3 or K_2CO_3, if the salt, for instance the HCl salt, of the hydroxylamine is used, at a temperature ranging from about 0°C to 65°C, preferably from 0°C to 25°C. The hydroxylamine of formula R^3ONH_2 may be prepared using one or more procedures disclosed in Bioconjugate Chemistry (1990), 2, 96; Journal of Pharmaceutical Science (1969) 58, 138; and Chem. Pharm. Bull (1967) 15, 345.

The compounds of formula 1 wherein R^1 is H and R^2 is $-NR^3R^4$, wherein R^3 and R^4 are as defined above, can be synthesized by reductive amination at the C-5" ketone site of hygromycin A. Combination of R^4NH_2 and hygromycin A in an inert solvent and treatment with a reducing agent such as $NaBH_4$, $NaBH(OAc)_3$ (Ac is acetyl), or $NaCNBH_3$ provides the product with R^3 = H. To convert R^3 to a group other than H, a second reductive amination can be carried out with an appropriate aldehyde or ketone of the formula RC(O)H or RC(O)R' (where R^3 is RCH_2- or RR'CH-, and R' and R are any of the moieties in the definition of R^3 that may be attached through a methylene group such as an alkyl, arylalkyl, or heterocyclicalkyl group). An Eschweiler-Clark reaction may be used to introduce a methyl group as the R^3 substituent. To provide an amide group, such as where R^1 is H and R^2 is $-NR^4C(O)R^3$, an amine of the formula $-NHR^4$ may be introduced as described above and then an acyl moiety of the formula $-C(O)R^3$ may be introduced by treating the intermediate with an activated form of the carboxylic acid, such as R^3COCl or $R^3C(O)OC(O)R^3$, or by using an amide coupling agent such as (2-ethoxy-1-ethoxycarbonyl-1,2-dihydroquinoline (EEDQ), 1,1'-carbonyl-diimidazole (CDI), or a carbodiimide such as 1,3-dicyclohexylcarbodiimide (DCC). During the above procedures, any of the hydroxyl groups of hygromycin A that are esterified can be liberated in a final deprotection step using K_2CO_3 in methanol.

Compounds of formula 1 where R^1 is H and R^2 is $-NR^4C(O)R^3$, wherein R^4 is H and R^3 is as defined above, may be prepared through use of the primary amine derived from reductive amination of hygromycin A with an ammonia equivalent, for instance through the use of ammonium acetate and sodium cyanoborohydride or sodium triacetoxyborohydride. Alternatively, this primary amine can be prepared via the corresponding azide: 1) the hydroxy groups of hygromycin A can be protected, for instance as their TBDMS (*tert*-butyldimethylsilyl) derivatives, for instance through the action of TBDMSCl and an amine base such as imidazole or pyridine; (2) the C-5" ketone of hygromycin A is then reduced, for instance with sodium

borohydride in methanol, to give persilylated 5"-hydroxy hygromycin; 3) the resulting alcohol is transformed into the mesylate, for instance through the action of methanesulfonyl chloride and triethylamine; 4) the mesylate is displaced by azide, for example using sodium azide in N,N-dimethylformamide (DMF); and 5) the azide is reduced to the primary amine using for instance triphenylphosphine followed by aqueous hydrolysis.

Reaction of the primary amine with an activated form of $R^3C(O)OH$, for instance $R^3C(O)Cl$ or $R^3C(O)OC(O)R^3$, provides the corresponding amide. Alternatively, amide coupling reagents can be used with $R^3C(O)OH$, such as 1-(3-dimethylaminopropyl)-3-ethyl-carbodiimide (EDC), diethyl phosphoryl cyanide (DEPC), DCC, CDI or EEDQ. Finally, any protecting groups are removed using an acid, such as acetic acid, hydrogen fluoride, hydrogen fluoride-pyridine complex, or fluoride ion, such as tetrabutylammonium fluoride (TBAF).

To incorporate an R^4 group other than H, the amide referred to above may be alkylated after protecting any free hydroxyl groups, for instance as silyl ethers. The alkylation may be carried out with a base and an alkylating agent, such as sodium hydride and an appropriate bromide of the formula R^4-Br. Deprotection of the hydroxyl groups is then carried out with an acid, such as acetic acid, hydrogen fluoride, hydrogen fluoride-pyridine complex, or fluoride ion, such as TBAF.

Alternatively, a reductive amination can be carried out on hygromycin A, or a protected version thereof, with R^4NH_2, mediated by sodium triacetoxyborohydride or sodium cyanoborohydride. The resulting secondary amine can be acylated as described above, with an activated form of $R^3C(O)OH$, or reacted with $R^3C(O)OH$ using an amide coupling reagent. Deprotection of the hydroxyl groups is then effected as described above.

Compounds of formula 1 where R^1 is H and R^2 is $-OC(O)NR^3R^4$ may be prepared by reacting persilylated 5"-hydroxy hygromycin A with isocyanate R^3NCO in toluene at temperatures from 40°C to 110°C, preferably 50 - 80°C. Addition of dimethylaminopyridine and triethylamine to the reaction may be advantageous. The product of this reaction, which has R^4 equal to H, may be alkylated to give R^4 equal to C_1 - C_{10} alkyl through use of a base such as sodium hydride and an alkylating agent such as a bromide of the formula R^4-Br. Deprotection of the hydroxyl groups can then be carried out by use of an acid such as acetic acid, hydrogen fluoride, hydrogen fluoride-pyridine complex, or fluoride ion, such as TBAF.

Compounds of formula 1 where R^1 is H and R^2 is $-OR^3$, wherein R^3 is an alkyl group or a substituted alkyl group, may be prepared by alkylation of the corresponding alcohol of hygromycin A. In this process, the hydroxy groups of hygromycin A are appropriately protected, for instance as their silyl ethers using an appropriate reagent such as triethylsilyl

chloride (TESCl), trimethylsilyl chloride (TMSCl) or TBDMS and an amine base, such as imidazole or pyridine. The C-5" ketone moiety is then reduced using an appropriate reducing agent such as sodium borohydride in methanol. The resulting alcohol can then be alkylated with R^3-X, wherein X is a leaving group such as Cl, Br or methanesulfonate, in the presence of a base, such as sodium hydride or potassium *tert*-butoxide. The protecting groups are then removed with acid, such as acetic acid, hydrogen fluoride, hydrogen fluoride-pyridine complex, or a fluoride source, such as TBAF.

Compounds of formula 1 where R^1 is H and R^2 is -OR^3, wherein R^3 is an aromatic or heterocyclic moiety, may be prepared via a Mitsunobu reaction. The protected hygromycin alcohol, prepared as described above, is subjected to a Mitsunobu reaction with R^3OH, mediated by triphenylphosphine and diethyl azodicarboxylate as described in D.L. Hughes, Org. Reactions (1992) 42 335. The resulting ether is then deprotected as described above.

Alternatively, when R^1 is H and R^2 is -OR^3, wherein R^3 is an aromatic or heterocyclic moiety, the protected hygromycin alcohol can be transformed into a leaving group, for instance the bromide or mesylate derivative. The leaving group can then be displaced by R^3OH using a base such as sodium hydride, potassium *tert*-butoxide or potassium carbonate.

Compounds of formula 1 wherein R^1 and R^2 are taken together to form =$CR^4C(O)R^3$, =$CR^4C(O)OR^3$, or =$CR^4C(O)NR^3R^4$, wherein R^3 and R^4 are as defined above, may be prepared through the corresponding α,β-unsaturated ester intermediates derived from Wittig or Horner-Emmons Wittig olefination of the C-5" ketone of hygromycin A. For instance, (carbethoxymethylene)triphenylphosphorane or (carbethoxyethylidene)triphenylphosphorane can be reacted with hygromycin A to provide the unsaturated ethyl ester. Hydrolysis of this ester, for instance with aqueous sodium hydroxide, provides the corresponding carboxylic acid (R^1 and R^2 taken together to form =CHC(O)OH). At this point, the hydroxyl groups of hygromycin can be protected, for instance as their TES or TBDMS ethers as described above. To prepare the esters described above, this carboxylic acid can be esterified with R^3OH, for instance through the action of DCC and DMAP, or CDI and a catalytic base such as sodium ethoxide.

Compounds of formula 1 wherein R^1 and R^2 are taken together to form =$CR^4C(O)NR^3R^4$ may be formed by treating the above carboxylic acid intermediate (R^1 and R^2 taken together to form =CHC(O)OH) with an amine of the formula R^3NH_2 with the use of an amide coupling agent such as DCC, CDI, EEDQ, DEPC, or EDC. On the protected derivative, R^4 can be introduced via alkylation, for instance with a base such as sodium hydride or potassium *tert*-butoxide and an alkylating agent such as R^4-X where is X is Br, Cl or methanesulfonate.

The compound of formula 1 (R^1 and R^2 are taken together to form $=CR^4C(O)R^3$) can be prepared either by direct Wittig or Horner-Emmons reaction of hygromycin A or a protected form of hygromycin A with for example the corresponding $R^3C(O)CHR^4$-PPh_3 (Ph is phenyl) or $R^3C(O)CHR^4$-$P=O(OEt)_2$ (Et is ethyl) reagent. Olefination can be carried out by procedures described in J. Boutagy and R. Thomas, Chem. Rev. (1974) 74, 87 and B.E. Maryanoff et al., Chem. Rev. (1989) 89 863. Alternatively, the protected, unsaturated carboxylic acid derivative of hygromycin A can be transformed into its Weinreb amide, for instance through treatment with CDI and N,O-dimethylhydroxylamine. This amide can then be reacted with R^3-M, where M is a metal ion such as Li or MgBr, to generate the ketone, according to the procedure of S. Nahm and S.M. Weinreb, Tet. Lett. (1981) 22 39.

Compounds of formula 1 wherein R^1 and R^2 are taken together to form $=CR^4R^3$, wherein R^3 and R^4 are as defined above, may be prepared by a Wittig or Horner-Emmons reaction of the ylid of R^4-$CH(PPh_3)$-R^3 or R^4-$CH(P=O(OEt)_2)$-R^3 with hygromycin A, or a protected derivative thereof, in which the hydroxyl groups have been modified as, for example, their silyl ethers such as TES or TBDMS as described above. The protecting groups can then be removed as described above.

Alternatively, the C-5" homologated ketone or aldehyde of hygromycin A can be utilized as an intermediate. These compounds can be accessed via Wittig or Horner-Emmons reaction with an oxygenated triphenylphosphonium salt or phosphorane such as Ph_3P-$C(R^3)OMe$ (Me is methyl). The resulting enol ether can be hydrolyzed with mild acid, such as acetic acid or dilute HCl, to provide the aldehyde or ketone. The aldehyde or ketone can then be reacted with an organometallic derivative R^4M, where M is, for example, Li or MgBr, to provide the corresponding alcohol, which can be dehydrated under the action of methanesulfonyl chloride to provide the corresponding olefin. Deprotection as described above then provides the compound of formula 1 wherein R^1 and R^2 are taken together to form $=CR^4R^3$.

The compound of formula 1 wherein R^1 and R^2 are taken together to form $=CR^4R^3$ and R^4 is aryl or heteroaryl and R^3 does not equal hydrogen, may be prepared using a palladium-catalyzed process. Conversion of the protected ketone CH_3-$CH(COR^3)$-hygro to the enol triflate can be carried out by the method of P.J. Stang and W. Treptow, Synthesis (1980) 283. The enol triflate can then be coupled in a Suzuki or Stille-type palladium-catalyzed process with aryl or heteroaryl boronic acids $R^4B(OH)_2$ or aryl tin species, for example R^4SnMe_3 or R^4SnBu_3 to provide the unsaturated aryl derivatives. Suzuki coupling reactions can be carried out as described by N. Miyaura and A. Suzuki, Chem. Rev. (1995) 95 2457. Stille reactions

are performed using conditions described in V. Farina et al., Org. Reactions (1997) 50 1. Deprotection as described above then provides the final compound.

The compounds of the present invention have asymmetric carbon atoms. Compounds having a mixture of isomers at one or more centers will exist as diastereomeric mixtures, which can be separated into their individual diastereomers on the basis of their physical chemical differences by methods known to those skilled in the art, for example, by chromatography or fractional crystallization. All such isomers, including diastereomer mixtures, are considered as part of the invention.

The compounds of the present invention that are basic in nature are capable of forming a wide variety of different salts with various inorganic and organic acids. Although such salts must be pharmaceutically acceptable for administration to animals, it is often desirable in practice to initially isolate the compound of the present invention from the reaction mixture as a pharmaceutically unacceptable salt and then simply convert the latter back to the free base compound by treatment with an alkaline reagent and subsequently convert the latter free base to a pharmaceutically acceptable acid addition salt. The acid addition salts of the basic compounds of this invention are readily prepared by treating the basic compound with a substantially equivalent amount of the chosen mineral or organic acid in an aqueous solvent medium or in a suitable organic solvent, such as methanol or ethanol. Upon careful evaporation of the solvent, the desired solid salt is readily obtained. The desired acid salt can also be precipitated from a solution of the free base in an organic solvent by adding to the solution an appropriate mineral or organic acid.

Those compounds of the present invention that are acidic in nature, are capable of forming base salts with various pharmacologically acceptable cations. Examples of such salts include the alkali metal or alkaline-earth metal salts and particularly, the sodium and potassium salts. These salts are all prepared by conventional techniques. The chemical bases which are used as reagents to prepare the pharmaceutically acceptable base salts of this invention are those which form non-toxic base salts with the acidic compounds of the present invention. Such non-toxic base salts include those derived from such pharmacologically acceptable cations as sodium, potassium, calcium and magnesium, etc. These salts can easily be prepared by treating the corresponding acidic compounds with an aqueous solution containing the desired alkali metal alkoxide or metal hydroxide, and then evaporating the resulting solution to dryness, preferably under reduced pressure. Alternatively, they may also be prepared by mixing lower alkanolic solutions of the acidic compounds and the desired alkali metal alkoxide or metal hydroxide together, and then evaporating the resulting solution to dryness in the same manner

as before. In either case, stoichiometric quantities of reagents are preferably employed in order to ensure completeness of reaction and maximum yields of the desired final product.

The antibacterial activity of the compounds of the present invention against bacterial pathogens is demonstrated by the compound's ability to inhibit growth of defined strains of pathogens.

Assay

The assay, described below, employs conventional methodology and interpretation criteria and is designed to provide direction for chemical modifications that may lead to compounds with antibacterial activity against susceptible and drug-resistant organisms including, but not limited to, beta-lactam, macrolide and vancomycin resistance. In the assay, a panel of bacterial strains is assembled to include a variety of target pathogenic species, including representatives of antibiotic resistant bacteria. Use of this panel enables the chemical structure/activity relationship to be determined with respect to potency and spectrum of activity. The assay is performed in microtiter trays and interpreted according to Performance Standards for Antimicrobial Disk Susceptibility Tests - Sixth Edition; Approved Standard, published by The National Committee for Clinical Laboratory Standards (NCCLS) guidelines; the minimum inhibitory concentration (MIC) is used to compare strains. Compounds are initially dissolved in dimethylsulfoxide (DMSO) as stock solutions.

The activity of the compounds of the present invention also may be assessed in accord with Steers replicator technique which is a standard in vitro bacterial testing method described by Steers et al., *Antibiotics and Chemotherapy* **1959**, 9, 307.

The in vivo activity of the compounds of the present invention can be determined by conventional animal protection studies well known to those skilled in the art, usually carried out in rodents.

According to one *in vivo* model, compounds are evaluated for efficacy in mouse models of acute bacterial infection. An example of one such *in vivo* system is provided as follows. Mice (CF1 mixed sex mice; 18-20 g) are allotted to cages upon their arrival, and allowed to acclimate 1-2 days before being placed in a study. The acute infection is produced by intraperitoneal inoculation of bacteria (*Staphylococcus aureus* strain 01A1095) suspended in 5% sterile hog gastric mucin. The inoculum is prepared by: growing the culture overnight at 37°C on blood agar, harvesting the resulting surface growth with sterile brain heart infusion broth, and adjusting this suspension to a turbidity that when diluted 1:10 into 5% sterile hog gastric mucin would produce 100% lethality.

Mice (10 per group) are treated subcutaneously, at 0.5 hour and 4 hours after challenge. Appropriate non-treated (infected but not treated) and positive (vancomycin or

minocycline, etc.) controls are included in each study. Percent survival is recorded after a 4-day observation period; the PD_{50} (mg/kg/dose calculated to protect 50% of infected animals) is determined by the probit method.

The compounds of the present invention, and the pharmaceutically acceptable salts thereof (hereinafter "the active compounds"), may be administered through oral, parenteral, topical, or rectal routes in the treatment of bacterial and protozoal infections. In general, these compounds are most desirably administered in dosages ranging from about 0.2 mg per kg body weight per day (mg/kg/day) to about 200 mg/kg/day in single or divided doses (i.e., from 1 to 4 doses per day), although variations will necessarily occur depending upon the species, weight and condition of the subject being treated and the particular route of administration chosen. However, a dosage level that is in the range of about 3 mg/kg/day to about 60 mg/kg/day is most desirably employed. Variations may nevertheless occur depending upon the species of mammal, fish or bird being treated and its individual response to said medicament, as well as on the type of pharmaceutical formulation chosen and the time period and interval at which such administration is carried out. In some instances, dosage levels below the lower limit of the aforesaid range may be more than adequate, while in other cases still larger doses may be employed without causing any harmful side effects, provided that such larger doses are first divided into several small doses for administration throughout the day.

The active compounds may be administered alone or in combination with pharmaceutically acceptable carriers or diluents by the routes previously indicated, and such administration may be carried out in single or multiple doses. More particularly, the active compounds may be administered in a wide variety of different dosage forms, i.e., they may be combined with various pharmaceutically acceptable inert carriers in the form of tablets, capsules, lozenges, troches, hard candies, powders, sprays, creams, salves, suppositories, jellies, gels, pastes, lotions, ointments, aqueous suspensions, injectable solutions, elixirs, syrups, and the like. Such carriers include solid diluents or fillers, sterile aqueous media and various non-toxic organic solvents, etc. Moreover, oral pharmaceutical compositions can be suitably sweetened and/or flavored. In general, the active compounds are present in such dosage forms at concentration levels ranging from about 5.0% to about 70% by weight.

For oral administration, tablets containing various excipients such as microcrystalline cellulose, sodium citrate, calcium carbonate, dicalcium phosphate and glycine may be employed along with various disintegrants such as starch (and preferably corn, potato or tapioca starch), alginic acid and certain complex silicates, together with granulation binders like polyvinylpyrrolidone, sucrose, gelatin and acacia. Additionally, lubricating agents such as magnesium stearate, sodium lauryl sulfate and talc are often very useful for tabletting purposes.

Solid compositions of a similar type may also be employed as fillers in gelatin capsules; preferred materials in this connection also include lactose or milk sugar as well as high molecular weight polyethylene glycols. When aqueous suspensions and/or elixirs are desired for oral adinistration, the active compound may be combined with various sweetening or flavoring agents, coloring matter or dyes, and, if so desired, emulsifying and/or suspending agents as well, together with such diluents as water, ethanol, propylene glycol, glycerin and various like combinations thereof.

For parenteral administration, solutions of an active compound in either sesame or peanut oil or in aqueous ethanol or propylene glycol may be employed. Use of a cyclodextrin derivative such as β-cyclodextrin sulfobutyl ether, sodium salt (see United States patent 5,134,127) may also be advantageous. The aqueous solutions should be suitably buffered if necessary and the liquid diluent first rendered isotonic. These aqueous solutions are suitable for intravenous injection purposes. The oily solutions are suitable for intraarticular, intramuscular and subcutaneous injection purposes. The preparation of all these solutions under sterile conditions is readily accomplished by standard pharmaceutical techniques known to those skilled in the art.

Additionally, it is also possible to administer the active compounds of the present invention topically and this may be done by way of creams, jellies, gels, pastes, patches, ointments and the like, in accordance with standard pharmaceutical practice.

For administration to animals other than humans, such as cattle or domestic animals, the active compounds may be administered in the feed of the animals or orally as a drench composition.

The active compounds may also be administered in the form of liposome delivery systems, such as small unilamellar vesicles, large unilamellar vesicles and multilamellar vesicles. Liposomes can be formed from a variety of phospholipids, such as cholesterol, stearylamine or phosphatidylcholines.

The active compounds may also be coupled with soluble polymers as targetable drug carriers. Such polymers can include polyvinylpyrrolidone, pyran copolymer, polyhydroxypropylmethacrylamide phenyl, polyhydroxyethylaspartamide-phenol, or polyethyleneoxide-polylysine substituted with palmitoyl residues. Furthermore, the active compounds may be coupled to a class of biodegradable polymers useful in achieving controlled release of a drug, for example, polylactic acid, polyglycolic acid, copolymers of polylactic and polyglycolic acid, polyepsilon caprolactone, polyhydroxy butyric acid, polyorthoesters, polyacetals, polydihydropyrans, polycyanoacrylates and cross-linked or amphipathic block copolymers of hydrogels.

The present invention is further described and exemplified in the preparations and examples described below. In the preparations and examples, "rt" means room or ambient temperature which is a temperature within the range of about 20-25°C.

Preparation 1

Five (5) mL of a frozen lot (stored at -80°C in 20% glycerol/80% inoculum medium) of the culture *Streptomyces hygroscopicus* NRRL 2388 was used to inoculate 1L of hygromycin inoculum medium (Corn Products Corp. cerelose 13 g/L, Hubinger starch 7 g/L, Roquette corn steep solids 3 g/L, Sheffield Brand Products NZ Amine YTT 7 g/L, Baker $CoCl_2.6H_2O$ 0.002 g/L, KH_2PO_4 0.7 g/L, $MgSO_4.7H_2O$ 1.3 g/L, ammonium sulfate 0.7 g/L, Dow Chemical P2000 defoamer 1 drop/flask, Colfax soybean oil 2 drops/flask, pH to 7.0 before autoclave) in a 2.8L Fernbach flask. The culture was grown for 3 days at 29°C with 200 rpm agitation on a 2-inch-throw shaker. This grown culture was used to inoculate 8L of sterile hygromycin fermentation medium (Albaglos calcium carbonate 1 g/L, Sheffield Brand Products NZ Amine YTT 5 g/L, Hubinger's starch 20 g/L, Archer Daniels Midland Nutrisoy flour 10 g/L, Dow Chemical P2000 defoamer 1 ml/L, Baker $CoCl_2.6H_2O$ 0.002 g/L, Colfax soybean oil 2 ml/L, cerelose 10 g/L, NaCl 5 g/L, pH to 7.0 before autoclave) in a 14 liter fermentor jar (New Brunswick Microferm, New Brunswick, New Jersey) equipped with two 4.75-inch Rushton impellers, spaced 3.75 inches from each other. The broth was incubated at 29°C with an aeration rate of 8 L/minute, and with stirring at 800 rpm. To minimize formation of *epi*-hygromycin, the pH was maintained between 6.5 and 6.9 for 126 hours, then to 6.2 to 6.6 with H_2SO_4 (15%) for the rest of the run. The fermentation was harvested after 143 hours total incubation. At this time, the ratio was 31:1 hygromycin A to *epi*-hygromycin.

Six liters of broth from the above fermentation was centrifuged at 8000 rpm for approximately 15 minutes. After centrifugation, the pellet was discarded and the supernatant (at pH 6.4, assayed by HPLC to contain approximately 4.12 gms of hygromycin A activity) was loaded on a column packed with 500 gms of an XAD-16 resin (Rohm and Haas (Philadelphia, Pennsylvania). The resin had previously been equilibrated with two bed volumes of 25 mM di-sodium phosphate, pH 6.0 ("buffer"). After loading, the column was washed with 2 bed volumes of buffer and 2 bed volumes of 80/20 buffer/methanol and the activity eluted with 5 bed volumes of 50/50 buffer/methanol. The cuts were assayed by HPLC and the cuts containing the bulk of the activity (2.730 gms of hygromycin A) were combined.

A part of this XAD-16 eluate (approximately 800 mg of hygromycin A) was diluted to 10% methanol by the addition of 1.8 liters of buffer and loaded on a 100 ml CG-161 column (TosoHaas (Montgomeryville, Pennsylvania)) which had been equilibrated with 4 bed volumes of 90/10 buffer/methanol. The product was eluted with 6 bed volumes of 50/50

buffer/methanol. The cuts were assayed by HPLC and the active cuts were combined. The combined cut was evaporated to dryness and the solids assayed to be approximately 65% pure by weight. A small part of these solids were transferred for assay.

About 500 mg of the solids were mixed with 500 ml of water and 500 ml of ethyl acetate and stirred for 20 minutes. The two layers were separated and part of the aqueous layer was dried to obtain solids which were assayed to be approximately 52% purity by weight. Both these solids (#34945-280-1 and 281-1) were assayed by NMR and TLC and found to contain hygromycin A activity. In addition, the NMR showed a hygromycin A/*epi*-hygromycin ratio of approximately 15:1.

Preparation 2

Five (5) mL of a frozen lot (stored at -80°C in 20% glycerol/80% inoculum medium) of the culture *Streptomyces hygroscopicus* NRRL 2388 was used to inoculate 1L of Hygromycin inoculum medium (CPC International Inc. cerelose 13 g/L, Hubinger's starch 7 g/L, Roquette corn steep solids 3 g/L, NZ Amine YTT 7 g/L, Baker $CoCl_2.6H_2O$ 0.002 g/L, KH_2PO_4 0.7 g/L, $MgSO_4.7H_2O$ 1.3 g/L, ammonium sulfate 0.7 g/L, Dow Chemical P2000 defoamer 1 drop/flask, Colfax soybean oil 2 drops/flask, pH to 7.0 before autoclave) in a 2.8 L Fernbach flask. The culture was grown for 2 to 3 days at 29°C with 200 rpm agitation on a 2-inch-throw shaker. Two five-hundred gallon, stainless steel fermentors were loaded with 380-400 gallons of the hygromycin fermentation medium (Mineral Technologies Calcium Carbonate 1 g/L, Sheffield Brand Products NZ Amine YTT 5 g/L, Hubinger's starch 20 g/L, Archer Daniels Midland Co., Soyflour 10 g/L, Dow Chemical P2000 defoamer 1 ml/L, Baker $CoCl_2.6H_2O$ 0.002 g/L, Colfax, Inc. soybean oil 2 gm/L, CPC International Inc. Cerelose 10 g/L, Cargill Inc. NaCl 5 g/L,). The medium was sterilized with 20 psig of steam for 60 minutes in the fermentors. After the medium was cooled using cooling coils in the fermentors, the pH was adjusted to 6.5-6.7. The fermentor conditions were set so that the airflow rate was 20 standard cubic feet per minute, the temperature was 28°C, the vent pressure was 5 psig, and the pH was maintained between 6.5 - 6.7 with 25% sodium hydroxide and 98% sulfuric acid. The agitation rates in the two fermentors were varied so as to maintain a dissolved oxygen level of greater than 20% of saturation level as measured in the broth immediately prior to inoculation. Upon setting the fermentor control conditions, five Fernbach inoculum flasks were combined in a sterile manner, into an 8 L aspirator bottle. This inoculum was then used for inoculation of a single, nominal, five-hundred gallon fermentor as described above. This procedure was repeated using 4 liters of inoculum so that one fermentor received four liters of inoculum and one fermenter received five liters of inoculum. Each fermentor ran for approximately 114 hours, at

which time the fermentations were stopped. The broth pH was adjusted to 6.3 using 98% sulfuric acid and transferred from the fermentors for recovery.

The two fermentors referred to above (pH= 6.3, having a ratio of hygromycin A to *epi*-hygromycin of approximately 51:1) were filtered on a ceramic filtration system. The filtrate (1450 gmsA, 506 gal) was loaded on a 70-gallon XAD-16 resin column. This column had been equilibrated previously with 4 bed volumes of a solution of trisodium phosphate buffer at pH 6.0 ("buffer"). After loading, the column was washed with 2 bed volumes of buffer and 2 bed volumes of 80/20 buffer/methanol. The activity was subsequently eluted from the column with 10 cuts (approximately 50 gallons each) of a solution of 50/50 buffer/methanol. The active cuts (approximately 1240 gmsA) were combined and diluted to a final concentration of 10% methanol by the addition of 1200 gallons of buffer. The use of dilution (rather than rotary evaporation) to reduce methanol concentration allowed the use of lower temperatures so as to minimize *epi*-hygromycin amounts, which tend to increase at higher temperatures. Half of this solution was loaded on a 40 liter CG-161 column (previously equilibrated with 4 bed volumes of a solution of 90/10 buffer/ methanol). After loading, the column was washed with 4 bed volumes of 80/20 buffer/methanol and eluted with 5.5 bed volumes of 50/50 buffer/ methanol. After regeneration and re-equilibration of the column, the second half of the activity was loaded on the column and eluted as described above. The combined cuts from both the runs (120 liters, approximately 1051 gmsA) were diluted to 10% methanol by the addition of buffer. This was re-loaded on the regenerated and re-equilibrated CG-161 resin column. Once the activity was adsorbed on the column, it was eluted with 4 bed volumes of methanol. This step served to both reduce the salts as well as increase the concentration of the sample prior to the final evaporation. The combined cuts from the final CG-161 column were evaporated to dryness to obtain a total of approximately 1 kgA of hygromycin A activity. The ratio of hygromycin A to *epi*-hygromycin in the final solids was about 14.5:1.

Experimental Procedures For Examples

In cases where final purification was effected using silica gel chromatography with an eluant system containing more than 10% methanol, the chromatographed product was taken up in 89:10:1 chloroform: methanol: concentrated ammonium hydroxide and filtered, or dissolved in methanol and passed through a 0.45 μM filter. Removal of solvent *in vacuo* provided the final product. In the procedures below, t-BOC refers to "*tert*-butoxycarbonyl".

5"-Oxime Ether Preparations

Preparation of hydroxylamine reagents for synthesis of oxime ethers, Examples 1-92, 1A-116A

The majority of hydroxylamine reagents employed were either commercially available (generally as an acid salt), or prepared from the corresponding alcohol or halide via the methods outlined below:

1) Preparation of phthalimide-protected benzylic or aliphatic hydroxylamines:

From the alcohol:

A Mitsunobu reaction with diethyl azodicarboxylate and triphenylphosphine was used to couple N-hydroxyphthalimide and the alcohol starting material, according to the procedure of E. Grochowski and J. Jurczak, Synthesis (1976) 682.

From the bromide or chloride:

Reaction of N-hydroxyphthalimide (1 equivalent) with the halide starting material (1.2 - 2 equivalents) was carried out in DMSO solution, using potassium carbonate (0.6 - 2 equivalents) as base. The reactions were carried out at room temperature, generally by stirring overnight. Pouring the reaction mixture into cold water provided a precipitate, which was filtered to give the phthalimide-protected hydroxylamine. In many cases, this material was directly deprotected; silica gel chromatography can also be employed, using ethyl acetate-hexane mixtures, to purify the phthalimide-protected hydroxylamine.

2) Removal of the phthalimide protecting group to provide the benzylic or aliphatic hydroxylamine:

Deprotection of the phthalimide-protected hydroxylamine was effected by reaction with hydrazine hydrate (1 - 2 equivalents) in ethanol solution, at temperatures ranging from room temperature to reflux, for periods ranging from 30 minutes to overnight. The reaction mixture was filtered, and the filtrate concentrated. This crude product can be taken to the next step as is, or can be further purified. Mixing the crude product with chloroform, removing solids by filtration and removal of solvent from the filtrate removes additional phthalhydrazide. Alternatively, the crude product was dissolved in 1N hydrochloric acid, and washed with ether or ethyl acetate. The aqueous layer was basified with saturated potassium carbonate solution and extracted with ether or ethyl acetate. Drying of the final organic layers and removal of solvent provided the hydroxylamine product.

3) Preparation of O-arylhydroxylamines:

Substituted phenols were converted into the corresponding O-arylhydroxylamines through the use of mesitylenesulfonylhydroxylamine, as described by Y. Endo, K. Shudo and T. Okamoto, Synthesis (1980) 461.

Preparation of miscellaneous alcohol and halide starting materials used in synthesis of hydroxylamines:

In general, benzyl alcohol derivatives could be transformed into the corresponding benzyl bromides, if desired, by treatment with 48% HBr at 65°C for 1-4 hours.

In a number of cases, alcohol starting materials were obtained by reduction of more highly oxidized commercially available compounds. 4-Cyclohexyl benzoic acid (Examples 46, 47) and 3-chloro-2-fluorobenzoic acid (Examples 13A, 14A) were reduced with lithium aluminum hydride (2 - 2.3 equivalents) in tetrahydrofuran to provide the corresponding alcohol. 3-(4-Chlorophenyl)propionic acid (Examples 56, 57), 3,4-dihydro-2H-1-benzopyran-2-carboxylic acid (Examples 36A, 37A), 4-chloro-3-sulfamoylbenzoic acid (Example 76A), 3-chlorothiophene-2-carboxylic acid (Examples 85A, 86A), 5-chlorothiophene-2-carboxylic acid (Examples 91A, 92A) and 2,6-dimethylbenzoic acid (Examples 98A, 99A) were reduced to the corresponding alcohols using diborane (1.1 - 2 equivalents) in tetrahydrofuran at 0°C to room temperature for 5 - 18 hours. 2-Fluoro-6-methoxybenzonitrile was hydrolyzed to 2-fluoro-6-methoxybenzoic acid by treatment with 30% aqueous KOH at reflux, and the acid reduced to 2-fluoro-6-methoxybenzyl alcohol (Example 80A) with diborane as above. 3-Trifluoromethoxybenzaldehyde (Examples 62, 68), 3-cyanobenzaldehyde (Example 63), benzofuran-2-carboxaldehyde (Examples 65, 66), 1,4-benzodioxan-6-carboxaldehyde (Examples 83, 84), 3-fluoro-4-methoxybenzaldehyde (Examples 85, 86), 6-fluoro-4-chromanone (Examples 16A, 17A) 3-chloro-4-fluorobenzaldehyde (Examples 19A, 22A), quinoline-3-carboxaldehyde (Examples 23A, 24A), 4-chloro-3-fluorobenzaldehyde (Examples 25A, 26A), 2,3-(methylenedioxy)benzaldehyde (Examples 28A, 29A), 2,4-dichlorobenzaldehyde (Examples 45A, 47A), 2-chloro-4-fluorobenzaldehyde (Examples 46A, 48A), 2-fluoro-6-(trifluoromethyl)benzaldehyde (Examples 66A, 67A), 2,3-difluorobenzaldehyde (Examples 68A, 69A), 2-(difluoromethoxy)benzaldehyde (Examples 93A, 94A) and 6-chlorochromanone (Examples 102A, 103A) were reduced to the alcohol derivatives using sodium borohydride (1 - 2 equivalents) in tetrahydrofuran or methanol at 0°C or room temperature.

Magnesium sulfate (4 equivalents) in methylene chloride was treated with concentrated sulfuric acid (1 equivalent), followed by 4-chloromethylbenzoic acid (1 equivalent) and tert-butanol (5.1 equivalents). Stirring overnight at room temperature provided the tert-butyl ester (Example 36).

4-Amino-3,5-dichlorobenzoic acid was N-acetylated by treatment with acetyl chloride (1.2 equivalents) in dimethylformamide at 90°C for 4 hours. The cooled reaction mixture was poured into cold water, chilled and filtered to provide the acetamide derivative. Reduction of

the carboxylic acid was effected with lithium aluminum hydride (2 equivalents) in tetrahydrofuran at 0°C for 2 hours, to provide N-(2,6-dichloro-4-hydroxymethyl-phenyl)acetamide (Example 51).

3-(Aminomethyl)benzyl alcohol and 4-(aminomethyl)benzyl alcohol were prepared by reduction of 3- and 4-cyanobenzaldehyde using diborane (4-5 equivalents) in THF at room temperature overnight. The amino groups of 3-(aminomethyl)benzyl alcohol (Examples 8A and 9A) and 4-(aminomethyl)benzyl alcohol (Example 55) as well as 3-aminobenzyl alcohol (Example 54) were protected as the N-*t*-BOC derivatives by treatment with di-tert-butyl dicarbonate (1.1 equivalent) in THF at reflux until the starting amino compound was consumed.

Reaction of ethyl 4-fluorobenzoate with piperidine (3 equivalents) in acetonitrile was carried out at reflux for 4 days. Dilution of the cooled reaction mixture with several volumes of water provided a precipitate, which was filtered to provide ethyl 4-(piperidin-1-yl)benzoate. Reduction of the ester with lithium aluminum hydride (2 equivalents) in tetrahydrofuran gave the corresponding alcohol (Examples 71, 72).

5-Hydroxymethylbenzofuran (Examples 79, 80) was prepared according to the procedure of K. Hiroya, K. Hashimura and K. Ogasawara, Heterocycles (1994) 38, 2463.

2-Phenylpyrimidine-5-carboxaldehyde (Examples 81, 82) was prepared according to the procedure of J. T. Gupton, J.E. Gall, S. W. Riesinger et al., J. Heterocyclic Chemistry (1991) 28, 1281. The aldehyde was reduced to the corresponding alcohol using sodium borohydride in methanol.

3-Hydroxymethyl-4-phenylfuran (Examples 6A, 7A) was prepared according to the procedure of B.A. Keay and J-L.J. Bontront, Canadian J. Chemistry (1991) 69, 1326.

5-Chloro-2-fluorobenzyl bromide (Examples 12A, 32A) was prepared by the method of A.P. Krapcho, C.E. Gallagher, A. Mammach, M. Ellis, E. Menta, and A. Oliva , J. Heterocyclic Chemistry (1997), 34, 27-32.

2-Chloro-3,4-dimethoxybenzaldehyde was converted to 4-chloro-1,3-benzodioxole-5-carboxaldehyde by the method of S.T. Ross, R.G. Franz, J.W. Wilson, R.A. Hahn and H.M. Sarau, J. Heterocyclic Chemistry, (1986) 23, 1805. Reduction of the aldehyde was then carried out with sodium borohydride (1 equivalent) in THF at 0°C to provide 4-chloro-1,3-benzodioxole-5-methanol (Examples 30A, 31A).

4-Phenylfuroic acid was prepared by the method of M.E. Alonso, P. Jano, M.I. Hernandez, R.S. Greenberg and E. Wenkert, J. Organic Chemistry (1983) 48, 3047. Reduction to 2-(hydroxymethyl)-4-phenylfuran (Examples 34A, 35A) was carried out

according to W.A. Scrivens, J.M.Tour, K.E. Creek, L. Pirisi, J. American Chemical Society (1994) 116, 4517.

3-Chloro-2,6-difluorobenzaldehyde was prepared from 1-chloro-2,4-difluorobenzene with n-buthyllithium and N,N-dimethylformamide by the method of A.S. Cantrell *et al.*, J. Medicinal Chemistry (1996) 21, 4261. Reduction with sodium borohydride in methanol provided 3-chloro-2,6-difluorobenzyl alcohol, which was transformed into 3-chloro-2,6-difluorobenzyl bromide (Examples 38A, 39A) by treatment with 48% HBr at 65°C for 3 hours. Similar treatment of 2,3,5,6-tetrafluorotoluene provided 2,3,5,6-tetrafluoro-4-methylbenzyl bromide (Examples 40A, 41A), and 3,5-difluorotoluene was similarly converted to 2,6-difluoro-4-methylbenzyl bromide (Examples 63A, 64A). 3,4-Difluoroanisole was similarly converted to 2,3-difluoro-6-(methoxy)benzyl bromide (Examples 74A, 75A), and 1-fluoro-3-(trifluoromethoxy)benzene converted to 2-fluoro-6-(trifluoromethoxy)benzyl bromide (Examples 77A, 78A). 2-Chloro-6-(trifluoromethoxy)benzyl alcohol (Examples 89A, 90A) was prepared in similar manner, except that lithium diisopropylamide was used in the formylation reaction, rather than n-butyllithium.

Vanillin was converted to 7-chloro-benzodioxole-5-carboxaldehyde by the method of T-T. Jong, P.G. Williard, and J.P. Porwoll, J. Organic Chemistry (1984) 49, 735. Reduction with sodium borohydride (1 equivalent) in methanol at room temperature then provided 7-chloro-1,3-benzodioxole-5-methanol (Examples 51A, 52A). In this case, transformation into the hydroxylamine reagent was carried out through intermediacy of a mesylate derivative, which was prepared by the method of R.K. Crossland and K.L. Servis, J. Organic Chemistry (1970) 35, 3195.

3-Chloro-5-fluorobenzyl alcohol (Examples 53A, 54A) was prepared according to W.R. Meindl, E. Von Angerer, H. Schoenenberger, and G. Ruckdeschel, J. Medicinal Chemistry (1984) 27, 1111.

4-Phenyl-2-thiazolecarboxaldehyde was prepared by a method analogus to K. Inami and T. Shiba, Bull. Chem. Soc. Jpn., (1985) 58, 352. The aldehyde was reduced to the corresponding alcohol using sodium borohydride in ethanol. The corresponding 2-chloromethyl thiazole derivative (Examples 104A, 105A) was prepared by treatment of the alcohol with thionyl chloride (4 equivalents) in methylene chloride at room temperature for 2-5 hours.

2,4-Difluoropropiophenone was reduced to the corresponding alcohol (Examples 106A, 107A) using sodium borohydride in ethanol.

1-(3-Chloro-2,6-difluorophenyl)ethanol and other phenylethanol derivatives (Examples 108A-116A) were prepared by treatment of the corresponding benzaldehyde derivative with

methylmagnesium bromide (1 equivalent) in THF at room temperature. These alcohols were then converted to the corresponding benzyl bromides by treatment with 48% HBr for 1-4 hours.

Preparation of oxime ethers, Methods (A - I), Examples 1-92, 1A-116A

Method A

A solution of hygromycin A (1 equivalent) and the hydrochloride salt of the appropriate hydroxylamine (1 - 2.2 equivalents) in methanol (roughly 0.1 M in hygromycin A) was treated with sodium carbonate (1.1-1.2 equivalents per equivalent of hydroxylamine salt) and heated to reflux for 15 minutes to 2 hours. The reactions can be followed by thin layer chromatography, using methanol/chloroform or methanol/chloroform/ammonium hydroxide eluants. The reaction mixture was then cooled to room temperature, and concentrated *in vacuo*. The crude product was purified by one of methods J to N.

Method B

A solution of hygromycin A (1 equivalent) and the hydrochloride salt of the appropriate hydroxylamine (1 - 2.2 equivalents) in methanol (roughly 0.1 M in hygromycin A) was treated with sodium carbonate (1.1-1.2 equivalents per equivalent of hydroxylamine salt) and heated to reflux for 18 hours. The reactions can be followed by thin layer chromatography, using methanol/chloroform or methanol/chloroform/ammonium hydroxide eluants. The reaction mixture was then cooled to room temperature, and concentrated *in vacuo*. The crude product was purified by one of methods J to N.

Method C

A solution of hygromycin A (1 equivalent) and the free base of the appropriate hydroxylamine (1 - 2.2 equivalents) in methanol (roughly 0.1 M in hygromycin A) was heated to reflux for 18 hours. The reactions can be followed by thin layer chromatography, using methanol/chloroform or methanol/chloroform/ammonium hydroxide eluants. The reaction mixture was then cooled to room temperature, and concentrated *in vacuo*. The crude product was purified by one of methods J to N.

Method D

A solution of hygromycin A (1 equivalent) and the free base of the appropriate hydroxylamine (1 - 2.2 equivalents) in methanol (roughly 0.1 M in hygromycin A) was heated to reflux for 5-6 hours. The reactions can be followed by thin layer chromatography, using methanol/chloroform or methanol/chloroform/ammonium hydroxide eluants. The reaction mixture was then cooled to room temperature, and concentrated *in vacuo*. The crude product was purified by one of methods J to N.

Method E

A solution of hygromycin A (1 equivalent) and the free base of the appropriate hydroxylamine (1 - 2.2 equivalents) in methanol (roughly 0.1 M in hygromycin A) was allowed to stir at room temperature for 18 hours. The reactions can be followed by thin layer chromatography, using methanol/chloroform or methanol/chloroform/ammonium hydroxide eluants. The reaction mixture was then concentrated *in vacuo*. The crude product was purified by one of methods J to N.

Method F

A solution of hygromycin A (1 equivalent) and the free base of the appropriate hydroxylamine (1 - 2.2 equivalents) in methanol (roughly 0.1 M in hygromycin A) was allowed to stir at room temperature for 1-5 hours. The reactions can be followed by thin layer chromatography, using methanol/chloroform or methanol/chloroform/ammonium hydroxide eluants. The reaction mixture was then concentrated *in vacuo*. The crude product was purified by one of methods J to N.

Method G

Separate solutions of hygromycin A (1 equivalent) and the free base of the appropriate hydroxylamine (1 - 2.2 equivalents) in methanol (final concentration, 0.5 - 0.1 M in hygromycin A) were combined at 0°C and allowed to warm to room temperature over 1-2 hours. The reactions can be followed by thin layer chromatography, using methanol/chloroform or methanol/chloroform/ammonium hydroxide eluants. The reaction mixture was then concentrated *in vacuo*. The crude product was purified by one of methods J to N.

Method H

A solution of hygromycin A (1 equivalent) and the free base of the appropriate hydroxylamine (1 - 2.2 equivalents) in methanol (final concentration, 0.5 - 0.1 M in hygromycin A) was stirred at 0°C for 2-3 hours. The reactions can be followed by thin layer chromatography, using methanol/chloroform or methanol/chloroform/ammonium hydroxide eluants. The reaction mixture was then concentrated *in vacuo*. The crude product was purified by one of methods J to N.

Method I

The substrate (see Tables for substrate employed) was dissolved in trifluoroacetic acid at a concentration of about 0.1 M, and allowed to stir at room temperature for 15 minutes, at which point the trifluoroacetic acid was removed *in vacuo*. Several volumes of a solution of 89:10:1 chloroform:methanol:concentrated ammonium hydroxide were added, and the

volatiles removed *in vacuo*. The neutralization was repeated, and concentrated *in vacuo* to provide the crude product.

Purification of oxime ethers, Methods (J - N-1)

Method J

Purification was carried out by silica gel chromatography. The crude product was generally preadsorbed onto silica gel through addition of dry silica gel to a methanol solution of the product, followed by complete removal of solvent. Column elution was carried out using a solution of methanol in chloroform, generally 5% to 20%, often run as a step gradient.

Method K

Purification was carried out by silica gel chromatography. The crude product was generally preadsorbed onto silica gel through addition of dry silica gel to a methanol solution of the product, followed by complete removal of solvent. Column elution was carried out using a solution of methanol in methylene chloride, generally 5 % to 20%, often run as a step gradient.

Method L

Purification was carried out by silica gel chromatography. The crude product was generally preadsorbed onto silica gel through addition of dry silica gel to a methanol solution of the product, followed by complete removal of solvent. Column elution was carried out using a ternary solution of chloroform: methanol: ammonium hydroxide, ranging in composition from 289:10:1 to 39:10:1, depending on the R_f of the products and starting materials. Columns were generally run as a step gradient. In the case of Example 55 the final column eluant was 73:25:2.

Method M

Purification was carried out by silica gel chromatography. The crude product was generally preadsorbed onto silica gel through addition of dry silica gel to a methanol solution of the product, followed by complete removal of solvent. Column elution was carried out using a ternary solution of methylene chloride: methanol: ammonium hydroxide, ranging from 322:10:1 to 56:10:1, often run as a step gradient.

Method N

Purification was carried out by C_{18} reversed-phase chromatography, eluting with a methanol-water solution of 10% to 100%, depending on the R_f of the products and starting materials. Columns were generally run as a step gradient.

Method N-1

Purification was carried out by C_{18} reversed-phase chromatography, eluting with a mixture of acetonitrile and 10 mM pH 7 potassium phosphate buffer. The isolated

components were minor products of the reaction mixture, obtained from epi-hygromycin (alpha stereochemistry at C-4") present in the hygromycin starting material.

5"-Amine Preparations, Examples 93-101

Methods (O - R) for preparation of amine derivatives

Method O

A solution of hygromycin A in methanol (0.1 M) was treated with the amine (1 equivalent) and allowed to stir at room temperature for 10 minutes. Acetic acid (3 equivalents) was added, followed by sodium triacetoxyborohydride (3 equivalents), and the reaction mixture was allowed to stir for an additional 24 hours. After treatment with a small volume of aqueous saturated sodium bicarbonate solution, solvents were removed *in vacuo*. The residue was purified by silica gel chromatography, eluting with a mixture of chloroform: methanol: ammonium hydroxide, ranging in composition from 89:10:1 to 70:28:2, often as a step gradient.

Method P

A solution of hygromycin A in methanol (0.1 M) was treated with the amine (2 - 4 equivalents) and allowed to stir at room temperature for 1 hour. In cases where imine formation is sluggish, 3 Angstrom molecular sieves were added, and the mixture stirred overnight. Sodium borohydride (1-2 equivalents) was then added, and the reaction stirred for 2 - 24 hours. After treatment with a small volume of aqueous saturated sodium bicarbonate solution (and removal of sieves, if present, by filtration), solvents were removed *in vacuo*, and the residue was purified by silica gel chromatography, eluting with a mixture of chloroform:methanol:ammonium hydroxide, ranging in composition from 89:10:1 to 80:19:1.

Method Q

The amino hygromycin A derivative in water (0.1 M) was treated with formaldehyde (5 equivalents) then formic acid (10 equivalents) and stirred at 90°C for 5 hours, then at room temperature for 48 hours. After addition of saturated aqueous sodium bicarbonate, the reaction mixture was stirred and then the clear supernatant was decanted off. The remaining residue was purified by column chromatography using as eluant chloroform: methanol: ammonium hydroxide in a ratio of 80:19:1.

Method R

A solution of hygromycin A in methanol (0.1 M) was treated with an aniline (4 equivalents) and crushed 3 Angstrom molecular sieves and stirred at 50°C for 2 hours or 70°C overnight. After the reaction mixture had cooled to room temperature, sodium borohydride (1 - 2 equivalents) was added and stirring was continued for 2 - 48 hours at room temperature. A small volume of saturated aqueous sodium bicarbonate was added, the sieves were

removed by filtration, and the filtrate was concentrated *in vacuo*. The crude residue was purified by column chromatography on silica gel, using 80:19:1 chloroform: methanol: ammonium hydroxide as eluant.

5"-Amide Preparations, Examples 102-104

Preparation of amide derivatives, Methods S - T

Synthesis of persilylated 5"-amino hygromycin A

a) A solution of hygromycin A, tert-butyldimethylsilyl chloride (12 equivalents), and imidazole (12 equivalents) in DMF (hygromycin concentration 0.25 M) were stirred at 80°C for 20 hours. After removal of the DMF under reduced pressure, the resulting residue was extracted with diethyl ether. The combined ether extracts were washed with water, then saturated sodium chloride solution, dried over sodium sulfate, filtered, and concentrated. The crude product was purified by silica gel chromatography, eluting with 10% ethyl acetate/ hexanes.

b) A solution of persilylated hygromycin A in 1:1 methanol: tetrahydrofuran (0.2 M) was treated with sodium borohydride (0.5 equivalents) and stirred at room temperature for 18 hours. After removal of solvents under reduced pressure, the residue was dissolved in chloroform, washed with saturated sodium bicarbonate solution, dried over sodium sulfate, filtered, and concentrated to give crude persilylated 5"-alcohol. Purification was carried out by column chromatography eluting with 10%-20% ethyl acetate/ hexanes. Subsequent analysis of Mosher esters showed the stereochemistry at 5" of the major product of this reaction to be *R*.

c) A solution of the 5"-alcohol in methylene chloride (0.2 M) at 0°C was treated with triethylamine (3 equivalents), followed by methanesulfonyl chloride (2 equivalents) and stirred at room temperature for 24 hours. The reaction mixture was then poured into water and extracted with methylene chloride. The combined organic layers were dried over sodium sulfate, filtered, and concentrated *in vacuo* to give the 5"-mesylate.

d) The 5"-mesylate in DMF (0.2 M) was treated with sodium azide (10 equivalents) and stirred at 95°C for 18 hours. The reaction mixture was poured into water, extracted with diethyl ether, washed with brine, dried with sodium sulfate, filtered, and concentrated *in vacuo*. The crude 5"-azide was purified by silica gel chromatography, eluting with 10% ethyl acetate/ hexanes.

e) A solution of the 5"-azide and triphenylphosphine (3 equivalents) in toluene (5"-azide concentration 0.2 M) was stirred at 105°C 18 hours. The toluene was removed under reduced pressure and replaced with tetrahydrofuran/ water (10/1) (hygromycin derivative concentration 0.1 M) and stirred at 75°C 5 hours. The reaction mixture was poured into water

and extracted with diethyl ether. The combined organic layers were washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*. The crude product was purified by silica gel chromatography, eluting with 20% ethyl acetate/ hexanes, to provide persilylated 5"-amino hygromycin A.

Method S

a) Persilylated 5"-amino hygromycin A and the appropriate carboxylic acid (2 equivalents) were stirred together with EEDQ (1-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline, 2 equivalents) in THF at 70°C for three hours (persilylated hygromycin concentration 0.1 M). The reaction mixture was poured into water and extracted with ether. The combined organic layers were washed with 5% sodium carbonate solution, water, and saturated sodium chloride solution. After being dried over sodium sulfate, the organic extracts were filtered and concentrated to provide a residue which was chromatographed on silica gel using a mixture of ethyl acetate and hexanes, to provide the desired amide as its persilyl protected derivative.

b) The silyl groups were removed by treatment of a solution of 5"-modified hexasilylhygromycin A (1 equivalent, 0.1 M) with a 1M solution of tetrabutylamonium fluoride (TBAF, 10 equivalents) in THF at room temperature for 14-24 hours. The THF was removed *in vacuo* and the crude material was dissolved in a mixture of water and methanol. This solution/suspension was applied to a column of Dowex (50X4-400) resin (10 -30 g of resin/ mmol of TBAF, which had been converted to the OH form by treatment with 0.1-0.2N sodium hydroxide and then washed with one column volume (CV) of water). The column was gravity eluted with 1-3 CV of water until the TBAF was removed and then eluted with 50% aqueous methanol with the aid of nitrogen pressure to provide the desired amide product. If additional purification was required, silica gel chromatography was performed (method J-N).

Method T

A solution of the appropriate carboxylic acid (1.2 equivalents) in tetrahydrofuran was treated with DEPC (diethyl phosphoryl cyanide, 1.2 equivalents) and triethylamine (1.2 equivalents) and the reaction mixture was stirred for 10 minutes. Persilylated 5"-amino hygromycin A (1 equivalent) was added (final hygromycin derivative concentration 0.17 M) and the reaction was allowed to proceed at room temperature for 48 hours. The reaction mixture was poured into water and extracted with ether. The combined organic layers were washed with aqueous sodium carbonate, water, and saturated sodium chloride solution, then dried over sodium sulfate, filtered, and concentrated *in vacuo*. The crude material was purified by silica gel chromatography, using a mixture of ethyl acetate and hexanes.

The silylated amide was deprotected with TBAF as in Method S, step b.

5"-Ether, Carbamate Preparations, Examples 105 - 131

Methods (U - Z)

Alkylation or acylation of persilylated 5"-hydroxy hygromycin A (see Examples 102-104 section, procedures a and b) was achieved through procedures U through Y and the silyl groups were subsequently removed using method S, step b.

Method U for the preparation of 5"-hygromycin A benzyl ethers.

Sodium hydride (60% dispersion in mineral oil, 10 equivalents) was weighed into an oven-dried round bottomed flask and washed 3 times with hexanes. The residual hexanes were removed *in vacuo* and to this was added tetrahydrofuran (THF) (persilylated 5"-hygromycin A concentration 0.1 M), persilylated 5"-hydroxy hygromycin A (1 equivalent) , and a benzyl bromide (10 equivalents) at rt. The resultant slurry was heated at 50°C for 1-4 hours. The reaction was cooled to rt, quenched with water and then extracted two times with chloroform ($CHCl_3$). The combined organics were washed with brine, dried over $MgSO_4$ and concentrated to a semisolid which was then chromatographed (SiO_2, 5-15 % EtOAc:toluene or EtOAc:hexanes)(EtOAc refers to ethyl acetate) to provide the desired ether.

Method V

Potassium *tert*-butoxide (5 equivalent of a 1M solution in THF) was added to a solution of persilylated 5"-hydroxy hygromycin A (1 equivalent) and a benzyl bromide (10 equivalents) in THF (0.1 M in persilylated 5"-hydroxy hygromycin A) at rt. The reaction was complete after 15 minutes. The reaction was quenched by the addition of water and the product was extracted into chloroform. The combined organic extracts were dried over $MgSO_4$, concentrated *in vacuo* and chromatographed (SiO_2, 5-15 % EtOAc:toluene or EtOAc:hexanes) to provide the desired product.

Method W

Potassium *tert*-butoxide (2 equivalents of a 1M solution in THF) was added in a dropwise fashion over 5 minutes to a solution of persilylated 5"-hydroxy hygromycin A (1 equivalent) and a benzyl bromide (5 equivalents) in dioxane (0.1 M in persilylated 5"-hydroxy hygromycin) at room temperature. The reaction was complete after 15 minutes. The reaction was quenched by the addition of water and the product was extracted into chloroform. The combined organic extracts were dried over $MgSO_4$, concentrated *in vacuo* and chromatographed (SiO_2, 5-15 % EtOAC:toluene or EtOAc:hexanes) to provide the desired product.

Method X

Phenyl isocyanate (7 equivalents) was added to a solution of persilylated 5"-hydroxy hygromycin A (1 equivalent) in toluene (0.05 M in persilylated 5"-hydroxy hygromycin) and

heated to 60°C for 12-24 hours. The crude reaction mixture was concentrated and chromatographed (SiO_2, 5-15 % EtOAc:toluene or EtOAc:hexanes) to provide the silylated product.

Method Y

Benzyl isocyanate (7 equivalents) was prepared by the method of Sigurdsson, S. Th.; Seeger, B.; Kutzke, U.; and Eckstein, F., J. Org. Chem. (1996) 61, 3883. This was added to a solution of persilylated 5"-hydroxy hygromycin A (1 equivalent), dimethylaminopyridine (0.2 equivalents) and triethylamine (4 equivalents) in toluene (0.05 M in persilylated 5"-hydroxy hygromycin) and heated to 70°C for 12-24 hours. The crude reaction mixture was concentrated and chromatographed (SiO_2, 5-7% EtOAc:hexanes) to provide the silylated material.

Method Z

Persilylated 5"-hydroxy hygromycin A was treated with K_2CO_3 (1.3 equivalents) in methanol (0.1 M) and stirred 14-20 hours. The methanol was removed *in vacuo* and the residue taken up in 1:1 EtOAc:hexanes and water. The organics were washed with $NaHCO_3$ and brine, dried over $MgSO_4$ and concentrated. Without further purification this material was then treated with allyl bromide (1-3 equivalents) and K_2CO_3 (1.4 equivalents) in DMF (0.1 M) for 14-24 hours. The reaction mixture was poured into hexane and washed with water. The organics were dried over $MgSO_4$, filtered and concentrated to a white foam consisting of the allyl-protected phenolic hydroxyl group, which was used without further purification. The 5"-alcohol was alkylated with benzyloxychloromethyl ether under the conditions of method X. The allyl group was removed using the method of Jaynes, B. H., Elliot, N. C. and Schicho, D. L. J. Antibiot. (1992) 45, 1705. The silyl groups were then removed using Method S, step b.

5"-Olefin Preparations, Examples 132 - 140

Preparation of olefin derivatives, Methods AA-EE

Method AA

A solution of hygromycin A and (carboethoxymethylene)triphenylphosphorane (2 equivalents) in DMF (0.1 M in hygromycin A) was stirred at 70°C for 15 hours. The DMF was removed under reduced pressure and the resulting residue was chromatographed on silica gel with a mixture of chloroform, methanol and ammonium hydroxide (80:19:1) to give the unsaturated ester of Example 132.

Method BB

The ethyl ester from Example 132 was dissolved in water and tetrahydrofuran (1:1) (0.25 M), treated with sodium hydroxide (3 equivalents) and stirred at room temperature for 6 hours. After removal of the tetrahydrofuran under reduced pressure, the pH was adjusted to 4

by the addition of 1N HCl. The aqueous solution was concentrated to dryness under reduced pressure and the resulting residue was slurried with MeOH and filtered. The filtrate was concentrated to give the carboxylic acid of Example 133.

Method CC

A solution of the carboxylic acid of Example 133, DCC (dicyclohexylcarbodiimide, 1 equivalent), and HOBT (hydroxybenzotriazole, 1 equivalent) in DMF (0.25 M) was treated with the appropriate amine (1 equivalent) and the reaction mixture was stirred at room temperature for 18 hours. After removal of the DMF under reduced pressure, the resulting oil was chromatographed on silica gel using a mixture of chloroform, methanol and ammonium hydroxide (89:10:1) to provide the desired amide.

Method DD

A mixture of the carboxylic acid of Example 133 and 1-(3-dimethylaminopropyl)-3-ethyl-carbodiimide hydrochloride (1 equivalent) in DMF (0.25 M) was treated with the appropriate amine (1 equivalent) and the reaction mixture was stirred at room temperature for 18 hours. After removal of the DMF under reduced pressure, the residue was purified by silica gel chromatography using chloroform, methanol and ammonium hydroxide, in concentrations ranging from 89:10:1 to 80:19:1.

Method EE

The product of Example 133 in dimethylformamide (0.25 M) was treated with EEDQ (1-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline, 1.2 - 2 equivalents) and the appropriate amine (1 equivalent) and stirred at 70°C overnight. After cooling, the reaction mixture was either concentrated *in vacuo* to provide a crude product for purification, or the reaction mixture was poured into chloroform, and the resulting solid filtered to provide the crude product.

Specific compounds prepared according to the above processes are illustrated in the tables below. In the tables, "Ex" means example, "Mol Wt" means molecular weight, "Stereo" means stereochemistry of the oxime moiety (E or Z), "Pro" means procedure used to prepare the compounds, and "Mass Spec" means mass spectrometry.

Using the specific and general chemistry described above, the compounds listed below may be prepared in analogous fashion. Each of the compounds listed below is part of the present invention and possesses activity against bacterial infections. Literature references or preparative information are provided for the requisite alcohol or halide when those starting materials are not commercially available.

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-*(E)*-propenyl]amino]-1,2-O-methylene-D-*neo*-inositol, *(E)*-O-[(2,3-dihydrobenzofuran-6-yl)methyl]oxime. 6-Benzofurancarboxaldehyde can be prepared by

the method of A.S. Tasker *et al.* J. Med. Chem. (1997) 40, 322. Reduction of the aldehyde with sodium borohydride and hydrogenation of the double bond over palladium on carbon provides 2,3-dihydro-6-benzofuranmethanol.

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-*(E)*-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(2,3-dihydrobenzofuran-6-yl)methyl]oxime. 6-Benzofurancarboxaldehyde can be prepared by the method of A.S. Tasker *et al.* J. Med. Chem. (1997) 40, 322. Reduction of the aldehyde with sodium borohydride and hydrogenation of the double bond over palladium on carbon provides 2,3-dihydro-6-benzofuranmethanol.

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-*(E)*-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, *(E)*-*O*-[(2,3-dihydrobenzofuran-5-yl)methyl]oxime. Reduction of 2,3-dihydro-5-benzofurancarboxaldehyde with sodium borohydride provides 2,3-dihydro-5-benzofuranmethanol.

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-*(E)*-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(2,3-dihydrobenzofuran-5-yl)methyl]oxime. Reduction of 2,3-dihydro-5-benzofurancarboxaldehyde with sodium borohydride provides 2,3-dihydro-5-benzofuranmethanol.

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-*(E)*-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, *(E)*-*O*-(1,2,3,4-tetrahydronaphthalen-1-yl)oxime.

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-*(E)*-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(1,2,3,4-tetrahydronaphthalen-1-yl)oxime.

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-*(E)*-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, *(E)*-*O*-(7-chloro-1,2,3,4-tetrahydronaphthalen-1-yl)oxime. 7-Chloro-3,4-dihydro-1(2*H*)-naphthalenone can be prepared by the method of W.M. Owton and M. Brunavs, Syn. Comm. (1991) 21, 981. Reduction with sodium borohydride provides 7-chloro-1,2,3,4-tetrahydro-1-naphthalenol.

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-*(E)*-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(7-chloro-1,2,3,4-tetrahydronaphthalen-1-yl)oxime. 7-Chloro-3,4-dihydro-1(2*H*)-naphthalenone can be prepared by the method of W.M. Owton and M. Brunavs, Syn. Comm.

(1991) 21, 981. Reduction with sodium borohydride provides 7-chloro-1,2,3,4-tetrahydro-1-naphthalenol.

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-*(E)*-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, *(E)*-*O*-(7-fluoro-1,2,3,4-tetrahydronaphthalen-1-yl)oxime. 7-Fluoro-3,4-dihydro-1(2*H*)-naphthalenone can be prepared by the method of W.M. Owton and M. Brunavs, Syn. Comm. (1991) 21, 981. Reduction with sodium borohydride provides 7-fluoro-1,2,3,4-tetrahydro-1-naphthalenol.

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-*(E)*-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(7-fluoro-1,2,3,4-tetrahydronaphthalen-1-yl)oxime. 7-Fluoro-3,4-dihydro-1(2*H*)-naphthalenone can be prepared by the method of W.M. Owton and M. Brunavs, Syn. Comm. (1991) 21, 981. Reduction with sodium borohydride provides 7-fluoro-1,2,3,4-tetrahydro-1-naphthalenol.

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-*(E)*-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, *(E)*-*O*-(8-chloro-3,4-dihydro-2*H*-1-benzopyran-4-yl)oxime. The procedure of G. Ariamala and K.K. Balasubramanian, Tet. Lett. (1988) 29, 3487 can be used to prepare 8-chloro-2,3-dihydro-4*H*-1-benzopyran-4-one; reduction with sodium borohydride then provides 8-chloro-3,4-dihydro-2*H*-1-benzopyran-4-ol.

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-*(E)*-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(8-chloro-3,4-dihydro-2*H*-1-benzopyran-4-yl)oxime. The procedure of G. Ariamala and K.K. Balasubramanian, Tet. Lett. (1988) 29, 3487 can be used to prepare 8-chloro-2,3-dihydro-4*H*-1-benzopyran-4-one; reduction with sodium borohydride then provides 8-chloro-3,4-dihydro-2*H*-1-benzopyran-4-ol.

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-*(E)*-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, *(E)*-*O*-(8-fluoro-3,4-dihydro-2*H*-1-benzopyran-4-yl)oxime. The procedure of R. Sarges *et al.*, J. Med. Chem. (1988) 31, 230 can be used to prepare 8-fluoro-2,3-dihydro-4*H*-1-benzopyran-4-one; reduction with sodium borohydride then provides 8-fluoro-3,4-dihydro-2*H*-1-benzopyran-4-ol.

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-*(E)*-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(8-fluoro-3,4-dihydro-2*H*-1-benzopyran-4-yl)oxime. The procedure of R. Sarges *et al.*, J. Med. Chem. (1988) 31, 230 can be used to prepare 8-fluoro-2,3-dihydro-4*H*-1-benzopyran-4-one; reduction with sodium borohydride then provides 8-fluoro-3,4-dihydro-2*H*-1-benzopyran-4-ol.

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-*(E)*-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, *(E)*-*O*-[4-(phenylmethyl)phenylmethyl]oxime. Reduction of 4-(phenylmethyl)benzoic acid with diborane provides 4-(phenylmethyl)benzenemethanol.

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-*(E)*-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, *(Z)*-*O*-[4-(phenylmethyl)phenylmethyl]oxime. Reduction of 4-(phenylmethyl)benzoic acid with diborane provides 4-(phenylmethyl)benzenemethanol.

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-*(E)*-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, *(E)*-*O*-[4-(phenoxy)phenylmethyl]oxime. Reduction of 4-phenoxybenzaldehyde with sodium borohydride provides 4-phenoxybenzenemethanol.

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-*(E)*-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, *(Z)*-*O*-[4-(phenoxy)phenylmethyl]oxime. Reduction of 4-phenoxybenzaldehyde with sodium borohydride provides 4-phenoxybenzenemethanol.

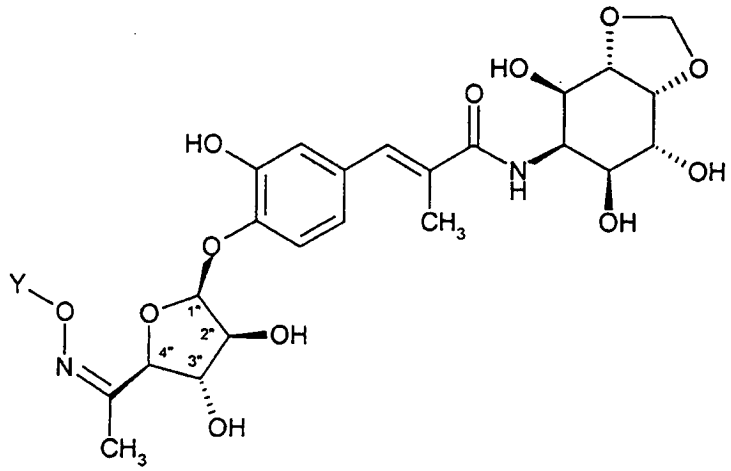
5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(3-difluoromethoxy-phenyl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-(3-difluoromethoxy-phenyl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(4-difluoromethoxy-phenyl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-(4-difluoromethoxy-phenyl)oxime;

Table 1



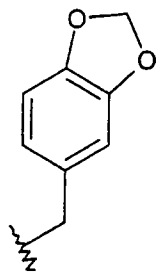
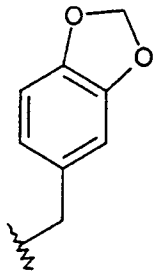
Most of the examples in Table 1 bear the C-4" stereochemistry shown, with the oxime moiety in the beta orientation. Some examples have the oxime in the alpha orientation; this is indicated in the Stereo column.

Ex.	Y	Mol Wt	Stereo	Pro.	Mass spec	1H NMR peaks (CD_3OD)
1	*tert*-butyl	582.61	E	A or B, L	583.1	5.69 (d, J = 4.2 Hz, 1H), 4.28 (d, J = 8.1 Hz, 1H), 1.22 (s, 9H)
2	2-propen-1-yl	566.57	E	B, L	567.1	5.93 (m, 1H), 5.55 (d, J = 4.4 Hz, 1H), 5.20 (dd, J = 17.2, 1.7 Hz, 1H), 5.11 (dd, J = 10.4, 1.7 Hz, 1H), 4.50 (d, J = 5.6 Hz, 2H), 4.23 (d, J = 7.9 Hz, 1H)
3	ethyl	554.46	E	B, L	555.1	5.69 (d, J = 4.2 Hz, 1H), 4.23 (d, J = 7.9 Hz, 1H), 4.04 (q, J = 7.1 Hz, 2H), 1.18 (t, J = 7.1 Hz, 3H)
4	ethyl	554.46	Z	B, L	555.1	5.64 (d, J = 4.2 Hz, 1H), 5.14 (d, J = 6.2 Hz, 1H), 4.03 (q, J = 7.1 Hz, 2H), 1.20 (t, J = 7.1 Hz, 3H)
5	isobutyl	582.61	Z	B, L	583.2	5.66 (d, J = 4.2 Hz, 1H), 5.18 (d, J = 6.2 Hz, 1H), 3.77 (d, J = 6.6 Hz, 2H), 1.95 (m, 1H), 0.92 (d, J = 6.8 Hz, 3H)
6	(4-nitrophenyl)methyl	661.63	E	B, L	662.1	8.14 (d, J = 8.9 Hz, 2H), 7.49 (d, J = 8.9 Hz, 2H), 5.54 (d, J = 4.6 Hz, 1H), 5.17 (s, 2H), 4.25 (d, J =

Ex.	Y	Mol Wt	Stereo	Pro.	Mass spec	1H NMR peaks (CD_3OD)
						7.9 Hz, 1H)
7	(4-chlorophenyl)methyl	651.07	Z	B, L	651.1	7.32 (m, 4H), 5.65 (d, J = 4.2 Hz, 1H), 5.20 (d, J = 6 Hz, 1H), 5.02 (AB quartet, Δν = 10.8 Hz, J = 12.8 Hz, 2H)
8	(4-chlorophenyl)methyl	651.07	E	B, L	651.1	7.28 (s, 4H), 5.55 (d, J = 4.6 Hz, 1H), 5.03 (s, 2H), 4.26 (d, J = 7.7 Hz, 1H)
9	(4-methylphenyl)methyl	630.66	Z	B, L	631.2	7.2 (d, J = 8 Hz, 2H), 7.1 (d, J = 8 Hz, 2H), 5.64 (d, J = 4.4 Hz, 1H), 5.18 (d, J = 6.4 Hz, 1H), 4.98 (AB quartet, Δν = 15.7 Hz, J = 12.1 Hz, 2H)
10	(4-methylphenyl)methyl	630.66	E	B, L	631.2	7.17 (d, J = 8 Hz, 2H), 7.10 (d, J = 8 Hz, 2H), 5.55 (d, J = 4.4 Hz, 1H), 4.99 (s, 2H), 4.25 (d. J = 7.9 Hz, 1H), 2.28 (s, 3H)
11	(4-methoxyphenyl)methyl	646.65	Z	B, L	647.2	7.27 (d, J = 8.7 Hz, 2H), 6.87 (d, J = 8.7 Hz, 2H), 5.64 (d, J = 4.4 Hz, 1H), 5.16 (d, J = 6.2 Hz, 1H), 4.95 (AB quartet, Δν = 16.0 Hz, J = 11.7 Hz, 2H)
12	(4-methoxyphenyl)methyl	646.65	E	B, L	647.2	7.22 (d, J = 8.3 Hz, 2H), 6.83 (d, J = 8.5 Hz, 2H), 5.55 (d, J = 4.6 Hz, 1H), 4.97 (s, 2H), 4.26 (d, J = 7.9 Hz, 1H), 3.75 (s, 3H)
13	(3,4-dichlorophenyl)methyl	685.52	Z	B, L	685.1, 687.1	7.51 (d, J = 1.9 Hz, 1H), 7.45 (d, J = 8.3 Hz, 1H), 7.26 (dd, J = 8.3, 2.1 Hz, 1H), 5.65 (d, J = 4.4 Hz, 1H), 5.22 (d, J = 6.2 Hz, 1H), 5.00 (AB quartet, Δν = 7.3 Hz, J = 13.3 Hz, 2H)
14	(3,4-dichlorophenyl)methyl	685.52	E	B, L	685.1, 687.1	7.44 (m, 2H), 7.23 (m, 1H), 5.55 (d, J = 4.4 Hz, 1H), 5.02 (s, 2H), 4.25 (d, J = 7.7 Hz, 1H)
15	4-pyridylmethyl	617.62	E	B, L	618.1	8.43 (d, J = 5.8 Hz, 2H), 7.32 (d, J = 5.8 Hz, 2H), 5.56 (d, J = 4.6 Hz, 1H), 5.13 (s, 2H), 4.25 (d, J = 7.7 Hz, 1H)
16	phenylmethyl	616.63	Z	B, L	617.2	7.34 (m, 5H), 5.65 (d, J = 4.4 Hz, 1H), 5.21 (d, J =

Ex.	Y	Mol Wt	Stereo	Pro.	Mass spec	1H NMR peaks (CD_3OD)
						6.2 Hz, 1H), 5.04 (AB quartet, Δν = 14.4 Hz, J = 12.3 Hz, 2H)
17	phenylmethyl	616.63	E	B, L	617.2	7.32 (m, 5H), 5.55 (d, J = 4.6 Hz, 1H), 5.05 (s, 2H), 4.26 (d, J = 7.7 Hz)
18	cyclohexylmethyl	622.68	Z	C, L	623.2	5.65 (d, J = 4.2 Hz, 1H), 5.16 (d, J = 6.2 Hz, 1H), 3.78 (m, 2H), 1.72 (m, 6H), 1.22 (m, 3H), 0.96 (m, 2H)
19	cyclohexylmethyl	622.68	E	C, L	623.2	5.55 (d, J = 4.6 Hz, 1H), 4.24 (d, J = 7.9 Hz, 1H), 3.82 (m, 2H), 1.68 (m, 6H), 1.21 (m, 3H), 0.94 (m, 2H)
20	2-pyridylmethyl	617.62	Z	C, L	618.1	8.49 (bd, J = 4.8 Hz, 1H), 7.82 (ddd, apparent td, J = 7.7, 1.7 Hz, 1H), 7.45 (d, J = 7.9 Hz, 1H), 7.32 (m, 1H), 5.66 (d, J = 4.2 Hz, 1H), 5.24 (d, J = 6.2 Hz, 1H), 5.15 (AB quartet, Δν = 10.9 Hz, J = 14.1 Hz, 2H)
21	2-pyridylmethyl	617.62	E	C, L	618.1	8.45 (bd, J = 5.0 Hz, 1H), 7.79 (ddd, apparent td, J = 7.8, 1.7 Hz, 1H), 7.40 (d, J = 7.9 Hz, 1H), 7.31 (dd, J = 7.6 Hz, 4.9 Hz, 1H), 5.56 (d, J = 4.6 Hz, 1H), 5.15 (s, 2H), 4.25 (d, J = 7.7 Hz, 1H)
22	(4-fluorophenyl)methyl	634.62	Z	C, L	635.1	7.36 (dd, J = 8,5 Hz, 2H), 7.04 (dd, apparent triplet, J = 8.8 Hz, 2H), 5.65 (d, J = 4.2 Hz, 1H), 5.20 (d, J = 6.4 Hz, 1H), 5.01 (AB quartet, Δν = 12.0 Hz, J = 12.6 Hz, 2H)
23	(4-fluorophenyl)methyl	634.62	E	C, L	635.1	7.32 (dd, J = 8.5, 5.4 Hz, 2H), 7.01 (dd, apparent t, J = 8.9 Hz, 2H), 5.55 (d, J = 4.36 Hz, 1H), 5.02 (s, 2H), 4.25 (d, J = 7.9 Hz, 1H)
24	(2,4-dichlorophenyl)methyl	685.52	E	C, L	685.1; 687.0	7.42 (d, J = 2.1 Hz, 1H), 7.34 (d, J = 8.3 Hz, 1H), 7.26 (dd, J = 8.3, 2.1 Hz, 1H), 5.56 (d, J = 4.6 Hz, 1H), 5.13 (s, 2H), 4.26 (d, J = 7.7 Hz, 1H)

Ex.	Y	Mol Wt	Stereo	Pro.	Mass spec	1H NMR peaks (CD_3OD)
25	(2,4-dichlorophenyl)methyl	685.52	Z	C, L	685.1; 687.0	7.46 (d, J = 8.3 Hz, 1H), 7.43 (d, J = 1.9 Hz, 1H), 7.30 (dd, J = 8.3, 2.1 Hz, 1H), 5.66 (d, J = 4.2 Hz, 1H), 5.25 (d, J = 6.4 Hz, 1H), 5.11 (AB quartet, Δv = 9.1 Hz, J = 14.0 Hz, 2H)
26	(2,3,4,5,6-pentafluorophenyl)-methyl	706.58	E	C, L	707.2	5.54 (d, J = 4.6 Hz, 1H), 5.16 (s, 2H), 4.21 (d, J = 7.9 Hz, 1H)
27	(3,4-difluorophenyl)methyl	652.61	E	C, L	653.2	7.17 (m, 3H), 5.56 (d, J = 4.4 Hz, 1H), 5.02 (s, 2H), 4.25 (d, J = 7.9 Hz, 1H)
28	(4-trifluoromethylphenyl)-methyl	684.63	E	C, L	685.2	7.58 (d, J = 8.1 Hz, 2H), 7.46 (d, J = 7.9 Hz, 2H), 5.54 (d, J = 4.4 Hz, 1H), 5.13 (s, 2H), 4.24 (d, J = 7.9 Hz, 1H)
29	(3-trifluoromethylphenyl)-methyl	684.63	E	C, L	685.2	7.57 (m, 3H), 7.49 (m, 1H), 5.55 (d, J = 4.4 Hz, 1H), 5.12 (s, 2H), 4.25 (d, J = 7.7 Hz, 1H)
30	(2-chlorophenyl)methyl	651.07	E	C, L	651.2; 653.1	7.35 (m, 2H), 7.24 (m, 2H), 5.56 (d, J = 4.6 Hz, 1H), 5.17 (s, 2H), 4.26 (d, J = 7.9 Hz, 1H)
31	(2,3-dichlorophenyl)-methyl	685.52	E	C, L	685.1; 687.1	7.42 (d, J = 7.7 Hz, 1H), 7.27 (m, 2H), 5.55 (d, J = 4.6 Hz, 1H), 5.17 (s, 2H), 4.25 (d, J = 7.7 Hz, 1H)
32	(4-acetamido phenyl)methyl	673.68	E	C, L	674.2	7.47 (d, J = 8.3 Hz, 2H), 7.24 (d, J = 8.3 Hz, 2H), 5.55 (d, J = 4.6 Hz, 1H), 5.00 (s, 2H), 4.25 (d, J = 7.9 Hz, 1H)
33	2-pyrazinylmethyl	618.6	E	C, L	619.2	8.59 (s, 1H), 8.54 (bs, 1H), 8.50 (bs, 1H), 5.55 (d, J = 4.4 Hz, 1H), 5.21 (s, 2H), 4.24 (d, J = 7.7 Hz, 1H)
34	4-pyrimidinylmethyl	618.6	E	C, L	619.2	9.03 (s, 1H), 8.67 (bd, J = 5.2 Hz, 1H), 7.40 (d, J = 5.2 Hz, 1H), 5.56 (d, J = 4.4 Hz, 1H), 5.15 (s, 2H), 4.25 (d, J = 7.5 Hz, 1H)
35	4-pyrimidinylmethyl	618.6	Z	C, L	619.2	9.07 (s, 1H), 8.73 (m, 1H), 7.57 (d, J = 5.2 Hz, 1H), 5.68 (d, J = 4.2 Hz, 1H), 5.29 (d, J = 6.4 Hz, 1H), 5.16 (bs, 2H)

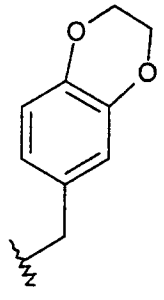
Ex.	Y	Mol Wt	Stereo	Pro.	Mass spec	1H NMR peaks (CD_3OD)
36	[4-(*tert*-butoxycarbonyl) phenyl]methyl	716.75	E	C, L	717.3	7.88 (d, J = 8 Hz, 2H), 7.36 (d, J = 8 Hz, 2H), 5.55 (d, J = 4.6 Hz, 1H), 5.12 (s, 2H), 4.25 (d, J = 7.7 Hz, 1H), 1.57 (s, 9H)
37	2-amino-5-thiazolylmethyl	638.66	E	C, L	639.1	6.44 (s, 1H), 5.55 (d, J = 4.4 Hz, 1H), 4.26 (d, J = 7.9 Hz, 1H)
38	[3-(*tert*-butoxycarbonylamino)-phenyl]methyl	731.76	E	E, L	732.3	7.36 (bs, 1H), 7.29 (bd, J = 8.5 Hz, 1H), 7.18 (dd, apparent t, J = 7.9 Hz, 1H), 6.94 (d, J = 7.7 Hz, 1H), 5.56 (d, J = 4.6 Hz, 1H), 5.01 (s, 2H), 4.26 (d, J = 7.9 Hz, 1H), 1.49 (s, 9H)
39	3-furanylmethyl	606.59	E	E, L	607.2	7.46 (s, 1H), 7.40 (s, 1H), 6.41 (s, 1H), 5.56 (d, J = 4.6 Hz, 1H), 4.92 (s, 2H), 4.26 (d, J = 7.9 Hz, 1H)
40	phenylmethyl	616.63	E	F, L	617.3	7.28 (m, 5H), 5.55 (d, J = 4.6 Hz, 1H), 5.05 (s, 2H), 4.26 (d, J = 7.9 Hz, 1H)
41		660.64	E	F, L	661.3	6.76 (m, 2H), 6.70 (d, J = 7.7 Hz, 1H), 5.88 (s, 2H), 5.53 (d, J = 4.6 Hz, 1H), 4.92 (s, 2H), 4.24 (d, J = 7.7 Hz, 1H)
42		660.64	Z	F, L	661.2	6.83 (d, J = 0.4 Hz, 1H), 6.79 (d, J = 7.9 Hz, 1H), 6.73 (dd, J = 7.9, 0.4 Hz, 1H), 5.88 (s, 2H), 5.62 (d, J = 4.4 Hz, 1H), 5.15 (d, J = 6.2 Hz, 1H), 4.90 (AB quartet, $\Delta\nu$ = 14.0 Hz, J = 12.0 Hz, 2H)
43	4-biphenylylmethyl	692.73	E	E, L	693.1	7.57 (m, 4H), 7.39 (m, 4H), 7.31 (m, 1H), 5.56 (d, J = 4.6 Hz, 1H), 5.10 (s, 2H), 4.28 (d, J = 7.9 Hz, 1H)
44	diphenylmethyl	692.73	E	E, L	693.1	7.24 (m, 10H), 6.14 (s, 1H), 5.52 (d, J = 4.4 Hz, 1H), 4.21 (d, J = 7.9 Hz,

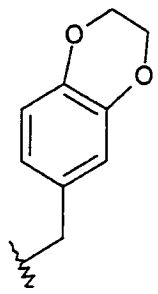
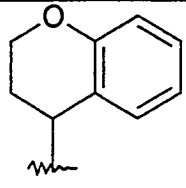
Ex.	Y	Mol Wt	Stereo	Pro.	Mass spec	1H NMR peaks (CD_3OD)
						1H)
45	(4-carboxy phenyl)methyl	660.64	E	I (using product of Example 36), N	661.2	7.94 (d, J = 8.1 Hz, 2H), 7.38 (d, J = 8.1 Hz, 2H), 5.55 (d, J = 4.4 Hz, 1H), 5.13 (s, 2H), 4.26 (d, J = 7.7 Hz, 1H)
46	(4-cyclohexyl phenyl)methyl	698.8	E	F, J	699.1	7.20 (d, J = 8.3 Hz, 2H), 7.13 (d, J = 8.1 Hz, 2H), 5.55 (d, J = 4.6 Hz, 1H), 5.01 (s, 2H), 4.26 (d, J = 7.9 Hz, 1H), 2.46 (m, 1H), 1.81 (m, 4H), 1.75 (m, 1H),1.41 (m, 4H), 1.28 (m, 1H)
47	(4-cyclohexyl phenyl)methyl	698.8	Z	F, J	699.3	7.16 (m, 4H), 5.65 (d, J = 4.2 Hz, 1H), 5.19 (d, J = 6.2 Hz, 1H), 4.99 (AB quartet, $\Delta\nu$ = 15.6 Hz, J = 12.0 Hz, 2H), 2.46 (m, 1H), 1.82 (m, 4H), 1.74 (m, 1H), 1.42 (m, 4H), 1.27 (m, 1H)
48	2-furanylmethyl	606.59	Z	E, L	607.2	7.46 (s, 1H), 6.37 (m, 2H), 5.64 (d, J = 4.4 Hz, 1H), 5.12 (d, J = 6.2 Hz, 1H), 4.95 (AB quartet, $\Delta\nu$ = 9.5 Hz, J = 13.1 Hz, 2H)
49	2-furanylmethyl	606.59	E	E, L	607.2	7.43 (s, 1H), 6.35 (m, 2H), 5.55 (d, J = 4.4 Hz, 1H), 4.96 (s, 2H), 4.26 (d, J = 7.9 Hz, 1H)
50	(3-fluoro phenyl)methyl	634.62	Z	G, L	635.2	7.32 (m, 1H), 7.15 (m, 1H), 7.11 (bd, J = 8 Hz, 1H), 6.99 (bdd, apparent bt, J = 8.3 Hz, 1H), 5.66 (d, J = 4.2 Hz, 1H), 5.24 (d, J = 6.4 Hz, 1H), 5.04 (AB quartet, $\Delta\nu$ = 9.9 Hz, J = 13.2 Hz, 2H)
51	(4-acetamido-3,5-dichlorophenyl)methyl	742.57	E	F, L	742.0; 743.9	7.37 (s, 2H), 5.54 (d, J = 4.6 Hz, 1H), 5.00 (s, 2H), 4.23 (d, J = 7.9 Hz, 1H), 2.13 (s, 3H)
52	[4-[(*tert*-butoxycarbonylamino)-methyl]phenyl]methyl	745.79	E	E, L	746.1	7.24 (AB quartet, $\Delta\nu$ = 18.4 Hz, J = 8.1 Hz, 4H), 5.55 (d, J = 4.6 Hz, 1H), 5.03 (s, 2H), 4.25 (d, J = 7.7 Hz, 1H) 4.19 (s, 2H), 1.43 (s, 9H)
53	[4-(*tert*-	745.79	Z	E, L	746.1	7.27 (AB quartet, $\Delta\nu$ =

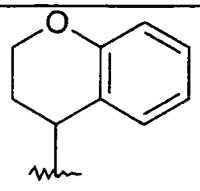
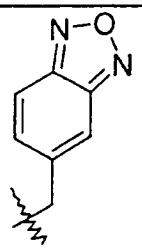
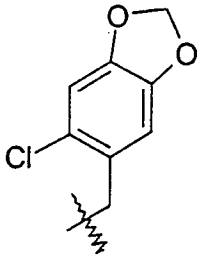
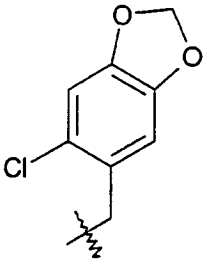
Ex.	Y	Mol Wt	Stereo	Pro.	Mass spec	1H NMR peaks (CD_3OD)
	butoxycarbonylamino)-methyl]phenyl]methyl					28.3 Hz, J = 8.1 Hz, 4H), 5.64 (d, J = 4.4 Hz, 1H), 5.20 (d, J = 6.4 Hz, 1H), 5.01 (AB quartet, Δν = 13.9 Hz, J = 12.3 Hz, 2H), 4.20 (s, 2H), 1.44 (s, 9H)
54	(3-aminophenyl)methyl	631.64	E	I (using product of Example 38), L	632.1	7.07 (t, J = 7.7 Hz, 1H), 6.76 (bs, 1H), 6.70 (m, 2H), 5.54 (d, J = 4.6 Hz, 1H), 4.95 (s, 2H), 4.24 (d, J = 7.9 Hz, 1H)
55	(4-aminomethylphenyl)-methyl	645.67	E	I (using product of Example 52), L	645.9	7.26 (s, 4H), 5.52 (d, J = 4.6 Hz, 1H), 5.02 (s, 2H), 4.22 (d, J = 7.9 Hz, 1H), 3.75 (s, 2H)
56	3-(4-chlorophenyl)prop-1-yl	679.13	Z	E, J	679.2; 681.2	7.24 (d, J = 8.3 Hz, 2H), 7.16 (d, J = 8.3 Hz, 2H), 5.67 (d, J = 4.2 Hz, 1H), 5.17 (d, J = 6.4 Hz, 1H), 4.00 (m, 2H), 2.68 (t, J = 7.6 Hz, 2H), 1.91 (m, 2H)
57	3-(4-chlorophenyl)prop-1-yl	679.13	E	E, J	679.2; 681.2	7.21 (d, J = 8.3 Hz, 2H), 7.12 (d, J = 8.5 Hz, 2H), 5.56 (d, J = 4.6 Hz, 1H), 4.26 (d, J = 7.7 Hz, 1H), 4.02 (t, J = 6.3 Hz, 2H), 2.62 (t, J = 7.6 Hz, 2H), 1.90 (m, 2H)
58	2-benzimidazolylmethyl	656.65	E	E, L	657.2	7.52 (m, 2H), 7.21 (m, 2H), 5.57 (d, J = 4.6 Hz, 1H), 5.27 (s, 2H), 4.28 (d, J = 7.9 Hz, 1H)
59	2-benzimidazolylmethyl	656.65	Z	E, L	657.1	7.54 (m, 2H), 7.22 (m, 2H), 5.67 (d, J = 4.4 Hz, 1H), 5.33 (d, J = 6.8 Hz, 1H), 5.27 (s, 2H)
60	2-phenylethyl	630.66	Z	E, J	631.1	7.22 (m, 5H), 5.63 (d, J = 4.2 Hz, 1H), 5.09 (d, J = 6.2 Hz, 1H), 4.15 (m, 2H), 2.90 (t, J = 7.0 Hz, 2H)
61	2-phenylethyl	630.66	E	E, J	631.1	7.12 (m, 5H), 5.53 (d, J = 4.6 Hz, 1H), 4.27 (d, J = 7.7 Hz, 1H), 4.17 (t, J = 6.7 Hz, 2H), 2.85 (t, J = 6.8 Hz, 2H)
62	[3-(trifluoromethoxy)	700.62	E	E, L	701	7.39 (t, J = 7.9 Hz, 1H),

Ex.	Y	Mol Wt	Stereo	Pro.	Mass spec	1H NMR peaks (CD_3OD)
	phenyl]methyl					7.30 (d, J = 7.9 Hz, 1H), 7.20 (bs, 1H), 7.16 (bd, J = 8.1 Hz, 1H), 5.55 (d, J = 4.6 Hz, 1H), 5.09 (s, 2H), 4.25 (d, J = 7.9 Hz, 1H)
63	(3-cyanophenyl)methyl	641.64	E	E, L	642.1	7.61 (m, 3H), 7.46 (dd, apparent t, J = 7.7 Hz, 1H), 5.53 (d, J = 4.6 Hz, 1H), 5.08 (s, 2H), 4.23 (d, J = 7.9 Hz, 1H)
64	(3,4-dimethoxyphenyl)-methyl	676.68	E	E, L	677.1	6.90 (m, 2H), 6.84 (s, 1H), 5.53 (d, J = 4.6 Hz, 1H), 4.96 (s, 2H), 4.25 (d, J = 7.9 Hz, 1H), 3.77 (s, 3H), 3.76 (s, 3H)
65	2-benzofuranylmethyl	656.65	E	E, L	657.1	7.51 (d, J = 7.7 Hz, 1H), 7.39 (d, J = 8.1 Hz, 1H), 7.22 (m, 1H), 7.15 (m, 1H), 6.71 (s, 1H), 5.53 (d, J = 4.6 Hz, 1H), 5.11 (s, 2H), 4.26 (d, J = 7.9 Hz, 1H)
66	2-benzofuranylmethyl	656.65	Z	E, L	657.1	7.53 (d, J = 7.1 Hz, 1H), 7.42 (d, J = 8.3 Hz, 1H), 7.24 (m, 1H), 7.17 (m, 1H), 6.75 (s, 1H), 5.62 (d, J = 4.2 Hz, 1H), 5.17 (d, J = 6.2 Hz, 1H), 5.10 (AB quartet, $\Delta\nu$ = 6.9 Hz, J = 13.7 Hz, 2H)
67	(3,4-dimethoxyphenyl)-methyl	676.68	Z	E, L	677.1	6.88 (m, 3H), 5.62 (d, J = 4.2 Hz, 1H), 5.17 (d, J = 6.4 Hz, 1H), 4.94 (AB quartet, $\Delta\nu$ = 17.2 Hz, J = 12.0 Hz, 2H), 3.80 (s, 3H), 3.79 (s, 3H)
68	[3-(trifluoromethoxy)-phenyl]methyl	700.63	Z	E,L	701.O	7.40 (m, 1H), 7.34 (bd, J = 6.4 Hz, 1H), 7.27 (bs, 1H), 7.16 (m, 1H), 5.66 (d, J = 3.9 Hz, 1H), 5.23 (d, J = 6.2 Hz, 1H), 5.07 (AB quartet, $\Delta\nu$ = 9.2 Hz, J = 13.1 Hz, 2H)
69	2-anilinoethyl	645.67	Z	E, L	646.2	7.08 (dd, J = 8.5, 7.5 Hz, 2H), 6.66 (dd, J = 8.6, 0.9 Hz, 2H), 6.62 (t, J = 7.3 Hz, 1H), 5.62 (d, J = 4.2 Hz, 1H), 5.18 (d, J = 6.4 Hz, 1H), 4.15 (m, 2H), 3.27 (m, 2H)

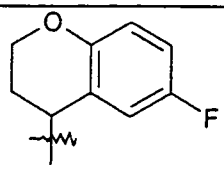
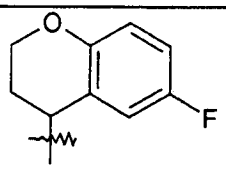
Ex.	Y	Mol Wt	Stereo	Pro.	Mass spec	1H NMR peaks (CD_3OD)
70	2-anilinoethyl	645.67	E	E, L	646.1	7.04 (dd, J = 8.6, 7.4 Hz, 2H), 6.60 (dd, J = 8.6, 0.9 Hz, 2H), 6.56 (t, J = 7.4 Hz, 1H), 5.55 (d, J = 4.6 Hz, 1H), 4.25 (d, J = 7.7 Hz, 1H), 4.16 (m, 2H), 3.31 (m, 2H)
71	[4-(1-piperidino)phenyl]-methyl	699.76	E	H, J	700.1	7.15 (d, J = 8.5 Hz, 2H), 6.87 (d, J = 8.7 Hz, 2H), 5.52 (d, J = 4.6 Hz, 1H), 4.92 (s, 2H), 4.24 (d, J = 7.7 Hz, 1H), 3.06 (dd, J = 5.4, 5.4 Hz, 4H), 1.65 (m, 4H), 1.54 (m, 2H)
72	[4-(1-piperidino)phenyl]-methyl	699.76	Z	H, J	700.1	7.23 (d, J = 8.8 Hz, 2H), 6.93 (d, J = 8.8 Hz, 2H), 5.63 (d, J = 4.3 Hz, 1H), 5.15 (d, J = 6.4 Hz, 1H), 4.93 (AB quartet, $\Delta\nu$ = 17.3 Hz, J = 11.8 Hz, 2H), 3.11 (dd, J = 5.4, 5.4 Hz, 4H), 1.69 (m, 4H), 1.58 (m, 2H)
73	3-phenylprop-1-yl	644.68	Z	E, J	645.1	7.20 (d, J = 7.3 Hz, 2H), 7.13 (m, 3H), 5.64 (d, J = 4.2 Hz, 1H), 5.18 (d, J = 6.4 Hz, 1H), 3.97 (m, 2H), 2.65 (t, J = 7.7 Hz, 2H), 1.90 (m, 2H)
74	3-phenylprop-1-yl	644.68	E	E, J	645.1	7.18 (d, J = 7.3 Hz, 2H), 7.11 (m, 3H), 5.54 (d, J = 4.4 Hz, 1H), 4.24 (d, J = 7.9 Hz, 1H) 4.01 (t, J = 6.3 Hz, 2H), 2.61 (t, J = 7.7 Hz, 2H), 1.89 (m, 2H)
75	(2-fluorophenyl)methyl	634.62	Z	G, L	635.2	7.44 (apparent td, J = 7.5, 1.8 Hz, 1H), 7.30 (m, 1H), 7.14 (m, 1H), 7.06 (dd, J = 10.2, 8.3 Hz, 1H), 5.65 (d, J = 4.2 Hz 1H), 5.20 (d, J = 6.4 Hz, 1H), 5.11 (AB quartet, $\Delta\nu$ = 9.1 Hz, J = 12.9 Hz, 1H)
76	(2-fluorophenyl)methyl	634.62	E	G, L	635.2	7.36 (apparent td, J = 7.5, 1.5 Hz, 1H), 7.28 (m, 1H), 7.12 (m, 1H), 7.04 (dd, J = 10.1, 8.4 Hz, 1H), 5.55 (d, J = 4.6 Hz, 1H), 5.12 (s, 2H), 4.26 (d, J = 7.9 Hz,

Ex.	Y	Mol Wt	Stereo	Pro.	Mass spec	1H NMR peaks (CD_3OD)
						1H)
77	2-(phenylthio)ethyl	662.71	Z	F, J	663.1	7.35 (d, J = 7.3 Hz, 2H), 7.26 (dd, apparent t, J = 7.7 Hz, 2H), 7.15 (m, 1H), 5.63 (d, J = 4.4 Hz, 1H), 5.09 (d, J = 6.2 Hz, 1H), 4.10 (t, J = 6.9 Hz, 2H), 3.15 (t, J = 6.7 Hz, 2H)
78	2-(phenylthio)ethyl	662.71	E	F, J	663.1	7.31 (d, J = 7.3 Hz, 2H), 7.22 (m, 2H), 7.10 (m, 1H), 5.55 (d, J = 4.4 Hz, 1H), 4.23 (d, J = 7.9 Hz, 1H), 4.18 (m, 2H), 3.12 (m, 2H)
79	5-benzofuranylmethyl	656.64	E	F, K	657.1	7.69 (d, J = 2.3 Hz, 1H), 7.54 (bs, 1H), 7.39 (d, J = 8.5 Hz, 1H), 7.23 (dd, J = 8.6, 1.6 Hz, 1H), 6.76 (m,1H), 5.53 (d, J = 4.6 Hz, 1H), 5.11 (s, 2H), 4.25 (d, J = 7.9 Hz, 1H)
80	5-benzofuranylmethyl	656.64	Z	F, K		7.71 (d, J = 2.3 Hz, 1H), 7.59 (bs, 1H), 7.43 (d, J = 8.5 Hz, 1H), 7.29 (dd, J = 8.5, 1.5 Hz, 1H). 6.79 (m, 1H), 5.62 (d, J = 4.2 Hz, 1H), 5.18 (d, J = 6.4 Hz, 1H), 5.10 (AB quartet, $\Delta\nu$ = 15.0 Hz, J = 11.9 Hz, 2H)
81	2-phenyl-5-pyrimidinylmethyl	694.69	Z	F, M	695.1	8.82 (s, 2H), 8.36 (m, 2H), 7.46 (m, 3H), 5.63 (d, J = 4.4 Hz, 1H), 5.2 (d, J obscured, 1H), 5.10 (s, 2H)
82	2-phenyl-5-pyrimidinylmethyl	694.69	E	F, M	695.1	8.75 (s, 2H), 8.33 (m, 2H), 7.45 (m, 3H), 5.52 (d, J = 4.6 Hz, 1H), 5.10 (s, 2H), 4.25 (d, J = 7.9 Hz, 1H)
83		674.66	Z	F, L	675.1	6.83 (d, J = 1.9 Hz, 1H), 6.78 (AB quartet, $\Delta\nu$ = 14.1 Hz, J = 8.2 Hz, 2H), 5.64 (d, J = 4.2 Hz, 1H), 5.16 (d, J = 6.2 Hz, 1H), 4.90 (AB quartet, $\Delta\nu$ = 15.2 Hz, J = 11.8 Hz, 2H), 4.20 (s, 4H)

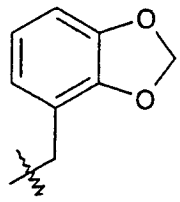
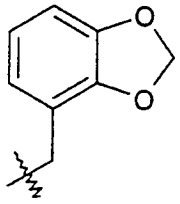
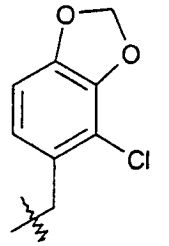
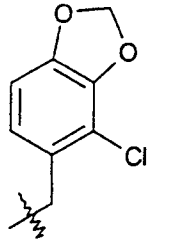
Ex.	Y	Mol Wt	Stereo	Pro.	Mass spec	1H NMR peaks (CD_3OD)
84		674.66	E	F, L	675.2	[D_2O] 6.73 (m, 3H), 5.51 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.14 (s, 4H), 4.06 (d, J = 7.9 Hz, 1H)
85	(3-fluoro-4-methoxyphenyl)methyl	664.65	E	E, L	665.1	7.05 (m, 2H), 7.00 (dd, apparent t, J = 8.2 Hz, 1H), 5.56 (d, J = 4.6 Hz, 1H), 4.97 (s, 2H), 4.26 (d, J = 7.9 Hz, 1H)
86	(3-fluoro-4-methoxyphenyl)methyl	664.65	Z	E, L	665.1	7.13 (m, 1H), 7.09 (bd, J = 6.8 Hz, 1H), 7.03 (m, 1H), 5.65 (d, J = 4.2 Hz, 1H), 5.19 (d, J = 6.4 Hz, 1H), 4.95 (AB quartet, $\Delta\nu$ = 12.2 Hz, J = 12.3 Hz, 2H)
87	2-phenoxyethyl	646.65	Z	E, J	647.2	7.25 (dd, apparent t, J = 7.3 Hz, 2H), 6.93 (m, 3H), 5.64 (d, J = 4.2 Hz, 1H), 5.13 (d, J = 6.0 Hz, 1H), 4.33 (m, 2H), 4.18 (m, 2H)
88	2-phenoxyethyl	646.65	E	E, J	647.2	7.21 (dd, apparent t, J = 7.7 Hz, 2H), 6.88 (m, 3H), 5.56 (d, J = 4.6 Hz, 1H), 4.34 (m, 2H), 4.27 (d, J = 7.9 Hz, 1H), 4.15 (m, 2H)
89	(3-fluorophenyl)methyl	634.62	E	G, L	635.1	7.30 (m, 1H), 7.11 (m, 1H), 7.03 (bd, J = 9.7 Hz, 1H), 6.98 (bdd, apparent bt, J = 8.6 Hz, 1H), 5.56 (d, J = 4.6 Hz, 1H), 5.06 (s, 2H), 4.26 (d, J = 7.9 Hz, 1H)
90		658.66	Z; major and minor diastereomer	F, J	659.2	7.33 (dd, J = 7.6, 1.8 Hz) and 7.25 (d, J = 7.7 Hz) [1H], 7.15 (m, 1H), 6.85 (m, 1H), 6.75 (d, J = 8.3 Hz, 1H), 5.61 (d, J = 4.4 Hz) and 5.59 (d, J = 4.4 Hz) [1H], 5.11 (d, J = 6.4 Hz) and 5.14 (d, J = 6.8 Hz)[1H], 5.07 (m) and 5.02 (m) [1H], 4.15 (m, 2H), 2.21 (bd, J = 14.5 Hz) and 2.29 (bd, J = 14.9 Hz)[1H],

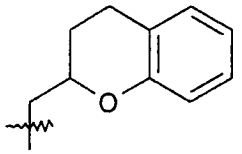
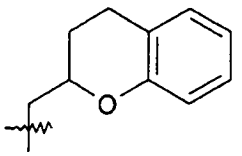
Ex.	Y	Mol Wt	Stereo	Pro.	Mass spec	1H NMR peaks (CD_3OD)
						2.03 (m, 1H)
91		658.66	E; mixture of 2 diastereomers	F, J	659.2	7.22 (m, 1H), 7.12 (m, 1H), 6.80 (m, 1H), 6.72 (d, J = 8.1 Hz, 1H), 5.56 (d, J = 3.5 Hz, 1H), 5.06 (m, 1H), 4.30 (d, J = 7.5 Hz) and 4.30 (d, J = 7.9 Hz) [1H], 4.15 (m, 2H), 2.23 (bd, J = 12.9 Hz) and 2.20 (bd, J = 13.6 Hz) [1H], 2.01 (m, 1H)
92	(3-chlorophenyl)methyl	651.07	E	D, L	651.1; 653.1	7.29 (bs, 1H), 7.23 (m, 3H), 5.54 (d, J = 4.4 Hz, 1H), 5.02 (s, 2H), 4.24 (d, J = 7.9 Hz, 1H)
1A		658.63	E	E, L	659.1	($DMSO-d_6$) 8.01 (d, J = 9.3 Hz, 1H), 7.87 (s, 1H), 7.51 (d, J = 9.1 Hz, 1H), 5.56 (d, J = 4.2 Hz, 1H), 5.17 (s, 2H), 4.10 (d, J = 7.9 Hz, 1H)
2A		695.08	E	F, L	695.1; 697.1	($DMSO-d_6$) 7.04 (s, 1H), 6.92 (s, 1H), 6.02 (s, 2H), 5.53 (d, J = 4.6 Hz, 1H), 4.96 (s, 2H), 4.07 (d, J = 7.9 Hz, 1H)
3A		695.08	Z	F, L	695.1; 697.1	6.96 (s, 1H), 6.86 (s, 1H), 5.97 (s, 2H), 5.66 (d, J = 4.2 Hz, 1H), 5.23 (obscured, presumed d, 1H), 5.04 (AB quartet, $\Delta\nu$ = 8.1 Hz, J = 13.2 Hz, 2H)
4A	(3,5-dichlorophenyl)methyl	685.52	Z	F, L	685.0; 687.0	7.30 (bs, 3H), 5.64 (d, J = 4.4 Hz, 1H), 5.22 (d, J = 6.4 Hz, 1H), 4.99 (bs, 2H)
5A	(3,5-dichlorophenyl)methyl	685.52	E	F, L	685.1; 687.1	7.30 (t, J = 2.0 Hz, 1H), 7.24 (d, J = 1.9 Hz, 2H), 5.53 (d, J = 4.4 Hz, 1H), 5.01 (s, 2H), 4.24 (d, J = 7.9 Hz, 1H)
6A	4-phenyl-3-	682.69	E	F, L	683.1	7.64 (d, J = 1.9 Hz, 1H),

Ex.	Y	Mol Wt	Stereo	Pro.	Mass spec	1H NMR peaks (CD_3OD)
	furanylmethyl					7.59 (bs, 1H), 7.43 (bd, J = 8 Hz, 2H), 7.31 (bt, J = 8 Hz, 2H), 7.25 (m, 1H), 5.56 (d, J = 4.6 Hz, 1H), 5.00 (s, 2H), 4.27 (d, J = 7.9 Hz, 1H)
7A	4-phenyl-3-furanylmethyl	682.69	Z	F, L	683.1	7.66 (d, J = 1.7 Hz, 1H), 7.64 (bs, 1H), 7.50 (bd, J = 8 Hz, 2H), 7.38 (bt, J = 8 Hz, 2H), 7.29 (m, 1H), 5.64 (d, J = 4.2 Hz, 1H), 5.13 (d, J = 6.4 Hz, 1H), 4.98 (AB quartet, $\Delta\nu$ = 21.6 Hz, J = 12.0 Hz, 2H)
8A	(3-[(*tert*-butoxycarbonyl)amino methyl]phenyl)methyl	745.79	Z	F, L	746.1	7.26 (m, 3H), 7.20 (m, 1H), 5.66 (d, J = 4.4 Hz, 1H), 5.21 (d, J = 6 Hz, 1H), 5.03 (AB quartet, $\Delta\nu$ = 13.4 Hz, J = 12.5 Hz, 2H), 4.21 (m, 2H)
9A	(3-[(*tert*-butoxycarbonyl)amino methyl]phenyl)methyl	745.79	E	F, L	746.1	7.24 (m, 2H), 7.19 (m, 2H), 5.56 (d, J = 4.6 Hz, 1H), 5.05 (s, 2H), 4.26 (d, J = 7.9 Hz, 1H), 4.20 (m, 2H)
10A	(3-chlorophenyl)methyl	651.07	Z	D, L	651.1; 653.1	7.35 (bs, 1H), 7.26 (m, 3H), 5.64 (d, J = 4.4 Hz, 1H), 5.21 (d, J = 6.4 Hz, 1H), 5.01 (AB quartet, $\Delta\nu$ = 10.2 Hz, J = 13.0 Hz, 2H)
11A	(3,5-difluorophenyl)methyl	652.61	E	F, L	653.1	6.90 (m, 2H), 6.82 (m, 1H), 5.56 (d, J = 4.6 Hz, 1H), 5.06 (s, 2H), 4.26 (d, J = 7.9 Hz, 1H)
12A	(5-chloro-2-fluorophenyl)methyl	669.06	E	F, L	669.0; 671.0	7.34 (dd, J = 6.2, 2.6 Hz), 7.27 (ddd, J = 8.8, 4.5, 3.0 Hz, 1H), 7.05 (dd, apparent t, J = 9.2 Hz, 1H), 5.54 (d, J = 4.4 Hz, 1H), 5.07 (s, 2H), 4.24 (d, J = 7.7 Hz, 1H)
13A	(3-chloro-2-fluorophenyl)methyl	669.06	Z	E, L	669.0; 671.0	7.37 (apparent dd, J = 7.7, 6.9 Hz, 2H), 7.1 (m, 1H), 5.64 (d, J = 4.4 Hz, 1H), 5.19 (d, J = 6.2 Hz, 1H), 5.10 (bs, 2H)
14A	(3-chloro-2-fluorophenyl)methyl	669.06	E	E, L	669.0; 671.0	7.36 (m, 1H), 7.28 (m, 1H), 7.08 (m, 1H), 5.54 (d, J = 4.4 Hz, 1H), 5.11 (s, 2H),

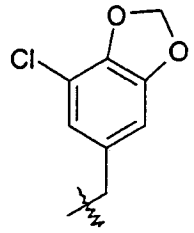
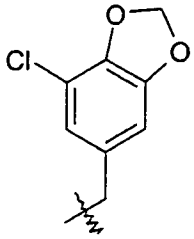
Ex.	Y	Mol Wt	Stereo	Pro.	Mass spec	1H NMR peaks (CD_3OD)
						4.23 (d, J = 7.7 Hz, 1H)
15A	(3,5-difluorophenyl)methyl	652.61	Z	F, L	653.1	6.94 (m, 2H), 6.80 (tt, J = 9.2, 2.4 Hz, 1H), 5.64 (d, J = 4.2 Hz, 1H), 5.23 (d, J = 6.4 Hz, 5.02 (presumed AB quartet, J = 14 Hz, 2H)
16A		676.66	Z	F, L	677.2	7.12 (m, 1H), 6.93 (m, 1H), 6.77 (dd, J = 9.1, 4.8 Hz, 1H), 5.64 (d, J = 4.4 Hz, 1H), 5.16 (d, J = 6.6 Hz, 1H), 5.07 (m, 1H), 4.12 (m, 1H), 2.21 (m, 1H), 2.06 (m, 1H)
17A		676.66	E; mixture of diastereomers	F, L	677.2	7.00 (ddd, apparent dt, J = 8.7, 2.8 Hz, 1H), 6.92 (m, 1H), 6.75 (dd, J = 8.9, 4.6 Hz, 1H), 5.60 and 5.59 (d, J = 4.4 and 4.6 Hz, 1H), 5.08 (m, 1H), 4.33 and 4.32 (d, J = 7.7 and 7.9 Hz, 1H), 4.22 (m, 1H), 4.04 (m, 1H), 2.22 (m, 1H), 2.03 (m, 1H)
18A	(3-aminomethylphenyl)methyl	645.67	E	I (using product of Example 9A), L	646.1	7.29 (m, 4H), 5.56 (d, J = 4.6 Hz, 1H), 5.07 (s, 2H), 4.26 (d, J = 7.9 Hz, 1H), 3.84 (s, 2H)
19A	(3-chloro-4-fluorophenyl)methyl	669.06	E	E, L	669.1; 671.1	7.39 (dd, J = 7.1, 2.1 Hz, 1H), 7.24 (ddd, J = 8.5, 4.8, 2.1 Hz, 1H), 7.14 (dd, J = 9.1, 8.5 Hz, 1H), 5.53 (d, J = 4.6 Hz, 1H), 4.99 (s, 2H), 4.23 (d, J = 7.9 Hz, 1H)
20A	2-quinolylmethyl	667.68	E	F, L	668.1	8.28 (d, J = 8.5 Hz, 1H), 7.98 (d, J = 8.5 Hz, 1H), 7.90 (d, J = 8.3 Hz, 1H), 7.74 (m, 1H), 7.57 (m, 1H), 7.52 (d, J = 8.5 Hz, 1H), 5.55 (d, J = 4.6 Hz, 1H), 5.33 (s, 2H), 4.27 (d, J =

Ex.	Y	Mol Wt	Stereo	Pro.	Mass spec	1H NMR peaks (CD_3OD)
						7.7 Hz, 1H)
21A	2-quinolylmethyl	667.68	Z	F, L	668.1	8.32 (d, J = 8.5 Hz, 1H), 8.12 (d, J = 8.3 Hz, 1H), 7.92 (d, J = 8.1 Hz, 1H), 7.76 (m, 1H), 7.59 (m, 1H), 7.53 (d, J = 8.5 Hz, 1H), 5.69 (d, J = 4.4 Hz, 1H), 5.36 (AB quartet, $\Delta\nu$ = 16.4 Hz, J = 14.8 Hz, 2H), 5.28 (d, J = 6.4 Hz, 1H)
22A	(3-chloro-4-fluorophenyl)methyl	669.06	Z	E, L	669.0; 671.0	7.46 (dd, J = 7.3, 2.1 Hz, 1H), 7.29 (ddd, J = 8.3, 4.7, 2.1 Hz, 1H), 7.17 (m, 1H), 5.64 (d, J = 4.2 Hz, 1H), 5.19 (d, J = 5.6 Hz, 1H), 4.98 (AB quartet, $\Delta\nu$ = 7.7, J = 13.2 Hz, 2H)
23A	3-quinolylmethyl	667.68	Z	F, L	668.1	8.84 (bd, J = 1.9 Hz, 1H), 8.30 (bs, 1H), 7.99 (d, J = 8.7 Hz, 1H), 7.91 (d, J = 8.1 Hz, 1H), 7.73 (m, 1H), 7.58 (m, 1H), 5.63 (d, J = 4.4 Hz, 1H), 5.24 (m, 3H)
24A	3-quinolylmethyl	667.68	E	F, L	668.1	8.80 (bd, J = 2.1 Hz, 1H), 8.26 (bd, J = 1.5 Hz, 1H), 7.98 (d, J = 8.5 Hz, 1H), 7.89 (bd, J = 8.3 Hz, 1H), 7.73 (m, 1H), 7.58 (m, 1H), 5.53 (d, J = 4.6 Hz, 1H), 5.27 (s, 2H), 4.25 (d, J = 7.7 Hz, 1H)
25A	(4-chloro-3-fluorophenyl)methyl	669.06	Z	F, L	669.1, 671.1	7.39 (dd, apparent t, J = 7.9 Hz, 1H), 7.23 (m, 1H), 7.14 (m, 1H), 5.64 (d, J = 4.4 Hz, 1H), 5.21 (d, J = 6.4 Hz, 1H), 5.00 (AB quartet, $\Delta\nu$ = 7.7 Hz, J = 13.3 Hz, 2H)
26A	(4-chloro-3-fluorophenyl)methyl	669.06	E	F, L	669.1, 671.1	7.42 (dd, apparent t, J = 7.9 Hz, 1H), 7.20 (dd, J = 10.1, 1.8 Hz, 1H), 7.14 (m, 1H), 5.59 (d, J = 4.6 Hz, 1H), 5.07 (s, 2H), 4.28 (d, J = 7.8 Hz, 1H)
27A	(3,4,5-trifluorophenyl)methyl	670.6	E	E, L	671.1	7.04 (dd, apparent t, J = 7.6 Hz, 2H), 5.54 (d, J = 4.6 Hz, 1H), 4.99 (s, 2H), 4.23 (d, J = 7.9 Hz, 1H)

Ex.	Y	Mol Wt	Stereo	Pro.	Mass spec	1H NMR peaks (CD_3OD)
28A		660.64	Z	F, L	661.1	6.76 (m, 3H), 5.92 (s, 2H), 5.63 (d, J = 4.2 Hz, 1H), 5.16 (d, J = 6.4 Hz, 1H), 5.00 (AB quartet, $\Delta\nu$ = 9.3 Hz, J = 12.5 Hz, 2H)
29A		660.64	E	F, L	661.1	6.73 (m, 3H), 5.89 (s, 2H), 5.54 (d, J = 4.6 Hz, 1H), 5.01 (s, 2H), 4.24 (d, J = 7.9 Hz, 1H)
30A		695.08	E	F, L	694.7; 696.4	[DMSO-d_6] 6.91 (d, J = 8.1 Hz, 1H), 6.84 (d, J = 8.3 Hz, 1H), 6.10 (s, 2H), 5.54 (d, J = 4.6 Hz, 1H), 4.99 (s, 2H), 4.08 (d, J = 7.9 Hz, 1H)
31A		695.08	Z	F, L	695.1; 697.1	6.96 (d, J = 8.1 Hz, 1H), 6.86 (d, J = 8.5 Hz, 1H), 6.03 (s, 2H), 5.65 (d, J = 4.2 Hz, 1H), 5.18 (d, J = 6.4 Hz, 1H), 5.05 (AB quartet, $\Delta\nu$ = 15.3 Hz, J = 12.5 Hz, 2H)
32A	(5-chloro-2-fluorophenyl)methyl	669.06	Z	F, L	669.2; 671.2	7.44 (dd, J = 6.3, 2.6 Hz, 1H), 7.27 (m, 1H), 7.06 (dd, J = 9.3, 8.9 Hz, 1H), 5.64 (d, J = 4.2 Hz, 1H), 5.20 (d, J = 6.2 Hz, 1H), 5.06 (bs, 2H)
33A	(4-fluorophenyl)methyl	634.62	E	F, L	635.2	7.31 (dd, J = 8.9, 5.6 Hz, 2H), 7.01 (dd, apparent t, J = 8.8 Hz, 2H), 5.55 (d, J = 4.6 Hz, 1H), 5.02 (s, 2H), 4.25 (d, J = 7.9 Hz, 1H)
34A	(4-phenyl-2-furanyl)methyl	682.69	Z	F, L	683.2	7.87 (s, 1H), 7.54 (d, J = 7.6 Hz, 2H), 7.37 (dd, apparent t, J = 7.6 Hz, 2H), 7.25 (t, J = 7.3 Hz, 1H), 6.80 (s, 1H), 5.68 (d, J = 4.3 Hz, 1H), 5.20 (d, J = 6.3 Hz, 1H), 5.02 (AB

Ex.	Y	Mol Wt	Stereo	Pro.	Mass spec	1H NMR peaks (CD_3OD)
						quartet, $\Delta\nu$ = 6.1 Hz, J = 13.3 Hz, 2H)
35A	(4-phenyl-2-furanyl)methyl	682.69	E	F, L	683.2	7.86 (s, 1H), 7.54 (d, J = 8.2 Hz, 2H), 7.38 (dd, J = 7.9, 6.9 Hz, 2H), 7.26 (t, J = 6.9 Hz, 1H), 6.80 (s, 1H), 5.61 (d, J = 4.6 Hz, 1H), 5.05 (s, 2H), 4.33 (d, J = 7.6 Hz, 1H)
36A		672.69	Z	F, L	673.1	7.01 (m, 2H), 6.78 (m, 2H), 5.65 (d, J = 4.2 Hz, 1H), 5.12 (d, J = 6.2 Hz, 1H), 2.84 (m, 1H), 2.75 (m, 1H), 2.02 (m, 1H), 1.74 (m, 1H)
37A		672.69	E; mixture of diastereomers	F, L	673.1	6.97 (m, 1H), 6.88 (dd, J = 7.9, 2.1 Hz, 1H), 6.74 (dd, apparent t, J = 7.5 Hz, 1H), 6.67 (m, 1H), 5.55 and 5.54 (d, 4.4 and 4.6 Hz, 1H), 4.26 and 4.25 (d, J = 7.7, 7.9 Hz, 1H), 2.79 (m, 1H), 2.71 (m, 1H), 1.98 (m, 1H), 1.67 (m, 1H)
38A	(3-chloro-2,6-difluorophenyl)methyl	687.05	Z	F, L	687.1; 689.1	7.47 (m, 1H), 6.70 (apparent bt, J = 8.8 Hz, 1H), 5.63 (d, J = 3.9 Hz, 1H), 5.12 (bs, 2H), 5.11 (d, J obscured, 1H)
39A	(3-chloro-2,6-difluorophenyl)methyl	687.05	E	F, L	687.1; 689.1	7.44 (ddd, apparent td, J = 9, 5 Hz, 1H), 6.96 (ddd, apparent td, J = 8.8, 1.8 Hz, 1H), 5.53 (d, J = 4.6 Hz, 1H), 5.13 (s, 2H), 4.21 (d, J = 7.9 Hz, 1H)
40A	(2,3,5,6-tetrafluoro-4-methylphenyl)methyl	702.62	Z	E, J	703.1	5.61 (d, J = 4.0 Hz, 1H), 5.11 (bs, 2H), 5.09 (d, J = 6.2 Hz, 1H), 2.24 (bs, 3H)
41A	(2,3,5,6-tetrafluoro-4-methylphenyl)methyl	702.62	E	E, J	703.1	5.52 (d, J = 4.6 Hz, 1H), 5.13 (s, 2H), 4.20 (d, J = 7.9 Hz, 1H), 2.22 (t, J = 2 Hz, 3H)
42A	(3,4,5-trifluorophenyl)methyl	670.6	Z	F, L	671.1	7.14 (m, 2H), 5.66 (d, J = 4.2 Hz, 1H), 5.24 (d, J = 6.6 Hz, 1H), 4.99 (s, 2H)
43A	(2,6-dichlorophenyl)methyl	685.52	Z	F, J	685.0; 687.0	7.37 (m, 2H), 7.27 (dd, J = 8.9, 7.1 Hz, 1H), 5.61 (d, J = 4.2 Hz, 1H), 5.30 (AB quartet, $\Delta\nu$ = 10.1, J = 11.0 Hz, 2H), 5.11 (d, J =

Ex.	Y	Mol Wt	Stereo	Pro.	Mass spec	1H NMR peaks (CD_3OD)
						6.2 Hz, 1H)
44A	(2,6-dichlorophenyl)methyl	685.52	E	F, J	685.0; 687.0	7.34 (m, 2H), 7.24 (dd, J = 8.8, 7.2 Hz, 1H), 5.54 (d, J = 4.6 Hz, 1H), 5.32 (s, 2H), 4.24 (d, J = 7.9 Hz, 1H)
45A	(2,4-dichlorophenyl)methyl	685.52	Z	F, L	685.0; 687.0	7.51 (d, J = 8.2 Hz, 1H), 7.47 (d, J = 2.3 Hz, 1H), 7.34 (dd, J = 8.2, 2.3 Hz, 1H), 5.70 (d, J = 4.3 Hz, 1H), 5.29 (d, J = 6.3 Hz, 1H), 5.15 (bs, 2H)
46A	(2-chloro-4-fluorophenyl)methyl	669.06	Z	F, L	669.1; 671.1	7.54 (dd, J = 8.6, 6.3 Hz, 1H), 7.24 (dd, J = 8.6, 2.6 Hz, 1H), 7.09 (ddd, apparent td, J = 8.6, 2.6, 1H), 5.70 (d, J = 4.3 Hz, 1H), 5.28 (d, J = 6.3 Hz, 1H), 5.15 (AB quartet, $\Delta\nu$ = 6.8 Hz, J = 13.5 Hz, 2H)
47A	(2,4-dichlorophenyl)methyl	685.52	E	F, L	685.1; 687.0	7.45 (d, J = 2.0 Hz, 1H), 7.37 (d, J = 8.2 Hz, 1H), 7.29 (dd, J = 8.6, 2.3 Hz, 1H), 5.59 (d, J = 4.6 Hz, 1H), 5.17 (s, 2H), 4.29 (d, J = 7.6 Hz, 1H)
48A	(2-chloro-4-fluorophenyl)methyl	669.06	E	F, L	669.1; 671.1	7.42 (dd, J = 8.6, 5.9 Hz, 1H), 7.22 (dd, J = 8.6, 2.6 Hz, 1H), 7.05 (ddd, apparent td, J = 8.6, 2.6 Hz, 1H), 5.59 (d, J = 4.6 Hz, 1H), 5.16 (s, 2H), 4.29 (d, J = 7.9 Hz, 1H)
49A	(2-chloro-6-fluorophenyl)methyl	669.06	Z	F, J	669.1; 671.1	7.33 (ddd, apparent td, J = 8.3, 6.0 Hz, 1H), 7.25 (presumed bd, J obscured, 1H), 7.08 (bdd, apparent bt, J = 8.3 Hz, 1H), 5.63 (d, J = 4.2 Hz, 1H), 5.20 (bs, 2H), 5.12 (d, J = 6.2 Hz, 1H)
50A	(2-chloro-6-fluorophenyl)methyl	669.06	E	F, J	669.1; 671.1	7.31 (ddd, apparent td, J = 8.1, 6.0, 1H), 7.22 (presumed bd, J obscured, 1H), 7.05 (presumed bt, J = 8.3 Hz, 1H), 5.55 (d, J = 4.6 Hz, 1H), 5.22 (s, 2H), 4.25 (d, J = 7.9 Hz, 1H)

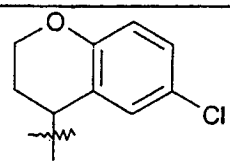
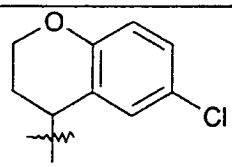
Ex.	Y	Mol Wt	Stereo	Pro.	Mass spec	1H NMR peaks (CD_3OD)
51A		695.08	Z	F, J	695.1; 697.0	6.83 (d, J = 1.3 Hz, 1H), 6.78 (d, J = 1.4 Hz, 1H), 6.00 (s, 2H), 5.63 (d, J = 4.2 Hz, 1H), 5.16 (d, J = 6.2 Hz, 1H), 4.89 (AB quartet, Δν = 10.1 Hz, J = 12.7 Hz, 2H)
52A		695.08	E	F, J	695.0; 697.0	6.78 (d, J = 1.4 Hz, 1H), 6.72 (d, J = 1.4 Hz, 1H), 5.98 (s, 2H), 5.53 (d, J = 4.6 Hz, 1H), 4.90 (s, 2H), 4.24 (d, J = 7.9 Hz, H)
53A	(3-chloro-5-fluorophenyl)methyl	669.06	Z	F, L	669.1; 671.0	7.24 (bs,1H), 7.12 (m, 2H), 5.70 (d, J = 4.3 Hz, 1H), 5.28 (d, J = 6.6 Hz, 1H), 5.06 (bs, 2H)
54A	(3-chloro-5-fluorophenyl)methyl	669.06	E	F, L	669.1; 671.1	7.18 (bs, 1H), 7.11 (m, 1H), 7.04 (m, 1H), 5.59 (d, J = 4.6 Hz, 1H), 5.08 (s, 2H), 4.29 (d, J = 7.9 Hz, 1H)
55A	(2,6-difluorophenyl)methyl	652.6	Z	F, L	653.1	7.40 (tt, J = 8.6, 6.6 Hz, 1H), 6.99 (dd, apparent t, J = 7.9 Hz, 2H), 5.66 (d, J = 4.3 Hz, 1H), 5.15 (m, 3H)
56A	(2,6-difluorophenyl)methyl	652.6	E	F, L	653.1	7.39 (tt, J = 8.6, 6.3 Hz, 1H), 6.87 (dd, apparent t, J = 7.6 Hz, 2H), 5.58 (d, J = 4.6 Hz, 1H), 5.17 (s, 2H), 4.28 (d, J = 7.9 Hz, 1H)
57A	(3,4-difluorophenyl)methyl	652.61	Z	F, L	653.1	7.31 (m, 1H), 7.23 (m, 1H), 7.15 (m, 1H), 5.69 (d, J = 4.0 Hz, 1H), 5.25 (d, J = 6.3 Hz, 1H), 5.03 (bs, 2H)
58A	(3,4-difluorophenyl)methyl	652.61	E	F, L	653.1	7.24 (m, 1H), 7.20 (dd, J = 10.7, 8.0 Hz, 1H), 7.14 (m, 1H), 5.59 (d, J = 4.3 Hz, 1H), 5.05 (s, 2H), 4.28 (d, J = 7.9 Hz, 1H)
59A	(2,3,6-trifluorophenyl)methyl	670.6	Z	F, L	671.1	7.25 (m, 1H), 6.94 (m, 1H), 5.61 (d, J = 4.2 Hz, 1H), 5.11 (AB quartet, Δν = 6.3 Hz, J = 9.8 Hz, 2H), 5.10 (d, J = 6.4 Hz, 1H)
60A	(2,3,6-	670.6	E	F, L	671.0	7.26 (m, 1H), 6.94 (m, 1H),

Ex.	Y	Mol Wt	Stereo	Pro.	Mass spec	1H NMR peaks (CD_3OD)
	trifluorophenyl)methyl					5.55 (d, J = 4.6 Hz, 1H), 5.15 (s, 2H), 4.23 (d, J = 7.9 Hz, 1H)
61A	(2,4-difluorophenyl)methyl	652.61	Z	F, L	653.2	7.50 (m, 1H), 6.95 (m, 2H), 5.68 (d, J = 4.0 Hz, 1H), 5.22 (d, J = 6.3 Hz, 1H), 5.09 (bs, 2H)
62A	(2,4-difluorophenyl)methyl	652.61	E	F, L	653.2	7.39 (m, 1H), 6.91 (m, 2H), 5.58 (d, J = 4.6 Hz, 1H), 5.09 (s, 2H), 4.30 (d, J = 7.9 Hz, 1H)
63A	(2,6-difluoro-4-methylphenyl)methyl	666.64	Z	F, L	667.1	6.77 (d, J = 8.1 Hz, 2H), 5.60 (d, J = 4.2 Hz, 1H), 5.08 (d, J = 6.2 Hz, 1H), 5.04 (bs, 2H), 2.32 (s, 3H)
64A	(2,6-difluoro-4-methylphenyl)methyl	666.64	E	F, L	667.1	6.75 (d, J = 8.1 Hz, 2H), 5.52 (d, J = 4.6 Hz, 1H), 5.06 (s, 2H), 4.22 (d, J = 7.9 Hz, 1H), 2.30 (s, 3H)
65A	(2,3,4,5,6-pentafluorophenyl)methyl	706.58	Z	F, L	707.1	5.62 (d, J = 4.0 Hz, 1H), 5.11 (bs, 2H), 5.08 (d, J = 6.2 Hz, 1H)
66A	(2-fluoro-6-trifluoromethylphenyl)methyl)	702.62	Z	F, L	703.1	7.54 (m, 2H), 7.40 (m, 1H), 5.60 (d, J = 4.2 Hz, 1H), 5.20 (AB quartet, $\Delta\nu$ = 15.4 Hz, J = 11.5 Hz, 2H), 5.07 (d, J = 6.4 Hz, 1H)
67A	(2-fluoro-6-trifluoromethylphenyl)methyl)	702.62	E	F, L	703.1	7.54 (m, 2H), 7.40 (m, 1H), 5.55 (d, J = 4.6 Hz, 1H), 5.24 (s, 2H), 4.25 (d, J = 7.9 Hz, 1H)
68A	(2,3-difluorophenyl)methyl	652.61	Z	F, L	653.1	7.25 (m, 1H), 7.17 (m, 2H), 5:69 (d, J = 4.0 Hz, 1H), 5.24 (presumed d, J obscured, 1H), 5.16 (bs, 2H)
69A	(2,3-difluorophenyl)methyl	652.61	E	F, L	653.1	7.16 (m, 3H), 5.59 (d, J = 4.6 Hz, 1H), 5.17 (bs, 2H), 4.28 (d, J = 7.9 Hz, 1H)
70A	(2,3,4-trifluorophenyl)methyl	670.6	E	F, L	671.1	7.17 (m, 1H), 7.03 (m, 1H), 5.53 (d, J = 4.6 Hz, 1H), 5.08 (s, 2H), 4.22 (d, J = 7.7 Hz, 1H)
71A	(2,3,4-trifluorophenyl)methyl	670.6	Z	F, L	671.1	7.22 (m, 1H), 7.09 (m, 1H), 5.65 (d, J = 4.2 Hz, 1H), 5.18 (d, J = 6.2 Hz, 1H), 5.08 (bs, 2H)
72A	(2,3,5,6-tetrafluorophenyl)methyl	688.59	Z	F, L	688.9	7.27 (m, 1H), 5.69 (d, J = 4.0 Hz, 1H), 5.24 (d, J =

Ex.	Y	Mol Wt	Stereo	Pro.	Mass spec	1H NMR peaks (CD_3OD)
	l					6.6 Hz, 1H), 5.12 (bs, 2H)
73A	(2,3,5,6-tetrafluorophenyl)methyl	688.59	E	F, L	689.0	7.17 (m, 1H), 5.58 (d, J = 4.3 Hz, 1H), 5.13 (bs, 2H), 4.27 (d, J = 7.6 Hz, 1H)
74A	2,3-difluoro-6-methoxyphenyl)methyl	682.64	E	F, L	683.0	7.20 (m, 1H), 6.76 (ddd, J = 9.2, 3.6, 2.3 Hz, 1H), 5.58 (d, J = 4.6 Hz, 1H), 5.16 (d, J = 2.0 Hz, 2H), 4.28 (d, J = 7.9 Hz, 1H), 3.83 (s, 3H)
75A	2,3-difluoro-6-methoxyphenyl)methyl	682.64	Z	F, L	683.0	7.22 (m, 1H), 6.80 (ddd, J = 9.2, 3.3, 2.0, 1H), 5.65 (d, J = 3.6 Hz, 1H), 5.14 (m, 2H), 5.09 (d, J = 5.6 Hz, 1H), 3.88 (s, 3H)
76A	(4-chloro-3-sulfonamidophenyl)methyl	730.15	E	F, L	730.0	8.21 (m, 1H), 7.90 (m, 1H), 7.52 (m, 1H), 5.58 (d, J = 4.6 Hz, 1H), 5.13 (s, 2H), 4.28 (d, J = 7.9 Hz, 1H)
77A	(2-fluoro-6-trifluoromethoxyphenyl) methyl	718.616	E	F, L	719.0	7.48 (ddd, apparent td, J = 8.2, 6.3 Hz, 1H), 7.18 (m, 2H), 5.58 (d, J = 4.3 Hz, 1H), 5.19 (d, J = 1.0 Hz, 2H), 4.27 (d, J = 7.9 Hz, 1H)
78A	(2-fluoro-6-trifluoromethoxyphenyl) methyl	718.616	Z	F, L	719.0	7.49 (ddd, apparent t, J = 8.6, 6.3 Hz, 1H), 7.19 (m, 2H), 5.65 (d, J = 4.3 Hz, 1H), 5.16 (bs, 2H), 5.14 (d, J = 6.3 Hz, 1H)
79A	3-chloro-4-fluorophenyl	655.04	E	E, J	654.8	7.28 (dd, J = 6.2, 2.7 Hz, 1H), 7.11 (dd, apparent t, J = 9 Hz, 1H), 7.02 (m, 1H), 5.65 (d, J = 4.4 Hz, 1H), 4.28 (dd, J = 8.3, 4.6 Hz, 1H)
80A	(2-fluoro-6-methoxyphenyl)methyl	664.65	E	F, L	665.1	7.26 (ddd, apparent td, J = 8.5, 6.9 Hz, 1H), 6.76 (d, J = 8.5 Hz, 1H), 6.65 (dd, apparent t, J = 8.5 Hz, 1H), 5.53 (d, J = 4.6 Hz, 1H), 5.09 (d, J = 1.4 Hz, 2H), 4.24 (d, J = 7.9 Hz, 1H), 3.79 (s, 3H)
81A	4-(methoxycarbonyl)phenyl	660.64	E	E, J	661.1	7.88 (d, J = 8.5 Hz, 2H), 7.12 (d, J = 8.5 Hz, 2H), 5.65 (d, J = 4.4 Hz, 1H), 4.29 (dd, J = 8.1, 5 Hz, 1H), 3.84 (s, 3H)

Ex.	Y	Mol Wt	Stereo	Pro.	Mass spec	1H NMR peaks (CD_3OD)
82A	3-chlorophenyl	637.04	E	E, J	637.3; 639.4	7.19 (dd, apparent t, J = 8.2 Hz, 1H), 7.18 (dd, apparent t, J = 2.2 Hz, 1H), 6.99 (ddd, J = 8.3, 2.3, 1.0 Hz, 1H), 6.95 (ddd, J = 8.1, 1.9, 1.0 Hz, 1H), 5.62 (d, J = 4.6 Hz, 1H), 4.25 (dd, J = 8.1, 4.6 Hz, 1H)
83A	2-fluorophenyl	620.58	E	E, J	621.0	7.34 (ddd, apparent td, J = 8.1, 1.7 Hz, 1H), 7.05 (m, 1H), 7.00 (m, 1H), 6.94 (m, 1H), 5.62 (d, J = 4.6 Hz, 1H), 4.26 (dd, J = 8.2, 4.7 Hz, 1H)
84A	3,5-dichlorophenyl	671.49	E	E, J	670.7; 673.2	7.14 (d, J = 1.9 Hz, 2H), 7.04 (bs, 1H), 5.65 (d J = 4.4 Hz, 1H), 4.29 (dd, J = 8.1, 4.6 Hz, 1H)
85A	(3-chloro-2-thienyl)methyl	657.098	Z	F, L	656.8; 658.9	7.46 (d, J = 5.3 Hz, 1H), 6.95 (d, J = 5.3 Hz, 1H), 5.68 (d, J = 4.3 Hz, 1H), 5.19 (m, 2H), 5.17 (d, J = 6.3 Hz, 1H)
86A	(3-chloro-2-thienyl)methyl	657.098	E	F, L	656.9; 658.9	7.43 (d, J = 5.3 Hz, 1H), 6.93 (d, J = 5.3 Hz, 1H), 5.59 (d, J = 4.6 Hz, 1H), 5.20 (s, 2H), 4.31 (d, J = 7.6 Hz, 1H)
87A	(2-thienyl)methyl	622.653	Z	F, L	622.9	7.38 (dd, J = 5.3, 1.3 Hz, 1H), 7.08 (bd, J = 3.6 Hz, 1H), 6.99 (dd, J = 5.3, 3.6 Hz, 1H), 5.67 (d, J = 4.3 Hz, 1H), 5.20 (bs, 2H), 5.16 (d, J = 6.3 Hz, 1H)
88A	(2-thienyl)methyl	622.653	E	F, L	622.9	7.35 (dd, J = 5.3, 1.3 Hz, 1H), 7.05 (bd, J = 3.3 Hz, 1H), 6.97 (dd, J = 4.9, 3.3 Hz, 1H), 5.59 (d, J = 4.6 Hz, 1H), 5.22 (s, 2H), 4.31 (d, J = 7.9 Hz, 1H)
89A	(2-chloro-6-trifluoromethoxyphenyl) methyl	735.07	Z	F, L	734.8; 737.0	7.46 (m, 2H), 7.33 (m, 1H), 5.66 (d, J = 4.3 Hz, 1H), 5.25 (AB quartet, $\Delta\nu$ = 4.9 Hz, J = 11.5 Hz, 2H), 5.14 (d, J = 6.3 Hz, 1H)
90A	(2-chloro-6-trifluoromethoxyphenyl) methyl	735.07	E	F, L	734.8; 736.9	7.45 (m, 2H), 7.31 (m, 1H), 5.58 (d, J = 4.3 Hz, 1H), 5.28 (s, 2H), 4.28 (d, J =

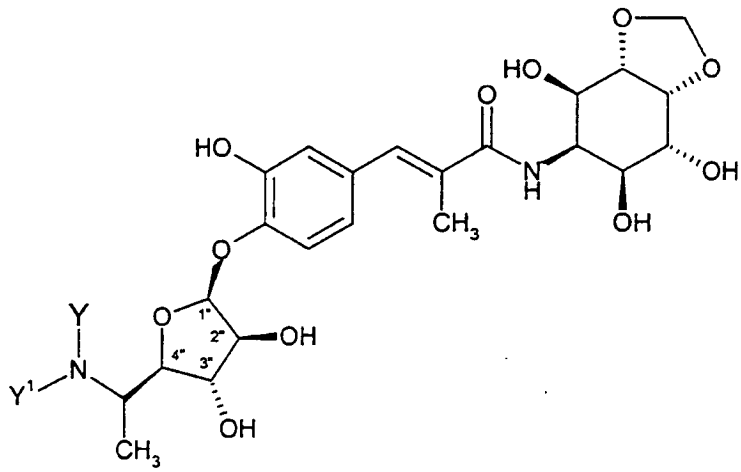
Ex.	Y	Mol Wt	Stereo	Pro.	Mass spec	1H NMR peaks (CD_3OD)
						7.9 Hz, 1H)
91A	(5-chloro-2-thienyl)methyl	657.098	Z	F, L	656.9; 658.9	6.89 (d, J = 4.0 Hz, 1H), 6.85 (d, J = 4.0 Hz, 1H), 5.68 (d, J = 4.0 Hz, 1H), 5.15 (d, J = 6.3 Hz, 1H), 5.10 (s, 2H)
92A	(5-chloro-2-thienyl)methyl	657.098	E	F, L	656.9; 658.9	6.86 (bd, J = 3.6 Hz, 1H), 6.82 (bd, J = 3.6 Hz, 1H), 5.59 (d, J = 4.3 Hz, 1H), 5.12 (s, 2H), 4.31 (d, J = 7.2 Hz, 1H)
93A	(2-difluoromethoxyphenyl) methyl	682.635	Z	F, L	683.1	7.49 (bd, J = 7.7 Hz, 1H), 7.33 (dd, apparent bt, J = 8 Hz, 1H), 7.22 (dd, apparent bt, J = 7.5 Hz, 1H), 7.16 (bd, J = 8 Hz, 1H), 6.79 (t, J = 74.4 Hz, 1H), 5.65 (d, J = 4.2 Hz, 1H), 5.22 (d, J = 6.4 Hz, 1H), 5.11 (AB quartet, $\Delta\nu$ = 9.2 Hz, J = 13.2 Hz, 2H)
94A	(2-difluoromethoxyphenyl) methyl	682.635	E	F, L	683.1	7.37 (d, J = 7.1 Hz, 1H), 7.29 (dd, apparent bt, J = 7 Hz, 1H), 7.16 (dd, apparent bt, J = 7.5 Hz, 1H), 7.10 (m, 1H), 6.72 (t, J = 74 Hz, 1H), 5.54 (d, J = 4.4 Hz, 1H), 5.11 (s, 2H), 4.24 (d, J = 7.9 Hz, 1H)
95A	(3-fluorophenyl)methyl	634.618	E; α-steroechem at 4"	F; N-1	634.9	7.36 (ddd, apparent td, J = 7.9, 5.9 Hz, 1H), 7.18 (m, 1H), 7.10 (m, 1H), 7.02 (m, 1H), 5.73 (d, J = 4.3 Hz, 1H), 5.12 (s, 2H), 4.79 (d, J = 6.9 Hz, 1H)
96A	(3-chlorophenyl)methyl	651.073	E; α-steroechem at 4"	F; N-1	650.8	7.32 (bs, 1H), 7.27 (m, 3H), 5.68 (d, J = 4.4 Hz, 1H), 5.05 (s, 2H), 4.74 (d, J = 7.1 Hz, 1H)
97A	(3,4-dichlorophenyl)methyl	685.518	E	F, L	684.9; 686.9	7.42 (m, 2H), 7.20 (dd, J = 8.3, 2.1 Hz, 1H), 5.53 (d, J = 4.6 Hz, 1H), 5.00 (s, 2H), 4.23 (d, J = 7.9 Hz, 1H)
98A	(2,6-dimethylphenyl)methyl	644.682	Z	F, L	644.9	7.05 (dd, J = 8.3, 6.4 Hz, 1H) 6.97 (bd, J = 7.5 Hz, 2H), 5.59 (d, J = 4.4 Hz, 1H), 5.11 (AB quartet, $\Delta\nu$ = 18.3 Hz, J = 10.9 Hz, 2H), 5.09 (d, J = 6.4 Hz,

Ex.	Y	Mol Wt	Stereo	Pro.	Mass spec	1H NMR peaks (CD_3OD)
						1H), 2.37 (s, 6H)
99A	(2,6-dimethylphenyl)methyl	644.682	E	F, L	645.1	7.03 (dd, J = 8.1, 6.4 Hz, 1H), 6.95 (bd, J = 7.3, 2H), 5.54 (d, J = 4.6 Hz, 1H), 5.13 (s, 2H), 4.25 (d, J = 7.7 Hz, 1H), 2.33 (s, 6H)
100A	(3-fluorophenyl)methyl	634.618	Z; α-steroechem at 4"	F; N-1	635.1	7.36 (ddd, apparent td, J = 7.9, 5.6 Hz, 1H), 7.16 (m, 1H), 7.13 (m, 1H), 7.02 (bt, J = 8.9 Hz, 1H), 5.80 (d, J = 4.0 Hz, 1H), 5.51 (d, J = 4.9 Hz, 1H), 5.07 (AB quartet, Δν = 11.8 Hz, J = 12.8 Hz, 1H)
101A	(3-chlorophenyl)methyl	651.073	Z; α-steroechem at 4"	F; N-1	650.9; 653.0	7.40 (bs, 1H), 7.29 (m, 3H), 5.80 (d, J = 4.0 Hz, 1H), 5.50 (d, J = 5.3 Hz, 1H), 5.06 (AB quartet, Δν = 11.89 Hz, J = 12.8 Hz, 2H)
102A		693.11	Z	E, J	693.1; 695.1	7.37 (d, J = 2.7 Hz, 1H), 7.14 (dd, J = 8.7, 2.7 Hz, 1H), 6.76 (d, J = 8.7 Hz, 1H), 5.63 (d, J = 4.4 Hz, 1H), 5.16 (d, J = 6.6 Hz, 1H), 5.05 (m, 1H), 2.21 (m, 1H), 2.04 (m, 1H)
103A		693.11	E; mixture of diastereomers	E, J	693.1; 695.1	7.24 (m, 1H), 7.11 (m, 1H), 6.73 (d, J = 8.9 Hz, 1H), 5.58 and 5.57 (d, J = 4.2 and 4.2 Hz, 1H), 5.04 (m, 1H), 4.31 and 4.30 (d, J = 7.7 and 7.7 Hz, 1H), 4.02 (m, 1H), 2.21 (m, 1H), 2.00 (m, 1H)
104A	(4-phenyl-2-thiazolyl)methyl	699.74	Z	G, L	700.2	7.87 (m, 2H), 7.74 (br s, 1H), 7.38 (m, 2H), 7.30 (m, 1H), 5.85 (d, J = 4.4, 1H), 5.83 (br s, 2H), 5.22 (d, J = 6.2 Hz, 1H)
105A	(4-phenyl-2-thiazolyl)methyl	699.74	E	G, L	700.2	7.82 (m, 2H), 7.67 (br s, 1H), 7.36 (m, 2H), 7.27 (m, 1H), 5.55 (d, J = 4.6, 1H), 5.84 (br s, 2H),
106A	1-(2,4-difluorophenyl)propyl	680.66	Z; mixture of diastereomer	G, L	681.0	7.48 and 7.32 (2m, 1H), 6.85 (m, 2H), 5.65 (m, 1H), 5.32 and 5.26 (2d, J = 6.4 and 6.2 Hz, 1H), 5.20 (m, 1H), 1.86 and 1.74 (2m,

Ex.	Y	Mol Wt	Stereo	Pro.	Mass spec	1H NMR peaks (CD_3OD)
			s			2H), 0.89 (m, 3H).
107A	1-(2,4-difluorophenyl)propyl	680.66	E; mixture of diastereomers	G, L	681.0	7.25 (m, 1H), 6.83 (m, 2H), 5.52 and 5.51 (2d, J = 4.5 and 4.5 Hz, 1H), 5.23 (m, 1H), 1.86 and 1.72 (2m, 2H), 0.86 (m, 3H).
108A	1-(3,4-difluorophenyl)ethyl	666.64	Z; mixture of diastereomers	G, L	667.0, 689.0	7.28 (m, 1H), 7.15 (m, 1H), 5.64 (d, J 4.2 Hz, 1H), 5.29 (d, J = 6.6 Hz, 1H), 5.09 (q, J = 6.6 Hz, 1H), 1.43 (d, J = 6.6 Hz, 3H).
109A	1-(3,4-difluorophenyl)ethyl	666.64	E; mixture of diastereomers	G, L	667.0, 689.0	7.13 (m, 3H), 5.52 (m, 1H), 5.14 (m, 1H), 1.43 and 1.42 (2d, J = 6.4 and 6.6 Hz, 3H).
110A	1-(2,4-difluorophenyl)ethyl	666.64	Z; mixture of diastereomers	G, L	667.1	7.51 and 7.37 (m, 1H), 8.85 (m, 1H), 5.65 (m, 1H), 5.38 (m, 1H), 5.30 and 5.24 (2 d, J = 6.6 and 6.4 Hz, 1H), 1.45 and 1.44(2d, J = 6.6 and 6.6 Hz, 3H).
111A	1-(2,4-difluorophenyl)ethyl	666.64	E; mixture of diastereomers	G, L	667.1	7.29 (m, 1H), 6.85 (m, 2H), 5.52 (m, 1H), 5.40 (m, 1H),1.47 and 1.46 (2 d, J = 6.6 and 6.6 Hz, 3H)
112A	1-(3,5-difluorophenyl)ethyl	666.64	Z; mixture of diastereomers	G, L	667.0	6/97 (m, 2H), 6.76 (m, 1H), 5.65 (d, J 4.2 Hz, 1H), 5.30 (d, J 6.6 Hz, 1H), 5.10 (q, J = 6.6 Hz, 1H), 1.4 (d, J = 6.6 Hz, 3H).
113A	1-(3,5-difluorophenyl)ethyl	666.64	E; mixture of diastereomers	G, L	667.0	6.83 (m., 2H), 6.75 (m, 1H), 5.52 (2 d, J = 4.8 and 4.6 Hz, 1H), 5.15 (m, 1H), 1.43 and 1.42 (2d , J = 6.6 and 6.6 Hz, 3H)
114A	1-(3-chloro-2,6-difluorophenyl)ethyl	701.081	Z; mixture of diastereomers	G, L	701.0, 703.0	7.39 (m, 1H), 6.94 (m, 1H), 5.64 (br d, J = 3.9 Hz, 1H), 5.49 (q, 6.8 Hz), 5.18 (m, 1H), 1.60 (d, 6.9 Hz).

Ex.	Y	Mol Wt	Stereo	Pro.	Mass spec	1H NMR peaks (CD_3OD)
115A	1-(3-chloro-2,6-difluorophenyl)ethyl	701.081	E; mixture of diastereomers	G, L	701.0, 703.0	7.35 (m, 1H), 6.89 (m, 1H), 5.58 (m, 1H), 5.49 (m, 1H), 1.56 and 1.55 (2 d, J = 6.8 and 6.8 Hz, 3H).
116A	1-(3-chlorophenyl)ethyl	665.10	E	E, L	665.1, 667.1	7.25 (m, 1H), 7.20 (m, 1H), 5.54 and 5.53 (2d, J = 4.8 and 4.8 Hz, 1H), 5.17 (m, 1H), 1.47 and 1.45 (2d, J = 6.2 and 6.6 Hz, 3H).

Table 2



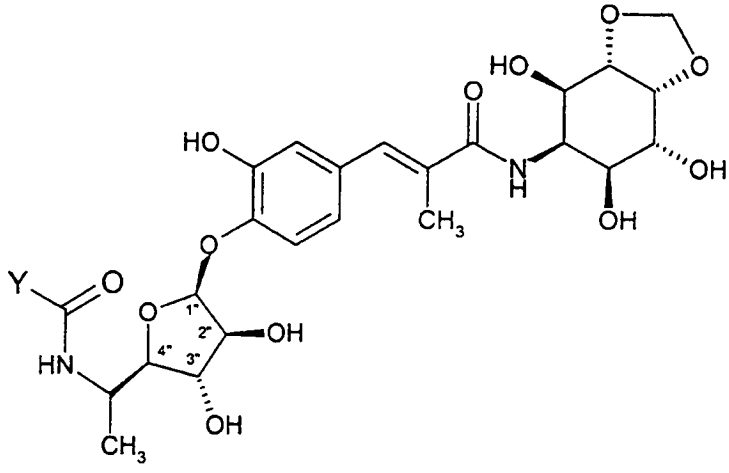
In the examples below for Table 2, Y^1 is H for all examples except Example 97 where it is methyl.

Ex.	Y	Mol Wt	Pro.	Mass spec.	1H NMR peaks (CD_3OD)
93	phenylmethyl	602.64	O	603.2	7.17 (m, 3H), 7.08 (m, 2H), 5.53 (d, J = 4.6 Hz, 1H), 3.87 (dd, J = 7.5, 4.4 Hz, 1H), 3.79 (d, J = 13.1 Hz, 1H), 3.61 (d, J = 13.1 Hz, 1H), 2.90 (m, 1H), 1.09 (d, J = 6.6 Hz, 3H)
94	(3,4-dimethoxyphenyl)-methyl	662.7	O	663.3	7.07 (s, 1H), 6.92 (m, 2H), 5.61 (d, J = 3.7 Hz, 1H), 4.07 (right half of AB quartet; left hand signal obscured, J = 13.1 Hz, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 3.41 (m, 1H), 1.26 (d,

Ex.	Y	Mol Wt	Pro.	Mass spec.	1H NMR peaks (CD_3OD)
					J = 6.9 Hz, 3H)
95	[2-(trifluoromethyl)phenyl] methyl	670.64	P	671.2	7.56 (bd, J = 7.9 Hz, 1H), 7.41 (m, 2H), 7.33 (bt, J = 7.5 Hz, 1H), 5.53 (d, J = 4.6 Hz, 1H), 3.87 (dd, J = 7.5, 4.4 Hz, 1H), 2.92 (m, 1H), 1.09 (d, J = 6.6 Hz, 3H)
96	(4-*tert*-butylphenyl)methyl	658.75	P	659.3	7.20 (d, J = 8.3 Hz, 2H), 6.97 (d, J = 8.3 Hz, 2H), 5.51 (d, J = 4.6 Hz, 1H), 3.84 (dd, J = 7.5, 4.4 Hz, 1H), 3.73 (d, J = 13.1 Hz, 1H), 3.55 (d, J = 13.1 Hz, 1H), 2.86 (m, 1H), 1.24 (s, 9H), 1.07 (d, J = 6.4 Hz, 3H)
97	phenylmethyl	616.67	Q (using the product of Example 93 as starting material)	617.2	7.30 (m, 5H), 5.55 (d, J = 3.9 Hz, 1H), 4.04 (dd, J = 7.1, 4.9 Hz, 1H), 3.54 (AB quartet, $\Delta\nu$ = 49.0 Hz, J = 13.2 Hz, 2H), 2.88 (m, 1H), 2.16 (s, 3H), 0.91 (d, J = 6.6 Hz, 3H)
98	phenyl	588.62	R	589.2	7.02 (dd, J = 8.6, 7.4 Hz, 2H), 6.58 (dd, J = 8.7, 1.0 Hz, 2H), 6.54 (dd, J = 7.3, 1.0 Hz, 1H), 5.57 (d, J = 4.4 Hz, 1H), 3.86 (dd, J = 6.8, 5.4 Hz, 1H), 3.59 (m, 1H), 1.04 (d, J = 6.4 Hz, 3H)
99	2-phenylethyl	616.67	P	617.3	7.19 (m, 2H), 7.08 (m, 3H), 5.52 (d, J = 4.4 Hz, 1H), 3.87 (dd, J = 7.2, 3.8 Hz, 1H), 2.88 (m, 3H), 2.67 (m, 2H), 1.03 (d, J = 6.4 Hz, 3H)
100	4-fluorophenyl	606.61	R	607.2	6.76 (dd, apparent t, J = 8.8 Hz, 2H), 6.56 (dd, J = 9.0, 4.5 Hz, 2H), 5.58 (d, J = 4.4 Hz, 1H), 3.53 (m, 1H), 1.04 (d, J = 6.4 Hz, 3H)
101	2-(4-chlorophenyl)ethyl	651.12	P	651.2; 653.2	7.19 (d, J = 8.3 Hz, 2H), 7.08 (d, J = 8.3 Hz, 2H), 5.53 (d, J = 4.4 Hz, 1H), 2.9 (m, 3H), 2.7 (m, 2H),

Ex.	Y	Mol Wt	Pro.	Mass spec.	1H NMR peaks (CD_3OD)
					1.07 (d, J = 6.4 Hz, 3H)

Table 3



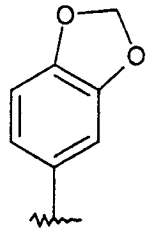
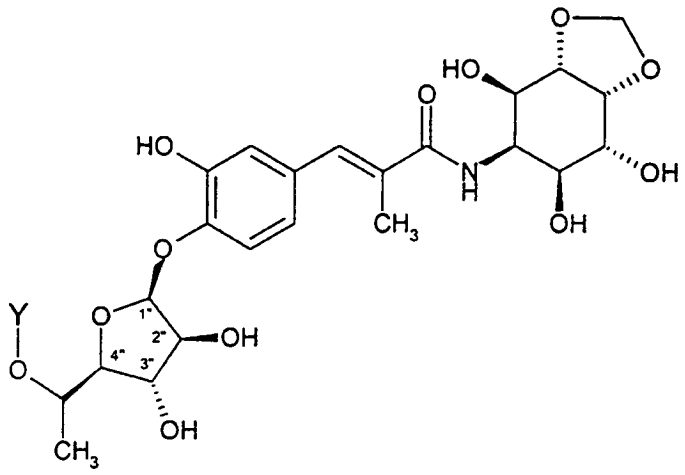
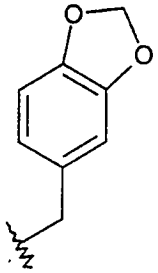
Ex.	Y	Mol wt	Pro.	Mass spec	1H NMR peaks (CD_3OD)
102	phenylmethyl	630.67	S	631.1	7.22 (m, 5H), 5.50 (d, J = 4.4 Hz, 1H), 3.39 (left half of AB quartet, right half obscured, J = 14.3 Hz, 1H), 1.03 (d, J = 6.6 Hz, 3H)
103	cyclopropyl	580.59	S	581.3	5.56 (d, J = 3.7 Hz, 1H), 1.47 (m, 1H), 1.06 (d, J = 6.6 Hz, 3H), 0.69 (m, 2H), 0.56 (m, 2H)
104		660.64	T	661.3	7.29 (dd, J = 8.1, 1.9 Hz, 1H), 7.21 (bs, 1H), 6.78 (d, J = 8.1 Hz, 1H), 5.97 (s, 2H), 5.50 (d, J = 4.6 Hz, 1H), 4.29 (m, 1H), 3.86 (dd, apparent t, J = 6.9 Hz, 1H), 1.18 (d, J = 6.8 Hz, 3H)

Table 4



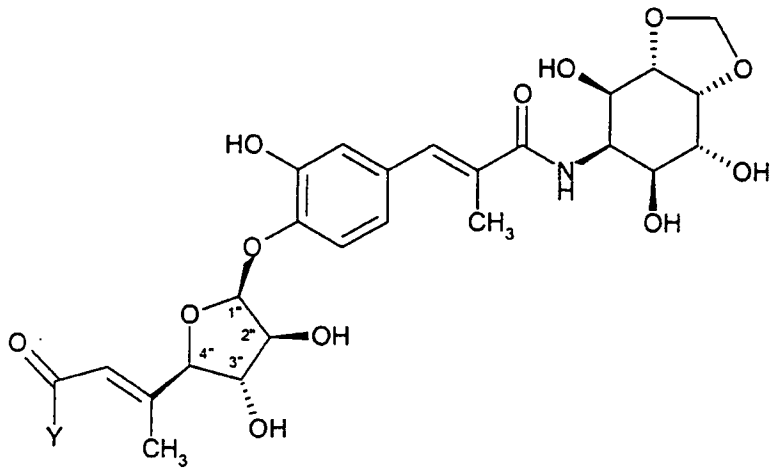
Ex.	Y	Mol Wt	Pro.	Mass Spec	1H NMR peaks (CD_3OD)
105	phenylmethyl	603.63	U	604.1	7.25 (br s, 1H), 7.2-7.13 (m, 6H), 6.92 (d, J = 1.3 Hz, 1H), 6.84 (dd, J = 8.5 and 1.9 Hz, 1H), 5.56 (d, J = 3.7 Hz, 1H), 4.42 (AB quartet, $\Delta\nu$ = 16 Hz, J = 11.8 Hz, 2H), 2.08 (d, J = 1.5 Hz, 3H), 1.16 (d, J = 6.4 Hz, 3H).
106	(3,4-dichlorophenyl)methyl	672.52	U	672.1, 674.1	7.30-7.26 (m, 2H); 7.22 (s, 1H); 7.13 (d, J = 8.5 Hz, 1H); 7.03 (dd, J = 8.3 and 2.0 Hz, 1H); 6.89 (d, J = 2 Hz, 1H); 6.85 (dd, J =8.5, 1.9 Hz, 1H); 5.56 (br dd, 1H); 4.34 (AB quartet, $\Delta\nu$ = 34.7 Hz, J = 12.7 Hz, 12H), 2.05 (d, J = 1.5 Hz, 3H); 1.16, (d, J = 6.2 Hz, 1H).
107	(4-fluorophenyl)methyl	621.62	U	622.2	7.22 (br s, 1H), 7.16-7.12 (m, 3H), 6.90-6.81 (m,4H), 5.54 (d, J = 4.0 Hz, 1H), 4.38 (AB quartet, $\Delta\nu$ = 25.1 Hz, J = 11.7 Hz, 2H), 2.06 (d, J = 1.4 Hz, 3H), 1.14 (d, J = 6.2 Hz)
108	(4-methylphenyl)methyl	617.66	U	618.3	7.25 (s, 1H), 7.17(d, J = 8.3 Hz, 1H), 7.04-6.99 (m, 4H), 6.93 (d, J = 1.8 Hz, 1H), 6.84 (dd, J = 8.5 and 2.1 Hz, 1H), 5.55 (d, J = 3.9 Hz, 1H), 4.37(AB quartet, $\Delta\nu$ = 16.0 Hz, J = 11.7 Hz, 2H), 2.25 (s, 3H), 2.08 (d, J = 2.2 Hz, 3H), 1.15 (d, J = 6.2 Hz, 3H)
109	(3-fluorophenyl)methyl	621.62	U	622	7.22 (d, J = 5.4 Hz, 1H), 7.2-7.16 (m, 1H) 7.16 (d, J = 8.5 Hz, 1H),

Ex.	Y	Mol Wt	Pro.	Mass Spec	1H NMR peaks (CD_3OD)
					6.94-6.89 (m, 4H), 6.82 (dd, J = 8.3 and 1.9 Hz, 1H), 5.57 (d, J = 3.5 Hz, 1H), 4.41 (AB quartet, Δν = 20.1 Hz, J = 12.5 Hz, 2H), 2.08 (d, J = 1.7 Hz, 3H), 1.18 (d, J = 6.4 Hz).
110		647.64	V	648.1	7.24 (brs, 1H), 7.15 (d, J = 8.3 Hz, 1 Hz), 6.92 (d, J = 2.0 Hz, 1H), 6.84 (dd, J = 8.4 and 2.0 Hz, 1H), 6.65-6.59 (m, 3H), 5.86, (s, 2H), 5.54 (d, J = 3.5 Hz, 1H), 4.30 (AB quartet, Δν = 23.6 Hz, J = 11.5 Hz, 2 H) , 2.08 (d, J = 1.3 Hz, 3H), 1.14 (d, J = 6.4 Hz, 3H).
111	(phenylmethyl)oxy-methyl	633.66	Z	634.2	7.28-7.18 (m, 5H), 7.11 (d, J = 8.5 Hz, 1H), 6.90 (d, J = 2.1 Hz, 1H) 6.78 (dd, J = 8.5 and 2.1 Hz, 1H), 5.54 (d, J = 4.2 Hz, 1H), 4.66 (AB quartet, Δν = 57.9, J = 6.8 Hz, 2H), 4.43 (AB quartet, Δν = 19.8 Hz, J = 11.9 Hz, 2H), 1.20 (d, J = 6.2 Hz, 3H).
112	(4-chlorophenyl)methyl	638	U	638.1, 640.1	7.25 (s, 1H), 7.19-7.11 (m, 4H), 6.92 (s, 1H), 6.84 (dd, J = 8.5 and 1.9 Hz, 1H), 5.56 (d, J = 3.5 Hz, 1H), 4.40 (AB quartet, Δν = 27.2 Hz, J = 12.0, 2H), 1.17 (d, J = 6.4 Hz).
113	(3-chlorophenyl)methyl	638	U	638.1, 640.1	7.24 (brs, 3H), 7.17-7.16 (m, 4H), 7.06-7.03 (m, 1H), 6.92, (d, J = 1.9 Hz, 1H), 6.83, (dd, J = 8.5 and 1.8 Hz, 1H), 5.58-5.57 (m, 1H), 4.38 (AB quartet, Δν = 24.0 Hz, J = 12.2 Hz, 2H), 1.18 (d, J = 6.4 Hz, 3H).
114	(4-cyclohexylphenyl)-methyl	685.8	U	685.9	7.26 (s, 1H), 7.19 (d, J = 8.5 Hz, 1H), 7.03 (AB quartet, Δν =13.8 Hz, J = 8.1 Hz, 4H), 6.93 (d, J = 1.8Hz, 1H), 6.86 (dd, J = 8.5 and 1.8 Hz, 1H), 5.55 (d, J = 3.5 Hz, 1H), 4.39 (AB quartet, Δν = 20.6 Hz, J = 11.6 Hz, 2H) 1.15 (d, J = 6.2 Hz, 3H).
115	(2-methylphenyl)methyl	617.6	U	617.9	7.23 (s, 1H), 7.16 (d, J = 8.3 Hz, 1H), 7.11-7.01 (m, 4H), 6.92 (d, J = 1.9 Hz, 1H), 6.82 (dd, J = 8.3 and 2.0 Hz, 1H), 5.56 (d, J = 3.9 Hz, 1H), 4.39 (brs, 2H), 1.18 (d, J = 6.2 Hz, 3H).

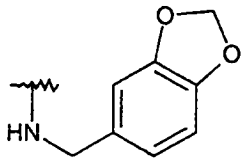
Ex.	Y	Mol Wt	Pro.	Mass Spec	1H NMR peaks (CD_3OD)
116	(2-fluorophenyl)methyl	621.6	U	621.8	7.28-7.19 (m, 3H), 7.17 (d, J = 8.3 Hz, 1H), 7.01-6.95 (m, 2H), 6.90 (d, J = 1.9 Hz, 1H), 6.81 (dd, J = 8.3 and 1.8 Hz, 1H), 5.54 (d, J = 4.2 Hz, 1H), 4.48 (brs, 2H), 1.19 (d, J = 6.5 Hz, 3H).
117	(4-methoxyphenyl)methyl	633.7	V	634.2	7.25 (s, 1H), 7.17 (d, J = 8.5 Hz, 1H), 7.06 (d, J = 8.5 Hz, 2H), 6.93 (d, J = 1.9 Hz, 1H), 6.85 (dd, J = 8.5 and 2.0 Hz, 1H), 6.73 (d, J = 8.5 Hz, 2H), 5.55 (d, J = 3.3 Hz, 1H), 4.35 (AB quartet, $\Delta\nu$ = 20.5 Hz, J = 11.4 Hz, 2H), 1.14 (d, J = 6.3 Hz, 3H).
118	(3-cyanophenyl)methyl	628.6	W	629.2	7.54 (d, J = 6.2 Hz, 1H), 7.46-7.35 (m, 2H), 7.23 (s, 1H), 7.15 (d, J = 8.3 Hz, 1H), 6.91 (d, J = 2.1 Hz, 1H), 6.84 (dd, J = 8.4 and 1.9 Hz, 1H), 5.6 (d, J = 3.7 Hz, 1H), 4.45 (AB quartet, $\Delta\nu$ = 42.3, J = 12.3, 2H), 1.20 (d, J = 6.2 Hz, 3H).
119	[(4-trifluoromethyl)phenyl] methyl	671.6	W	672.1	7.47 (d, J = 8.1 Hz, 2H), 7.33 (d, J = 8.1 Hz, 2H), 7.24 (s, 1H), 7.15 (d, J = 8.3 Hz, 1H), 6.91 (d, J = 1.9 Hz, 1H), 6.84 (dd, J = 8.4 and 1.9 Hz, 1H), 5.59 (d, J = 3.7 Hz, 1H), 4.50 (AB quartet, $\Delta\nu$ = 27.1 Hz, J = 12.7 Hz, 2H), 1.20 (d, J = 6.5 Hz, 3H)
120	(4-cyanophenyl)methyl	628.6	W	629.2	7.52 (d, J = 8.1 Hz, 1H), 7.31 (d, J = 8.1, 2H), 7.24 (s, 1H), 7.15 (d, J = 8.5 Hz, 1H), 6.91 (d, J = 1.9 Hz, 1H), 6.83 (dd, J = 8.5 and 1.9 Hz, 1H), 5.59 (d, J = 3.7 Hz, 1H), 4.48 (AB quartet, $\Delta\nu$ = 32.3 Hz, J = 13.4 Hz, 2H), 1.21 (d, J = 6.4 Hz, 3H).
121	(3-methylphenyl)methyl	617.6	W	618.3	7.25 (s, 1H), 7.18 (d, J = 8.5 Hz, 1H), 7.15-6.95 (3m, 3H), 6.93 (d, J = 2.1 Hz, 1H), 6.85 (dd, J = 8.5 and 2.1 Hz, 1H), 5.55 (d, J = 3.5 Hz, 1H) 4.38 (AB quartet, $\Delta\nu$ = 14.1 Hz, J = 11.7 Hz, 2H), 2.24 (s, 3H) 1.15 (d, J = 6.4 Hz, 3H).
122	(3,4-dimethylphenyl)methyl	631.7	W	632.2	7.25 (s, 1H), 7.18 (d, J = 8.5 Hz, 1H), 6.96-6.93 (m, 2H), 6.87-6.83 (m, 3H), 5.54 (d, J = 3.3 Hz, 1H), 4.34 (AB quartet, $\Delta\nu$ = 12.9 Hz, J = 11.5 Hz, 2H), 2.17 (s, 3H), 2.15 (s, 3H), 1.13 (d, J = 6.2 Hz, 3H).
123	phenylaminocarbonyl	632.63	X	633.1	7.35-7.19 (2 m, 5H), 7.11 (d, J = 8.6

Ex.	Y	Mol Wt	Pro.	Mass Spec	1H NMR peaks (CD_3OD)
					Hz, 1 H) 6.96 (t, J = 7.4 Hz, 1H) 6.91 (d, J = 2.1 Hz, 1H), 6.73 (dd, J = 8.5 and 2.1 Hz, 1H), 5.56 (d, J = 3.5 Hz, 1H), 1.22 (d, J = 6.4 Hz, 3H).
124	3-fluorophenylamino-carbonyl	650.62	X	651.1	7.26-7.20 (m , 3H), 7.15, (d, J = 8.5 Hz, 1H), 7.05 (dd, J = 8.1 and 1.8 Hz, 1H), 6.93 (d, J = 2.1 Hz, 1H), 6.76-6.68 (m, 2H), 5.58 (d, J = 3.5 Hz, 1H), 1.24 (d, J = 6.4 Hz, 3H).
125	3,4-dichlorophenylamino-carbonyl	701.52	X	701, 703	7.62 (s, 1H), 7.33 (d, J = 8.9 Hz, 1H), 7.23-7.20 (m, 2H), 7.11 (d, J = 8.5 Hz, 1H), 6.92 (d, J = 2.1 Hz, 1H), 6.74 (dd, J = 8.5 and 2.1 Hz, 1H), 5.56 (d, J = 3.1 Hz, 1H), 4.91-4.8 (m, 1H), 1.25 (d, J = 6.4 Hz, 3H).
126	4-chlorophenylamino-carbonyl	667.07	X	667,669	7.35-7.32 (m, 2H), 7.20-7.19 (m, 3H), 7.12 (d, J = 8.5 Hz, 1H), 6.93 (d, J = 2.1 Hz, 1H), 6.75 (dd, J = 8.5 and 2.1 Hz, 1H), 5.57 (d, J = 3.1 Hz, 1H), 1.24 (d, J = 6.4 Hz, 3H).
127	4-methoxyphenylamino-carbonyl	662.65	X	663	7.23-7.21 (m , 3H), 7.13 (d, J = 8.5 Hz, 1H), 6.93, (d, J = 1.9 Hz, 1H), 6.80-6.76 (m, 3H), 5.58 (brs, 1H), 1.23, (d, J = 6.4 Hz, 3H).
128	[(4-fluorophenyl)methyl]-aminocarbonyl	664.5	Y	665.1	7.24 (br s, 3H), 7.10 (d, J = 8.3 Hz, 1H), 7.00 (m, 2H), 6.6 (br s, 1H), 6.77 (br d, J = 8.1 Hz, 1H), 5.52 (br s, 1H), 4.9-4.80 (m, 1H), 1.19 (br d, J = 6.4 Hz, 1H).
129	(phenylmethyl)amino-carbonyl	646.6	Y	647.2	7.7.3-7.1(m, 6H), 7.5 (d, J = 8.3 Hz, 1H), 6.82 (br s, 1H), 6.66 (d, J = 8.3, 1H) , 5.50 (d, J = 5.2 Hz, 1H), 4.83-4.80 (m, 1H), 1.20 (d, J = 6.9 Hz, 3H).
130	[(3,4-dichloro phenyl)methyl]amino-carbonyl	715.5	Y	715, 717	7.39 (s, 1H), 7.23 (s, 1H), 7.18-7.01 (m, 3H), 6.86 (d, J = 1.6 Hz. 1H), 6.77-6.72 (m, 1H), 5.52 (d, J = 2.5 Hz, 1H), 4.85-4.82 (m, 1H), 1.20 (d, J = 6.5 Hz, 3H).
131	[(4-chlorophenyl)methyl]-aminocarbonyl	681.1	Y	681.1, 683.1	7.3-7.2 (m, 4H) 7.11 (d, J = 8.5 Hz, 1H), 6.77 (d, J = 7.7, 1H), 5.5 (br s, 1H), 4.84-4.80 (m, 1H), 1.19 (d, J = 6.4 Hz).

Table 5

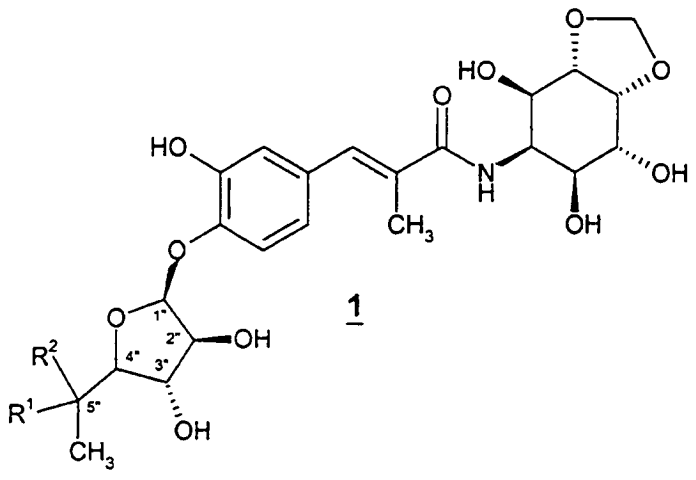


Ex.	Y	Mol Wt	Pro.	Mass spec.	1H NMR peaks (CD_3OD)
132	ethoxy	581.58	AA	582.2	5.80 (bs, 1H), 5.59 (d, J = 4.6 Hz, 1H), 4.02 (q, J = 7.1 Hz, 2H), 2.04 (d, J = 1.2 Hz, 3H), 1.15 (t, J = 7.1 Hz, 3H)
133	hydroxy	553.52	BB	554.1	5.84 (bs, 1H), 5.56 (d, J = 3.9 Hz, 1H), 1.95 (d, J = 1.2 Hz, 3H)
134	(phenylmethyl)amino	642.67	CC	643.3	7.21 (m, 5H), 5.90 (s, 1H), 5.60 (d, J = 2.3 Hz, 1H), 4.32 (s, 2H), 1.99 (s, 3H)
135	[(3-fluorophenyl)methyl]-amino	660.66	DD	661.2	7.30 (m, 1H), 7.03 (d, J = 7.9 Hz, 1H), 6.94 (m, 2H), 5.93 (s, 1H), 5.61 (d, J = 3.8 Hz, 1H), 4.34 (s, 2H), 2.00 (d, J = 1.3 Hz, 3H)
136	cyclohexylamino	634.69	EE, L	635.1	5.82 (s, 1H), 5.60 (d, J = 3.9 Hz, 1H), 3.59 (m, 1H), 1.95 (d, J = 1.2 Hz, 3H),1.78 (bd, J = 11.8 Hz, 2H), 1.70 (bd, J = 13.3 Hz, 2H), 1.59 (bd, J = 12.7 Hz, 1H), 1.31 (m, 2H), 1.14 (m, 3H)
137	4-pyridylmethylamino	643.65	EE, J	644.3	8.39 (m, 2H), 7.23 (m, 2H), 5.93 (bs, 1H), 5.60 (d, J = 3.7 Hz, 1H), 4.36 (AB quartet, $\Delta\nu$ = 20.3 Hz, J = 16.2 Hz, 2H), 1.99 (d, J = 1.2 Hz, 3H)

Ex.	Y	Mol Wt	Pro.	Mass spec.	1H NMR peaks (CD_3OD)
138		686.68	EE, L	687.2	6.68 (m, 3H), 5.87 (s, 2H), 5.87 (bs, 1H), 5.59 (d, J = 3.7 Hz, 1H), 1.97 (d, J = 1.2 Hz, 3H)
139	2-(dimethylamino)ethyl-amino	623.66	EE, N	623.8	5.84 (bs, 1H), 5.57 (d, J = 3.7 Hz, 1H), 3.27 (t, J = 6.8 Hz, 2H), 2.39 (t, J = 6.7 Hz, 2H), 2.21 (s, 6H), 1.96 (d, J = 1.2 Hz, 3H)
140	2-furanylmethylamino	632.63	EE, J	632.8	7.35 (dd, J = 1.9, 0.8 Hz, 1H), 6.28 (dd, J = 3.3, 1.9 Hz, 1H), 6.15 (dd, J = 3.2, 0.7 Hz, 1H), 5.85 (bs, 1H), 5.57 (d, J = 3.7 Hz, 1H), 4.29 (s, 2H), 1.96 (d, J = 1.2 Hz, 3H)

CLAIMS

1. A compound of the formula



1

or a pharmaceutically acceptable salt, prodrug or solvate thereof wherein:

R^1 is H and R^2 is $-NR^3R^4$, $-NR^4C(O)R^3$, $-OC(O)NR^3R^4$ or $-OR^3$;

or R^1 and R^2 are taken together to form $=N-OR^3$, $=CR^4R^3$, $=CR^4C(O)R^3$, $=CR^4C(O)OR^3$, or $=CR^4C(O)NR^3R^4$;

each R^3 is independently selected from H, C_1-C_{10} alkyl, C_2-C_{10} alkenyl, $-(CH_2)_t(C_3$-C_{10} cycloalkyl), $-(CH_2)_t(C_6$-C_{10} aryl), and $-(CH_2)_t$(4-10 membered heterocyclic), wherein t is an integer ranging from 0 to 5, said alkyl group optionally contains 1 or 2 hetero moieties selected from O, $-S(O)_j-$ wherein j is an integer ranging from 0 to 2, and $-N(R^7)-$ with the proviso that two O atoms, two S atoms, or an O and S atom are not attached directly to each other; said cycloalkyl, aryl and heterocyclic R^3 groups are optionally fused to a benzene ring, a C_5-C_8 saturated cyclic group, or a 4-10 membered heterocyclic group; the $-(CH_2)_t-$ moieties of the foregoing R^3 groups optionally include a carbon-carbon double or triple bond where t is an integer between 2 and 5; and the foregoing R^3 groups, except H but including any optional fused rings referred to above, are optionally substituted by 1 to 5 R^5 groups, with the proviso that R^3 is not H, methyl or ethyl where R^1 is H and R^2 is $-OR^3$;

each R^4 is independently H or C_1-C_{10} alkyl;

each R^5 is independently selected from C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, halo, cyano, nitro, trifluoromethyl, difluoromethoxy, trifluoromethoxy, azido, $-OR^6$, $-C(O)R^6$, $-C(O)OR^6$, $-NR^7C(O)OR^9$, $-OC(O)R^6$, $-NR^7SO_2R^9$, $-SO_2NR^6R^7$, $-NR^7C(O)R^6$, $-C(O)NR^6R^7$, $-NR^6R^7$, $-S(O)_j(CH_2)_m(C_6$-C_{10} aryl), $-S(O)_j(C_1$-C_6 alkyl), wherein j is an integer ranging from 0 to 2, $-(CH_2)_m(C_6$-C_{10} aryl), $-O(CH_2)_m(C_6$-C_{10} aryl), $-NR^7(CH_2)_m(C_6$-C_{10} aryl), and $-(CH_2)_m$(4-10 membered heterocyclic), wherein m is an integer ranging from 0 to 4; said alkyl group

optionally contains 1 or 2 hetero moieties selected from O, -S(O)$_j$- wherein j is an integer ranging from 0 to 2, and -N(R^7)- with the proviso that two O atoms, two S atoms, or an O and S atom are not attached directly to each other; said cycloalkyl, aryl and heterocyclic R^5 groups are optionally fused to a C_6-C_{10} aryl group, a C_5-C_8 saturated cyclic group, or a 4-10 membered heterocyclic group; and said alkyl, cycloalkyl, aryl and heterocyclic R^5 groups are optionally substituted by 1 to 5 substituents independently selected from halo, cyano, nitro, trifluoromethyl, difluoromethoxy, trifluoromethoxy, azido, -$NR^7SO_2R^9$, -$SO_2NR^6R^7$, -C(O)R^6, -C(O)OR^6, -OC(O)R^6, -NR^7C(O)OR^9, -NR^7C(O)R^6, -C(O)NR^6R^7, -NR^6R^7, -OR^6, C_1-C_{10} alkyl, -$(CH_2)_m$(C_6-C_{10} aryl), and -$(CH_2)_m$(4-10 membered heterocyclic), wherein m is an integer ranging from 0 to 4;

each R^6 is independently selected from H, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, -$(CH_2)_m$(C_6-C_{10} aryl), and -$(CH_2)_m$(4-10 membered heterocyclic), wherein m is an integer ranging from 0 to 4; said alkyl group optionally includes 1 or 2 hetero moieties selected from O, -S(O)$_j$- wherein j is an integer ranging from 0 to 2, and -N(R^7)- with the proviso that two O atoms, two S atoms, or an O and S atom are not attached directly to each other; said cycloalkyl, aryl and heterocyclic R^6 groups are optionally fused to a C_6-C_{10} aryl group, a C_5-C_8 saturated cyclic group, or a 4-10 membered heterocyclic group; and the foregoing R^6 substituents, except H, are optionally substituted by 1 to 5 substituents independently selected from halo, cyano, nitro, trifluoromethyl, difluoromethoxy, trifluoromethoxy, azido, -C(O)R^7, -C(O)OR^7, -OC(O)R^7, -NR^7C(O)R^8, -C(O)NR^7R^8, -NR^7R^8, hydroxy, C_1-C_6 alkyl, and C_1-C_6 alkoxy;

each R^7 and R^8 is independently H or C_1-C_6 alkyl; and,

R^9 is selected from the substituents provided in the definition of R^6 except H.

2. A compound according to claim 1 wherein R^1 and R^2 are taken together to form =N-OR^3, and R^3 is C_1-C_4 alkyl, C_2-C_4 alkenyl, -$(CH_2)_t$(C_6-C_{10} aryl) or -$(CH_2)_t$(4-10 membered heterocyclic), wherein t is an integer ranging from 0 to 3, the heterocyclic group is optionally fused to a benzene ring, the aryl group is optionally fused to a 5 or 6 membered heterocyclic group, and the foregoing R^3 groups, including said optionally fused moieties, are optionally substituted by 1 to 5 substituents independently selected from nitro, halo, C_1-C_3 alkoxy, C_1-C_4 alkyl, trifluoromethyl, acetamido, *tert*-butoxycarbonylamino, *tert*-butoxycarbonylaminomethyl, *tert*-butoxycarbonyl, -NR^6R^7, phenyl, cyclohexyl, carboxy, aminomethyl, difluoromethoxy, trifluoromethoxy, cyano, piperidinyl, morpholino, phenoxy, and phenylthio.

3. A compound according to claim 1 wherein R^1 and R^2 are taken together to form =N-OR^3, and R^3 is -$(CH_2)_t$(C_6-C_{10} aryl) or -$(CH_2)_t$(4-10 membered heterocyclic), wherein t is an integer ranging from 0 to 3, the heterocyclic group is optionally fused to a benzene ring, the aryl group is optionally fused to a 5 or 6 membered heterocyclic group, and the foregoing R^3

groups, including said optionally fused moieties, are optionally substituted by 1 to 5 substituents independently selected from nitro, halo, C_1-C_3 alkoxy, C_1-C_4 alkyl, trifluoromethyl, acetamido, *tert*-butoxycarbonyl, *tert*-butoxycarbonylamino, -NR^6R^7, phenyl, cyclohexyl, carboxy, *tert*-butoxycarbonylaminomethyl, aminomethyl, difluoromethoxy, trifluoromethoxy, cyano, piperidinyl, morpholino, phenoxy, and phenylthio.

4. A compound according to claim 1 wherein R^1 is H, R^2 is -NR^3R^4, R^4 is H or methyl, and R^3 is -$(CH_2)_t$(C_6-C_{10} aryl) or -$(CH_2)_t$(4-10 membered heterocyclic), wherein t is an integer ranging from 0 to 2, and the R^3 group is optionally substituted by 1 to 5 substituents independently selected from halo, C_1-C_3 alkoxy, C_1-C_4 alkyl, and trifluoromethyl.

5. A compound according to claim 1 wherein R^1 is H, R^2 is -$NR^4C(O)R^3$, R^4 is H, and R^3 is C_3-C_6 cycloalkyl, -$(CH_2)_t$(C_6-C_{10} aryl) or -$(CH_2)_t$(4-10 membered heterocyclic), wherein t is an integer ranging from 0 to 2, the aryl group is optionally fused to a 5 or 6 membered heterocyclic group, the heterocyclic group is optionally fused to a benzene ring, and the foregoing R^3 groups, including said optionally fused moieties, are optionally substituted by 1 to 5 substituents independently selected from halo, C_1-C_3 alkoxy, C_1-C_4 alkyl, and trifluoromethyl.

6. A compound according to claim 1 wherein R^1 and R^2 are taken together to form =$CR^4C(O)OR^3$ or =$CR^4C(O)NR^3R^4$, R^4 is H, and R^3 is H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, -$(CH_2)_t$(4-10 membered heterocyclic), or -$(CH_2)_t$(C_6-C_{10} aryl) wherein t is an integer ranging from 0 to 2, the aryl group is optionally fused to a 5 or 6 membered heterocyclic group, the heterocyclic group is optionally fused to a benzene ring, and the foregoing R^3 groups, except H but including said optionally fused moieties, are optionally substituted by 1 to 5 substituents independently selected from halo, C_1-C_3 alkoxy, C_1-C_4 alkyl, -NR^6R^7 and trifluoromethyl.

7. A compound according to claim 1 wherein R^1 is H, R^2 is -OR^3, and R^3 is C_1-C_4 alkyl, -$(CH_2)_t$(4-10 membered heterocyclic), or -$(CH_2)_t$(C_6-C_{10} aryl) wherein t is an integer ranging from 1 to 2, the aryl group is optionally fused to a 5 or 6 membered heterocyclic group, the heterocyclic group is optionally fused to a benzene ring, and the foregoing R^3 groups, including said optionally fused moieties, are optionally substituted by 1 to 5 substituents independently selected from halo, C_1-C_3 alkoxy, C_1-C_4 alkyl, cyclohexyl, cyano, trifluoromethyl, benzyloxy and trifluoromethyl.

8. A compound according to claim 1 wherein R^1 is H, R^2 is -$OC(O)NR^3R^4$, R^4 is H, and R^3 is -$(CH_2)_t$(C_6-C_{10} aryl) wherein t is an integer ranging from 0 to 2, and the R^3 group is optionally substituted by 1 to 5 substituents independently selected from halo, C_1-C_3 alkoxy, C_1-C_4 alkyl, and trifluoromethyl.

9. A compound according to claim 1 wherein said compound is selected from the group consisting of:

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(benzofuran-2-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(benzofuran-2-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-phenylmethyloxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-phenylmethyloxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(4-chlorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3,4-dichlorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3,4-dichlorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(4-pyridinyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(4-(4-morpholinyl)phenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[cyclohexylmethyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(4-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-b-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(2,4-dichlorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3,4-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(furan-3-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(furan-3-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(1,3-benzodioxol-5-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(1,3-benzodioxol-5-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3-chlorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(4-cyclohexylphenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3-aminophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[[(4-aminomethyl)phenyl]methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[3-(4-chlorophenyl)propyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[3-(4-chlorophenyl)propyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3-(trifluoromethoxy)phenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(4-(1-piperidinyl)phenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(2-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[2-(phenylthio)ethyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(benzofuran-5-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(benzofuran-5-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(2-phenylpyrimidin-5-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3-fluoro-4-methoxyphenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3,4-dihydro-2H-1-benzopyran-4-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(5,6-dideoxy-5-(methyl(phenylmethyl)amino-α-L-*galacto*-furanos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol;

5-Deoxy-5-[[3-[4-[(5,6-dideoxy-5-phenylamino-α-L-*galacto*-furanos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol;

5-Deoxy-5-[[3-[4-[(6-deoxy-5-*O*-[(3,4-dichlorophenyl)methyl]-β-D-*altro*-furanos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(furan-2-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(5-methyl-β-D-*arabino*-hept-5-(*E*)-enofuranuron-1-ylic acid)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, ethyl ester;

5-Deoxy-5-[[3-[4-[[N-(furan-2-yl)methyl]-(5-methyl-β-D-*arabino*-hept-5-(*E*)-enofuranuron-1-yl-amide)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[3-(phenyl)propyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(2-propen-1-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-(2-propen-1-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(4-methylphenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(4-methoxyphenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3-(trifluoromethyl)phenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-5-*O*-[(4-chlorophenyl)methyl]-β-D-*altro*-furanos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[diphenylmethyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-5-phenylcarbamate-β-D-*altro*-furanos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol;

5-Deoxy-5-[[3-[4-[(6-deoxy-5-[(3,4-dichlorophenyl)methyl]carbamate-β-D-*altro*-furanos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3-chlorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3-chloro-2-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3-chloro-2-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3-chloro-4-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3-chloro-4-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3-chloro-5-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3-chloro-5-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-*(E)*-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(5-chloro-2-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-*(E)*-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, *(E)*-*O*-[(5-chloro-2-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3,5-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3,5-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(4-chloro-3-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(4-chloro-3-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(4-chloro-1,3-benzodioxol-6-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(4-chloro-1,3-benzodioxol-6-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(5-chloro-1,3-benzodioxol-6-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(5-chloro-1,3-benzodioxol-6-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(4-chloro-1,3-benzodioxol-5-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(4-chloro-1,3-benzodioxol-5-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-*(E)*-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, *(E)*-*O*-[(2,3-dihydrobenzofuran-6-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-*(E)*-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(2,3-dihydrobenzofuran-6-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(2,3-dihydrobenzofuran-5-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(2,3-dihydrobenzofuran-5-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-(1,2,3,4-tetrahydronaphthalen-1-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(1,2,3,4-tetrahydronaphthalen-1-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-(7-chloro-1,2,3,4-tetrahydronaphthalen-1-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(7-chloro-1,2,3,4-tetrahydronaphthalen-1-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-(7-fluoro-1,2,3,4-tetrahydronaphthalen-1-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(7-fluoro-1,2,3,4-tetrahydronaphthalen-1-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-(8-chloro-3,4-dihydro-2*H*-1-benzopyran-4-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(8-chloro-3,4-dihydro-2*H*-1-benzopyran-4-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-(6-chloro-3,4-dihydro-2*H*-1-benzopyran-4-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(6-chloro-3,4-dihydro-2*H*-1-benzopyran-4-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-(8-fluoro-3,4-dihydro-2*H*-1-benzopyran-4-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(8-fluoro-3,4-dihydro-2*H*-1-benzopyran-4-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-(6-fluoro-3,4-dihydro-2*H*-1-benzopyran-4-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(6-fluoro-3,4-dihydro-2*H*-1-benzopyran-4-yl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(quinolin-2-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(quinolin-2-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(quinolin-3-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(quinolin-3-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[4-(phenylmethyl)phenylmethyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[4-(phenylmethyl)phenylmethyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[4-(phenoxy)phenylmethyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[4-(phenoxy)phenylmethyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3,5-dichlorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3,5-dichlorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(phenyl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-(phenyl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(3-chloro-4-fluorophenyl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-(3-chloro-4-fluorophenyl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(4-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(4-chlorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3,4-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(2,4-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(2,4-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(2,1,3-benzoxadiazol-5-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(2,1,3-benzoxadiazol-5-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(2,3,5,6-tetrafluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(2,3,5,6-tetrafluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-O-methylene-D-*neo*-inositol, (*E*)-O-[(2,3-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-O-methylene-D-*neo*-inositol, (*Z*)-O-[(2,3-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-O-methylene-D-*neo*-inositol, (*E*)-O-[(4-phenyl-furan-3-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-O-methylene-D-*neo*-inositol, (*Z*)-O-[(4-phenyl-furan-3-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-O-methylene-D-*neo*-inositol, (*E*)-O-[(4-phenyl-furan-2-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-O-methylene-D-*neo*-inositol, (*Z*)-O-[(4-phenyl-furan-2-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-O-methylene-D-*neo*-inositol, (*E*)-O-[(2,3-difluoro-6-methoxyphenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-O-methylene-D-*neo*-inositol, (*Z*)-O-[(2,3-difluoro-6-methoxyphenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-O-methylene-D-*neo*-inositol, (*E*)-O-[(3-chloro-thiophen-2-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-O-methylene-D-*neo*-inositol, (*Z*)-O-[(3-chloro-thiophen-2-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-O-methylene-D-*neo*-inositol, (*E*)-O-[(5-chloro-thiophen-2-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(5-chloro-thiophen-2-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3-chloro-2,6-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3-chloro-2,6-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(2-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[1-(3-chlorophenyl)ethyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(3-difluoromethoxy-phenyl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-(3-difluoromethoxy-phenyl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(4-difluoromethoxy-phenyl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-(4-difluoromethoxy-phenyl)oxime;

and the pharmaceutically acceptable salts and solvates of said compounds.

10. A compound according to claim 1 wherein said compound is selected from the group consisting of:

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(1,3-benzodioxol-5-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3-chlorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3-chlorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(benzofuran-2-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3,5-dichlorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3,5-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3,5-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3-chloro-2-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3-chloro-2-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3-chloro-4-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3-chloro-4-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(4-chloro-3-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(4-chloro-3-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(4-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(4-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(4-chlorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(4-chlorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(4-phenyl-furan-2-yl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3-chloro-5-fluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(3,4-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(3,4-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(2,3-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(2,4-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-[(2,4-difluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(2,3,5,6-tetrafluorophenyl)methyl]oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-(3-chloro-4-fluorophenyl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*E*)-*O*-(3-chloro-4-fluorophenyl)oxime;

5-Deoxy-5-[[3-[4-[(6-deoxy-β-D-*arabino*-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-(*E*)-propenyl]amino]-1,2-*O*-methylene-D-*neo*-inositol, (*Z*)-*O*-[(5-chloro-thiophen-2-yl)methyl]oxime;

and the pharmaceutically acceptable salts and solvates of said compounds.

11. A pharmaceutical composition for the treatment of a bacterial infection, a protozoal infection, or a disorder related to a bacterial infection or a protozoal infection, in a mammal, fish, or bird which comprises a therapeutically effective amount of a compound of claim 1 and a pharmaceutically acceptable carrier.

12. A method of treating a bacterial infection, a protozoal infection, or a disorder related to a bacterial infection or a protozoal infection, in a mammal, fish, or bird which comprises administering to said mammal, fish or bird a therapeutically effective amount of a compound of claim 1.

13. A method of preparing a composition containing hygromycin A and *epi*-hygromycin, wherein the ratio of hygromycin A to *epi*-hygromycin is at least 10:1, which comprises fermenting *Streptomyces hygroscopicus* in media having a pH less than 6.9 at a temperature ranging from 25°C to 35°C.

14. A method according to claim 12 wherein said *Streptomyces hygroscopicus* is *Streptomyces hygroscopicus* NRRL2388, or a mutant thereof, said pH ranges from 6.2 to 6.7, said temperature is about 29°C, and the ratio of hygromycin A to *epi*-hygromycin is at least 14:1.

15. The method of claim 12 and further comprising maintaining said composition at a pH of about 6.0 to 6.4 and maintaining the temperature of said composition at a temperature ranging from 25°C to 35°C during purification of said hygromycin A to an oil.

16. The method of claim 14 wherein said pH is maintained at about 6.0.

17. A method of preparing a compound of claim 1 wherein R^1 and R^2 are taken together to form =N-OR^3, which comprises treating hygromycin A with a hydroxylamine of the formula H_2N-OR^3, or a salt of said compound, where R^3 is as defined above, in an inert solvent, optionally in the presence of a base if the salt of the hydroxylamine is used, at a temperature ranging from about 0°C to 65°C.

18. The method of claim 17 wherein said inert solvent is methanol, ethanol, or pyridine, or a mixture of the foregoing solvents, said base is Na_2CO_3 or K_2CO_3, and said temperature ranges from from 0°C to 25°C.

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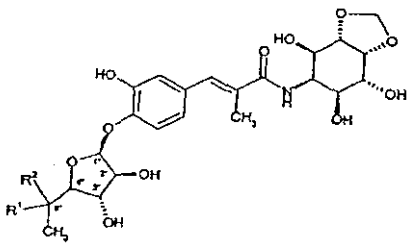
[54]发明名称 潮霉素A衍生物

[57]摘要

本发明涉及式(1)化合物及其可药用盐、药物前体和溶剂化物，其中R^1和R^2如本文中所定义。式(1)化合物是抗细菌剂和抗原生动 物剂，它们可以用于治疗各种细菌和原生动物感染以及与这些感染有 关的疾病。本发明也涉及含有式(1)化合物的药物组合物以及通过施 用式(1)化合物来治疗细菌和原生动物感染的方法。



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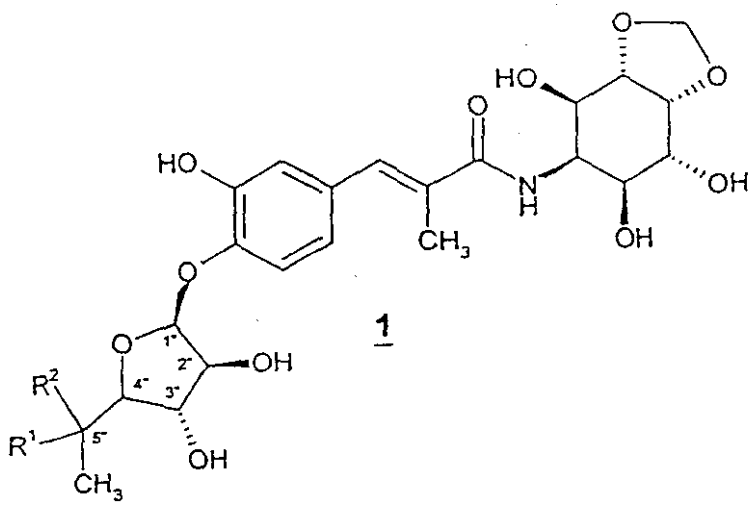
1、式1化合物:



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或其可药用盐、药物前体或溶剂化物，其中:

R^1是H，R^2是$-NR^3R^4$，$-NR^4C(O)R^3$，$-OC(O)NR^3R^4$或$-OR^3$;

或者R^1和R^2共同构成$=N-OR^3$，$=CR^4R^3$，$=CR^4C(O)R^3$，$=CR^4C(O)OR^3$或$=CR^4C(O)NR^3R^4$;

每个R^3独立地选自H，C_1-C_{10}烷基，C_2-C_{10}链烯基，$-(CH_2)_t(C_3-C_{10}$环烷基)，$-(CH_2)_t(C_6-C_{10}$芳基)和$-(CH_2)_t$(4-10元杂环)，其中t是0-5的整数，所述烷基可选地含有1个或2个选自O，$-S(O)_j-$，其中j是0-2的整数，和$-N(R^7)-$的杂基，条件是两个O原子、两个S原子或者O和S原子彼此不直接相连；所述环烷基、芳基和杂环R^3基可选地与一个苯环、C_5-C_8饱和环基或4-10元杂环基稠合；前述R^3基团的$-(CH_2)_t-$部分可选地包括一个碳-碳双键或三键，其中t是2-5之间的整数；前述R^3基团，不包括H但包括上述任一个可选的稠环，可选地被1-5个R^5基团取代，条件是R^1为H且R^2为$-OR^3$时，R^3不为H、甲基或乙基;

每个R^4独立地为H或C_1-C_{10}烷基;

每个R^5独立地选自：C_1-C_{10}烷基，C_3-C_{10}环烷基，卤素，氰基，硝基，三氟甲基，二氟甲氧基，三氟甲氧基，叠氮基，$-OR^6$，$-C(O)R^6$，$-C(O)OR^6$，

$-NR^7C(O)OR^9$，$-OC(O)R^6$，$-NR^7SO_2R^9$，$-SO_2NR^6R^7$，$-NR^7C(O)R^6$，$-C(O)NR^6R^7$，$-NR^6R^7$，$-S(O)_j(CH_2)_m$(C_6-C_{10}芳基)，$-S(O)_j$(C_1-C_6烷基)，其中j是0-2的整数，$-(CH_2)_m$(C_6-C_{10}芳基)，$-O(CH_2)_m$(C_6-C_{10}芳基)，$-NR^7(CH_2)_m$(C_6-C_{10}芳基)和$-(CH_2)_m$(4-10元杂环)，其中m是0-4的整数；所述烷基可选地含有1个或2个选自O，$-S(O)_j-$，其中j是0-2的整数，和$-N(R^7)-$的杂基，条件是两个O原子、两个S原子或者O和S原子彼此不直接相连；所述环烷基、芳基和杂环R^5基可选地与一个C_6-C_{10}芳基、C_5-C_8饱和环基或4-10元杂环基稠合；所述烷基、环烷基、芳基和杂环R^5基可选地被1-5个独立地选自下列的取代基取代：卤素，氰基，硝基，三氟甲基，二氟甲氧基，三氟甲氧基，叠氮基，$-NR^7SO_2R^9$，$-SO_2NR^6R^7$，$-C(O)R^6$，$-C(O)OR^6$，$-OC(O)R^6$，$-NR^7C(O)OR^9$，$-NR^7C(O)R^6$，$-C(O)NR^6R^7$，$-NR^6R^7$，$-OR^6$，C_1-C_{10}烷基，$-(CH_2)_m$(C_6-C_{10}芳基)和$-(CH_2)_m$(4-10元杂环)，其中m是0-4的整数；

每个R^6独立地选自：H，C_1-C_{10}烷基，C_3-C_{10}环烷基，$-(CH_2)_m$(C_6-C_{10}芳基)和$-(CH_2)_m$(4-10元杂环)，其中m是0-4的整数；所述烷基可选地包括1个或2个选自O，$-S(O)_j-$，其中j是0-2的整数，和$-N(R^7)-$的杂基，条件是两个O原子、两个S原子或者O和S原子彼此不直接相连；所述环烷基、芳基和杂环R^6基可选地与一个C_6-C_{10}芳基、C_5-C_8饱和环基或4-10元杂环基稠合；前述R^6取代基，除H以外，可选地被1-5个独立地选自下列的取代基取代：卤素，氰基，硝基，三氟甲基，二氟甲氧基，三氟甲氧基，叠氮基，$-C(O)R^7$，$-C(O)OR^7$，$-OC(O)R^7$，$-NR^7C(O)R^8$，$-C(O)NR^7R^8$，$-NR^7R^8$，羟基，C_1-C_6烷基和C_1-C_6烷氧基；

每个R^7和R^8独立地为H或C_1-C_6烷基；

R^9选自R^6的定义中规定的除H以外的取代基。

2、按照权利要求1的化合物，其中R^1和R^2共同构成$=N-OR^3$，而R^3为C_1-C_4烷基、C_2-C_4链烯基、$-(CH_2)_t$(C_6-C_{10}芳基)或$-(CH_2)_t$(4-10元杂环)，其中t是0-3的整数，杂环基可选地与一个苯环稠合，芳基可选地与一个5或6元杂环基稠合，而前述R^3基，包括所述可选地稠合的部分，可选地被1-5个独立地选自下列的取代基取代：硝基，卤素，C_1-C_3烷氧基，

C_1-C_4烷基，三氟甲基，乙酰氨基，叔丁氧羰基氨基，叔丁氧羰基氨基甲基，叔丁氧羰基，$-NR^6R^7$，苯基，环己基，羧基，氨基甲基，二氟甲氧基，三氟甲氧基，氰基，哌啶基，吗啉代，苯氧基和苯硫基。

3、按照权利要求1的化合物，其中R^1和R^2共同构成=N-OR^3，而R^3为$-(CH_2)_t$(C_6-C_{10}芳基)或$-(CH_2)_t$(4-10元杂环)，其中t是0-3的整数，杂环基可选地与一个苯环稠合，芳基可选地与一个5或6元杂环基稠合，而前述R^3基，包括所述可选地稠合的部分，可选地被1-5个独立地选自下列的取代基取代：硝基，卤素，C_1-C_3烷氧基，C_1-C_4烷基，三氟甲基，乙酰氨基，叔丁氧羰基，叔丁氧羰基氨基，$-NR^6R^7$，苯基，环己基，羧基，叔丁氧羰基氨基甲基，氨基甲基，二氟甲氧基，三氟甲氧基，氰基，哌啶基，吗啉代，苯氧基和苯硫基。

4、按照权利要求1的化合物，其中R^1为H，R^2为$-NR^3R^4$，R^4为H或甲基，R^3为$-(CH_2)_t$(C_6-C_{10}芳基)或$-(CH_2)_t$(4-10元杂环)，其中t是0-2的整数，而R^3基可选地被1-5个独立地选自卤素、C_1-C_3烷氧基，C_1-C_4烷基和三氟甲基的取代基取代。

5、按照权利要求1的化合物，其中R^1为H，R^2为$-NR^4C(O)R^3$，R^4为H，R^3为C_3-C_6环烷基、$-(CH_2)_t$(C_6-C_{10}芳基)或$-(CH_2)_t$(4-10元杂环)，其中t是0-2的整数，芳基可选地与一个5或6元杂环基稠合，杂环基可选地与一个苯环稠合，而前述R^3基，包括所述可选地稠合的部分，可选地被1-5个独立地选自卤素、C_1-C_3烷氧基，C_1-C_4烷基和三氟甲基的取代基取代。

6、按照权利要求1的化合物，其中R^1和R^2共同构成=$CR^4C(O)OR^3$或=$CR^4C(O)NR^3R^4$，R^4为H，R^3为H、C_1-C_6烷基、C_3-C_6环烷基、$-(CH_2)_t$(4-10元杂环)或$-(CH_2)_t$(C_6-C_{10}芳基)，其中t是0-2的整数，芳基可选地与一个5或6元杂环基稠合，杂环基可选地与一个苯环稠合，而前述R^3基，

不包括H但包括所述可选地稠合的部分，可选地被1-5个独立地选自卤素、C_1-C_3烷氧基，C_1-C_4烷基、$-NR^6R^7$和三氟甲基的取代基取代。

7、按照权利要求1的化合物，其中R^1为H，R^2为$-OR^3$，而R^3为C_1-C_4烷基、$-(CH_2)_t$(4-10元杂环)或$-(CH_2)_t$(C_6-C_{10}芳基)，其中t是1-2的整数，芳基可选地与一个5或6元杂环基稠合，杂环基可选地与一个苯环稠合，而前述R^3基，包括所述可选地稠合的部分，可选地被1-5个独立地选自卤素、C_1-C_3烷氧基，C_1-C_4烷基、环己基、氰基、三氟甲基、苄氧基和三氟甲基的取代基取代。

8、按照权利要求1的化合物，其中R^1为H，R^2为$-OC(O)NR^3R^4$，R^4为H，R^3为$-(CH_2)_t$(C_6-C_{10}芳基)，其中t是0-2的整数，而R^3基可选地被1-5个独立地选自卤素、C_1-C_3烷氧基，C_1-C_4烷基和三氟甲基的取代基取代。

9、按照权利要求1的化合物，其中所述化合物选自下组：

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(苯并呋喃-2-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(苯并呋喃-2-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲

基-D-新肌醇，(*Z*)-*O*-苯甲基肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-苯甲基肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(4-氯苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3,4-二氯苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3,4-二氯苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(4-吡啶基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(4-(4-吗啉基)苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[环己基甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(4-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(2,4-二氯苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)

氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3,4-二氟苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(呋喃-3-基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(呋喃-3-基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(1,3-苯并二氧杂环戊烯-5-基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(1,3-苯并二氧杂环戊烯-5-基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3-氯苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(4-环己基苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3-氨基苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[[(4-氨基甲基)苯基]甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[3-(4-氯苯基)丙基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[3-(4-氯苯基)丙基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3-(三氟甲氧基)苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(4-(1-哌啶基)苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(2-氟苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[2-(苯硫基)乙基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(苯并呋喃-5-基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(苯并呋喃-5-基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(2-苯基嘧啶-5-基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3-氟-4-甲氧基苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲

基-D-新肌醇，（*E*）-*O*-[(3,4-二氢-2H-1-苯并吡喃-4-基)甲基]肟；

5-脱氧-5-[[3-[4-[(5,6-二脱氧-5-(甲基(苯甲基)氨基-α-L-半乳糖型-呋喃糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇；

5-脱氧-5-[[3-[4-[(5,6-二脱氧-5-苯氨基-α-L-半乳糖型-呋喃糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇；

5-脱氧-5-[[3-[4-[(6-脱氧-5-*O*-[(3,4-二氯苯基)甲基]-β-D-阿卓糖型-呋喃糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，（*E*）-*O*-[(呋喃-2-基)甲基]肟；

5-脱氧-5-[[3-[4-[(5-甲基-β-D-阿糖型-庚-5-(*E*)-烯呋喃糖醛-1-基酸)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，乙酯；

5-脱氧-5-[[3-[4-[[N-(呋喃-2-基)甲基]-(5-甲基-β-D-阿糖型-庚-5-(*E*)-烯呋喃糖醛-1-基-酰胺)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，（*E*）-*O*-[3-(苯基)丙基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，（*Z*）-*O*-(2-丙烯-1-基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，（*E*）-*O*-(2-丙烯-1-基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)

氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(4-甲基苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(4-甲氧基苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3-(三氟甲基)苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-5-*O*-[(4-氯苯基)甲基]-β-D-阿卓糖型-呋喃糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[二苯甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-5-苯氨基甲酸酯-β-D-阿卓糖型-呋喃糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇；

5-脱氧-5-[[3-[4-[(6-脱氧-5-[(3,4-二氯苯基)甲基]氨基甲酸酯-β-D-阿卓糖型-呋喃糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3-氯苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3-氯-2-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3-氯-2-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3-氯-4-氟苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3-氯-4-氟苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3-氯-5-氟苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3-氯-5-氟苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(5-氯-2-氟苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(5-氯-2-氟苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3,5-二氟苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3,5-二氟苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(4-氯-3-氟苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲

基-D-新肌醇，(*E*)-*O*-[(4-氯-3-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(4-氯-1,3-苯并二氧杂环戊烯-6-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(4-氯-1,3-苯并二氧杂环戊烯-6-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(5-氯-1,3-苯并二氧杂环戊烯-6-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(5-氯-1,3-苯并二氧杂环戊烯-6-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(4-氯-1,3-苯并二氧杂环戊烯-5-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(4-氯-1,3-苯并二氧杂环戊烯-5-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(2,3-二氢苯并呋喃-6-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(2,3-二氢苯并呋喃-6-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(2,3-二氢苯并呋喃-5-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)

氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(2,3-二氢苯并呋喃-5-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-(1,2,3,4-四氢化萘-1-基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-(1,2,3,4-四氢化萘-1-基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-(7-氯-1,2,3,4-四氢化萘-1-基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-(7-氯-1,2,3,4-四氢化萘-1-基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-(7-氟-1,2,3,4-四氢化萘-1-基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-(7-氟-1,2,3,4-四氢化萘-1-基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-(8-氯-3,4-二氢-2*H*-1-苯并吡喃-4-基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-(8-氯-3,4-二氢-2*H*-1-苯并吡喃-4-基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-(6-氯-3,4-二氢-2*H*-1-苯并吡喃-4-基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇,(*Z*)-*O*-(6-氯-3,4-二氢-2*H*-1-苯并吡喃-4-基)肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇,(*E*)-*O*-(8-氟-3,4-二氢-2*H*-1-苯并吡喃-4-基)肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇,(*Z*)-*O*-(8-氟-3,4-二氢-2*H*-1-苯并吡喃-4-基)肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇,(*E*)-*O*-(6-氟-3,4-二氢-2*H*-1-苯并吡喃-4-基)肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇,(*Z*)-*O*-(6-氟-3,4-二氢-2*H*-1-苯并吡喃-4-基)肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇,(*E*)-*O*-[(喹啉-2-基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇,(*Z*)-*O*-[(喹啉-2-基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇,(*E*)-*O*-[(喹啉-3-基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇,(*Z*)-*O*-[(喹啉-3-基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲

基-D-新肌醇，(*E*)-*O*-[4-(苯甲基)苯甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[4-(苯甲基)苯甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[4-(苯氧基)苯甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[4-(苯氧基)苯甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3,5-二氯苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3,5-二氯苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-(苯基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-(苯基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-(3-氯-4-氟苯基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-(3-氯-4-氟苯基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)

氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(4-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(4-氯苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3,4-二氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(2,4-二氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(2,4-二氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(2,1,3-苯并噁二唑-5-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(2,1,3-苯并噁二唑-5-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(2,3,5,6-四氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(2,3,5,6-四氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(2,3-二氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(2,3-二氟苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(4-苯基-呋喃-3-基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(4-苯基-呋喃-3-基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(4-苯基-呋喃-2-基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(4-苯基-呋喃-2-基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(2,3-二氟-6-甲氧基苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(2,3-二氟-6-甲氧基苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3-氯-噻吩-2-基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3-氯-噻吩-2-基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲

基-D-新肌醇，(*E*)-*O*-[(5-氯-噻吩-2-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(5-氯-噻吩-2-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3-氯-2,6-二氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3-氯-2,6-二氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(2-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[1-(3-氯苯基)乙基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-(3-二氟甲氧基-苯基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-(3-二氟甲氧基-苯基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-(4-二氟甲氧基-苯基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-(4-二氟甲氧基-苯基)肟；

以及所述化合物的可药用盐和溶剂化物。

10、按照权利要求1的化合物，其中所述化合物选自下组:

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(1,3-苯并二氧杂环戊烯-5-基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3-氯苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3-氯苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3-氟苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3-氟苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(苯并呋喃-2-基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3,5-二氯苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3,5-二氟苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3,5-二氟苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3-氯-2-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3-氯-2-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3-氯-4-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3-氯-4-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(4-氯-3-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(4-氯-3-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(4-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(4-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(4-氯苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲

基-D-新肌醇，(*E*)-*O*-[(4-氯苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(4-苯基-呋喃-2-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3-氯-5-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3,4-二氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3,4-二氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(2,3-二氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(2,4-二氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(2,4-二氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(2,3,5,6-四氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-(3-氯-4-氟苯基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)

氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-(3-氯-4-氟苯基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(5-氯-噻吩-2-基)甲基]肟；

以及所述化合物的可药用盐和溶剂化物。

11、一种用于治疗哺乳动物、鱼或鸟的细菌感染、原生动物感染、或者与细菌感染或原生动物感染有关的疾病的药物组合物，它包含治疗有效量的权利要求1所述化合物和可药用载体。

12、一种治疗哺乳动物、鱼或鸟的细菌感染、原生动物感染或者与细菌感染或原生动物感染有关的疾病的方法，该方法包含对所述哺乳动物、鱼或鸟施用治疗有效量的权利要求1所述化合物。

13、一种含有潮霉素A和表潮霉素的组合物的制备方法，所述组合物中潮霉素A与表潮霉素的比至少为10:1，该方法包含使吸水链霉菌在25℃-35℃的温度范围内、在pH小于6.9的培养基中发酵。

14、按照权利要求12的方法，其中所述吸水链霉菌是吸水链霉菌NRRL2388或其突变株，所述pH范围为6.2-6.7，所述温度为约29℃，而潮霉素A与表潮霉素的比至少为14:1。

15、权利要求12的方法，它还包含使所述组合物保持在约pH6.0-6.4下，并且在将所述潮霉素A纯化为油的过程中，使所述组合物的温度保持在25℃-35℃范围内。

16、权利要求14所述的方法，其中所述pH保持为约6.0。

17、其中R^1和R^2共同构成=N-OR^3的权利要求1所述化合物的制备方法，该方法包含用式H_2N-OR^3的羟胺处理潮霉素A，或所述化合物的盐，此时R^3如上所定义，反应在惰性溶剂中进行，如果使用羟胺的盐的话，可选地在碱的存在下进行，反应的温度范围是约0℃-65℃。

18、权利要求17所述的方法，其中所述惰性溶剂是甲醇、乙醇或吡啶，或前述溶剂的混合物，所述碱是Na_2CO_3或K_2CO_3，而所述温度范围是0℃-25℃。

说　明　书

潮霉素A衍生物

发明背景

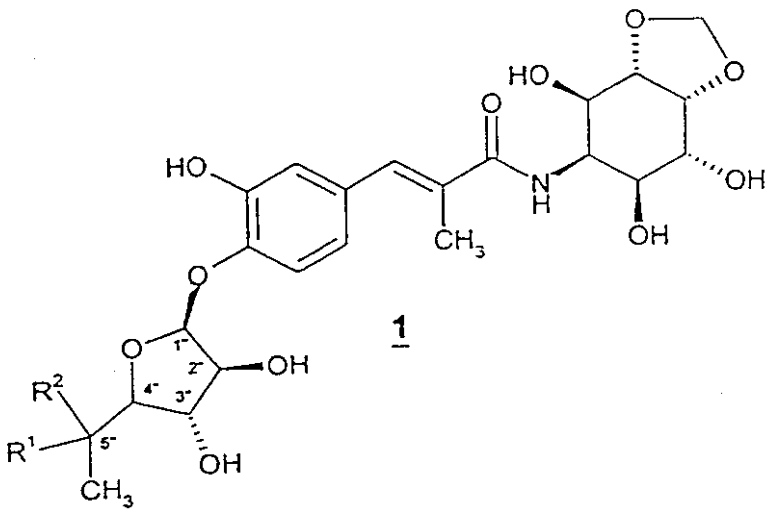
本发明涉及新的潮霉素A衍生物，它们可用作哺乳动物，包括人，以及鱼和鸟类的抗菌剂和抗原生动物剂。本发明也涉及含有所述新化合物的药物组合物，以及通过对需要这种治疗的哺乳动物、鱼和鸟类施用所述新化合物来治疗哺乳动物、鱼和鸟类的细菌和原生动物感染的方法。

潮霉素A是一种发酵产生的天然产物，于1953年首次从吸水链霉菌中分离出来。作为一种抗生素，潮霉素A具有对抗人病原体的活性，并有报道说其具有对抗引起猪痢疾的猪痢疾小蛇菌的强体外活性。有几篇参考文献提到了潮霉素A的半合成修饰，包括：K. Isono等人在《抗生素杂志》1957，10，21中和R. L. Mann与D. O. Woolf在《美国化学会会志》1957，79，120中提到潮霉素A的5"酮衍生化成2,4-二硝基苯腙。K. Isono等人（同上）也提到在5"上的缩氨基硫脲；R. L. Mann与D. O. Woolf（同上）以及S. J. Hecker等人在《生物有机医药化学快报》1992，2，533中和S. J. Hecker等人在《生物有机医药化学快报》1993，3，295中提到了将潮霉素A的5"酮还原为5"醇；B. H. Jaynes等人在《生物有机医药化学快报》1993，3，1531中和B. H. Jaynes等人在《抗生素杂志》1992，45，1705中提到了呋喃糖类似物；S. J. Hecker等人在《生物有机医药化学快报》1993，3，289中和C. B. Cooper等人在《生物有机医药化学快报》1997，7，1747中提到了芳环类似物；S. J. Hecker等人在《生物有机医药化学快报》1992，2，533中提到了烯酰胺类似物；S. J. Hecker等人在《生物有机医药化学快报》1992，2，1015中和S. J. Hecker等人在《生物有机医药化学快报》1992，2，1043中提到了氨基环醇类似物。本发明的潮霉素A衍生物具有对抗革兰氏阴性和革兰氏阳性细菌和原生动物的活性。

与本申请同时提出的、1998年5月4日提出的、题目为“2”-脱氧潮霉素衍生物”的（代理人摘要号PC 10186）、指定发明人为R. G. Linde II的美国临时专利申请第60/084058号中也提到了潮霉素类似物，该文献全文引入本文作为参考。

发明概述

本发明涉及式1化合物：



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及其可药用盐、药物前体和溶剂化物，其中：

R^1是H，R^2是$-NR^3R^4$，$-NR^4C(O)R^3$，$-OC(O)NR^3R^4$或$-OR^3$；

或者R^1和R^2共同构成=N-OR^3，$=CR^4R^3$，$=CR^4C(O)R^3$，$=CR^4C(O)OR^3$或$=CR^4C(O)NR^3R^4$；

每个R^3独立地选自H，C_1-C_{10}烷基，C_2-C_{10}链烯基，$-(CH_2)_t$(C_3-C_{10}环烷基)，$-(CH_2)_t$(C_6-C_{10}芳基)和$-(CH_2)_t$(4-10元杂环)，其中t是0-5的整数，所述烷基可选地含有1个或2个选自O，$-S(O)_j-$（其中j是0-2的整数）和$-N(R^7)-$的杂基，条件是两个O原子、两个S原子或者O和S原子彼此不直接相连；所述环烷基、芳基和杂环R^3基可选地与苯环、C_5-C_8饱和环基或4-10元杂环基稠合；前述R^3基团的$-(CH_2)_t-$部分可选地包括一个碳-碳双键或三键，其中t是2-5之间的整数；前述R^3基团，不包括H但包括上述任一个可选的稠环，可选地被1-5个R^5基团取代，条件是R^1为H且R^2为$-OR^3$时，R^3不为H、甲基或乙基；

每个R^4独立地为H或C_1-C_{10}烷基;

每个R^5独立地选自: C_1-C_{10}烷基, C_3-C_{10}环烷基, 卤素, 氰基, 硝基, 三氟甲基, 二氟甲氧基, 三氟甲氧基, 叠氮基, $-OR^6$, $-C(O)R^6$, $-C(O)OR^6$, $-NR^7C(O)OR^9$, $-OC(O)R^6$, $-NR^7SO_2R^9$, $-SO_2NR^6R^7$, $-NR^7C(O)R^6$, $-C(O)NR^6R^7$, $-NR^6R^7$, $-S(O)_j(CH_2)_m$(C_6-C_{10}芳基), $-S(O)_j$(C_1-C_6烷基), 其中j是0-2的整数, $-(CH_2)_m$(C_6-C_{10}芳基), $-O(CH_2)_m$(C_6-C_{10}芳基), $-NR^7(CH_2)_m$(C_6-C_{10}芳基)和$-(CH_2)_m$(4-10元杂环), 其中m是0-4的整数; 所述烷基可选地含有1个或2个选自O, $-S(O)_j-$(其中j是0-2的整数)和$-N(R^7)-$的杂基, 条件是两个O原子、两个S原子或者O和S原子彼此不直接相连; 所述环烷基、芳基和杂环R^5基可选地与C_6-C_{10}芳基、C_5-C_8饱和环基或4-10元杂环基稠合; 所述烷基、环烷基、芳基和杂环R^5基可选地被1-5个独立地选自下列的取代基取代: 卤素, 氰基, 硝基, 三氟甲基, 二氟甲氧基, 三氟甲氧基, 叠氮基, $-NR^7SO_2R^9$, $-SO_2NR^6R^7$, $-C(O)R^6$, $-C(O)OR^6$, $-OC(O)R^6$, $-NR^7C(O)OR^9$, $-NR^7C(O)R^6$, $-C(O)NR^6R^7$, $-NR^6R^7$, $-OR^6$, C_1-C_{10}烷基, $-(CH_2)_m$(C_6-C_{10}芳基)和$-(CH_2)_m$(4-10元杂环), 其中m是0-4的整数;

每个R^6独立地选自: H, C_1-C_{10}烷基, C_3-C_{10}环烷基, $-(CH_2)_m$(C_6-C_{10}芳基)和$-(CH_2)_m$(4-10元杂环), 其中m是0-4的整数; 所述烷基可选地包括1个或2个选自O, $-S(O)_j-$(其中j是0-2的整数)和$-N(R^7)-$的杂基, 条件是两个O原子、两个S原子或者O和S原子彼此不直接相连; 所述环烷基、芳基和杂环R^6基可选地与C_6-C_{10}芳基、C_5-C_8饱和环基或4-10元杂环基稠合; 前述R^6取代基, 除H以外, 可选地被1-5个独立地选自下列的取代基取代: 卤素, 氰基, 硝基, 三氟甲基, 二氟甲氧基, 三氟甲氧基, 叠氮基, $-C(O)R^7$, $-C(O)OR^7$, $-OC(O)R^7$, $-NR^7C(O)R^8$, $-C(O)NR^7R^8$, $-NR^7R^8$, 羟基, C_1-C_6烷基和C_1-C_6烷氧基;

每个R^7和R^8独立地为H或C_1-C_6烷基;

R^9选自R^6的定义中规定的除H以外的取代基。

优选的式1化合物包括那些化合物, 即, 其中R^1和R^2共同构成=N-OR^3且R^3为C_1-C_4烷基、C_2-C_4链烯基、$-(CH_2)_t$(C_6-C_{10}芳基)或$-(CH_2)_t$(4-10元杂环), 其中t是0-3的整数, 杂环基可选地与苯环稠合, 芳基可选地与

一个5或6元杂环基稠合，而前述R^3基，包括所述可选地稠合的部分，可选地被1-5个独立地选自下列的取代基取代：硝基，卤素，C_1-C_3烷氧基，C_1-C_4烷基，三氟甲基，乙酰氨基，叔丁氧羰基氨基，叔丁氧羰基氨基甲基，叔丁氧羰基，$-NR^6R^7$，苯基，环己基，羧基，氨基甲基，二氟甲氧基，三氟甲氧基，氰基，哌啶基，吗啉代，苯氧基和苯硫基。

其他优选的式1化合物包括那些化合物，即，其中R^1和R^2共同构成$=N-OR^3$且R^3为$-(CH_2)_t(C_6-C_{10}$芳基)或$-(CH_2)_t$(4-10元杂环)，其中t是0-3的整数，杂环基可选地与苯环稠合，芳基可选地与一个5或6元杂环基稠合，而前述R^3基，包括所述可选地稠合的部分，可选地被1-5个独立地选自下列的取代基取代：硝基，卤素，C_1-C_3烷氧基，C_1-C_4烷基，三氟甲基，乙酰氨基，叔丁氧羰基，叔丁氧羰基氨基，$-NR^6R^7$，苯基，环己基，羧基，叔丁氧羰基氨基甲基，氨基甲基，二氟甲氧基，三氟甲氧基，氰基，哌啶基，吗啉代，苯氧基和苯硫基。

其他优选的式1化合物包括那些化合物，即，其中R^1为H、R^2为$-NR^3R^4$、R^4为H或甲基、R^3为$-(CH_2)_t(C_6-C_{10}$芳基)或$-(CH_2)_t$(4-10元杂环)，其中t是0-2的整数，而R^3基可选地被1-5个独立地选自卤素、C_1-C_3烷氧基，C_1-C_4烷基和三氟甲基的取代基取代。

其他优选的式1化合物包括那些化合物，即，其中R^1为H、R^2为$-NR^4C(O)R^3$、R^4为H、R^3为C_3-C_6环烷基、$-(CH_2)_t(C_6-C_{10}$芳基)或$-(CH_2)_t$(4-10元杂环)，其中t是0-2的整数，芳基可选地与一个5或6元杂环基稠合，杂环基可选地与一个苯环稠合，而前述R^3基，包括所述可选地稠合的部分，可选地被1-5个独立地选自卤素、C_1-C_3烷氧基，C_1-C_4烷基和三氟甲基的取代基取代。

其他优选的式1化合物包括那些化合物，即，其中R^1和R^2共同构成$=CR^4C(O)OR^3$或$=CR^4C(O)NR^3R^4$、R^4为H、R^3为H、C_1-C_6烷基、C_3-C_6环烷基、$-(CH_2)_t$(4-10元杂环)或$-(CH_2)_t(C_6-C_{10}$芳基)，其中t是0-2的整数，芳基可选地与一个5或6元杂环基稠合，杂环基可选地与一个苯环稠合，而前述R^3基，不包括H但包括所述可选地稠合的部分，可选地被1-5个独立地选自卤素、C_1-C_3烷氧基，C_1-C_4烷基、$-NR^6R^7$和三氟甲基的取代基取

代。

其他优选的式1化合物包括那些化合物，即，其中R^1为H、R^2为$-OR^3$、R^3为C_1-C_4烷基、$-(CH_2)_t$(4-10元杂环)或$-(CH_2)_t$(C_6-C_{10}芳基)，其中t是1-2的整数，芳基可选地与一个5或6元杂环基稠合，杂环基可选地与一个苯环稠合，而前述R^3基，包括所述可选地稠合的部分，可选地被1-5个独立地选自卤素、C_1-C_3烷氧基，C_1-C_4烷基、环己基、氰基、三氟甲基、苄氧基和三氟甲基的取代基取代。

其他优选的式1化合物包括那些化合物，即，其中R^1为H、R^2为$-OC(O)NR^3R^4$、R^4为H、R^3为$-(CH_2)_t$(C_6-C_{10}芳基)，其中t是0-2的整数，而R^3基可选地被1-5个独立地选自卤素、C_1-C_3烷氧基，C_1-C_4烷基和三氟甲基的取代基取代。

特别优选的式1化合物包括选自下列的那些:

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3-氟苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3-氟苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(苯并呋喃-2-基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(苯并呋喃-2-基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-苯甲基肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲

基-D-新肌醇，(*E*)-*O*-苯甲基肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(4-氯苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3,4-二氯苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3,4-二氯苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(4-吡啶基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(4-(4-吗啉基)苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[环己基甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(4-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(2,4-二氯苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3,4-二氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)

氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(呋喃-3-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(呋喃-3-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(1,3-苯并二氧杂环戊烯-5-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(1,3-苯并二氧杂环戊烯-5-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3-氯苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(4-环己基苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3-氨基苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[[(4-氨基甲基)苯基]甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[3-(4-氯苯基)丙基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[3-(4-氯苯基)丙基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3-(三氟甲氧基)苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(4-(1-哌啶基)苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(2-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[2-(苯硫基)乙基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(苯并呋喃-5-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(苯并呋喃-5-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(2-苯基嘧啶-5-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3-氟-4-甲氧基苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3,4-二氢-2H-1-苯并吡喃-4-基)甲基]肟；

5-脱氧-5-[[3-[4-[(5,6-二脱氧-5-(甲基(苯甲基)氨基-α-L-半乳糖型-呋喃糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯

基]氨基]-1,2-*O*-亚甲基-D-新肌醇;

5-脱氧-5-[[3-[4-[(5,6-二脱氧-5-苯氨基-α-L-半乳糖型-呋喃糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇;

5-脱氧-5-[[3-[4-[(6-脱氧-5-*O*-[(3,4-二氯苯基)甲基]-β-D-阿卓糖型-呋喃糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇, (*E*)-*O*-[(呋喃-2-基)甲基]肟;

5-脱氧-5-[[3-[4-[(5-甲基-β-D-阿糖型-庚-5-(*E*)-烯呋喃糖醛-1-基酸)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇, 乙酯;

5-脱氧-5-[[3-[4-[[N-(呋喃-2-基)甲基]-(5-甲基-β-D-阿糖型-庚-5-(*E*)-烯呋喃糖醛-1-基-酰胺)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇, (*E*)-*O*-[3-(苯基)丙基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇, (*Z*)-*O*-(2-丙烯-1-基)肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇, (*E*)-*O*-(2-丙烯-1-基)肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇, (*E*)-*O*-[(4-甲基苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)

氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(4-甲氧基苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3-(三氟甲基)苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-5-O-[(4-氯苯基)甲基]-β-D-阿卓糖型-呋喃糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[二苯甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-5-苯氨基甲酸酯-β-D-阿卓糖型-呋喃糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇；

5-脱氧-5-[[3-[4-[(6-脱氧-5-[(3,4-二氯苯基)甲基]氨基甲酸酯-β-D-阿卓糖型-呋喃糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*Z*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3-氯苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3-氯-2-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3-氯-2-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3-氯-4-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3-氯-4-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3-氯-5-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3-氯-5-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(5-氯-2-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(5-氯-2-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3,5-二氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3,5-二氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(4-氯-3-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(4-氯-3-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲

基-D-新肌醇，(*E*)-*O*-[(4-氯-1,3-苯并二氧杂环戊烯-6-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(4-氯-1,3-苯并二氧杂环戊烯-6-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(5-氯-1,3-苯并二氧杂环戊烯-6-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(5-氯-1,3-苯并二氧杂环戊烯-6-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(4-氯-1,3-苯并二氧杂环戊烯-5-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(4-氯-1,3-苯并二氧杂环戊烯-5-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(2,3-二氢苯并呋喃-6-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(2,3-二氢苯并呋喃-6-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(2,3-二氢苯并呋喃-5-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(2,3-二氢苯并呋喃-5-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)

氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-(1,2,3,4-四氢化萘-1-基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-(1,2,3,4-四氢化萘-1-基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-(7-氯-1,2,3,4-四氢化萘-1-基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-(7-氯-1,2,3,4-四氢化萘-1-基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-(7-氯-1,2,3,4-四氢化萘-1-基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-(7-氯-1,2,3,4-四氢化萘-1-基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-(8-氯-3,4-二氢-2*H*-1-苯并吡喃-4-基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-(8-氯-3,4-二氢-2*H*-1-苯并吡喃-4-基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-(6-氯-3,4-二氢-2*H*-1-苯并吡喃-4-基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-(6-氯-3,4-二氢-2*H*-1-苯并吡喃-4-基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-(8-氟-3,4-二氢-2*H*-1-苯并吡喃-4-基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-(8-氟-3,4-二氢-2*H*-1-苯并吡喃-4-基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-(6-氟-3,4-二氢-2*H*-1-苯并吡喃-4-基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-(6-氟-3,4-二氢-2*H*-1-苯并吡喃-4-基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(喹啉-2-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(喹啉-2-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(喹啉-3-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(喹啉-3-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[4-(苯甲基)苯甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲

基-D-新肌醇，(*Z*)-*O*-[4-(苯甲基)苯甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[4-(苯氧基)苯甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[4-(苯氧基)苯甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3,5-二氯苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3,5-二氯苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-(苯基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-(苯基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-(3-氯-4-氟苯基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-(3-氯-4-氟苯基)肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(4-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)

氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(4-氯苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3,4-二氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(2,4-二氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(2,4-二氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(2,1,3-苯并噁二唑-5-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(2,1,3-苯并噁二唑-5-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(2,3,5,6-四氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(2,3,5,6-四氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(2,3-二氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(2,3-二氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(4-苯基-呋喃-3-基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(4-苯基-呋喃-3-基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(4-苯基-呋喃-2-基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(4-苯基-呋喃-2-基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(2,3-二氟-6-甲氧基苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(2,3-二氟-6-甲氧基苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3-氯-噻吩-2-基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3-氯-噻吩-2-基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(5-氯-噻吩-2-基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲

基-D-新肌醇，(*Z*)-*O*-[(5-氯-噻吩-2-基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3-氯-2,6-二氟苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3-氯-2,6-二氟苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(2-氟苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[1-(3-氯苯基)乙基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-(3-二氟甲氧基-苯基)肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-(3-二氟甲氧基-苯基)肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-(4-二氟甲氧基-苯基)肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-(4-二氟甲氧基-苯基)肟;

以及所述化合物的可药用盐和溶剂化物。

在一个更特别的实施方案中，本发明包括以下化合物:

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲

基-D-新肌醇，(*Z*)-*O*-[(1,3-苯并二氧杂环戊烯-5-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3-氯苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3-氯苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(苯并呋喃-2-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3,5-二氯苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3,5-二氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3,5-二氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3-氯-2-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)

氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3-氯-2-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3-氯-4-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3-氯-4-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(4-氯-3-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(4-氯-3-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(4-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(4-氟苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(4-氯苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(4-氯苯基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(4-苯基-呋喃-2-基)甲基]肟；

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3-氯-5-氟苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(3,4-二氟苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(3,4-二氟苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(2,3-二氟苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(2,4-二氟苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(2,4-二氟苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(2,3,5,6-四氟苯基)甲基]肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-(3-氯-4-氟苯基)肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-(3-氯-4-氟苯基)肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲

基-D-新肌醇，(*Z*)-*O*-[(5-氯-噻吩-2-基)甲基]肟;

以及所述化合物的可药用盐和溶剂化物。

本发明也涉及一种药物组合物，该组合物可用于治疗哺乳动物、鱼或鸟的下列疾病：细菌感染、原生动物感染、以及与细菌感染或原生动物感染有关的疾病，该组合物包含治疗有效量的式1化合物或其可药用盐，和可药用载体。

本发明也涉及一种治疗哺乳动物、鱼或鸟的选自细菌感染、原生动物感染或者与细菌感染或原生动物感染有关的疾病的方法，该方法包含对所述哺乳动物、鱼或鸟施用治疗有效量的式1化合物或其可药用盐。

本发明也涉及含有潮霉素A和表潮霉素的组合物的制备方法，所述组合物中潮霉素A与表潮霉素的比至少为10:1，该方法包含使吸水链霉菌在25℃-35℃的温度范围内、在pH小于6.9的培养基中发酵。在所述方法的一个优选实施方案中，所述吸水链霉菌是吸水链霉菌NRRL2388或其突变株，所述pH范围为6.2-6.7，所述温度为约29℃，而潮霉素A与表潮霉素的比至少为14:1。在上述方法的另一个方面，所述组合物保持在pH6.0-6.4下，优选约6.0，并且在将所述潮霉素A纯化为油的过程中，所述组合物的温度保持在25℃-35℃范围内。

除非另有说明，否则本文中所用的术语“治疗”是指逆转、减轻、抑制该术语所指的疾病或病况的进展，或者预防其所指的疾病或病况，或是这类疾病或病况的一种或多种症状。本文中所用的名词“治疗”是指治疗行为，此“治疗行为”中的“治疗”即上面刚刚定义的“治疗”。

除非另有说明，否则本文中所用的术语或短语“细菌感染”、“原生动物感染”和“与细菌感染或原生动物感染有关的疾病”包括下列这些：与肺炎链球菌、流感嗜血菌、粘膜炎莫拉氏菌、金黄色葡萄球菌、粪肠球菌、屎肠球菌、铅黄肠球菌、表皮葡萄球菌、溶血葡萄球菌或消化链球菌的感染有关的肺炎，中耳炎，窦炎，支气管炎，扁桃体炎和乳突炎；与酿脓链球菌、C群和G群链球菌、白喉棒杆菌或溶血

放线杆菌的感染有关的咽炎、风湿热和肾小球性肾炎；与肺炎枝原体、侵肺军团菌、肺炎链球菌、流感嗜血菌或肺炎衣原体的感染有关的呼吸道感染；血液和组织感染，包括心内膜炎和骨髓炎，它们是由金色链球菌、溶血链球菌、粪肠球菌、屎肠球菌、耐久肠球菌引起的，这些细菌中包括对已知抗细菌剂有抗性的菌株，所述已知抗细菌剂是诸如但不限于：β-内酰胺类、万古霉素、氨基苷类、喹诺酮类、氯霉素、四环素类和大环内酯类；与金黄色葡萄球菌、凝固酶阴性的葡萄球菌（即表皮葡萄球菌、溶血葡萄球菌等）、酿脓链球菌、无乳链球菌、C-F族链球菌（小菌落链球菌）、绿色链球菌、极小棒杆菌、梭菌或汉氏巴尔通氏体的感染有关的无并发症的皮肤和软组织感染和脓肿以及产褥热；与金黄色葡萄球菌、凝固酶阴性的葡萄球菌或肠球菌的感染有关的无并发症的急性泌尿道感染；尿道炎和子宫颈炎；与砂眼衣原体、杜氏嗜血菌、苍白密螺旋体、解脲尿枝原体或淋病奈瑟氏球菌的感染有关的性传播疾病；与金黄色葡萄球菌（食物中毒和中毒性休克综合征）或A、B和C群链球菌的感染有关的毒素疾病；与幽门螺杆菌感染有关的溃疡；与回归热疏螺旋体感染有关的全身性发热综合征；与布氏疏螺旋体感染有关的莱姆病；与砂眼衣原体、淋病奈瑟氏球菌、金色链球菌、肺炎链球菌、酿脓链球菌、流感嗜血菌或利斯特氏菌的感染有关的结膜炎、角膜炎和泪囊炎；与鸟分枝杆菌或胞内分枝杆菌的感染有关的播散性鸟分枝杆菌复合体（MAC）疾病；由结核分枝杆菌、麻风分枝杆菌、副结核分枝杆菌、堪萨斯分枝杆菌或龟分枝杆菌引起的感染；与空肠弯曲杆菌空肠亚种感染有关的胃肠炎；与隐孢子虫感染有关的肠原生动物感染；与绿色链球菌感染有关的牙原性感染；与百日咳博德特氏菌感染有关的持续咳嗽；与产气荚膜梭菌或拟杆菌的感染有关的气性坏疽；以及与幽门螺杆菌或肺炎衣原体的感染有关的动脉粥样硬化或心血管疾病。可以治疗或预防的动物的细菌感染和原生动物感染以及与这类感染有关的疾病包括以下这些：与溶血巴斯德氏菌、多杀巴斯德氏菌、牛枝原体或博德特氏菌的感染有关的牛呼吸疾病；与原生动物（即球虫、隐孢子虫等）感染有关的母牛肠疾病；与

金黄色葡萄球菌、乳房链球菌、无乳链球菌、停乳链球菌、棒杆菌或肠球菌的感染有关的乳牛场母牛乳腺炎；与大叶性肺炎放线杆菌（A.pleuro）、多杀巴斯德氏菌或枝原体感染有关的猪呼吸疾病；与胞内散沫花（*Lawsonia intracellularis*）、沙门氏菌或猪痢疾小蛇菌的感染有关的猪肠疾病；与梭杆菌感染有关的母牛腐蹄病；与坏死梭杆菌或节瘤偶蹄形菌感染有关的母牛毛状疣；与牛莫拉氏菌感染有关的母牛红眼病；与原生动物（即新孢子虫（neosporium））感染有关的母牛早期流产；与表皮葡萄球菌、中间葡萄球菌、凝固酶阴性葡萄球菌或多杀巴斯德氏菌感染有关的狗和猫的皮肤和软组织感染；以及与产碱菌、拟杆菌、梭菌、肠杆菌、真杆菌、消化链球菌、卟啉单胞菌或普雷沃氏菌的感染有关的狗和猫的牙或口腔感染。可以按照本发明的方法治疗或预防的其他细菌感染和原生动物感染以及与这类感染有关的疾病参见J.P.Sanford等人的《Sanford抗微生物治疗指南》第26版（Antimicrobial Therapy, Inc., 1996年）。

除非另有说明，否则本文中所用的术语“卤素”包括氟、氯、溴或碘。优选的卤基是氟、氯和溴。

除非另有说明，否则本文中所用的术语“烷基”包括带有直链或分支部分的饱和一价烃基。所述烃基可以包括一个或两个双键或三键。应当理解，对于所述烃基来说，为了包括一个碳-碳双键或三键，在所述烃基中至少需要两个碳原子。

除非另有说明，否则本文中所用的术语“芳基”包括芳烃去除一个氢后形成的有机基，诸如苯基或萘基。

除非另有说明，否则本文中所用的术语“4-10元杂环”包括含有一个或多个各选自O、S和N的杂原子的芳族和非芳族杂环基，其中每个杂环基在其环系统中具有4-10个原子。非芳族杂环基包括环系统中仅有4个原子的基团，而芳族杂环基的环系统中必需有至少5个原子。杂环基包括苯并稠合环系统和由一个或多个氧代部分取代的环系统。4元杂环基的实例是氮杂环丁基（来源于氮杂环丁烷）。5元杂环基的实例是噻唑基，10元杂环基的实例是喹啉基。非芳族杂环基的实例是吡

咯烷基、四氢呋喃基、四氢噻吩基、四氢吡喃基、四氢噻喃基、哌啶子基、吗啉代、硫代吗啉代、噻嗯烷基、哌嗪基、氮杂环丁基、氧杂环丁基、硫杂环丁基、高哌啶基、氧杂环庚基、硫杂环庚基、氧氮杂萘基、二氮杂萘基、硫氮杂萘基、1,2,3,6-四氢吡啶基、2-吡咯啉基、3-吡咯啉基、二氢吲哚基、2H-吡喃基、4H-吡喃基、二噁烷基、1,3-二氧戊环基、吡唑啉基、二噻烷基、二硫戊环基、二氢吡喃基、二氢噻吩基、二氢呋喃基、吡唑烷基、咪唑啉基、咪唑烷基、3-氮杂二环[3.1.0]己基、3-氮杂二环[4.1.0]庚基、3H-吲哚基和喹嗪基。芳族杂环基的实例是吡啶基、咪唑基、嘧啶基、吡唑基、三唑基、吡嗪基、四唑基、呋喃基、噻吩基、异噁唑基、噻唑基、噁唑基、异噻唑基、吡咯基、喹啉基、异喹啉基、吲哚基、苯并咪唑基、苯并呋喃基、噌啉基、吲唑基、中氮茚基、2,3-二氮杂萘基、哒嗪基、三嗪基、异吲哚基、蝶啶基、嘌呤基、噁二唑基、噻二唑基、呋咱基、苯并呋咱基、苯并噻吩基、苯并噻唑基、苯并噁唑基、喹唑啉基、喹喔啉基、1,5-二氮杂萘基和呋吡啶基。前述基团，当从上述化合物衍生时，有可能是与C连接或与N连接的。例如，从吡咯衍生的基团可能是吡咯-1-基（N连接的）或者是吡咯-3-基（C连接的）。

除非另有说明，否则本文中所用的短语“可药用盐”包括本发明化合物中可能存在的酸性基或碱性基的盐。本发明的性质上为碱性的化合物能与各种无机和有机酸形成各种各样的盐。可以用于制备这类碱性化合物的可药用酸加成盐的酸是可以形成无毒酸加成盐（即含有药理学上可接受的阴离子的盐）的那些，诸如盐酸盐、氢溴酸盐、氢碘酸盐、硝酸盐、硫酸盐、酸式硫酸盐、磷酸盐、酸式磷酸盐、异烟酸盐、乙酸盐、乳酸盐、水杨酸盐、柠檬酸盐、酸式柠檬酸盐、酒石酸盐、泛酸盐、酒石酸氢盐、抗坏血酸盐、琥珀酸盐、马来酸盐、龙胆酸盐、富马酸盐、葡糖酸盐、葡糖醛酸盐、蔗糖盐、甲酸盐、苯甲酸盐、谷氨酸盐、甲磺酸盐、乙磺酸盐、苯磺酸盐、对甲苯磺酸盐和扑酸盐（即，1,1'-亚甲基-双-(2-羟基-3-萘甲酸盐)）。除了上面所提到的酸以外，包括碱性部分、诸如氨基的本发明化合物还可以与各种

氨基酸形成可药用盐。

本发明的性质上为酸性的那些化合物能与各种药理学上可接受的阳离子形成碱式盐。这类盐的实例包括本发明化合物的碱金属和碱土金属盐，特别是钙盐、镁盐、钠盐和钾盐。

本发明化合物具有不对称中心，因此存在不同的对映形和非对映形。本发明涉及本发明化合物的所有旋光异构体和立体异构体及其混合物的使用，也涉及所有药物组合物以及可能应用或含有它们的治疗方法。关于这一点，如果R^1和R^2共同构成式=N-OR^3的肟部分的话，则本发明包括与氮相连的-OR^3基的E和Z构型。式1化合物也可以作为互变异构体存在。本发明涉及所有这些互变异构体及其混合物的使用。

本发明也包括同位素标记的化合物，及其可药用盐，它们与式1表示的化合物是相同的，只不过一个或多个原子被取代为原子质量或质量数不同于自然界中常见的原子质量或质量数的原子。可以引入到本发明化合物中的同位素的实例包括氢、碳、氮、氧、磷、氟和氯的同位素，诸如^2H、^3H、^{13}C、^{14}C、^{15}N、^{18}O、^{17}O、^{35}S、^{18}F和^{36}Cl。含有上述同位素和/或其他原子的其他同位素的本发明化合物、其药物前体、以及所述化合物或所述药物前体的可药用盐也在本发明的范围内。本发明的某些同位素标记的化合物，例如其中引入了放射性同位素诸如^3H和^{14}C的那些，可以用于药物和/或底物的组织分布测定。氚（即^3H）和碳-14（即^{14}C）同位素是特别优选的，因为它们容易制备和检测。另外，用较重的同位素诸如氘（即^2H）取代可以产生某些医疗优点，这些优点的产生是因为代谢稳定性更大了，例如体内半衰期增加了，或者所需剂量减少了，因此，在某些情况下可能是优选的。本发明的同位素标记的式1化合物及其药物前体一般可以通过进行下列流程和/或实施例和制备例中公开的操作，通过用容易获得的同位素标记的试剂代替非同位素标记的试剂而制得。

本发明也包括含有式1化合物的药物前体的药物组合物，以及通过施用式1化合物的药物前体而治疗细菌感染的方法。带有游离氨基、酰氨基、羟基或羧基的式1化合物可以转化为药物前体。在药物前体包括

的化合物中，有一个氨基酸残基、或者两个或多个（例如两个、三个或四个）氨基酸残基的多肽链通过酰胺或酯键与式1化合物的游离氨基、羟基或羧酸基共价连接。氨基酸残基包括但不限于通常由三字母符号指定的20个天然氨基酸，也包括4-羟基脯氨酸、羟基赖氨酸、锁链赖氨素(demosine)、异锁链赖氨素、3-甲基组氨酸、正缬氨酸、β-丙氨酸、γ-氨基丁酸、瓜氨酸、高半胱氨酸、高丝氨酸、鸟氨酸和甲硫氨酸砜。

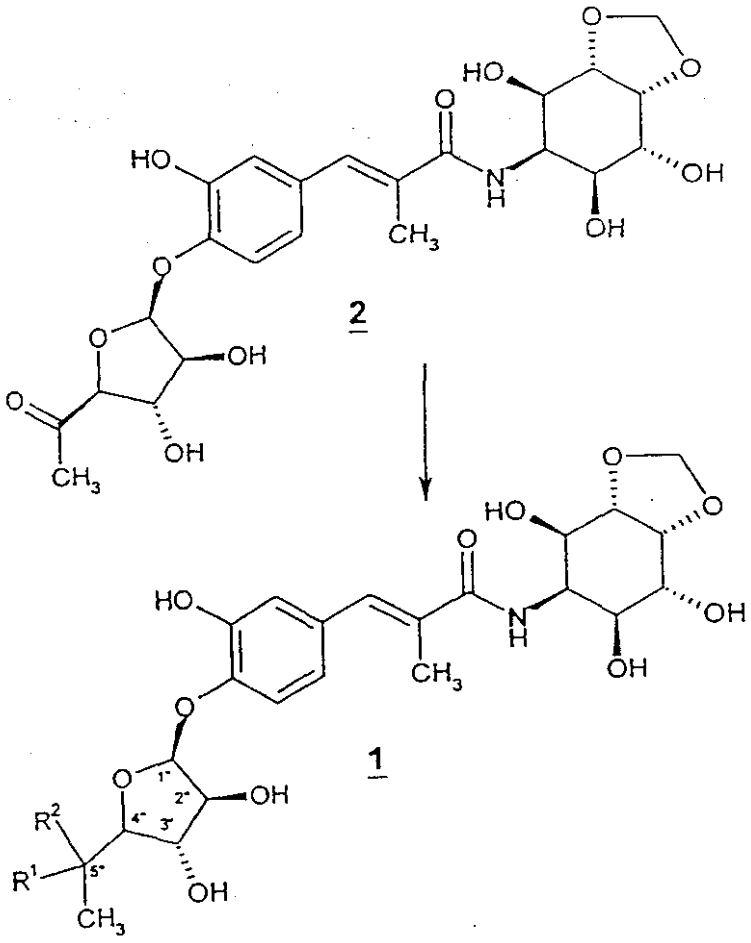
也包括其他类型的药物前体。例如，游离羧基可以衍生为酰胺或烷基酯。酰胺和酯部分可以引入包括但不限于醚、胺和羧酸官能度的基团。游离羟基可以使用包括但不限于半琥珀酸酯、磷酸酯、二甲氨基乙酸酯和磷酰氧甲氧羰基等的基团衍生，如D. Fleisher, R. Bong, B. H. Stewart, 在《高级药物释放评论》（1996年）19, 115中概述的。也包括羟基和氨基的氨基甲酸酯药物前体，如羟基的碳酸酯药物前体和硫酸酯。也包括羟基衍生为(酰氧基)甲基和(酰氧基)乙基醚，其中酰基可以是一个烷基酯，可选地被包括但不限于醚、胺和羧酸官能度的基团取代，或者该酰基是一个如上所述的氨基酸酯。R. P. Robinson等人在《医药化学杂志》(1996年)39, 10中描述了此类型的药物前体。

药物前体侧链的选择性引进可以在潮霉素A核心分子的羟基上进行。例如，可以用叔丁基二甲硅烷基氯将潮霉素A的6个羟基彻底甲硅烷基化。该六甲硅烷基衍生物在室温下经受碳酸钾的甲醇溶液的作用，选择性除去酚式甲硅烷基，使得可以在该位置作进一步的选择性修饰。在另一个例子中，将潮霉素A不完全甲硅烷基化（参见PC 10186, R. Linde, 2"-脱氧潮霉素A衍生物，美国临时专利申请第60/084,058号，1998年5月4日申请）得到五甲硅烷基衍生物，其中C-2"羟基是游离的。可以对此衍生物进行选择性酰基化、烷基化等，从而得到在C-2"上连接的药物前体。

发明详述

下列流程图说明了本发明化合物的制备方法。

流程图



本发明化合物是容易制备的。根据上述流程图，式2表示的起始化合物是潮霉素A，它可以按照本领域技术人员熟知的方法制备，诸如通过吸水链霉菌NRRL2388的发酵。潮霉素A分子的呋喃糖4"位上的甲基酮可以在该呋喃糖上以S构型（潮霉素A）或R构型（表潮霉素）存在。当用已公开的方案作为发酵和回收潮霉素A的模型时（美国专利3,100,176;《抗生素化学疗法》(1953年)3: 1268-1278, 1279-1282），潮霉素产物是如图所示带有在呋喃糖上的β取向的甲基酮的潮霉素A（4"-(S)差向异构体）和表潮霉素的近似3:1的混合物。从文献中知道（《抗生素杂志》33（7），695-704，1980年），纯潮霉素A在碱性溶液中将转化为表潮霉素。通过小心地将发酵过程中的pH控制在6.9以下，和控制纯化过程中的pH、温度和溶剂，可以将最终回收产物中的潮霉

素A与表潮霉素的比例提高到至少为14:1。使用此原料，可以制备用作进一步合成修饰用的模板的、来源于4"-(S)潮霉素的基本上单一的异构体。

通过吸水链霉菌NRRL2388或其突变株的发酵来生产富集在4"-(S)差向异构体中的潮霉素A，在整个发酵过程中，将培养基的pH控制在6.9以下，优选为6.2-6.7。该培养基含有可同化的碳、氮和微量元素源，正如本领域技术人员熟知的。发酵在约25-35℃、优选约29℃的温度下进行。例如，利用高压液相色谱法对发酵进行监控。培养持续至化合物的产率达到最大，一般持续大约3-10天，优选约4-6天。

在纯化过程中，通过使用缓冲水溶液（而不是未缓冲的水）和将活性物流的pH控制在接近6.0，可使表潮霉素的形成减至最小。也可以通过将回收物质经受较高温度的时间最小化而使表潮霉素的形成最小化。因此，如果需要降低溶剂浓度，优选用缓冲水溶液稀释活性物流并避免在提高的温度下使用旋转蒸发。并且，作为避免较高温度的手段，可以在最后的纯化步骤之前，用树脂柱浓缩活性溶液，以减少必须被煮沸的溶液的体积。在该过程中，最后的纯化步骤是利用真空和大约35-50℃的水浴温度将活性馏份浓缩成固体。可以通过分阶段地煮沸而将溶液经受高温的期间减到最短。

其中R^1和R^2共同构成式=NOR^3（其中R^3如上所定义）表示的肟的式1化合物可以利用下述方法制备：用式R^3ONH_2表示的羟胺处理潮霉素A（式2化合物），其中使用羟胺的游离碱或盐，优选羟胺的游离碱。该反应在惰性溶剂、诸如甲醇、乙醇或吡啶中进行，如果使用羟胺的盐、例如盐酸盐的话，溶剂中还加入碱，诸如Na_2CO_3或K_2CO_3，该反应在约0-65℃、优选0-25℃的温度范围内进行。可以使用《生物共轭化学》（1990年）2，96；《药物科学杂志》（1969年）58，138和《化学与药学通报》（1967年）15，345中公开的一种或多种方法制备式R^3ONH_2表示的羟胺。

其中R^1为H、R^2为-NR^3R^4、而R^3和R^4如上所定义的式1化合物可以通过在潮霉素A的C-5"酮位点进行还原胺化而合成。R^4NH_2和潮霉素A在惰性溶剂中化合并用还原剂诸如$NaBH_4$、$NaBH(OAc)_3$(Ac是乙酰基）或

$NaCNBH_3$进行处理得到R^3 = H的产物。为了将R^3转化为H以外的基团，可以用适宜的式RC(O)H或RC(O)R'表示的醛或酮进行第二次还原胺化（如果R^3是RCH_2-或RR'CH-，且R'和R是R^3定义内的任何一个部分，它们可以通过一个亚甲基连接，诸如烷基、芳基烷基或杂环烷基）。可以用Eschweiler-Clark反应引进一个甲基作为R^3取代基。为了提供一个酰胺基，诸如当R^1为H而R^2为$-NR^4C(O)R^3$时，可以如上所述引入一个式$-NHR^4$表示的胺，然后通过用活化形式的羧酸、诸如R^3COCl或$R^3C(O)OC(O)R^3$处理中间体而引入一个式$-C(O)R^3$的酰基部分，或者通过使用酰胺偶联剂，诸如(2-乙氧基-1-乙氧基羰基-1,2-二氢喹啉(EEDQ)，1,1'-羰基-二咪唑(CDI)或碳化二亚胺，诸如1,3-二环己基碳化二亚胺(DCC)。在上述方法中，可以在最后的脱保护步骤中使用K_2CO_3的甲醇溶液将潮霉素A中的任何一个已酯化的羟基释放出来。

通过使用利用氨等价物将潮霉素A还原胺化而产生的伯胺，例如通过使用醋酸铵和氰基硼氢化钠或三乙酰氧基硼氢化钠，可以制得其中R^1为H、R^2为$-NR^4C(O)R^3$、而R^4为H、R^3如上所定义的式1化合物。另一方面，此伯胺可以经相应的叠氮化物制备：1）例如，通过TBDMSCI和胺型碱如咪唑或吡啶的作用，可以将潮霉素A的羟基保护为它们的TBDMS（叔丁基二甲基甲硅烷基）衍生物；2）然后例如用硼氢化钠的甲醇溶液将潮霉素A的C-5"酮还原得到全甲硅烷化的5"-羟基潮霉素；3）例如通过甲磺酰氯和三乙胺的作用，将所得醇转化为甲磺酸酯；4）例如使用叠氮化钠的N,N-二甲基甲酰胺（DMF）溶液将该甲磺酸酯置换为叠氮化物；5）使用例如三苯基膦后接着进行水解而将该叠氮化物还原为伯胺。

该伯胺与$R^3C(O)OH$的活化形式、例如$R^3C(O)Cl$或$R^3C(O)OC(O)R^3$反应得到相应的酰胺。另一方面，可以与$R^3C(O)OH$一起使用酰胺偶联剂，诸如1-(3-二甲氨基丙基)-3-乙基碳化二亚胺（EDC）、二乙基氰化磷酰（DEPC）、DCC、CDI或EEDQ。最后，使用酸诸如乙酸、氟化氢、氟化氢-吡啶复合物或氟离子诸如氟化四丁基铵（TBAF）除去任何保护基。

为了加入不是H的R4基，可以在将任何游离羟基保护后，将上述酰

胺烷基化为例如甲硅烷基醚。该烷基化作用可以用碱和烷化剂进行，诸如氢化钠和适宜的式R4-Br表示的溴化物。然后用酸诸如乙酸、氟化氢、氟化氢-吡啶复合物或氟离子诸如TBAF将羟基脱保护。

或者，可以经三乙酰氧基硼氢化钠或氰基硼氢化钠介导，用R^4NH_2对潮霉素A或其被护变型进行还原胺化。所得仲胺可以如上所述用$R^3C(O)OH$的活化形式将其酰化，或者通过使用酰胺偶联剂与$R^3C(O)OH$反应。然后如上所述完成羟基的脱保护。

全甲硅烷化的5"-羟基潮霉素A与在甲苯中的异氰酸酯R^3NCO在40-110℃、优选50-80℃的温度下进行反应，可以制得其中R^1为H、R^2为$-OC(O)NR^3R^4$的式1化合物。向该反应中加入二甲氨基吡啶和三乙胺可能是有益的。该反应的产物中R^4等于氢，可以通过使用碱诸如氢化钠和烷化剂诸如式R^4-Br表示的溴化物将其烷基化，使R^4等于C_1-C_{10}烷基。然后可以利用酸诸如乙酸、氟化氢、氟化氢-吡啶复合物或氟离子诸如TBAF进行羟基的脱保护。

其中R^1为H、R^2为$-OR^3$、而R^3为烷基或取代烷基的式1化合物可以通过相应的潮霉素A的醇的烷基化制备。在此过程中，使用一种适宜的试剂诸如三乙基甲硅烷基氯(TESCl)、三甲基硅烷基氯(TMSCIl)或TBDMS和一种胺型碱诸如咪唑或吡啶，将潮霉素A的羟基合适地保护为例如它们的甲硅烷醚。然后使用适宜的还原剂诸如在甲醇中的硼氢化钠将该C-5"酮部分还原。所得醇可以在碱、诸如氢化钠或叔丁醇钾的存在下，用R^3-X（其中X是一个离去基如Cl、Br或甲磺酸酯）烷基化。然后用酸诸如乙酸、氟化氢、氟化氢-吡啶复合物或一个氟源诸如TBAF除去保护基。

其中R^1为H、R^2为$-OR^3$、而R^3为芳族或杂环部分的式1化合物可以经Mitsunobu反应制备。如D. L. Hughes在《有机反应》(1992年)42，335中所述，使如上所述制备的被护的潮霉素醇与R^3OH经三苯基膦和二乙基偶氮二羧酸酯介导发生Mitsunobu反应。然后如上所述将所得醚脱保护。

或者，当R^1为H、R^2为$-OR^3$、而R^3为芳族或杂环部分时，被护的潮霉

素醇可以转化为一个离去基，例如溴化物或甲磺酸酯衍生物。然后使用碱诸如氢化钠、叔丁醇钾或碳酸钾将该离去基置换为R^3OH。

通过相应的从潮霉素A的C-5"酮的Wittig或Horner-Emmons Wittig烯化作用而产生的α,β-不饱和酯中间体，可以制备其中R^1和R^2共同构成$=CR^4C(O)R^3$、$=CR^4C(O)OR^3$或$=CR^4C(O)NR^3R^4$、而R^3和R^4如上所定义的式1化合物。例如，(乙酯基亚甲基)三苯基正膦或(乙酯基亚乙基)三苯基正膦可以与潮霉素A反应得到不饱和乙酯。例如用含水氢氧化钠将该酯水解得到相应的羧酸（R^1和R^2共同构成$=CHC(O)OH$）。此时，潮霉素的羟基可以如上所述保护为例如它们的TES或TBDMS醚。为了制备上述酯，可以通过例如DCC和DMAP、或CDI和一种催化碱诸如乙醇钠的作用，用R^3OH将该羧酸酯化。

其中R^1和R^2共同构成$=CR^4C(O)NR^3R^4$的式1化合物可以通过用式R^3NH_2的胺处理上述羧酸中间体（R^1和R^2共同构成$=CHC(O)OH$）进行制备，同时使用一种酰胺偶联剂，诸如DCC、CDI、EEDQ、DEPC或EDC。关于被护衍生物，可以经烷基化引入R^4，例如用一种碱诸如氢化钠或叔丁醇钾和一种烷化剂诸如R^4-X，其中X是Br、Cl或甲磺酸酯。

通过潮霉素A的直接的Wittig或Horner Emmons反应，或者通过被护形式的潮霉素A与例如相应的$R^3C(O)CHR^4-PPh_3$（Ph为苯基）或$R^3C(O)CHR^4-P=O(OEt)_2$（Et为乙基）试剂反应，可以制备式1化合物（R^1和R^2共同构成$=CR^4C(O)\ R^3$）。可以利用J. Boutagy和R. Thomas在《化学评论》（1974年）74，87中和B. E. Maryanoff等在《化学评论》（1989年）89，863中描述的方法进行烯化。或者，潮霉素A的被护的不饱和羧酸衍生物可以例如通过用CDI和N,O-二甲基羟胺处理而转化为其Weinreb酰胺。然后按照S. Nahm和S. M. Weinreb在《四面体快报》（1981年）22，39中公开的方法，该酰胺可与R^3-M（其中M是一个金属离子如Li或MgBr）反应生成酮。

利用$R^4-CH(PPh_3)-R^3$或$R^4-CH(P=O(OEt)_2)-R^3$的内鎓盐与潮霉素A或其被护衍生物的Wittig或Hormer-Emmons反应，可以制备其中R^1和R^2共同构成$=CR^4R^3$、而R^3和R^4如上所定义的式1化合物，其中羟基已如上所述

被修饰为例如它们的甲硅烷醚如TES或TBDMS。然后可如上所述除去保护基。

或者，可以利用潮霉素A的C-5"同系化的酮或醛作为一个中间体。这些化合物可以借助于与氧化三苯基鏻盐或正膦如$Ph_3P-C(R^3)OMe$（Me是甲基）的Wittig或Hormer-Emmons反应获得。所得烯醇醚可以用温和的酸诸如乙酸或稀盐酸水解得到醛或酮。然后该醛或酮可以与有机金属衍生物R^4M（其中M是例如Li或MgBr）反应得到相应的醇，该醇可以在甲磺酰氯的作用下脱水得到相应的烯烃。然后如上所述脱保护，得到其中R^1和R^2共同构成$=CR^4R^3$的式1化合物。

其中R^1和R^2共同构成$=CR^4R^3$、而R^4为芳基或杂芳基、R^3不为氢的式1化合物可以利用钯催化法制备。被护酮$CH_3-CH(COR^3)$-hygro向三氟甲基磺酸烯醇酯的转化可以利用P. J. Stang和W. Treptow在《合成》（1980年）283中公开的方法进行。然后该三氟甲基磺酸烯醇酯可以用Suzuki或Stille型钯催化法与芳基或杂芳基二羟基甲硼酸$R^4B(OH)_2$或芳基锡类、例如R^4SnMe_3或R^4SnBu_3偶合得到不饱和芳基衍生物。Suzuki偶合反应可以按照N. Miyaura和A. Suzuki在《化学评论》（1995年）95，2457中的描述进行。Stille反应利用V. Farina等在《有机反应》（1997年）50，1中描述的条件进行。然后如上所述脱保护得到最终的化合物。

本发明的化合物具有不对称碳原子。带有在一个或多个中心的异构体的混合物的化合物将作为非对映体混合物存在，它们可以用本领域技术人员熟知的方法、例如层析法或分级结晶法，在它们的物理化学差异的基础上分离成单独的非对映体。所有这类异构体，包括非对映体混合物，都被认为是本发明的组成部分。

本发明的性质上为碱性的化合物能与各种无机和有机酸形成各种各样的不同盐。尽管这类盐必须是药学上可接受的用于对动物给药的，但在实践中经常希望从作为药学上不可接受的盐的反应混合物开始分离本发明化合物，然后通过用碱性试剂处理该药学上不可接受的盐而简单地将其转变为游离碱化合物，随后将该游离碱转变为药学上可接受的酸加成盐。通过在含水溶剂介质或在合适的有机溶剂如甲醇或乙

醇中，用实质上等当量的选定的无机酸或有机酸处理该碱性化合物，就可以容易地制备本发明的碱性化合物的酸加成盐。随着溶剂的细心蒸发，可容易地得到所需的固体盐。所需酸式盐也可通过向溶液中加入适宜的无机或有机酸而从游离碱在有机溶剂中的溶液中沉淀出来。

本发明的性质上为酸性的那些化合物能与各种药理学上可接受的阳离子形成碱式盐。这类盐的实例包括碱金属或碱土金属盐，特别是钠盐和钾盐。这些盐都是用常规技术制备的。用作制备本发明的可药用碱式盐用的试剂的化学碱是与本发明的酸性化合物形成无毒碱式盐的那些。这类无毒碱式盐包括从诸如钠、钾、钙和镁等药理学上可接受的阳离子衍生的那些。这些盐可以通过用含有所需碱金属醇盐或金属氢氧化物的水溶液处理相应的酸性化合物、然后优选在减压条件下将所得溶液蒸发至干而容易地制备。或者，它们也可以通过将酸性化合物的低级链烷酸溶液与所需碱金属醇盐或金属氢氧化物混合在一起、然后用与前面相同的方式将所得溶液蒸发至干而制备。在这两种情况下，优选使用化学计量量的各种试剂，以确保反应完全和所需最终产物的最大产率。

借助于化合物抑制定义的病原体菌株生长的能力来证明本发明化合物对抗细菌病原体的抗菌活性。

测定

该测定，如下所述，采用常规的方法和解释标准，并设计用于对化学修饰提供指导，这些化学修饰可能导致具有对抗敏感和耐药有机体的抗菌活性的化合物，所述耐药的包括但不限于β-内酰胺、大环内酯和万古霉素抗性的。在该测定中，装配一组细菌菌株，使包括各种目标病原体物质，包括典型的抗生素抗性细菌。使用这组实验对象使得能够根据活性的效能和光谱确定化学结构/活性关系。该测定用微量滴定盘进行，并按照National Committee for Clinical Laboratory Standards(NCCLS)出版的"抗微生物圆盘敏感性试验的行为标准-第六版，核定标准"指标进行解释；用最小抑制浓度（MIC）对比各菌株。开始时将化合物溶于二甲基亚砜（DMSO）作为储液。

本发明化合物的活性也可按照Steers复制基因技术进行评定，该技术是由Steers等人在《抗生素与化学疗法》1959年，9，307中描述的一种标准体外细菌测试法。

本发明化合物的体内活性可以利用本领域技术人员熟知的常规动物保护研究来确定，该研究通常用啮齿动物进行。

根据一个体内模型，用小鼠急性细菌感染模型评估化合物的效力。下面提供一个这样的体内系统的例子。将小鼠（CF1混合性别小鼠；18-20g）随到达随分配到笼子中，并使它们在被用于研究之前适应新环境1-2天。通过腹膜内接种悬浮于5%无菌猪胃粘蛋白中的细菌（金黄色葡萄球菌菌株01A1095）产生急性感染。接种物通过下述方法制备：使培养物在37℃下在血琼脂上生长过夜，收获所得到的带有脑-心浸剂肉汤的表面生长物，调节该悬浮液的浊度，使得当稀释1:10到5%无菌猪胃粘蛋白中时，将产生100%致死率。

在进行了刺激后的0.5小时和4小时的时候，对小鼠（每组10只）进行皮下治疗。每个研究中都包括适宜的未治疗的（感染了，但未治疗）和阳性（万古霉素或米诺环素等）对照小鼠。经过4天观察期后，记录存活百分率；利用概率法确定PD_{50}（计算为保护了50%的受感染动物的mg/kg/剂量）。

本发明化合物及其可药用盐（下文中称作“活性化合物”）在治疗细菌和原生动物感染时可以通过口服、胃肠外、局部或直肠途径给药。一般说来，这些化合物大多希望以从约0.2mg/kg体重/天（mg/kg/天）至约200mg/kg/天的剂量范围以单剂或均分剂（即每天1-4剂）给药，尽管根据受治疗者的种类、体重和健康状况以及所选定的特定给药途径需要对此进行调整。不过，最希望采用的剂量水平范围是从约3mg/kg/天至60mg/kg/天。然而，根据所治疗的哺乳动物、鱼或鸟的种类和其个体对所述药物疗法的反应，以及所选定的药物制剂的类型和进行这种给药的时间周期与间隔，上述所给剂量范围有可能发生变化。在有些情况下，低于上述范围下限的剂量水平可能是更加适当的，而在另一些情况下可能采用更大的剂量而不会引起任何有害的副作用，

只要将这种大剂量首先分成数个小剂量后在一天内给药就行。

活性化合物可以利用前述途径单独给药或与可药用载体或稀释剂结合给药，并且这种给药可以以单剂或多剂进行。更具体地说，活性化合物可以以各种不同剂型给药，即，它们可以与各种可药用惰性载体混合，制成片剂、胶囊剂、锭剂、糖锭、硬糖、粉末剂、喷雾剂、膏霜、软膏、栓剂、胶冻、凝胶、糊剂、洗剂、油膏、含水悬浮液、可注射溶液、酏剂、糖浆剂等剂型。这类载体包括固体稀释剂或填充剂、无菌含水介质和各种无毒有机溶剂等。另外，可以对口服药物组合物进行适当的增甜和/或调味。一般说来，活性化合物以约5.0%至约70重量%范围内的浓度水平、以这类剂型的形式存在。

对于口服给药，可以采用含有各种赋形剂如微晶纤维素、柠檬酸钠、碳酸钙、磷酸二钙和甘氨酸的片剂，该片剂中同时还含有各种崩解剂，诸如淀粉（优选玉米、马铃薯或木薯淀粉）、藻酸和某些复合硅酸盐，以及颗粒粘合剂，象聚乙烯吡咯烷酮、蔗糖、明胶和阿拉伯胶。此外，对于压片来说，诸如硬脂酸镁、十二烷基硫酸钠和滑石等润滑剂经常是非常有用的。类似形式的固体组合物也可用作明胶胶囊中的填充物；在这种联合中的优选物质还包括乳糖或奶糖以及高分子量的聚乙二醇。当希望用含水悬浮液和/或酏剂进行口服给药时，该活性化合物可以与各种甜味剂或调味剂、着色物质或染料混合，以及如果需要的话，与乳化剂和/或悬浮剂混合，还可加上诸如水、乙醇、丙二醇、甘油及其各种类似混合物等稀释剂。

对于胃肠外给药，可以采用活性化合物在芝麻油或花生油中的溶液，或是在含水乙醇或丙二醇中的溶液。使用环糊精衍生物诸如β-环糊精磺基丁醚，钠盐（参见美国专利5,134,127）也可能是有益的。如果必要的话，水溶液应当适当地缓冲，而液体稀释剂首先使成为等渗的。这些水溶液适于静脉注射给药。油性溶液适于关节内、肌内和皮下注射给药。所有这些溶液在无菌状态下的制剂是用本领域技术人员熟知的标准制药技术容易地制得的。

此外，依照标准药学实践，也可能将本发明的活性化合物局部给

药，这可以利用膏霜、胶冻、凝胶、糊剂、贴敷片、油膏剂等实现。

至于对人以外的动物、诸如家畜或家养动物给药，可以将活性化合物加在这些动物的饲料中，或是作为兽用组合物经口服给予。

该活性化合物也可以以脂质体释放系统的形式给药，诸如小单层囊泡、大单层囊泡和多层囊泡。脂质体可以由各种磷脂、诸如胆固醇、硬脂酰胺或磷脂酰胆碱形成。

活性化合物也可以与可溶性聚合物如可定向的药物载体结合。这类聚合物可包括聚乙烯吡咯烷酮、吡喃共聚物、聚羟基丙基甲基丙烯酰胺苯基、聚羟基乙基天冬酰胺-酚、或被棕榈酰残基取代的聚环氧乙烷-聚赖氨酸。另外，该活性化合物可以与一类用于实现药物的可控释放的生物降解性聚合物结合，例如聚乳酸、聚乙醇酸、聚乳酸和聚乙醇酸的共聚物、聚ε己内酯、聚羧基丁酸、聚原酸酯、聚缩醛、聚二氢吡喃、聚氰基丙烯酸酯和水凝胶的交联或两亲嵌段共聚物。

本发明用下述制备例和实施例作了进一步的描述和例证。在这些制备例和实施例中，“rt”是指室温，即约20-25℃。

制备1

在一个2.8L冯巴赫瓶中，用5mL培养物吸水链霉菌NRRL2388的冷冻样品（在-80℃下储存于20%甘油/80%种菌培养基中）接种1L潮霉素种菌培养基（Corn Products公司，脑糖(cerelose) 13g/L，Hubinger淀粉 7g/L，Roquette玉米浸渍固体3g/L，Sheffield Brand Products NZ胺YTT 7g/L，Baker $CoCl_2 \cdot 6H_2O$ 0.002g/L，KH_2PO_4 0.7g/L，$MgSO_4 \cdot 7H_2O$ 1.3g/L，硫酸铵 0.7g/L，Dow Chemical P2000消泡剂 1滴/瓶，Colfax大豆油 2滴/瓶，加入高压灭菌器之前pH调节至7.0）。该培养物在29℃下在一个2英寸行程的摇动器上在200rpm摇动速率下生长3天。在一个14升的、配备了两个彼此间隔3.75英寸的4.75英寸Rushton叶轮的发酵罐（New Brunswick Microferm，New Brunswick，New Jersey）中，用该生长后的培养物接种8L无菌潮霉素发酵培养基（Albaglos碳酸钙 1g/L，Sheffield Brand Products NZ胺YTT 5g/L，Hubinger淀粉 20g/L，Archer Daniels Midland营养豆粉 10g/L，Dow Chemical P2000

消泡剂 1ml/L，Baker $CoCl_2 \cdot 6H_2O$ 0.002g/L，Colfax大豆油 2ml/L，脑糖 10g/L，NaCl 5g/L，加入高压灭菌器之前pH调节至7.0)。该培养液在29℃、8L/分钟的通气速率和800rpm搅拌速率下培养。为了将表潮霉素的形成减至最小，使pH保持在6.5-6.9之间达126小时，然后在其余时间内，用H_2SO_4(15%)将pH调节至6.2-6.6。总共培养143小时后收获发酵物。此时，潮霉素A与表潮霉素的比例为31:1。

将从上述发酵得到的6升培养液以8000rpm离心大约15分钟。离心后，弃去粒状沉淀，将上清液（pH6.4，HPLC测定其含有大约4.12gms潮霉素A活性）加载到填塞了500gms XAD-16树脂（Rohm & Haas(Philadelphia, Pennsylvania)）的层析柱上。该树脂先前已用2柱床体积的25mM磷酸二钠，pH6.0（"缓冲剂"）进行了平衡。加样后，该层析柱用2柱床体积的缓冲剂和2柱床体积的80/20缓冲剂/甲醇洗涤，活性用5柱床体积的50/50缓冲剂/甲醇洗脱。各馏份用HPLC测定，将含有大多数活性（2.730gms潮霉素A）的馏份合并。

通过加入1.8升缓冲剂将该XAD-16洗脱液的一部分（大约800mg潮霉素A）稀释到10%甲醇，并将其加载到已用4柱床体积的90/10缓冲剂/甲醇平衡的100ml CG-161柱（TosoHaas(Montgomeryville, Pennsylvania)）上。产物用6柱床体积的50/50缓冲剂/甲醇洗脱。各馏份用HPLC测定并将活性馏份合并。将合并后的馏份蒸发至干，测得固体的纯度大约为65重量%。将这些固体的一小部分转移用于测定。

将大约500mg固体与500ml水和500ml乙酸乙酯混合并搅拌20分钟。分离成两层，将水层干燥得到固体，经测定该固体大约为52重量%纯度。这两种固体（#34945-280-1和281-1）进行NMR和TLC测定，发现它们含有潮霉素A活性。此外，NMR显示潮霉素A/表潮霉素比大约为15:1。

制备2

在一个2.8L冯巴赫瓶中，用5mL培养物吸水链霉菌NRRL2388的冷冻样品（在-80℃下储存于20%甘油/80%种菌培养基中）接种1L潮霉素种菌培养基（CPC国际有限公司，脑糖(cerelose) 13g/L，Hubinger淀粉 7g/L，Roquette玉米浸渍固体3g/L，NZ胺YTT 7g/L，Baker

$CoCl_2 \cdot 6H_2O$ 0.002g/L，KH_2PO_4 0.7g/L，$MgSO_4 \cdot 7H_2O$ 1.3g/L，硫酸铵0.7g/L，Dow Chemical P2000消泡剂 1滴/瓶，Colfax大豆油 2滴/瓶，加入高压灭菌器之前pH调节至7.0)。该培养物在29℃下在一个2英寸行程的摇动器上在200rpm摇动速率下生长2-3天。向两个500加仑的不锈钢发酵罐中加入380-400加仑的潮霉素发酵培养基（Mineral Technologies碳酸钙 1g/L，Sheffield Brand Products NZ胺YTT 5g/L，Hubinger淀粉 20g/L，Archer Daniels Midland公司，大豆粉10g/L，Dow Chemical P2000消泡剂 1ml/L，Baker $CoCl_2 \cdot 6H_2O$ 0.002g/L，Colfax公司的大豆油 2gm/L，CPC国际有限公司的脑糖10g/L，Cargill公司的NaCl 5g/L)。该培养基在发酵罐中用20psig蒸汽灭菌60分钟。该培养基在发酵罐中利用冷却螺旋管冷却后，将pH调节至6.5-6.7。将发酵罐的条件设定为：气流速率为20标准立方英尺/分钟，温度为28℃，通气孔压力为5psig，用25%氢氧化钠和98%硫酸使pH保持在6.5-6.7。改变两个发酵罐中的搅拌速率，以使在接种前立即测量的培养基中的溶解氧浓度保持大于20%饱和浓度。设定了发酵罐的控制条件后，将5个冯巴赫种菌瓶以无菌方式合并到一个8L的吸气瓶中。然后如上所述用此种菌接种一个单一的、标称的500加仑发酵罐。此操作使用4升种菌重复进行，使一个发酵罐接受了4升种菌，另一个发酵罐接受了5升种菌。每个发酵罐运转大约114小时，此时终止发酵。用98%硫酸将培养液的pH调节至6.3，并将其从发酵罐中移出用于回收。

将上述这两个发酵罐（pH=6.3，潮霉素A与表潮霉素的比近似为51:1）在一个陶瓷过滤系统上过滤。将滤液（1450gmsA，506gal）加载到一个70加仑的XAD-16树脂柱上。该柱事先已用4柱床体积的磷酸三钠缓冲溶液，pH6.0（“缓冲剂”）平衡。加样后，该层析柱用2柱床体积的缓冲剂和2柱床体积的80/20缓冲剂/甲醇洗涤。随后用10馏份（每份大约50加仑）的50/50缓冲剂/甲醇溶液从柱上洗脱出活性。将活性馏份（大约1240gmsA）合并，通过加入1200加仑的缓冲剂稀释至终浓度为10%甲醇。使用稀释（而不是旋转蒸发）来降低甲醇浓度，使得可以使用较低的温度，以最大程度地减少容易在较高温度下增加的表潮

霉素的量。将此溶液的一半加载到一个40升的CG-161柱（事先已用4柱床体积的90/10缓冲剂/甲醇溶液平衡）上。加样后，该层析柱用4柱床体积的80/20缓冲剂/甲醇洗涤，并用5.5柱床体积的50/50缓冲剂/甲醇洗脱。将该层析柱再生并再次平衡后，将另一半活性加载到柱上并如上所述洗脱。将从这两次操作合并的馏份（120升，大约1051gmsA）通过加入缓冲剂而稀释到10%甲醇。将其再次加载到再生并再平衡的CG-161树脂柱上。一旦活性被吸附到柱上，就用4柱床体积的甲醇进行洗脱。此步骤用于在最后的蒸发之前减少盐以及提高样品的浓度。将合并后的从最后的CG-161柱得到的馏份蒸发至干得到总量约为1kgA的潮霉素A活性。在最终的固体中，潮霉素A与表潮霉素的比为约14.5:1。

用于实施例的实验方法

当用含有10%以上甲醇的洗脱剂系统使用硅胶层析法完成了最后的纯化步骤后，将层析产物溶于89:10:1的氯仿:甲醇:浓氢氧化铵并过滤，或者溶于甲醇并通过一个0.45μM的滤器。真空除去溶剂得到最终产物。在以下步骤中，t-BOC是指“叔丁氧羰基”

5”-肟醚制剂

用于合成肟醚的羟胺试剂的制备，实施例1-92，1A-116A

所用的大多数羟胺试剂既可以从市场上购得（一般是作为酸盐），也可以借助于下列方法从相应的醇或卤化物制备:

1）邻苯二甲酰亚胺保护的芳型或脂族羟胺的制备:

从醇制备:

按照E.Grochowski和J.Jurczak在《合成》（1976年）682中公开的方法，将与二乙基偶氮二羧酸酯和三苯基膦进行的Mitsunobu反应用于偶合N-羟基邻苯二甲酰亚胺和醇起始物。

从溴化物或氯化物制备:

N-羟基邻苯二甲酰亚胺（1当量）与卤化物起始物（1.2-2当量）的反应在DMSO溶液中进行，使用碳酸钾（0.6-2当量）作为碱。该反应在室温下，一般通过搅拌过夜而完成。将该反应混合物倒入冷水中，产生沉淀，将沉淀过滤得到邻苯二甲酰亚胺保护的羟胺。在许多情况

下，直接将此物质脱保护；也可以采用使用乙酸乙酯-己烷混合物的硅胶层析法来纯化该邻苯二甲酰亚胺保护的羟胺。

2）除去邻苯二甲酰亚胺保护基，得到苄型或脂族羟胺：

邻苯二甲酰亚胺保护的羟胺的脱保护通过与水合肼（1-2当量）在乙醇溶液中的反应来完成，该反应在室温至回流的温度范围内进行30分钟至过夜的时间。将反应混合物过滤，将滤液浓缩。此粗产物可以就照这样用于下一个步骤，也可以进一步纯化。将该粗产物与氯仿混合，通过过滤除去固体并从滤液中除去溶剂，从而除去了额外的邻苯二甲酰肼。或者，将该粗产物溶于1N盐酸，用乙醚或乙酸乙酯洗涤。水层用饱和碳酸钾溶液碱化并用乙醚或乙酸乙酯萃取。将最终的有机层干燥并除去溶剂，得到羟胺产物。

3）O-芳基羟胺的制备：

如Y. Endo, K. Shudo和T. Okamoto在《合成》（1980年）461中所述，通过使用均三甲基苯磺酰羟胺，将取代的酚转化为相应的O-芳基羟胺。

用于合成羟胺的各种醇和卤化物起始物的制备：

一般说来，如果需要，通过用48% HBr在65℃下处理1-4小时，可以将苯甲醇衍生物转化为相应的苄基溴。

在许多情况下，醇起始物是通过还原更高氧化程度的可从商业上获得的化合物得到的。4-环己基苯甲酸（实施例46，47）和3-氯-2-氟苯甲酸（实施例13A，14A）用在四氢呋喃中的氢化铝锂（2-2.3当量）还原得到相应的醇。3-(4-氯苯基)丙酸（实施例56，57）、3,4-二氢-2H-1-苯并吡喃-2-羧酸（实施例36A，37A）、4-氯-3-氨磺酰苯甲酸（实施例76A）、3-氯噻吩-2-羧酸（实施例85A，86A）、5-氯噻吩-2-羧酸（实施例91A，92A）和2,6-二甲基苯甲酸（实施例98A，99A）使用在四氢呋喃中的乙硼烷（1.1-2当量）在0℃-室温下反应5-18小时而还原成相应的醇。2-氟-6-甲氧基苄腈通过用30%的含水KOH在回流温度下处理而水解为2-氟-6-甲氧基苯甲酸，该酸如上所述用乙硼烷还原为2-氟-6-甲氧基苯甲醇（实施例80A）。3-三氟甲氧基苯甲醛（实施例62，68）、3-氰基苯甲醛（实施例63）、苯并呋喃-2-甲醛（实施例65，66）、1,4-

苯并二噁烷-6-甲醛（实施例83，84）、3-氟-4-甲氧基苯甲醛（实施例85，86）、6-氟-4-苯并二氢吡喃酮（实施例16A，17A）、3-氯-4-氟苯甲醛（实施例19A，22A）、喹啉-3-甲醛（实施例23A，24A）、4-氯-3-氟苯甲醛（实施例25A，26A）、2,3-(亚甲二氧基)苯甲醛（实施例28A，29A）、2,4-二氯苯甲醛（实施例45A，47A）、2-氯-4-氟苯甲醛（实施例46A，48A）、2-氟-6-(三氟甲基)苯甲醛（实施例66A，67A）、2,3-二氟苯甲醛（实施例68A，69A）、2-(二氟甲氧基)苯甲醛（实施例93A，94A）和6-氯苯并二氢吡喃-4-酮（实施例102A，103A）使用在四氢呋喃或甲醇中的硼氢化钠（1-2当量）在0℃或室温下还原为醇衍生物。

在二氯甲烷中的硫酸镁（4当量）用浓硫酸（1当量）进行处理，接着用4-氯甲基苯甲酸（1当量）和叔丁醇（5.1当量）处理。在室温下搅拌过夜得到叔丁酯（实施例36）。

4-氨基-3,5-二氯苯甲酸通过用在二甲基甲酰胺中的乙酰氯（1.2当量）在90℃下处理4小时而N-乙酰化。将冷却后的反应混合物倒入冷水中，冷冻并过滤得到乙酰胺衍生物。羧酸的还原用在四氢呋喃中的氢化铝锂（2当量）在0℃下进行2小时，得到N-(2,6-二氯-4-羟基甲基苯基)乙酰胺（实施例51）。

3-(氨基甲基)苯甲醇和4-(氨基甲基)苯甲醇通过在室温下用在THF中的乙硼烷(4-5当量)将3-和4-氰基苯甲醛还原过夜而制备。3-(氨基甲基)苯甲醇（实施例8A和9A）和4-(氨基甲基)苯甲醇（实施例55）以及3-氨基苯甲醇（实施例54）中的氨基，通过在回流温度下用在THF中的重碳酸二叔丁酯（1.1当量）处理直到起始的氨基化合物被耗尽而保护为N-t-BOC衍生物。

4-氟苯甲酸乙酯与在乙腈中的哌啶（3当量）的反应在回流下进行4天。用数体积的水稀释冷却后的反应混合物得到沉淀，将沉淀过滤得到4-(哌啶-1-基)苯甲酸乙酯。该酯用在四氢呋喃中的氢化铝锂（2当量）还原得到相应的醇（实施例71，72）。

5-羟甲基苯并呋喃（实施例79，80）按照K.Hiroya，K.Hashimura和K.Ogasawara在《杂环》（1994年）38，2463中公开的过程制备。

2-苯基嘧啶-5-甲醛（实施例81，82）按照J. T. Gupton, J. E. Gall, S. W. Riesinger等在《杂环化学杂志》（1991年）28，1281中公开的过程制备。该醛使用在甲醇中的硼氢化钠还原为相应的醇。

3-羟基甲基-4-苯基呋喃（实施例6A，7A）按照B. A. Keay和J-L. J. Bontront在《加拿大化学杂志》（1991年）69，1326中公开的方法制备。

5-氯-2-氟苄基溴（实施例12A，13A）利用A. P. Krapcho, C. E. Gallagher, A. Mammach, M. Ellis, E. Menta和A. Oliva在《杂环化学杂志》（1997年）34，27-32中公开的方法制备。

利用S. T. Ross, R. G. Franz, J. W. Wilson, R. A. Hahn和H. M. Sarau在《杂环化学杂志》（1986年）23，1805中公开的方法将2-氯-3,4-二甲氧基苯甲醛转化为4-氯-1,3-苯并二氧杂环戊烯-5-甲醛。然后该醛用在THF中的硼氢化钠（1当量）在0℃下进行还原，得到4-氯-1,3-苯并二氧杂环戊烯-5-甲醇（实施例30A，31A）。

4-苯基糠酸利用M. E. Alonso, P. Jano, M. I. Hernandez, R. S. Greenberg和E. Wenkert在《有机化学杂志》（1983年）48，3047中公开的方法制备。按照W. A. Scrivens, J. M. Tour, K. E. Creek, L. Pirisi在《美国化学会会志》（1994年）116，4517中公开的方法将其还原为2-(羟基甲基)-4-苯基呋喃（实施例34A，35A）。

利用A. S. Cantrell等在《医药化学杂志》（1996年）21，4261中公开的方法，用正丁基锂和N,N-二甲基甲酰胺从1-氯-2,4-二氟代苯制备3-氯-2,6-二氟苯甲醛。用在甲醇中的硼氢化钠还原得到3-氯-2,6-二氟苯甲醇，通过用48%HBr在65℃下处理3小时将其转化为3-氯-2,6-二氟苄基溴（实施例38A，39A）。类似地处理2,3,5,6-四氟甲苯得到2,3,5,6-四氟-4-甲基苄基溴（实施例40A，41A），而3,5-二氟甲苯被类似地转化为2,6-二氟-4-甲基苄基溴（实施例63A，64A）。3,4-二氟苯甲醚类似地转化为2,3-二氟-6-(甲氧基)苄基溴（实施例74A，75A），而1-氟-3-(三氟甲氧基)苯转化为2-氟-6-(三氟甲氧基)苄基溴（实施例77A，78A）。以类似的方式制备2-氯-6-(三氟甲氧基)苯甲醇（实施

例89A，90A），只是在甲酰化反应中使用二异丙基酰胺锂而不是正丁基锂。

利用T-T.Jong，P.G.Williard和J.P.Porwoll在《有机化学杂志》（1984年）49，735中公开的方法，将香草醛转化为7-氯-苯并二氧杂环戊烯-5-甲醛。然后用在甲醇中的硼氢化钠（1当量）在室温下还原得到7-氯-1,3-苯并二氧杂环戊烯-5-甲醇（实施例51A，52A）。在这种情况下，转化成羟胺试剂是通过甲磺酸酯衍生物的中介进行的，该甲磺酸酯衍生物是利用R.K.Crossland和K.L.Servis在《有机化学杂志》（1970年）35，3195中公开的方法制备的。

按照W.R.Meindl，E.Von Angerer，H.Schoenenberger和G.Ruckdeschel在《医药化学杂志》（1984年）27，1111中公开的方法制备3-氯-5-氟苯甲醇（实施例53A，54A）。

利用K.Inami和T.Shiba在《日本化学会通报》（1985年）58，352中公开的方法的类似方法制备4-苯基-2-噻唑甲醛。使用在乙醇中的硼氢化钠将该醛还原为相应的醇。通过用在二氯甲烷中的亚硫酰氯（4当量）在室温下处理该醇2-5小时而制备相应的2-氯甲基噻唑衍生物（实施例104A，105A）。

使用在乙醇中的硼氢化钠将2,4-二氟苯基·乙基酮还原为相应的醇（实施例106A，107A）。

通过用在THF中的溴化甲基镁（1当量）在室温下处理相应的苯甲醛衍生物而制备1-(3-氯-2,6-二氟苯基)乙醇和其他苯基乙醇衍生物（实施例108A-116A）。然后用48％HBr处理1－4小时而将这些醇转化为相应的苄基溴。

肟醚的制备，方法（A-I），实施例1-92，1A-116A

方法A

潮霉素A（1当量）和适宜羟胺的盐酸盐（1-2.2当量）的甲醇溶液（约0.1M潮霉素A）用碳酸钠（1.1-1.2当量/羟胺盐当量）进行处理并加热至回流持续15分钟至2小时。该反应后可以接着使用甲醇/氯仿或甲醇/氯仿/氢氧化铵洗脱剂进行薄层层析。然后将该反应混合物冷却

至室温并真空浓缩。粗产物利用J-N中的方法之一进行纯化。

方法B

潮霉素A（1当量）和适宜羟胺的盐酸盐（1-2.2当量）的甲醇溶液（约0.1M潮霉素A）用碳酸钠（1.1-1.2当量/羟胺盐当量）进行处理并加热至回流持续18小时。该反应后可以接着使用甲醇/氯仿或甲醇/氯仿/氢氧化铵洗脱剂进行薄层层析。然后将该反应混合物冷却至室温并真空浓缩。粗产物利用J-N中的方法之一进行纯化。

方法C

将潮霉素A（1当量）和适宜羟胺的游离碱（1-2.2当量）的甲醇溶液（约0.1M潮霉素A）加热至回流持续18小时。该反应后可以接着使用甲醇/氯仿或甲醇/氯仿/氢氧化铵洗脱剂进行薄层层析。然后将该反应混合物冷却至室温并真空浓缩。粗产物利用J-N中的方法之一进行纯化。

方法D

将潮霉素A（1当量）和适宜羟胺的游离碱（1-2.2当量）的甲醇溶液（约0.1M潮霉素A）加热至回流持续5-6小时。该反应后可以接着使用甲醇/氯仿或甲醇/氯仿/氢氧化铵洗脱剂进行薄层层析。然后将该反应混合物冷却至室温并真空浓缩。粗产物利用J-N中的方法之一进行纯化。

方法E

将潮霉素A（1当量）和适宜羟胺的游离碱（1-2.2当量）的甲醇溶液（约0.1M潮霉素A）在室温下搅拌18小时。该反应后可以接着使用甲醇/氯仿或甲醇/氯仿/氢氧化铵洗脱剂进行薄层层析。然后将该反应混合物真空浓缩。粗产物利用J-N中的方法之一进行纯化。

方法F

将潮霉素A（1当量）和适宜羟胺的游离碱（1-2.2当量）的甲醇溶液（约0.1M潮霉素A）在室温下搅拌1-5小时。该反应后可以接着使用甲醇/氯仿或甲醇/氯仿/氢氧化铵洗脱剂进行薄层层析。然后将该反应混合物真空浓缩。粗产物利用J-N中的方法之一进行纯化。

方法G

将分离的潮霉素A(1当量)的甲醇溶液和适宜羟胺的游离碱(1-2.2当量)的甲醇溶液在0℃下混合(终浓度，0.5-0.1M潮霉素A)并加热至室温1-2小时。该反应后可以接着使用甲醇/氯仿或甲醇/氯仿/氢氧化铵洗脱剂进行薄层层析。然后将该反应混合物真空浓缩。粗产物利用J-N中的方法之一进行纯化。

方法H

将潮霉素A(1当量)和适宜羟胺的游离碱(1-2.2当量)的甲醇溶液(终浓度，0.5-0.1M潮霉素A)在0℃下搅拌2-3小时。该反应后可以接着使用甲醇/氯仿或甲醇/氯仿/氢氧化铵洗脱剂进行薄层层析。然后将该反应混合物真空浓缩。粗产物利用J-N中的方法之一进行纯化。

方法I

将被作用物(参见有关所使用的被作用物的表)以约0.1M的浓度溶于三氟乙酸，并在室温下搅拌15分钟。此时真空除去三氟乙酸。加入数体积的89:10:1的氯仿:甲醇:浓氢氧化铵溶液，并真空除去挥发物。反复中和并真空浓缩得到粗产物。

肟醚的纯化，方法(J-N-1)

方法J

纯化利用硅胶层析法进行。通过将干燥硅胶加入到粗产物的甲醇溶液中，接着完全除去溶剂，而使该粗产物普遍预吸附到硅胶上。使用一般为5%至20%的甲醇的氯仿溶液进行柱洗脱，经常以梯度洗脱方式进行。

方法K

纯化利用硅胶层析法进行。通过将干燥硅胶加入到粗产物的甲醇溶液中，接着完全除去溶剂，而使该粗产物普遍预吸附到硅胶上。使用一般为5%至20%的甲醇的二氯甲烷溶液进行柱洗脱，经常以梯度洗脱方式进行。

方法L

纯化利用硅胶层析法进行。通过将干燥硅胶加入到粗产物的甲醇

溶液中，接着完全除去溶剂，而使该粗产物普遍预吸附到硅胶上。根据产物和起始物的R_f值，使用组成为289:10:1-39:10:1的氯仿:甲醇:氢氧化铵的三元溶液进行柱洗脱。柱洗脱通常以梯度方式进行。在实施例55的情形下，最后的柱洗脱剂为73:25:2。

方法M

纯化利用硅胶层析法进行。通过将干燥硅胶加入到粗产物的甲醇溶液中，接着完全除去溶剂，而使该粗产物普遍预吸附到硅胶上。使用范围从322:10:1至56:10:1的二氯甲烷:甲醇:氢氧化铵的三元溶液进行柱洗脱，通常以梯度洗脱方式进行。

方法N

纯化利用C_{18}反相色谱法进行，根据产物和起始物的R_f值，用10%至100%的甲醇-水溶液进行洗脱。柱洗脱通常以梯度方式进行。

方法N-1

纯化利用C_{18}反相色谱法进行，用乙腈和10mM pH7磷酸钾缓冲剂的混合物进行洗脱。分离出的组分是该反应混合物的次要产物，是从潮霉素起始物中存在的表潮霉素（C-4"上的α立体化学）得到的。

5"-胺制剂，实施例93-101

用于制备胺衍生物的方法（O-R）

方法O

潮霉素A的甲醇溶液（0.1M）用胺（1当量）进行处理并使其在室温下搅拌10分钟。加入乙酸（3当量），接着加入三乙酰氧基硼氢化钠（3当量），将该反应混合物再搅拌24小时。用少量的碳酸氢钠饱和水溶液处理后，真空除去溶剂。残余物用硅胶层析法纯化，用组成范围从89:10:1至70:28:2的氯仿:甲醇:氢氧化铵的混合物进行洗脱，通常以梯度洗脱方式进行。

方法P

潮霉素A的甲醇溶液（0.1M）用胺（2-4当量）进行处理并使其在室温下搅拌1小时。当亚胺的形成迟缓时，加入3埃分子筛，将该混合物搅拌过夜。然后加入硼氢化钠（1-2当量），将该反应搅拌2-24小时。

用少量的碳酸氢钠饱和水溶液处理（并且如果存在的话，通过过滤除去分子筛）后，真空除去溶剂，残余物用硅胶层析法纯化，用组成范围从89:10:1至80:19:1的氯仿:甲醇:氢氧化铵的混合物进行洗脱。

方法Q

在水中的氨基潮霉素A衍生物（0.1M）用甲醛（5当量）处理后用甲酸（10当量）处理，在90℃下搅拌5小时，然后在室温下搅拌48小时。加入饱和碳酸氢钠水溶液后，搅拌该反应混合物，然后滗出澄清的上清液。剩余的残余物用柱色谱法纯化，使用比例为80:19:1的氯仿:甲醇:氢氧化铵作为洗脱剂。

方法R

潮霉素A的甲醇溶液（0.1M）用苯胺（4当量）和碎3埃分子筛进行处理并在50℃下搅拌2小时，或在70℃下搅拌过夜。该反应混合物已冷却至室温后，加入硼氢化钠（1-2当量）并在室温下继续搅拌2-48小时。加入少量饱和含水碳酸氢钠，通过过滤除去分子筛，将滤液真空浓缩。粗残余物用硅胶柱色谱法纯化，使用80:19:1的氯仿:甲醇:氢氧化铵作为洗脱剂。

5"-酰胺制剂，实施例102-104

酰胺衍生物的制备，方法S-T

全甲硅烷基化的5"-氨基潮霉素A的合成

a）将潮霉素A、叔丁基二甲硅烷基氯（12当量）和咪唑（12当量）的DMF溶液（潮霉素浓度为0.25M）在80℃下搅拌20小时。减压条件下除去DMF后，所得残余物用二乙醚萃取。合并后的醚萃取液用水洗涤后用饱和氯化钠溶液洗涤，用硫酸钠干燥，过滤，浓缩。该粗产物用硅胶层析法纯化，用10%乙酸乙酯/己烷洗脱。

b）全甲硅烷基化的潮霉素A在1:1的甲醇:四氢呋喃中的溶液(0.2M)用硼氢化钠(0.5当量)处理并在室温下搅拌18小时。在减压条件下除去溶剂后，将残余物溶于氯仿，用饱和碳酸氢钠溶液洗涤，用硫酸钠干燥，过滤，并浓缩得到粗制全甲硅烷基化的5"-醇。纯化利用柱色谱法进行，用10%-20%的乙酸乙酯/己烷洗脱。随后对Mosher酯的分析显示，

此反应主要产物的5"位的立体化学是*R*。

c）5"-醇的二氯甲烷溶液（0.2M）在0℃下用三乙胺（3当量）处理后用甲磺酰氯（2当量）处理，并在室温下搅拌24小时。然后将该反应混合物倒入水中并用二氯甲烷萃取。合并后的有机层用硫酸钠干燥，过滤，真空浓缩得到5"-甲磺酸酯。

d）该5"-甲磺酸酯的DMF溶液（0.2M）用叠氮化钠（10当量）处理并在95℃下搅拌18小时。将该反应混合物倒入水中，用二乙醚萃取，用盐水洗涤，用硫酸钠干燥，过滤，真空浓缩。该粗制5"-叠氮化物用硅胶层析法纯化，用10%乙酸乙酯/己烷洗脱。

e）将5"-叠氮化物和三苯基膦（3当量）的甲苯溶液（5"-叠氮化物的浓度为0.2M）在105℃下搅拌18小时。在减压条件下除去甲苯并替换为四氢呋喃/水（10/1）（潮霉素衍生物浓度为0.1M），在75℃下搅拌5小时。将该反应混合物倒入水中并用二乙醚萃取。合并后的有机层用盐水洗涤，用硫酸钠干燥，过滤，真空浓缩。该粗产物用硅胶层析法纯化，用20%乙酸乙酯/己烷洗脱，得到全甲硅烷基化的5"-氨基潮霉素A。

方法S

a）将全甲硅烷基化的5"-氨基潮霉素A和适宜的羧酸（2当量）与在THF中的EEDQ（1-乙氧羰基-2-乙氧基-1,2-二氢喹啉，2当量）一起在70℃下搅拌3小时（全甲硅烷基化的潮霉素的浓度为0.1M）。将该反应混合物倒入水中并用醚萃取。合并后的有机层用5%碳酸钠溶液、水和饱和氯化钠溶液洗涤。用硫酸钠干燥后，过滤该有机萃取液并浓缩得到残余物，该残余物在硅胶上使用乙酸乙酯和己烷的混合物进行层析，得到作为其全甲硅烷基保护的衍生物的所需酰胺。

b）5"-改性六甲硅烷基潮霉素A的溶液（1当量，0.1M）用四丁基氟化铵（TBAF，10当量）的1M THF溶液在室温下处理14-24小时，从而除去甲硅烷基。真空除去THF，将该粗物质溶于水和甲醇的混合物。将该溶液/悬浮液应用到Dowex（50X4-400）树脂柱上（10-30g树脂/mmol TBAF，其已通过用0.1-0.2N的氢氧化钠处理后用1柱体积(CV)水洗涤而

转化为OH形式）。该柱用1-3CV的水重力洗脱直至TBAF被除去，然后在氮压力的帮助下用50%含水甲醇洗脱得到所需的酰胺产物。如果需要进一步纯化，可进行硅胶层析（方法J-N）。

方法T

适宜羧酸（1.2当量）的四氢呋喃溶液用DEPC（二乙基氰化磷酰，1.2当量）和三乙胺（1.2当量）处理，将该反应混合物搅拌10分钟。加入全甲硅烷基化的5"-氨基潮霉素A(1当量)（最终的潮霉素衍生物浓度为0.17M），使该反应在室温下继续进行48小时。将该反应混合物倒入水中并用醚萃取。合并后的有机层用含水碳酸钠、水和饱和氯化钠溶液洗涤，然后用硫酸钠干燥，过滤，并真空浓缩。该粗物质利用硅胶层析法纯化，使用乙酸乙酯和己烷的混合物。

按照方法S中的步骤b，用TBAF将该硅烷化的酰胺脱保护。

5"-醚，氨基甲酸酯制剂，实施例105-131

方法（U-Z）

通过方法U至Y将全甲硅烷基化的5"-羟基潮霉素A烷基化或酰化（参见实施例102-104部分，步骤a和b），随后使用方法S的步骤b除去甲硅烷基。

用于制备5"-潮霉素A苄醚的方法U

将氢化钠（在矿物油中的60%分散体，10当量）称取到一个用烘箱干燥过的圆底烧瓶中并用己烷洗涤3次。真空除去残余的己烷并在室温下向其中加入四氢呋喃（THF）（全甲硅烷基化的5"-潮霉素A的浓度为0.1M）、全甲硅烷基化的5"-羟基潮霉素A（1当量）和苄基溴（10当量）。将生成物浆液在50℃下加热1-4小时。将该反应冷却至室温，加入水终止反应，然后用氯仿（$CHCl_3$）萃取两次。合并后的有机相用盐水洗涤，用硫酸镁干燥并浓缩成半固体，对该半固体进行层析（SiO_2，5-15% EtOAc:甲苯或EtOAc:己烷）（EtOAc指的是乙酸乙酯）得到所需醚。

方法V

在室温下将叔丁醇钾（1M的THF溶液，5当量）加入到全甲硅烷基化的5"-羟基潮霉素A（1当量）和苄基溴（10当量）的THF溶液中（全

甲硅烷基化的5"-羟基潮霉素A浓度为0.1M)。15分钟后反应完成。加入水使反应终止并将产物萃取到氯仿中。合并后的有机萃取液用硫酸镁干燥，真空浓缩并进行层析（SiO_2，5-15% EtOAc:甲苯或EtOAc:己烷）得到所需产物。

方法W

在室温下将叔丁醇钾（1M的THF溶液，2当量）在5分钟内逐滴加入到全甲硅烷基化的5"-羟基潮霉素A（1当量）和苄基溴（5当量）的二噁烷溶液中（全甲硅烷基化的5"-羟基潮霉素浓度为0.1M)。15分钟后反应完成。加入水使反应终止并将产物萃取到氯仿中。合并后的有机萃取液用硫酸镁干燥，真空浓缩并进行层析（SiO_2，5-15% EtOAc:甲苯或EtOAc:己烷）得到所需产物。

方法X

将异氰酸苯酯（7当量）加入到全甲硅烷基化的5"-羟基潮霉素A（1当量)的甲苯溶液中(全甲硅烷基化的5"-羟基潮霉素浓度为0.05M）并加热至60℃持续12-24小时。将该粗反应混合物浓缩并进行层析（SiO_2，5-15% EtOAc:甲苯或EtOAc:己烷）得到甲硅烷基化的产物。

方法Y

利用S.Th.；Seeger,B.；Kutzke,U.和Eckstein在《有机化学杂志》(1996年）61，3883中公开的方法制备异氰酸苄酯（7当量)。将其加入到全甲硅烷基化的5"-羟基潮霉素A(1当量)、二甲氨基吡啶（0.2当量）和三乙胺（4当量）的甲苯溶液中（全甲硅烷基化的5"-羟基潮霉素浓度为0.05M）并加热至70℃持续12-24小时。将该粗反应混合物浓缩并进行层析（SiO_2，5-7% EtOAc:己烷）得到甲硅烷基化物质。

方法Z

全甲硅烷基化的5"-羟基潮霉素A用在甲醇中的K_2CO_3（1.3当量）（0.1M）处理并搅拌14-20小时。真空除去甲醇，将残余物溶于1:1的EtOAc:己烷和水。有机相用碳酸氢钠和盐水洗涤，用硫酸镁干燥并浓缩。不必进一步纯化，将该物质用烯丙基溴（1-3当量）和K_2CO_3（1.4当量）的DMF溶液（0.1M）处理14-24小时。将该反应混合物倒入己烷

中并用水洗涤。有机相用硫酸镁干燥，过滤，浓缩得到由烯丙基保护的酚式羟基组成的白色泡沫，其不必进一步纯化即可使用。该5"-醇在方法X的条件下用苄氧基氯甲基醚烷基化。使用Jaynes, B.H., Elliot, N.C.和Schicho, D.L.在《抗生素杂志》(1992年) 45, 1705中公开的方法除去烯丙基，然后使用方法S的步骤b除去甲硅烷基。

5"-烯烃制剂，实施例132-140

烯烃衍生物的制备，方法AA-EE

方法AA

将潮霉素A和(乙酯基亚甲基)三苯基正膦(2当量)的DMF溶液(0.1M潮霉素A)在70℃下搅拌15小时。在减压条件下除去DMF，所得残余物在硅胶上用氯仿、甲醇和氢氧化铵的混合物(80:19:1)进行层析，得到实施例132的不饱和酯。

方法BB

将实施例132的乙酯溶于水和四氢呋喃(1:1)(0.25M)，用氢氧化钠(3当量)处理并在室温下搅拌6小时。在减压条件下除去四氢呋喃后，加入1N HCl将pH调节至pH4。将该水溶液在减压条件下浓缩至干，所得残余物与MeOH混合并过滤。将滤液浓缩得到实施例133的羧酸。

方法CC

实施例133的羧酸、DCC(二环己基碳化二亚胺，1当量)和HOBT(羟基苯并三唑，1当量)的DMF溶液(0.25M)用适宜的胺(1当量)处理，将该反应混合物在室温下搅拌18小时。在减压条件下除去DMF后，所得油在硅胶上用氯仿、甲醇和氢氧化铵的混合物(80:19:1)进行层析，得到所需的酰胺。

方法DD

实施例133的羧酸和盐酸1-(3-二甲氨基丙基)-3-乙基-碳化二亚胺(1当量)在DMF中的混合物(0.25M)用适宜的胺(1当量)处理，将该反应混合物在室温下搅拌18小时。在减压条件下除去DMF后，残余物利用硅胶层析法纯化，使用浓度范围从89:10:1至80:19:1的氯仿、甲醇和氢氧化铵洗脱。

方法EE

存在于二甲基甲酰胺中的实施例133的产物（0.25M）用EEDQ（1-乙氧羰基-2-乙氧基-1,2-二氢喹啉，1.2-2当量）和适宜的胺（1当量）处理，并在70℃下搅拌过夜。冷却后，或者将该反应混合物真空浓缩得到粗产物用于纯化；或者将该反应混合物倒入氯仿中，将所得固体过滤得到粗产物。

在下面的表中阐明了按照上述方法制备的具体化合物。在这些表中，“Ex”指实施例，“Mol Wt”指分子量，“Stereo”指肟部分的立体化学（E或Z），“Pro”指用于制备该化合物的方法，“Mass Spec”指质谱法。

使用上述特定化学和普通化学，可以用类似的方式制备下列化合物。下面所列的每种化合物都是本发明的一部分，并具有对抗细菌感染的活性。当必要的醇或卤化物起始物不是从商业上购得时，给出了有关它们的参考文献或制备信息。

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(2,3-二氢苯并呋喃-6-基)甲基]肟。6-苯并呋喃甲醛可以用A.S.Tasker等在《医药化学杂志》（1997年）40，322中公开的方法制备。用硼氢化钠将该醛还原，双键在披钯碳上氢化，得到2,3-二氢-6-苯并呋喃甲醇。

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(2,3-二氢苯并呋喃-6-基)甲基]肟。6-苯并呋喃甲醛可以用A.S.Tasker等在《医药化学杂志》（1997年）40，322中公开的方法制备。用硼氢化钠将该醛还原，双键在披钯碳上氢化，得到2,3-二氢-6-苯并呋喃甲醇。

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-[(2,3-二氢苯并呋喃-5-基)甲基]肟。2,3-二氢

-5-苯并呋喃甲醛用硼氢化钠还原得到2,3-二氢-5-苯并呋喃甲醇。

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-[(2,3-二氢苯并呋喃-5-基)甲基]肟。2,3-二氢-5-苯并呋喃甲醛用硼氢化钠还原得到2,3-二氢-5-苯并呋喃甲醇。

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-(1,2,3,4-四氢化萘-1-基)肟。

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-(1,2,3,4-四氢化萘-1-基)肟。

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-(7-氯-1,2,3,4-四氢化萘-1-基)肟。7-氯-3,4-二氢-1(2*H*)-萘酮可以用W.M.Owton和M.Brunavs在《合成通讯》(1991年) 21，981中公开的方法制备。用硼氢化钠还原得到7-氯-1,2,3,4-四氢-1-萘醇。

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-(7-氯-1,2,3,4-四氢化萘-1-基)肟。7-氯-3,4-二氢-1(2*H*)-萘酮可以用W.M.Owton和M.Brunavs在《合成通讯》(1991年) 21，981中公开的方法制备。用硼氢化钠还原得到7-氯-1,2,3,4-四氢-1-萘醇。

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-(7-氟-1,2,3,4-四氢化萘-1-基)肟。7-氟-3,4-二氢-1(2*H*)-萘酮可以用W.M.Owton和M.Brunavs在《合成通讯》(1991年) 21，981中公开的方法制备。用硼氢化钠还原得到7-氟-1,2,3,4-四氢-1-萘醇。

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-(7-氟-1,2,3,4-四氢化萘-1-基)肟。7-氟-3,4-二氢-1(2*H*)-萘酮可以用W.M.Owton和M.Brunavs在《合成通讯》(1991年)21，981中公开的方法制备。用硼氢化钠还原得到7-氟-1,2,3,4-四氢-1-萘醇。

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-(8-氯-3,4-二氢-2*H*-1-苯并吡喃-4-基)肟。可以用G.Ariamala和K.K.Balasubramanian在《四面体快报》(1988年)29，3487中公开的方法制备8-氯-2,3-二氢-4*H*-1-苯并吡喃-4-酮；然后用硼氢化钠还原得到8-氯-3,4-二氢-2*H*-1-苯并吡喃-4-醇。

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-(8-氯-3,4-二氢-2*H*-1-苯并吡喃-4-基)肟。可以用G.Ariamala和K.K.Balasubramanian在《四面体快报》(1988年)29，3487中公开的方法制备8-氯-2,3-二氢-4*H*-1-苯并吡喃-4-酮；然后用硼氢化钠还原得到8-氯-3,4-二氢-2*H*-1-苯并吡喃-4-醇。

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*E*)-*O*-(8-氟-3,4-二氢-2*H*-1-苯并吡喃-4-基)肟。可以用R.Sarges等在《医药化学杂志》(1988年)31，230中公开的方法制备8-氟-2,3-二氢-4*H*-1-苯并吡喃-4-酮；然后用硼氢化钠还原得到8-氟-3,4-二氢-2*H*-1-苯并吡喃-4-醇。

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇，(*Z*)-*O*-(8-氟-3,4-二氢-2*H*-1-苯并吡喃-4-基)肟。可以用R.Sarges等在《医药化学杂志》(1988年)31，230中公开的方法制备8-氟-2,3-二氢-4*H*-1-苯并吡喃-4-酮；然后用硼氢化钠还原得到

8-氟-3,4-二氢-2*H*-1-苯并吡喃-4-醇。

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇,(*E*)-*O*-[4-(苯甲基)苯甲基]肟。4-(苯甲基)苯甲酸用乙硼烷还原为4-(苯甲基)苯甲醇。

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇,(*Z*)-*O*-[4-(苯甲基)苯甲基]肟。4-(苯甲基)苯甲酸用乙硼烷还原为4-(苯甲基)苯甲醇。

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇,(*E*)-*O*-[4-(苯氧基)苯甲基]肟。4-苯氧基苯甲醛用硼氢化钠还原为4-苯氧基苯甲醇。

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇,(*Z*)-*O*-[4-(苯氧基)苯甲基]肟。4-苯氧基苯甲醛用硼氢化钠还原为4-苯氧基苯甲醇。

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇,(*Z*)-*O*-(3-二氟甲氧基-苯基)肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇,(*E*)-*O*-(3-二氟甲氧基-苯基)肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇,(*Z*)-*O*-(4-二氟甲氧基-苯基)肟;

5-脱氧-5-[[3-[4-[(6-脱氧-β-D-阿糖型-己呋喃-5-酮糖-1-基)氧]-3-羟基苯基]-2-甲基-1-氧代-2-(*E*)-丙烯基]氨基]-1,2-*O*-亚甲基-D-新肌醇,(*E*)-*O*-(4-二氟甲氧基-苯基)肟;

表1

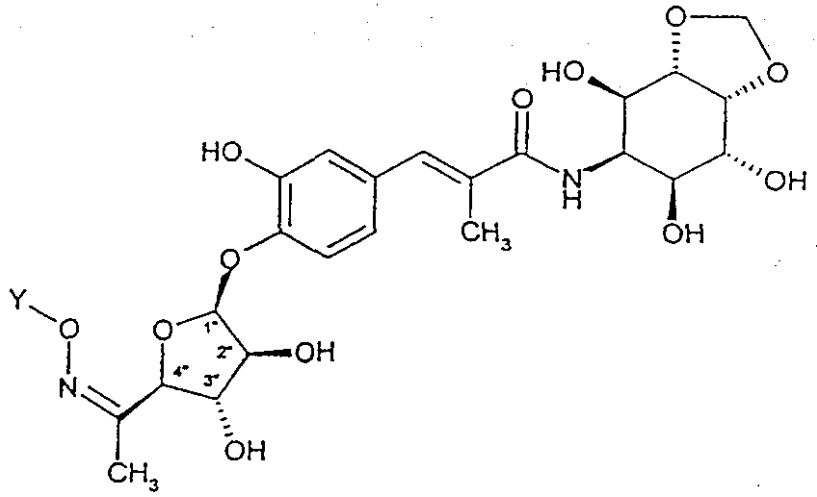


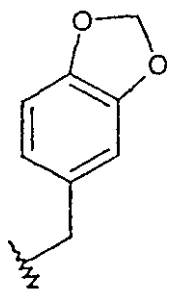
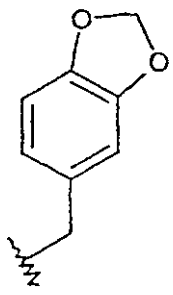
表1中的大多数实施例带有显示的C-4"立体化学，肟部分是β取向的。有些实施例具有α取向的肟；这些指示在"立体化学"一栏中。

实施例	Y	分子量	立体化学	制备方法	质 谱	1H NMR峰 值 (CD_3OD)
1	叔丁基	582.61	E	A或B, L	583.1	5.69 (d, J = 4.2 Hz, 1H), 4.28 (d, J = 8.1 Hz, 1H), 1.22 (s, 9H)
2	2-丙烯-1-基	566.57	E	B, L	567.1	5.93 (m, 1H), 5.55 (d, J = 4.4 Hz, 1H), 5.20 (dd, J = 17.2, 1.7 Hz, 1H), 5.11 (dd, J = 10.4, 1.7 Hz, 1H), 4.50 (d, J = 5.6 Hz, 2H), 4.23 (d, J = 7.9 Hz, 1H)
3	乙 基	554.46	E	B, L	555.1	5.69 (d, J = 4.2 Hz, 1H), 4.23 (d, J = 7.9 Hz, 1H), 4.04 (q, J = 7.1 Hz, 2H), 1.18 (t, J = 7.1 Hz, 3H)
4	乙 基	554.46	Z	B, L	555.1	5.64 (d, J = 4.2 Hz, 1H), 5.14 (d, J = 6.2 Hz, 1H), 4.03 (q, J = 7.1 Hz, 2H), 1.20 (t, J = 7.1 Hz, 3H)
5	异丁基	582.61	Z	B, L	583.2	5.66 (d, J = 4.2 Hz, 1H), 5.18 (d, J = 6.2 Hz, 1H), 3.77 (d, J = 6.6 Hz, 2H), 1.95 (m, 1H), 0.92 (d, J = 6.8 Hz, 3H)
6	(4-硝基苯基)甲基	661.63	E	B, L	662.1	8.14 (d, J = 8.9 Hz, 2H), 7.49 (d, J = 8.9 Hz, 2H), 5.54 (d, J = 4.6 Hz, 1H), 5.17 (s, 2H), 4.25 (d, J =

实施例	Y	分子量	立体化学	制备方法	质 谱	1H NMR 峰 值 (CD_3OD)
						7.9 Hz, 1H)
7	(4-氯苯基) 甲基	651.07	Z	B, L	651.1	7.32 (m, 4H), 5.65 (d, J = 4.2 Hz, 1H), 5.20 (d, J = 6 Hz, 1H), 5.02 (AB 四重峰, Δv = 10.8 Hz, J = 12.8 Hz, 2H)
8	(4-氯苯基) 甲基	651.07	E	B, L	651.1	7.28 (s, 4H), 5.55 (d, J = 4.6 Hz, 1H), 5.03 (s, 2H), 4.26 (d, J = 7.7 Hz, 1H)
9	(4-甲基苯基) 甲基	630.66	Z	B, L	631.2	7.2 (d, J = 8 Hz, 2H), 7.1 (d, J = 8 Hz, 2H), 5.64 (d, J = 4.4 Hz, 1H), 5.18 (d, J = 6.4 Hz, 1H), 4.98 (AB 四重峰, Δv = 15.7 Hz, J = 12.1 Hz, 2H)
10	(4-甲基苯基) 甲基	630.66	E	B, L	631.2	7.17 (d, J = 8 Hz, 2H), 7.10 (d, J = 8 Hz, 2H), 5.55 (d, J = 4.4 Hz, 1H), 4.99 (s, 2H), 4.25 (d, J = 7.9 Hz, 1H), 2.28 (s, 3H)
11	(4-甲氧苯基) 甲基	646.65	Z	B, L	647.2	7.27 (d, J = 8.7 Hz, 2H), 6.87 (d, J = 8.7 Hz, 2H), 5.64 (d, J = 4.4 Hz, 1H), 5.16 (d, J = 6.2 Hz, 1H), 4.95 (AB 四重峰, Δv = 16.0 Hz, J = 11.7 Hz, 2H)
12	(4-甲氧苯基) 甲基	646.65	E	B, L	647.2	7.22 (d, J = 8.3 Hz, 2H), 6.83 (d, J = 8.5 Hz, 2H), 5.55 (d, J = 4.6 Hz, 1H), 4.97 (s, 2H), 4.26 (d, J = 7.9 Hz, 1H), 3.75 (s, 3H)
13	(3, 4-二氯苯基) 甲基	685.52	Z	B, L	685.1, 687.1	7.51 (d, J = 1.9 Hz, 1H), 7.45 (d, J = 8.3 Hz, 1H), 7.26 (dd, J = 8.3, 2.1 Hz, 1H), 5.65 (d, J = 4.4 Hz, 1H), 5.22 (d, J = 6.2 Hz, 1H), 5.00 (AB 四重峰, Δv = 7.3 Hz, J = 13.3 Hz, 2H)
14	(3, 4-二氯苯基) 甲基	685.52	E	B, L	685.1, 687.1	7.44 (m, 2H), 7.23 (m, 1H), 5.55 (d, J = 4.4 Hz, 1H), 5.02 (s, 2H), 4.25 (d, J = 7.7 Hz, 1H)
15	4-吡啶基甲基	617.62	E	B, L	618.1	8.43 (d, J = 5.8 Hz, 2H), 7.32 (d, J = 5.8 Hz, 2H), 5.56 (d, J = 4.6 Hz, 1H), 5.13 (s, 2H), 4.25 (d, J = 7.7 Hz, 1H)
16	苯甲基	616.63	Z	B, L	617.2	7.34 (m, 5H), 5.65 (d, J = 4.4 Hz, 1H), 5.21 (d, J =

实施例	Y	分子量	立体化学	制备方法	质 谱	1H NMR 峰 值 (CD_3OD)
						6.2 Hz, 1H), 5.04 (AB 四重峰, Δv = 14.4 Hz, J = 12.3 Hz, 2H)
17	苯甲基	616.63	E	B, L	617.2	7.32 (m, 5H), 5.55 (d, J = 4.6 Hz, 1H), 5.05 (s, 2H), 4.26 (d, J = 7.7 Hz)
18	环己基甲基	622.68	Z	C, L	623.2	5.65 (d, J = 4.2 Hz, 1H), 5.16 (d, J = 6.2 Hz, 1H), 3.78 (m, 2H), 1.72 (m, 6H), 1.22 (m, 3H), 0.96 (m, 2H)
19	环己基甲基	622.68	E	C, L	623.2	5.55 (d, J = 4.6 Hz, 1H), 4.24 (d, J = 7.9 Hz, 1H), 3.82 (m, 2H), 1.68 (m, 6H), 1.21 (m, 3H), 0.94 (m, 2H)
20	2-吡啶基甲基	617.62	Z	C, L	618.1	8.49 (bd, J = 4.8 Hz, 1H), 7.82 (ddd, 清晰的 td, J = 7.7, 1.7 Hz, 1H), 7.45 (d, J = 7.9 Hz, 1H), 7.32 (m, 1H), 5.66 (d, J = 4.2 Hz, 1H), 5.24 (d, J = 6.2 Hz, 1H), 5.15 (AB 四重峰, Δv = 10.9 Hz, J = 14.1 Hz, 2H)
21	2-吡啶基甲基	617.62	E	C, L	618.1	8.45 (bd, J = 5.0 Hz, 1H), 7.79 (ddd, 清晰的 td, J = 7.8, 1.7 Hz, 1H), 7.40 (d, J = 7.9 Hz, 1H), 7.31 (dd, J = 7.6 Hz, 4.9 Hz, 1H), 5.56 (d, J = 4.6 Hz, 1H), 5.15 (s, 2H), 4.25 (d, J = 7.7 Hz, 1H)
22	(4-氟苯基) 甲基	634.62	Z	C, L	635.1	7.36 (dd, J = 8,5 Hz, 2H), 7.04 (dd, 清晰的三重峰 , J = 8.8 Hz, 2H), 5.65 (d, J = 4.2 Hz, 1H), 5.20 (d, J = 6.4 Hz, 1H), 5.01 (AB 四重峰, Δv = 12.0 Hz, J = 12.6 Hz, 2H)
23	(4-氟苯基) 甲基	634.62	E	C, L	635.1	7.32 (dd, J = 8.5, 5.4 Hz, 2H), 7.01 (dd, 清晰的 t, J = 8.9 Hz, 2H), 5.55 (d, J = 4.36 Hz, 1H), 5.02 (s, 2H), 4.25 (d, J = 7.9 Hz, 1H)
24	(2, 4-二氯苯基) 甲基	685.52	E	C, L	685.1; 687.0	7.42 (d, J = 2.1 Hz, 1H), 7.34 (d, J = 8.3 Hz, 1H), 7.26 (dd, J = 8.3, 2.1 Hz, 1H), 5.56 (d, J = 4.6 Hz, 1H), 5.13 (s, 2H), 4.26 (d, J = 7.7 Hz, 1H)

实施例	Y	分子量	立体化学	制备方法	质 谱	1H NMR 峰 值 (CD_3OD)
25	(2,4-二氯苯基)甲基	685.52	Z	C, L	685.1; 687.0	7.46 (d, J = 8.3 Hz, 1H), 7.43 (d, J = 1.9 Hz, 1H), 7.30 (dd, J = 8.3, 2.1 Hz, 1H), 5.66 (d, J = 4.2 Hz, 1H), 5.25 (d, J = 6.4 Hz, 1H), 5.11 (AB 四重峰, Δv = 9.1 Hz, J = 14.0 Hz, 2H)
26	(2,3,4,5,6-五氟苯基)-甲基	706.58	E	C, L	707.2	5.54 (d, J = 4.6 Hz, 1H), 5.16 (s, 2H), 4.21 (d, J = 7.9 Hz, 1H)
27	(3,4-二氟苯基)甲基)	652.61	E	C, L	653.2	7.17 (m, 3H), 5.56 (d, J = 4.4 Hz, 1H), 5.02 (s, 2H), 4.25 (d, J = 7.9 Hz, 1H)
28	(4-三氟甲苯基)甲基	684.63	E	C, L	685.2	7.58 (d, J = 8.1 Hz, 2H), 7.46 (d, J = 7.9 Hz, 2H), 5.54 (d, J = 4.4 Hz, 1H), 5.13 (s, 2H), 4.24 (d, J = 7.9 Hz, 1H)
29	(3-三氟甲基苯基)甲基	684.63	E	C, L	685.2	7.57 (m, 3H), 7.49 (m, 1H), 5.55 (d, J = 4.4 Hz, 1H), 5.12 (s, 2H), 4.25 (d, J = 7.7 Hz, 1H)
30	(2-氯苯基)甲基	651.07	E	C, L	651.2; 653.1	7.35 (m, 2H), 7.24 (m, 2H), 5.56 (d, J = 4.6 Hz, 1H), 5.17 (s, 2H), 4.26 (d, J = 7.9 Hz, 1H)
31	(2,3-二氯苯基)甲基	685.52	E	C, L	685.1; 687.1	7.42 (d, J = 7.7 Hz, 1H), 7.27 (m, 2H), 5.55 (d, J = 4.6 Hz, 1H), 5.17 (s, 2H), 4.25 (d, J = 7.7 Hz, 1H)
32	(4-乙酰氨基苯基)甲基	673.68	E	C, L	674.2	7.47 (d, J = 8.3 Hz, 2H), 7.24 (d, J = 8.3 Hz, 2H), 5.55 (d, J = 4.6 Hz, 1H), 5.00 (s, 2H), 4.25 (d, J = 7.9 Hz, 1H)
33	2-吡嗪基甲基	618.6	E	C, L	619.2	8.59 (s, 1H), 8.54 (bs, 1H), 8.50 (bs, 1H), 5.55 (d, J = 4.4 Hz, 1H), 5.21 (s, 2H), 4.24 (d, J = 7.7 Hz, 1H)
34	4-嘧啶基甲基	618.6	E	C, L	619.2	9.03 (s, 1H), 8.67 (bd, J = 5.2 Hz, 1H), 7.40 (d, J = 5.2 Hz, 1H), 5.56 (d, J = 4.4 Hz, 1H), 5.15 (s, 2H), 4.25 (d, J = 7.5 Hz, 1H)
35	4-嘧啶基甲基	618.6	Z	C, L	619.2	9.07 (s, 1H), 8.73 (m, 1H), 7.57 (d, J = 5.2 Hz, 1H), 5.68 (d, J = 4.2 Hz, 1H), 5.29 (d, J = 6.4 Hz, 1H), 5.16 (bs, 2H)

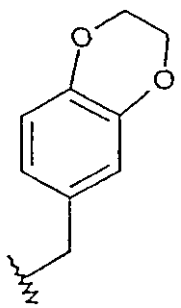
实施例	Y	分子量	立体化学	制备方法	质 谱	1H NMR 峰值 (CD_3OD)
36	[4-(叔丁氧羰基)苯基]甲基	716.75	E	C, L	717.3	7.88 (d, J = 8 Hz, 2H), 7.36 (d, J = 8 Hz, 2H), 5.55 (d, J = 4.6 Hz, 1H), 5.12 (s, 2H), 4.25 (d, J = 7.7 Hz, 1H), 1.57 (s, 9H)
37	3-氨基-5-噻唑基甲基	638.66	E	C, L	639.1	6.44 (s, 1H), 5.55 (d, J = 4.4 Hz, 1H), 4.26 (d, J = 7.9 Hz, 1H)
38	[3-(叔丁氧羰基氨基)苯基]甲基	731.76	E	E, L	732.3	7.36 (bs, 1H), 7.29 (bd, J = 8.5 Hz, 1H), 7.18 (dd, 清晰的 t, J = 7.9 Hz, 1H), 6.94 (d, J = 7.7 Hz, 1H), 5.56 (d, J = 4.6 Hz, 1H), 5.01 (s, 2H), 4.26 (d, J = 7.9 Hz, 1H), 1.49 (s, 9H)
39	3-呋喃基甲基	606.59	E	E, L	607.2	7.46 (s, 1H), 7.40 (s, 1H), 6.41 (s, 1H), 5.56 (d, J = 4.6 Hz, 1H), 4.92 (s, 2H), 4.26 (d, J = 7.9 Hz, 1H)
40	苯甲基	616.63	E	F, L	617.3	7.28 (m, 5H), 5.55 (d, J = 4.6 Hz, 1H), 5.05 (s, 2H), 4.26 (d, J = 7.9 Hz, 1H)
41		660.64	E	F, L	661.3	6.76 (m, 2H), 6.70 (d, J = 7.7 Hz, 1H), 5.88 (s, 2H), 5.53 (d, J = 4.6 Hz, 1H), 4.92 (s, 2H), 4.24 (d, J = 7.7 Hz, 1H)
42		660.64	Z	F, L	661.2	6.83 (d, J = 0.4 Hz, 1H), 6.79 (d, J = 7.9 Hz, 1H), 6.73 (dd, J = 7.9, 0.4 Hz, 1H), 5.88 (s, 2H), 5.62 (d, J = 4.4 Hz, 1H), 5.15 (d, J = 6.2 Hz, 1H), 4.90 (AB 四重峰, Δν = 14.0 Hz, J = 12.0 Hz, 2H)
43	4-联苯基甲基	692.73	E	E, L	693.1	7.57 (m, 4H), 7.39 (m, 4H), 7.31 (m, 1H), 5.56 (d, J = 4.6 Hz, 1H), 5.10 (s, 2H), 4.28 (d, J = 7.9 Hz, 1H)
44	二苯甲基	692.73	E	E, L	693.1	7.24 (m, 10H), 6.14 (s, 1H), 5.52 (d, J = 4.4 Hz, 1H), 4.21 (d, J = 7.9 Hz,

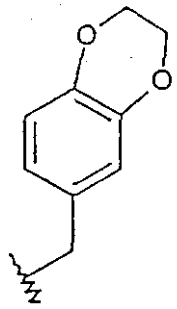
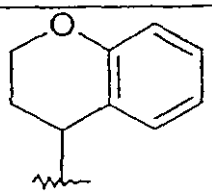
实施例	Y	分子量	立体化学	制备方法	质 谱	1H NMR 峰 值 (CD_3OD)
						1H)
45	(4-羧基苯基)甲基	660.64	E	I (使用实施例36的产物), N	661.2	7.94 (d, J = 8.1 Hz, 2H), 7.38 (d, J = 8.1 Hz, 2H), 5.55 (d, J = 4.4 Hz, 1H), 5.13 (s, 2H), 4.26 (d, J = 7.7 Hz, 1H)
46	(4-环己基苯基)甲基	698.8	E	F, J	699.1	7.20 (d, J = 8.3 Hz, 2H), 7.13 (d, J = 8.1 Hz, 2H), 5.55 (d, J = 4.6 Hz, 1H), 5.01 (s, 2H), 4.26 (d, J = 7.9 Hz, 1H), 2.46 (m, 1H), 1.81 (m, 4H), 1.75 (m, 1H),1.41 (m, 4H), 1.28 (m, 1H)
47	(4-环己基苯基)甲基	698.8	Z	F, J	699.3	7.16 (m, 4H), 5.65 (d, J = 4.2 Hz, 1H), 5.19 (d, J = 6.2 Hz, 1H), 4.99 (AB 四重峰, Δv = 15.6 Hz, J = 12.0 Hz, 2H), 2.46 (m, 1H), 1.82 (m, 4H), 1.74 (m, 1H), 1.42 (m, 4H), 1.27 (m, 1H)
48	2-呋喃基甲基	606.59	Z	E, L	607.2	7.46 (s, 1H), 6.37 (m, 2H), 5.64 (d, J = 4.4 Hz, 1H), 5.12 (d, J = 6.2 Hz, 1H), 4.95 (AB 四重峰, Δv = 9.5 Hz, J = 13.1 Hz, 2H)
49	2-呋喃基甲基	606.59	E	E, L	607.2	7.43 (s, 1H), 6.35 (m, 2H), 5.55 (d, J = 4.4 Hz, 1H), 4.96 (s, 2H), 4.26 (d, J = 7.9 Hz, 1H)
50	(3-氟苯基)甲基	634.62	Z	G, L	635.2	7.32 (m, 1H), 7.15 (m, 1H), 7.11 (bd, J = 8 Hz, 1H), 6.99 (bdd, 清晰的 bt, J = 8.3 Hz, 1H), 5.66 (d, J = 4.2 Hz, 1H), 5.24 (d, J = 6.4 Hz, 1H), 5.04 (AB 四重峰, Δv = 9.9 Hz, J = 13.2 Hz, 2H)
51	(4-乙酰氨基-3, 5-二氯苯基)甲基	742.57	E	F, L	742.0; 743.9	7.37 (s, 2H), 5.54 (d, J = 4.6 Hz, 1H), 5.00 (s, 2H), 4.23 (d, J = 7.9 Hz, 1H), 2.13 (s, 3H)
52	[4-[(叔丁氧羰基氨基)-甲基]丁基]甲基	745.79	E	E, L	746.1	7.24 (AB 四重峰, Δv = 18.4 Hz, J = 8.1 Hz, 4H), 5.55 (d, J = 4.6 Hz, 1H), 5.03 (s, 2H), 4.25 (d, J = 7.7 Hz, 1H) 4.19 (s, 2H), 1.43 (s, 9H)
53		745.79	Z	E, L	746.1	7.27 (AB 四重峰, Δv =

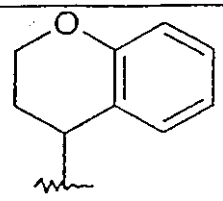
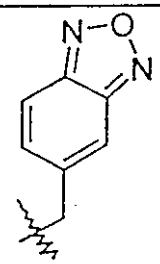
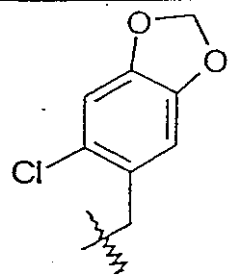
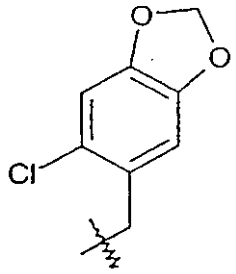
实施例	Y	分子量	立体化学	制备方法	质谱	1H NMR 峰值 (CD_3OD)
	[4-(叔丁氧羰基氨基)甲基]苯基]甲基					28.3 Hz, J = 8.1 Hz, 4H), 5.64 (d, J = 4.4 Hz, 1H), 5.20 (d, J = 6.4 Hz, 1H), 5.01 (AB 四重峰 Δν = 13.9 Hz, J = 12.3 Hz, 2H), 4.20 (s, 2H), 1.44 (s, 9H)
54	(3-氨基苯基) 甲基	631.64	E	I (使用实施例38的产物), L	632.1	7.07 (t, J = 7.7 Hz, 1H), 6.76 (bs, 1H), 6.70 (m, 2H), 5.54 (d, J= 4.6 Hz, 1H), 4.95 (s, 2H), 4.24 (d, J = 7.9 Hz, 1H)
55	(4-氨基甲基苯基) 甲基	645.67	E	I (使用实施例52的产物), L	645.9	7.26 (s, 4H), 5.52 (d, J = 4.6 Hz, 1H), 5.02 (s, 2H), 4.22 (d, J = 7.9 Hz, 1H), 3.75 (s, 2H)
56	3- (4-氯苯基) 丙-1-基	679.13	Z	E, J	679.2; 681.2	7.24 (d, J = 8.3 Hz, 2H), 7.16 (d, J = 8.3 Hz, 2H), 5.67 (d, J = 4.2 Hz, 1H), 5.17 (d, J = 6.4 Hz, 1H), 4.00 (m, 2H), 2.68 (t, J = 7.6 Hz, 2H), 1.91 (m, 2H)
57	3- (4-氯苯基) 丙-1-基	679.13	E	E, J	679.2; 681.2	7.21 (d, J = 8.3 Hz, 2H), 7.12 (d, J = 8.5 Hz, 2H), 5.56 (d, J = 4.6 Hz, 1H), 4.26 (d, J = 7.7 Hz, 1H), 4.02 (t, J = 6.3 Hz, 2H), 2.62 (t, J = 7.6 Hz, 2H), 1.90 (m, 2H)
58	2-苯并咪唑基甲基	656.65	E	E, L	657.2	7.52 (m, 2H), 7.21 (m, 2H), 5.57 (d, J = 4.6 Hz, 1H), 5.27 (s, 2H), 4.28 (d, J = 7.9 Hz, 1H)
59	2-苯并咪唑基甲基	656.65	Z	E, L	657.1	7.54 (m, 2H), 7.22 (m, 2H), 5.67 (d, J = 4.4 Hz, 1H), 5.33 (d, J = 6.8 Hz, 1H), 5.27 (s, 2H)
60	2-苯乙基	630.66	Z	E, J	631.1	7.22 (m, 5H), 5.63 (d, J = 4.2 Hz, 1H), 5.09 (d, J = 6.2 Hz, 1H), 4.15 (m, 2H), 2.90 (t, J = 7.0 Hz, 2H)
61	2-苯乙基	630.66	E	E, J	631.1	7.12 (m, 5H), 5.53 (d, J = 4.6 Hz, 1H), 4.27 (d, J = 7.7 Hz, 1H), 4.17 (t, J = 6.7 Hz, 2H), 2.85 (t, J = 6.8 Hz, 2H)
62		700.62	E	E, L	701	7.39 (t, J = 7.9 Hz, 1H),

实施例	Y	分子量	立体化学	制备方法	质谱	1H NMR 峰值 (CD_3OD)
	[3-（三氟甲氧基）苯基]甲基					7.30 (d, J = 7.9 Hz, 1H), 7.20 (bs, 1H), 7.16 (bd, J = 8.1 Hz, 1H), 5.55 (d, J = 4.6 Hz, 1H), 5.09 (s, 2H), 4.25 (d, J = 7.9 Hz, 1H)
63	（3-氰基苯基）甲基	641.64	E	E, L	642.1	7.61 (m, 3H), 7.46 (dd, 清晰的 t, J = 7.7 Hz, 1H), 5.53 (d, J = 4.6 Hz, 1H), 5.08 (s, 2H), 4.23 (d, J = 7.9 Hz, 1H)
64	(3, 4-二甲氧苯基）甲基	676.68	E	E, L	677.1	6.90 (m, 2H), 6.84 (s, 1H), 5.53 (d, J = 4.6 Hz, 1H), 4.96 (s, 2H), 4.25 (d, J = 7.9 Hz, 1H), 3.77 (s, 3H), 3.76 (s, 3H)
65	2-苯并呋喃基甲基	656.65	E	E, L	657.1	7.51 (d, J = 7.7 Hz, 1H), 7.39 (d, J = 8.1 Hz, 1H), 7.22 (m, 1H), 7.15 (m, 1H), 6.71 (s, 1H), 5.53 (d, J = 4.6 Hz, 1H), 5.11 (s, 2H), 4.26 (d, J = 7.9 Hz, 1H)
66	2-苯并呋喃基甲基	656.65	Z	E, L	657.1	7.53 (d, J = 7.1 Hz, 1H), 7.42 (d, J = 8.3 Hz, 1H), 7.24 (m, 1H), 7.17 (m, 1H), 6.75 (s, 1H), 5.62 (d, J = 4.2 Hz, 1H), 5.17 (d, J = 6.2 Hz, 1H), 5.10 (AB 四重峰, Δv = 6.9 Hz, J = 13.7 Hz, 2H)
67	(3, 4-二甲氧苯基）甲基	676.68	Z	E, L	677.1	6.88 (m, 3H), 5.62 (d, J = 4.2 Hz, 1H), 5.17 (d, J = 6.4 Hz, 1H), 4.94 (AB 四重峰, Δv = 17.2 Hz, J = 12.0 Hz, 2H), 3.80 (s, 3H), 3.79 (s, 3H)
68	[3-(三氟甲氧基）苯基]甲基	700.63	Z	E,L	701.O	7.40 (m, 1H), 7.34 (bd, J = 6.4 Hz, 1H), 7.27 (bs, 1H), 7.16 (m, 1H), 5.66 (d, J = 3.9 Hz, 1H), 5.23 (d, J = 6.2 Hz, 1H), 5.07 (AB 四重峰, Δv = 9.2 Hz, J = 13.1 Hz, 2H)
69	2-苯胺基乙基	645.67	Z	E, L	646.2	7.08 (dd, J = 8.5, 7.5 Hz, 2H), 6.66 (dd, J = 8.6, 0.9 Hz, 2H), 6.62 (t, J = 7.3 Hz, 1H), 5.62 (d, J = 4.2 Hz, 1H), 5.18 (d, J = 6.4 Hz, 1H), 4.15 (m, 2H), 3.27 (m, 2H)

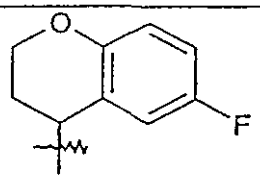
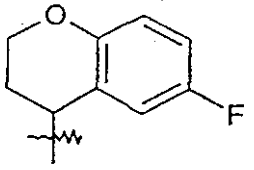
实施例	Y	分子量	立体化学	制备方法	质谱	1H NMR 峰值 (CD_3OD)
70	2-苯胺基乙基	645.67	E	E, L	646.1	7.04 (dd, J = 8.6, 7.4 Hz, 2H), 6.60 (dd, J = 8.6, 0.9 Hz, 2H), 6.56 (t, J = 7.4 Hz, 1H), 5.55 (d, J = 4.6 Hz, 1H), 4.25 (d, J = 7.7 Hz, 1H), 4.16 (m, 2H), 3.31 (m, 2H)
71	[4-(1-哌啶子基)苯基]甲基	699.76	E	H, J	700.1	7.15 (d, J = 8.5 Hz, 2H), 6.87 (d, J = 8.7 Hz, 2H), 5.52 (d, J = 4.6 Hz, 1H), 4.92 (s, 2H), 4.24 (d, J = 7.7 Hz, 1H), 3.06 (dd, J = 5.4, 5.4 Hz, 4H), 1.65 (m, 4H), 1.54 (m, 2H)
72	[4-(1-哌啶子基)苯基]甲基	699.76	Z	H, J	700.1	7.23 (d, J = 8.8 Hz, 2H), 6.93 (d, J = 8.8 Hz, 2H), 5.63 (d, J = 4.3 Hz, 1H), 5.15 (d, J = 6.4 Hz, 1H), 4.93 (AB四重峰, Δv = 17.3 Hz, J = 11.8 Hz, 2H), 3.11 (dd, J = 5.4, 5.4 Hz, 4H), 1.69 (m, 4H), 1.58 (m, 2H)
73	3-苯基丙-1-基	644.68	Z	E, J	645.1	7.20 (d, J = 7.3 Hz, 2H), 7.13 (m, 3H), 5.64 (d, J = 4.2 Hz, 1H), 5.18 (d, J = 6.4 Hz, 1H), 3.97 (m, 2H), 2.65 (t, J = 7.7 Hz, 2H), 1.90 (m, 2H)
74	3-苯基丙-1-基	644.68	E	E, J	645.1	7.18 (d, J = 7.3 Hz, 2H), 7.11 (m, 3H), 5.54 (d, J = 4.4 Hz, 1H), 4.24 (d, J = 7.9 Hz, 1H) 4.01 (t, J = 6.3 Hz, 2H), 2.61 (t, J = 7.7 Hz, 2H), 1.89 (m, 2H)
75	(2-氟苯基)甲基	634.62	Z	G, L	635.2	7.44 (清晰的 , J = 7.5, 1.8 Hz, 1H), 7.30 (m, 1H), 7.14 (m, 1H), 7.06 (dd, J = 10.2, 8.3 Hz, 1H), 5.65 (d, J = 4.2 Hz 1H), 5.20 (d, J = 6.4 Hz, 1H), 5.11 (AB 四重峰, Δv = 9.1 Hz, J = 12.9 Hz, 1H)
76	(2-氟苯基)甲基	634.62	E	G, L	635.2	7.36 (清晰的 , J = 7.5, 1.5 Hz, 1H), 7.28 (m, 1H), 7.12 (m, 1H), 7.04 (dd, J = 10.1, 8.4 Hz, 1H), 5.55 (d, J = 4.6 Hz, 1H), 5.12 (s, 2H), 4.26 (d, J = 7.9 Hz,

实施例	Y	分子量	立体化学	制备方法	质谱 spec	1H NMR 峰值 (CD_3OD)
						1H)
77	2-(苯硫基)乙基	662.71	Z	F, J	663.1	7.35 (d, J = 7.3 Hz, 2H), 7.26 (dd, 清晰的 t, J = 7.7 Hz, 2H), 7.15 (m, 1H), 5.63 (d, J = 4.4 Hz, 1H), 5.09 (d, J = 6.2 Hz, 1H), 4.10 (t, J = 6.9 Hz, 2H), 3.15 (t, J = 6.7 Hz, 2H)
78	2-(苯硫基)乙基	662.71	E	F, J	663.1	7.31 (d, J = 7.3 Hz, 2H), 7.22 (m, 2H), 7.10 (m, 1H), 5.55 (d, J = 4.4 Hz, 1H), 4.23 (d, J = 7.9 Hz, 1H), 4.18 (m, 2H), 3.12 (m, 2H)
79	5-苯并呋喃基甲基	656.64	E	F, K	657.1	7.69 (d, J = 2.3 Hz, 1H), 7.54 (bs, 1H), 7.39 (d, J = 8.5 Hz, 1H), 7.23 (dd, J = 8.6, 1.6 Hz, 1H), 6.76 (m,1H), 5.53 (d, J = 4.6 Hz, 1H), 5.11 (s, 2H), 4.25 (d, J = 7.9 Hz, 1H)
80	5-苯并呋喃基甲基	656.64	Z	F, K		7.71 (d, J = 2.3 Hz, 1H), 7.59 (bs, 1H), 7.43 (d, J = 8.5 Hz, 1H), 7.29 (dd, J = 8.5, 1.5 Hz, 1H), 6.79 (m, 1H), 5.62 (d, J = 4.2 Hz, 1H), 5.18 (d, J = 6.4 Hz, 1H), 5.10 (AB四重峰, Δv = 15.0 Hz, J = 11.9 Hz, 2H)
81	2-苯基-5-嘧啶基甲基	694.69	Z	F, M	695.1	8.82 (s, 2H), 8.36 (m, 2H), 7.46 (m, 3H), 5.63 (d, J = 4.4 Hz, 1H), 5.2 (d, J 模糊的 , 1H), 5.10 (s, 2H)
82	2-苯基-5-嘧啶基甲基	694.69	E	F, M	695.1	8.75 (s, 2H), 8.33 (m, 2H), 7.45 (m, 3H), 5.52 (d, J = 4.6 Hz, 1H), 5.10 (s, 2H), 4.25 (d, J = 7.9 Hz, 1H)
83		674.66	Z	F, L	675.1	6.83 (d, J = 1.9 Hz, 1H), 6.78 (AB四重峰, Δv = 14.1 Hz, J = 8.2 Hz, 2H), 5.64 (d, J = 4.2 Hz, 1H), 5.16 (d, J = 6.2 Hz, 1H), 4.90 (AB四重峰, Δv = 15.2 Hz, J = 11.8 Hz, 2H), 4.20 (s, 4H)

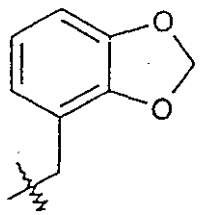
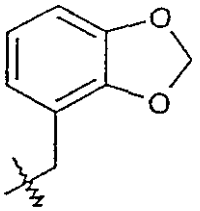
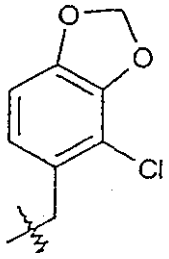
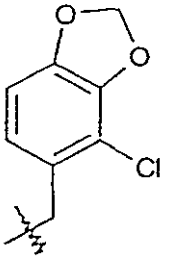
实施例	Y	分子量	立体化学	制备方法	质谱	1H NMR 峰值 (CD_3OD)
84		674.66	E	F, L	675.2	[D_2O] 6.73 (m, 3H), 5.51 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.14 (s, 4H), 4.06 (d, J = 7.9 Hz, 1H)
85	（3-氟-4-甲氧苯基）甲基	664.65	E	E, L	665.1	7.05 (m, 2H), 7.00 (dd, 清晰的 t, J = 8.2 Hz, 1H), 5.56 (d, J = 4.6 Hz, 1H), 4.97 (s, 2H), 4.26 (d, J = 7.9 Hz, 1H)
86	（3-氟-4-甲氧苯基）甲基	664.65	Z	E, L	665.1	7.13 (m, 1H), 7.09 (bd, J = 6.8 Hz, 1H), 7.03 (m, 1H), 5.65 (d, J = 4.2 Hz, 1H), 5.19 (d, J = 6.4 Hz, 1H), 4.95 (AB 四重峰, Δν = 12.2 Hz, J = 12.3 Hz, 2H)
87	2-苯氧乙基	646.65	Z	E, J	647.2	7.25 (dd, 清晰的 t, J = 7.3 Hz, 2H), 6.93 (m, 3H), 5.64 (d, J = 4.2 Hz, 1H), 5.13 (d, J = 6.0 Hz, 1H), 4.33 (m, 2H), 4.18 (m, 2H)
88	2-苯氧乙基	646.65	E	E, J	647.2	7.21 (dd, 清晰的 t, J = 7.7 Hz, 2H), 6.88 (m, 3H), 5.56 (d, J = 4.6 Hz, 1H), 4.34 (m, 2H), 4.27 (d, J = 7.9 Hz, 1H), 4.15 (m, 2H)
89	（3-氟苯基）甲基	634.62	E	G, L	635.1	7.30 (m, 1H), 7.11 (m, 1H), 7.03 (bd, J = 9.7 Hz, 1H), 6.98 (bdd, 清晰的 bt, J = 8.6 Hz, 1H), 5.56 (d, J = 4.6 Hz, 1H), 5.06 (s, 2H), 4.26 (d, J = 7.9 Hz, 1H)
90		658.66	Z; 主要和次要的非对映体	F, J	659.2	7.33 (dd, J = 7.6, 1.8 Hz) 和 7.25 (d, J = 7.7 Hz) [1H], 7.15 (m, 1H), 6.85 (m, 1H), 6.75 (d, J = 8.3 Hz, 1H), 5.61 (d, J = 4.4 Hz) 和 5.59 (d, J = 4.4 Hz) [1H], 5.11 (d, J = 6.4 Hz) 和 5.14 (d, J = 6.8 Hz)[1H], 5.07 (m) 和 5.02 (m) [1H], 4.15 (m, 2H), 2.21 (bd, J = 14.5 Hz) 和 2.29 (bd, J = 14.9 Hz)[1H],

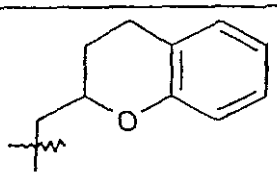
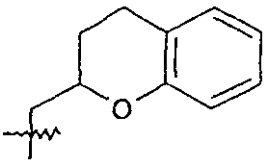
实施例	Y	分子量	立体化学	制备方法	质谱	1H NMR 峰值 (CD_3OD)
						2.03 (m, 1H)
91		658.66	E; 2种非对映体的混合物	F, J	659.2	7.22 (m, 1H), 7.12 (m, 1H), 6.80 (m, 1H), 6.72 (d, J = 8.1 Hz, 1H), 5.56 (d, J = 3.5 Hz, 1H), 5.06 (m, 1H), 4.30 (d, J = 7.5 Hz) 和 4.30 (d, J = 7.9 Hz) [1H], 4.15 (m, 2H), 2.23 (bd, J = 12.9 Hz) 和 2.20 (bd, J = 13.6 Hz) [1H], 2.01 (m, 1H)
92	(3-氯苯基) 甲基	651.07	E	D, L	651.1; 653.1	7.29 (bs, 1H), 7.23 (m, 3H), 5.54 (d, J = 4.4 Hz, 1H), 5.02 (s, 2H), 4.24 (d, J = 7.9 Hz, 1H)
1A		658.63	E	E, L	659.1	(DMSO-d_6) 8.01 (d, J = 9.3 Hz, 1H), 7.87 (s, 1H), 7.51 (d, J = 9.1 Hz, 1H), 5.56 (d, J = 4.2 Hz, 1H), 5.17 (s, 2H), 4.10 (d, J = 7.9 Hz, 1H)
2A		695.08	E	F, L	695.1; 697.1	(DMSO-d_6) 7.04 (s, 1H), 6.92 (s, 1H), 6.02 (s, 2H), 5.53 (d, J = 4.6 Hz, 1H), 4.96 (s, 2H), 4.07 (d, J = 7.9 Hz, 1H)
3A		695.08	Z	F, L	695.1; 697.1	6.96 (s, 1H), 6.86 (s, 1H), 5.97 (s, 2H), 5.66 (d, J = 4.2 Hz, 1H), 5.23 (模糊的，推测的 d, 1H), 5.04 (AB四重峰, Δv = 8.1 Hz, J = 13.2 Hz, 2H)
4A	(3, 5-二氯苯基) 甲基	685.52	Z	F, L	685.0; 687.0	7.30 (bs, 3H), 5.64 (d, J = 4.4 Hz, 1H), 5.22 (d, J = 6.4 Hz, 1H), 4.99 (bs, 2H)
5A	(3, 5-二氯苯基) 甲基	685.52	E	F, L	685.1; 687.1	7.30 (t, J = 2.0 Hz, 1H), 7.24 (d, J = 1.9 Hz, 2H), 5.53 (d, J = 4.4 Hz, 1H), 5.01 (s, 2H), 4.24 (d, J = 7.9 Hz, 1H)
6A		682.69	E	F, L	683.1	7.64 (d, J = 1.9 Hz, 1H),

实施例	Y	分子量	立体化学	制备方法	质谱	1H NMR 峰值 (CD_3OD)
	4-苯基-3-呋喃基甲基					7.59 (bs, 1H), 7.43 (bd, J = 8 Hz, 2H), 7.31 (bt, J = 8 Hz, 2H), 7.25 (m, 1H), 5.56 (d, J = 4.6 Hz, 1H), 5.00 (s, 2H), 4.27 (d, J = 7.9 Hz, 1H)
7A	4-苯基-3-呋喃基甲基	682.69	Z	F, L	683.1	7.66 (d, J = 1.7 Hz, 1H), 7.64 (bs, 1H), 7.50 (bd, J = 8 Hz, 2H), 7.38 (bt, J = 8 Hz, 2H), 7.29 (m, 1H), 5.64 (d, J = 4.2 Hz, 1H), 5.13 (d, J = 6.4 Hz, 1H), 4.98 (AB 四重峰, Δν = 21.6 Hz, J = 12.0 Hz, 2H)
8A	(3-[(叔丁氧羰基)氨基甲基]苯基)甲基	745.79	Z	F, L	746.1	7.26 (m, 3H), 7.20 (m, 1H), 5.66 (d, J = 4.4 Hz, 1H), 5.21 (d, J = 6 Hz, 1H), 5.03 (AB 四重峰, Δν = 13.4 Hz, J = 12.5 Hz, 2H), 4.21 (m, 2H)
9A	(3-[(叔丁氧羰基)氨基甲基]苯基)甲基	745.79	E	F, L	746.1	7.24 (m, 2H), 7.19 (m, 2H), 5.56 (d, J = 4.6 Hz, 1H), 5.05 (s, 2H), 4.26 (d, J = 7.9 Hz, 1H), 4.20 (m, 2H)
10A	(3-氯苯基) 甲基	651.07	Z	D, L	651.1; 653.1	7.35 (bs, 1H), 7.26 (m, 3H), 5.64 (d, J = 4.4 Hz, 1H), 5.21 (d, J = 6.4 Hz, 1H), 5.01 (AB 四重峰, Δν = 10.2 Hz, J = 13.0 Hz, 2H)
11A	(3, 5-二氟苯基) 甲基	652.61	E	F, L	653.1	6.90 (m, 2H), 6.82 (m, 1H), 5.56 (d, J = 4.6 Hz, 1H), 5.06 (s, 2H), 4.26 (d, J = 7.9 Hz, 1H)
12A	(5-氯-2-氟苯基)甲基	669.06	E	F, L	669.0; 671.0	7.34 (dd, J = 6.2, 2.6 Hz), 7.27 (ddd, J = 8.8, 4.5, 3.0 Hz, 1H), 7.05 (dd, 清晰的 t, J = 9.2 Hz, 1H), 5.54 (d, J = 4.4 Hz, 1H), 5.07 (s, 2H), 4.24 (d, J = 7.7 Hz, 1H)
13A	(3-氯-2-氟苯基)甲基	669.06	Z	E, L	669.0; 671.0	7.37 (清晰的 dd, J = 7.7, 6.9 Hz, 2H), 7.1 (m, 1H), 5.64 (d, J = 4.4 Hz, 1H), 5.19 (d, J = 6.2 Hz, 1H), 5.10 (bs, 2H)
14A	(3-氯-2-氟苯基)甲基	669.06	E	E, L	669.0; 671.0	7.36 (m, 1H), 7.28 (m, 1H), 7.08 (m, 1H), 5.54 (d, J = 4.4 Hz, 1H), 5.11 (s, 2H),

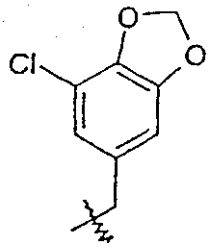
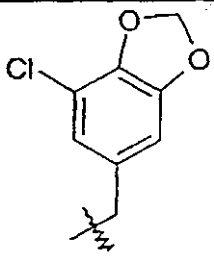
实施例	Y	分子量	立体化学	制备方法	质谱	1H NMR 峰值 (CD_3OD)
						4.23 (d, J = 7.7 Hz, 1H)
15A	(3, 5-二氟苯基）甲基	652.61	Z	F L	653.1	6.94 (m, 2H), 6.80 (tt, J = 9.2, 2.4 Hz, 1H), 5.64 (d, J = 4.2 Hz, 1H), 5.23 (d, J = 6.4 Hz, 5.02 (推测的AB四重峰 , J = 14 Hz, 2H)
16A		676.66	Z	F, L	677.2	7.12 (m, 1H), 6.93 (m, 1H), 6.77 (dd, J = 9.1, 4.8 Hz, 1H), 5.64 (d, J = 4.4 Hz, 1H), 5.16 (d, J = 6.6 Hz, 1H), 5.07 (m, 1H), 4.12 (m, 1H), 2.21 (m, 1H), 2.06 (m, 1H)
17A		676.66	E; 非对映体的混合物	F, L	677.2	7.00 (ddd, 清晰的 dt, J = 8.7, 2.8 Hz, 1H), 6.92 (m, 1H), 6.75 (dd, J = 8.9, 4.6 Hz, 1H), 5.60 和 5.59 (d, J = 4.4 and 4.6 Hz, 1H), 5.08 (m, 1H), 4.33 和 4.32 (d, J = 7.7 和 7.9 Hz, 1H), 4.22 (m, 1H), 4.04 (m, 1H), 2.22 (m, 1H), 2.03 (m, 1H)
18A	（3-氨基甲基苯基）甲基	645.67	E	I（使用实施例9A的产物）, L	646.1	7.29 (m, 4H), 5.56 (d, J = 4.6 Hz, 1H), 5.07 (s, 2H), 4.26 (d, J = 7.9 Hz, 1H), 3.84 (s, 2H)
19A	（3-氯-4-氟苯基）甲基	669.06	E	E, L	669.1; 671.1	7.39 (dd, J = 7.1, 2.1 Hz, 1H), 7.24 (ddd, J = 8.5, 4.8, 2.1 Hz, 1H), 7.14 (dd, J = 9.1, 8.5 Hz, 1H), 5.53 (d, J = 4.6 Hz, 1H), 4.99 (s, 2H), 4.23 (d, J = 7.9 Hz, 1H)
20A	2-喹啉基甲基	667.68	E	F, L	668.1	8.28 (d, J = 8.5 Hz, 1H), 7.98 (d, J = 8.5 Hz, 1H), 7.90 (d, J = 8.3 Hz, 1H), 7.74 (m, 1H), 7.57 (m, 1H), 7.52 (d, J = 8.5 Hz, 1H), 5.55 (d, J = 4.6 Hz, 1H), 5.33 (s, 2H), 4.27 (d, J =

实施例	Y	分子量	立体化学	制备方法	质谱	1H NMR 峰值 (CD_3OD)
						7.7 Hz, 1H)
21A	2-喹啉基甲基	667.68	Z	F, L	668.1	8.32 (d, J = 8.5 Hz, 1H), 8.12 (d, J = 8.3 Hz, 1H), 7.92 (d, J = 8.1 Hz, 1H), 7.76 (m, 1H), 7.59 (m, 1H), 7.53 (d, J = 8.5 Hz, 1H), 5.69 (d, J = 4.4 Hz, 1H), 5.36 (AB 四重峰, Δν = 16.4 Hz, J = 14.8 Hz, 2H), 5.28 (d, J = 6.4 Hz, 1H)
22A	(3-氯-4-氟苯基)甲基	669.06	Z	E, L	669.0; 671.0	7.46 (dd, J = 7.3, 2.1 Hz, 1H), 7.29 (ddd, J = 8.3, 4.7, 2.1 Hz, 1H), 7.17 (m, 1H), 5.64 (d, J = 4.2 Hz, 1H), 5.19 (d, J = 5.6 Hz, 1H), 4.98 (AB 四重峰, Δν = 7.7, J = 13.2 Hz, 2H)
23A	3-喹啉基甲基	667.68	Z	F, L	668.1	8.84 (bd, J = 1.9 Hz, 1H), 8.30 (bs, 1H), 7.99 (d, J = 8.7 Hz, 1H), 7.91 (d, J = 8.1 Hz, 1H), 7.73 (m, 1H), 7.58 (m, 1H), 5.63 (d, J = 4.4 Hz, 1H), 5.24 (m, 3H)
24A	3-喹啉基甲基	667.68	E	F, L	668.1	8.80 (bd, J = 2.1 Hz, 1H), 8.26 (bd, J = 1.5 Hz, 1H), 7.98 (d, J = 8.5 Hz, 1H), 7.89 (bd, J = 8.3 Hz, 1H), 7.73 (m, 1H), 7.58 (m, 1H), 5.53 (d, J = 4.6 Hz, 1H), 5.27 (s, 2H), 4.25 (d, J = 7.7 Hz, 1H)
25A	(4-氯-3-氟苯基)甲基	669.06	Z	F, L	669.1, 671.1	7.39 (dd, 清晰的 t, J = 7.9 Hz, 1H), 7.23 (m, 1H), 7.14 (m, 1H), 5.64 (d, J = 4.4 Hz, 1H), 5.21 (d, J = 6.4 Hz, 1H), 5.00 (AB 四重峰, Δν = 7.7 Hz, J = 13.3 Hz, 2H)
26A	(4-氯-3-氟苯基)甲基	669.06	E	F, L	669.1, 671.1	7.42 (dd, 清晰的 t, J = 7.9 Hz, 1H), 7.20 (dd, J = 10.1, 1.8 Hz, 1H), 7.14 (m, 1H), 5.59 (d, J = 4.6 Hz, 1H), 5.07 (s, 2H), 4.28 (d, J = 7.8 Hz, 1H)
27A	(3, 4, 5-三氟苯基)甲基	670.6	E	E, L	671.1	7.04 (dd, 清晰的 t, J = 7.6 Hz, 2H), 5.54 (d, J = 4.6 Hz, 1H), 4.99 (s, 2H), 4.23 (d, J = 7.9 Hz, 1H)

实施例	Y	分子量	立体化学	制备方法	质谱	1H NMR 峰值 (CD_3OD)
28A		660.64	Z	F, L	661.1	6.76 (m, 3H), 5.92 (s, 2H), 5.63 (d, J = 4.2 Hz, 1H), 5.16 (d, J = 6.4 Hz, 1H), 5.00 (AB 四重峰 Δν = 9.3 Hz, J = 12.5 Hz, 2H)
29A		660.64	E	F, L	661.1	6.73 (m, 3H), 5.89 (s, 2H), 5.54 (d, J = 4.6 Hz, 1H), 5.01 (s, 2H), 4:24 (d, J = 7.9 Hz, 1H)
30A		695.08	E	F, L	694.7; 696.4	[DMSO-d_6] 6.91 (d, J = 8.1 Hz, 1H), 6.84 (d, J = 8.3 Hz, 1H), 6.10 (s, 2H), 5.54 (d, J = 4.6 Hz, 1H), 4.99 (s, 2H), 4.08 (d, J = 7.9 Hz, 1H)
31A		695.08	Z	F, L	695.1; 697.1	6.96 (d, J = 8.1 Hz, 1H), 6.86 (d, J = 8.5 Hz, 1H), 6.03 (s, 2H), 5.65 (d, J = 4.2 Hz, 1H), 5.18 (d, J = 6.4 Hz, 1H), 5.05 (AB 四重峰, Δν = 15.3 Hz, J = 12.5 Hz, 2H)
32A	（5-氯-2-氟苯基）甲基	669.06	Z	F, L	669.2; 671.2	7.44 (dd, J = 6.3, 2.6 Hz, 1H), 7.27 (m, 1H), 7.06 (dd, J = 9.3, 8.9 Hz, 1H), 5.64 (d, J = 4.2 Hz, 1H), 5.20 (d, J = 6.2 Hz, 1H), 5.06 (bs, 2H)
33A	（4-氟苯基）甲基	634.62	E	F, L	635.2	7.31 (dd, J = 8.9, 5.6 Hz, 2H), 7.01 (dd, 清晰的 t, J = 8.8 Hz, 2H), 5.55 (d, J = 4.6 Hz, 1H), 5.02 (s, 2H), 4.25 (d, J = 7.9 Hz, 1H)
34A	（4-苯基-2-呋喃基）甲基	682.69	Z	F, L	683.2	7.87 (s, 1H), 7.54 (d, J = 7.6 Hz, 2H), 7.37 (dd, 清晰的 t, J = 7.6 Hz, 2H), 7.25 (t, J = 7.3 Hz, 1H), 6.80 (s, 1H), 5.68 (d, J = 4.3 Hz, 1H), 5.20 (d, J = 6.3 Hz, 1H), 5.02 (AB

实施例	Y	分子量	立体化学	制备方法	质 谱	1H NMR 峰 值 (CD_3OD)
						四重峰, Δv = 6.1 Hz, J = 13.3 Hz, 2H)
35A	(4-苯基-2-呋喃基) 甲基	682.69	E	F, L	683.2	7.86 (s, 1H), 7.54 (d, J = 8.2 Hz, 2H), 7.38 (dd, J = 7.9, 6.9 Hz, 2H), 7.26 (t, J = 6.9 Hz, 1H), 6.80 (s, 1H), 5.61 (d, J = 4.6 Hz, 1H), 5.05 (s, 2H), 4.33 (d, J = 7.6 Hz, 1H)
36A		672.69	Z	F, L	673.1	7.01 (m, 2H), 6.78 (m, 2H), 5.65 (d, J = 4.2 Hz, 1H), 5.12 (d, J = 6.2 Hz, 1H), 2.84 (m, 1H), 2.75 (m, 1H), 2.02 (m, 1H), 1.74 (m, 1H)
37A		672.69	E; 非对映体的混合物	F, L	673.1	6.97 (m, 1H), 6.88 (dd, J = 7.9, 2.1 Hz, 1H), 6.74 (dd, 清晰的 t, J = 7.5 Hz, 1H), 6.67 (m, 1H), 5.55 5.54 (d, 4.4 和 4.6 Hz, 1H), 4.26 和 4.25 (d, J = 7.7, 7.9 Hz, 1H), 2.79 (m, 1H), 2.71 (m, 1H), 1.98 (m, 1H), 1.67 (m, 1H)
38A	(3-氯-2, 6-二氟苯基) 甲基	687.05	Z	F, L	687.1; 689.1	7.47 (m, 1H), 6.70 (清晰的 bt, J = 8.8 Hz, 1H), 5.63 (d, J = 3.9 Hz, 1H), 5.12 (bs, 2H), 5.11 (d, J 模糊的 , 1H)
39A	(3-氯-2, 6-二氟苯基) 甲基	687.05	E	F, L	687.1; 689.1	7.44 (ddd, 清晰的 td, J = 9, 5 Hz, 1H), 6.96 (ddd, 清晰的 td, J = 8.8, 1.8 Hz, 1H), 5.53 (d, J = 4.6 Hz, 1H), 5.13 (s, 2H), 4.21 (d, J = 7.9 Hz, 1H)
40A	(2, 3, 5, 6-四氟-4-甲基苯基) 甲基	702.62	Z	E, J	703.1	5.61 (d, J = 4.0 Hz, 1H), 5.11 (bs, 2H), 5.09 (d, J = 6.2 Hz, 1H), 2.24 (bs, 3H)
41A	(2, 3, 5, 6-四氟-4-甲基苯基) 甲基	702.62	E	E, J	703.1	5.52 (d, J = 4.6 Hz, 1H), 5.13 (s, 2H), 4.20 (d, J = 7.9 Hz, 1H), 2.22 (t, J = 2 Hz, 3H)
42A	(3, 4, 5-三氟苯基) 甲基	670.6	Z	F, L	671.1	7.14 (m, 2H), 5.66 (d, J = 4.2 Hz, 1H), 5.24 (d, J = 6.6 Hz, 1H), 4.99 (s, 2H)
43A	(2, 6-二氯苯基) 甲基	685.52	Z	F, J	685.0; 687.0	7.37 (m, 2H), 7.27 (dd, J = 8.9, 7.1 Hz, 1H), 5.61 (d, J = 4.2 Hz, 1H), 5.30 (AB 四重峰 , Δv = 10.1, J = 11.0 Hz, 2H), 5.11 (d, J =

实施例	Y	分子量	立体化学	制备方法	质 谱	1H NMR 峰值 (CD_3OD)
						6.2 Hz, 1H)
44A	(2, 6-二氯苯基)甲基	685.52	E	F, J	685.0; 687.0	7.34 (m, 2H), 7.24 (dd, J = 8.8, 7.2 Hz, 1H), 5.54 (d, J = 4.6 Hz, 1H), 5.32 (s, 2H), 4.24 (d, J = 7.9 Hz, 1H)
45A	(2, 4-二氯苯基)甲基	685.52	Z	F, L	685.0; 687.0	7.51 (d, J = 8.2 Hz, 1H), 7.47 (d, J = 2.3 Hz, 1H), 7.34 (dd, J = 8.2, 2.3 Hz, 1H), 5.70 (d, J = 4.3 Hz, 1H), 5.29 (d, J = 6.3 Hz, 1H), 5.15 (bs, 2H)
46A	(2-氯-4-氟苯基)甲基	669.06	Z	F, L	669.1; 671.1	7.54 (dd, J = 8.6, 6.3 Hz, 1H), 7.24 (dd, J = 8.6, 2.6 Hz, 1H), 7.09 (ddd, 清晰的td, J = 8.6, 2.6, 1H), 5.70 (d, J = 4.3 Hz, 1H), 5.28 (d, J = 6.3 Hz, 1H), 5.15 (AB 四重峰, Δν = 6.8 Hz, J = 13.5 Hz, 2H)
47A	(2, 4-二氯苯基)甲基	685.52	E	F, L	685.1; 687.0	7.45 (d, J = 2.0 Hz, 1H), 7.37 (d, J = 8.2 Hz, 1H), 7.29 (dd, J = 8.6, 2.3 Hz, 1H), 5.59 (d, J = 4.6 Hz, 1H), 5.17 (s, 2H), 4.29 (d, J = 7.6 Hz, 1H)
48A	(2-氯-4-氟苯基)甲基	669.06	E	F, L	669.1; 671.1	7.42 (dd, J = 8.6, 5.9 Hz, 1H), 7.22 (dd, J = 8.6, 2.6 Hz, 1H), 7.05 (ddd, 清晰的, J = 8.6, 2.6 Hz, 1H), 5.59 (d, J = 4.6 Hz, 1H), 5.16 (s, 2H), 4.29 (d, J = 7.9 Hz, 1H)
49A	(2-氯-6-氟苯基)甲基	669.06	Z	F, J	669.1; 671.1	7.33 (ddd, 清晰的 td, J = 8.3, 6.0 Hz, 1H), 7.25 (推测的 bd, J 模糊的 , 1H), 7.08 (bdd, 清晰的 bt, J = 8.3 Hz, 1H), 5.63 (d, J = 4.2 Hz, 1H), 5.20 (bs, 2H), 5.12 (d, J = 6.2 Hz, 1H)
50A	(2-氯-6-氟苯基)甲基	669.06	E	F, J	669.1; 671.1	7.31 (ddd, 清晰的 td, J = 8.1, 6.0, 1H), 7.22 (推测的 bd, J 模糊的 , 1H), 7.05 (推测的 bt, J = 8.3 Hz, 1H), 5.55 (d, J = 4.6 Hz, 1H), 5.22 (s, 2H), 4.25 (d, J = 7.9 Hz, 1H)

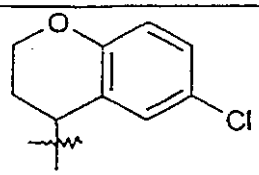
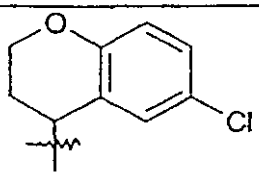
实施例	Y	分子量	立体化学	制备方法	质 谱	1H NMR 峰 值 (CD_3OD)
51A		695.08	Z	F, J	695.1; 697.0	6.83 (d, J = 1.3 Hz, 1H), 6.78 (d, J = 1.4 Hz, 1H), 6.00 (s, 2H), 5.63 (d, J = 4.2 Hz, 1H), 5.16 (d, J = 6.2 Hz, 1H), 4.89 (AB 四重峰, Δν = 10.1 Hz, J = 12.7 Hz, 2H)
52A		695.08	E	F, J	695.0; 697.0	6.78 (d, J = 1.4 Hz, 1H), 6.72 (d, J = 1.4 Hz, 1H), 5.98 (s, 2H), 5.53 (d, J = 4.6 Hz, 1H), 4.90 (s, 2H), 4.24 (d, J = 7.9 Hz, H)
53A	(3-氯-5-氟苯基)甲基	669.06	Z	F, L	669.1; 671.0	7.24 (bs,1H), 7.12 (m, 2H), 5.70 (d, J = 4.3 Hz, 1H), 5.28 (d, J = 6.6 Hz, 1H), 5.06 (bs, 2H)
54A	(3-氯-5-氟苯基)甲基	669.06	E	F, L	669.1; 671.1	7.18 (bs, 1H), 7.11 (m, 1H), 7.04 (m, 1H), 5.59 (d, J = 4.6 Hz, 1H), 5.08 (s, 2H), 4.29 (d, J = 7.9 Hz, 1H)
55A	(2, 6-二氟苯基)甲基	652.6	Z	F, L	653.1	7.40 (tt, J = 8.6, 6.6 Hz, 1H), 6.99 (dd, 清晰的 t, J = 7.9 Hz, 2H), 5.66 (d, J = 4.3 Hz, 1H), 5.15 (m, 3H)
56A	(2, 6-二氟苯基)甲基	652.6	E	F, L	653.1	7.39 (tt, J = 8.6, 6.3 Hz, 1H), 6.87 (dd, 清晰的 t, J = 7.6 Hz, 2H), 5.58 (d, J = 4.6 Hz, 1H), 5.17 (s, 2H), 4.28 (d, J = 7.9 Hz, 1H)
57A	(3, 4-二氟苯基)甲基	652.61	Z	F, L	653.1	7.31 (m, 1H), 7.23 (m, 1H), 7.15 (m, 1H), 5.69 (d, J = 4.0 Hz, 1H), 5.25 (d, J = 6.3 Hz, 1H), 5.03 (bs, 2H)
58A	(3, 4-二氟苯基)甲基	652.61	E	F, L	653.1	7.24 (m, 1H), 7.20 (dd, J = 10.7, 8.0 Hz, 1H), 7.14 (m, 1H), 5.59 (d, J = 4.3 Hz, 1H), 5.05 (s, 2H), 4.28 (d, J = 7.9 Hz, 1H)
59A	(2, 3, 6-三氟苯基)甲基	670.6	Z	F, L	671.1	7.25 (m, 1H), 6.94 (m, 1H), 5.61 (d, J = 4.2 Hz, 1H), 5.11 (AB 四重峰, Δν = 6.3 Hz, J = 9.8 Hz, 2H), 5.10 (d, J = 6.4 Hz, 1H)
60A		670.6	E	F, L	671.0	7.26 (m, 1H), 6.94 (m, 1H),

实施例	Y	分子量	立体化学	制备方法	质 谱	1H NMR 峰 值 (CD_3OD)
	(2, 3, 6-三氟苯基)甲基					5.55 (d, J = 4.6 Hz, 1H), 5.15 (s, 2H), 4.23 (d, J = 7.9 Hz, 1H)
61A	(2, 4-二氟苯基)甲基	652.61	Z	F, L	653.2	7.50 (m, 1H), 6.95 (m, 2H), 5.68 (d, J = 4.0 Hz, 1H), 5.22 (d, J = 6.3 Hz, 1H), 5.09 (bs, 2H)
62A	(2, 4-二氟苯基)甲基	652.61	E	F, L	653.2	7.39 (m, 1H), 6.91 (m, 2H), 5.58 (d, J = 4.6 Hz, 1H), 5.09 (s, 2H), 4.30 (d, J = 7.9 Hz, 1H)
63A	(2, 6-二氟-4-甲苯基)甲基	666.64	Z	F, L	667.1	6.77 (d, J = 8.1 Hz, 2H), 5.60 (d, J = 4.2 Hz, 1H), 5.08 (d, J = 6.2 Hz, 1H), 5.04 (bs, 2H), 2.32 (s, 3H)
64A	(2, 6-二氟-4-甲苯基)甲基	666.64	E	F, L	667.1	6.75 (d, J = 8.1 Hz, 2H), 5.52 (d, J = 4.6 Hz, 1H), 5.06 (s, 2H), 4.22 (d, J = 7.9 Hz, 1H), 2.30 (s, 3H)
65A	(2, 3, 4, 5, 6-五氟苯基)甲基	706.58	Z	F, L	707.1	5.62 (d, J = 4.0 Hz, 1H), 5.11 (bs, 2H), 5.08 (d, J = 6.2 Hz, 1H)
66A	(2-氟-6-三氟甲基苯基)甲基	702.62	Z	F, L	703.1	7.54 (m, 2H), 7.40 (m, 1H), 5.60 (d, J ≈ 4.2 Hz, 1H), 5.20 (AB 四重峰, Δν = 15.4 Hz, J ≈ 11.5 Hz, 2H), 5.07 (d, J ≈ 6.4 Hz, 1H)
67A	(2-氟-6-三氟甲基苯基)甲基	702.62	E	F, L	703.1	7.54 (m, 2H), 7.40 (m, 1H), 5.55 (d, J ≈ 4.6 Hz, 1H), 5.24 (s, 2H), 4.25 (d, J = 7.9 Hz, 1H)
68A	(2, 3-二氟苯基)甲基	652.61	Z	F, L	653.1	7.25 (m, 1H), 7.17 (m, 2H), 5:69 (d, J ≈ 4.0 Hz, 1H), 5.24 (推测的 d, J 模糊的 , 1H), 5.16 (bs, 2H)
69A	(2, 3-二氟苯基)甲基	652.61	E	F, L	653.1	7.16 (m, 3H), 5.59 (d, J = 4.6 Hz, 1H), 5.17 (bs, 2H), 4.28 (d, J = 7.9 Hz, 1H)
70A	(2, 3, 4-三氟苯基)甲基	670.6	E	F, L	671.1	7.17 (m, 1H), 7.03 (m, 1H), 5.53 (d, J = 4.6 Hz, 1H), 5.08 (s, 2H), 4.22 (d, J = 7.7 Hz, 1H)
71A	(2, 3, 4-三氟苯基)甲基	670.6	Z	F, L	671.1	7.22 (m, 1H), 7.09 (m, 1H), 5.65 (d, J ≈ 4.2 Hz, 1H), 5.18 (d, J ≈ 6.2 Hz, 1H), 5.08 (bs, 2H)
72A	(2, 3, 5, 6-四氟苯基)甲基	688.59	Z	F, L	688.9	7.27 (m, 1H), 5.69 (d, J = 4.0 Hz, 1H), 5.24 (d, J =

实施例	Y	分子量	立体化学	制备方法	质 谱	1H NMR 峰 值 (CD_3OD)
	I					6.6 Hz, 1H), 5.12 (bs, 2H)
73A	(2, 3, 5, 6-四氟苯基) 甲基	688.59	E	F, L	689.0	7.17 (m, 1H), 5.58 (d, J = 4.3 Hz, 1H), 5.13 (bs, 2H), 4.27 (d, J = 7.6 Hz, 1H)
74A	2, 3-二氟-6-甲氧基苯基) 甲基	682.64	E	F, L	683.0	7.20 (m, 1H), 6.76 (ddd, J = 9.2, 3.6, 2.3 Hz, 1H), 5.58 (d, J = 4.6 Hz, 1H), 5.16 (d, J = 2.0 Hz, 2H), 4.28 (d, J = 7.9 Hz, 1H), 3.83 (s, 3H)
75A	2, 3-二氟-6-甲氧基苯基) 甲基	682.64	Z	F, L	683.0	7.22 (m, 1H), 6.80 (ddd, J = 9.2, 3.3, 2.0, 1H), 5.65 (d, J = 3.6 Hz, 1H), 5.14 (m, 2H), 5.09 (d, J = 5.6 Hz, 1H), 3.88 (s, 3H)
76A	(4-氯-3-磺酰氨基苯基) 甲基	730.15	E	F, L	730.0	8.21 (m, 1H), 7.90 (m, 1H), 7.52 (m, 1H), 5.58 (d, J = 4.6 Hz, 1H), 5.13 (s, 2H), 4.28 (d, J = 7.9 Hz, 1H)
77A	(2-氟-6-三氟甲氧基苯基) 甲基	718.616	E	F, L	719.0	7.48 (ddd, 清晰的 td, J = 8.2, 6.3 Hz, 1H), 7.18 (m, 2H), 5.58 (d, J = 4.3 Hz, 1H), 5.19 (d, J = 1.0 Hz, 2H), 4.27 (d, J = 7.9 Hz, 1H)
78A	(2-氟-6-三氟甲氧基苯基) 甲基	718.616	Z	F, L	719.0	7.49 (ddd, 清晰的 , J = 8.6, 6.3 Hz, 1H), 7.19 (m, 2H), 5.65 (d, J = 4.3 Hz, 1H), 5.16 (bs, 2H), 5.14 (d, J = 6.3 Hz, 1H)
79A	3-氯-4-氟苯基	655.04	E	E, J	654.8	7.28 (dd, J = 6.2, 2.7 Hz, 1H), 7.11 (dd, 清晰的 t, J = 9 Hz, 1H), 7.02 (m, 1H), 5.65 (d, J = 4.4 Hz, 1H), 4.28 (dd, J = 8.3, 4.6 Hz, 1H)
80A	(2-氟-6-甲氧基苯基) 甲基	664.65	E	F, L	665.1	7.26 (ddd, 清晰的 td, J = 8.5, 6.9 Hz, 1H), 6.76 (d, J = 8.5 Hz, 1H), 6.65 (dd, 清晰的 t, J = 8.5 Hz, 1H), 5.53 (d, J = 4.6 Hz, 1H), 5.09 (d, J = 1.4 Hz, 2H), 4.24 (d, J = 7.9 Hz, 1H), 3.79 (s, 3H)
81A	4-(甲氧羰基) 苯基	660.64	E	E, J	661.1	7.88 (d, J = 8.5 Hz, 2H), 7.12 (d, J = 8.5 Hz, 2H), 5.65 (d, J = 4.4 Hz, 1H), 4.29 (dd, J = 8.1, 5 Hz, 1H), 3.84 (s, 3H)

实施例	Y	分子量	立体化学	制备方法	质 谱	1H NMR 峰 值 (CD_3OD)
82A	3-氯苯基	637.04	E	E, J	637.3; 639.4	7.19 (dd, 清晰的 t, J = 8.2 Hz, 1H), 7.18 (dd, 清晰的 t, J = 2.2 Hz, 1H), 6.99 (ddd, J = 8.3, 2.3, 1.0 Hz, 1H), 6.95 (ddd, J = 8.1, 1.9, 1.0 Hz, 1H), 5.62 (d, J = 4.6 Hz, 1H), 4.25 (dd, J = 8.1, 4.6 Hz, 1H)
83A	2-氟苯基	620.58	E	E, J	621.0	7.34 (ddd, 清晰的 , J = 8.1, 1.7 Hz, 1H), 7.05 (m, 1H), 7.00 (m, 1H), 6.94 (m, 1H), 5.62 (d, J = 4.6 Hz, 1H), 4.26 (dd, J = 8.2, 4.7 Hz, 1H)
84A	3, 5-二氯苯基	671.49	E	E, J	670.7; 673.2	7.14 (d, J = 1.9 Hz, 2H), 7.04 (bs, 1H), 5.65 (d J = 4.4 Hz, 1H), 4.29 (dd, J = 8.1, 4.6 Hz, 1H)
85A	(3-氯-2-噻吩基) 甲基	657.098	Z	F, L	656.8; 658.9	7.46 (d, J = 5.3 Hz, 1H), 6.95 (d, J = 5.3 Hz, 1H), 5.68 (d, J = 4.3 Hz, 1H), 5.19 (m, 2H), 5.17 (d, J = 6.3 Hz, 1H)
86A	(3-氯-2-噻吩基) 甲基	657.098	E	F, L	656.9; 658.9	7.43 (d, J = 5.3 Hz, 1H), 6.93 (d, J = 5.3 Hz, 1H), 5.59 (d, J = 4.6 Hz, 1H), 5.20 (s, 2H), 4.31 (d, J = 7.6 Hz, 1H)
87A	(2-噻吩基) 甲基	622.653	Z	F, L	622.9	7.38 (dd, J = 5.3, 1.3 Hz, 1H), 7.08 (bd, J = 3.6 Hz, 1H), 6.99 (dd, J = 5.3, 3.6 Hz, 1H), 5.67 (d, J = 4.3 Hz, 1H), 5.20 (bs, 2H), 5.16 (d, J = 6.3 Hz, 1H)
88A	(2-噻吩基) 甲基	622.653	E	F, L	622.9	7.35 (dd, J = 5.3, 1.3 Hz, 1H), 7.05 (bd, J = 3.3 Hz, 1H), 6.97 (dd, J = 4.9, 3.3 Hz, 1H), 5.59 (d, J = 4.6 Hz, 1H), 5.22 (s, 2H), 4.31 (d, J = 7.9 Hz, 1H)
89A	(2-氯-6-三氟甲氧苯基) 甲基	735.07	Z	F, L	734.8; 737.0	7.46 (m, 2H), 7.33 (m, 1H), 5.66 (d, J = 4.3 Hz, 1H), 5.25 (AB四重峰 , Δν = 4.9 Hz, J = 11.5 Hz, 2H), 5.14 (d, J = 6.3 Hz, 1H)
90A	(2-氯-6-三氟甲氧苯基) 甲基	735.07	E	F, L	734.8; 736.9	7.45 (m, 2H), 7.31 (m, 1H), 5.58 (d, J = 4.3 Hz, 1H), 5.28 (s, 2H), 4.28 (d, J =

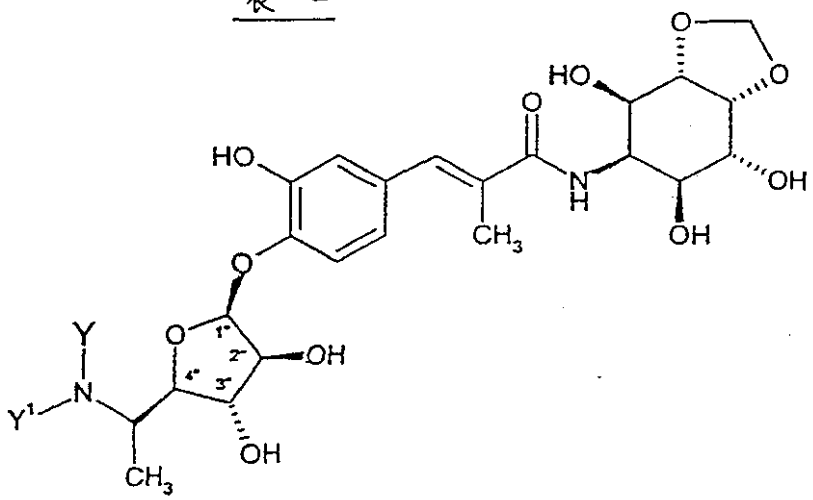
实施例	Y	分子量	立体化学	制备方法	质 谱	1H NMR 峰 值 (CD_3OD)
						7.9 Hz, 1H)
91A	(5-氯-2-噻吩基)甲基	657.098	Z	F, L	656.9; 658.9	6.89 (d, J = 4.0 Hz, 1H), 6.85 (d, J = 4.0 Hz, 1H), 5.68 (d, J = 4.0 Hz, 1H), 5.15 (d, J = 6.3 Hz, 1H), 5.10 (s, 2H)
92A	(5-氯-2-噻吩基)甲基	657.098	E	F, L	656.9; 658.9	6.86 (bd, J = 3.6 Hz, 1H), 6.82 (bd, J = 3.6 Hz, 1H), 5.59 (d, J = 4.3 Hz, 1H), 5.12 (s, 2H), 4.31 (d, J = 7.2 Hz, 1H)
93A	(2-二氟甲氧苯基)甲基	682.635	Z	F, L	683.1	7.49 (bd, J = 7.7 Hz, 1H), 7.33 (dd, 清晰的 bt, J = 8 Hz, 1H), 7.22 (dd, 清晰的bt, J = 7.5 Hz, 1H), 7.16 (bd, J = 8 Hz, 1H), 6.79 (t, J = 74.4 Hz, 1H), 5.65 (d, J = 4.2 Hz, 1H), 5.22 (d, J = 6.4 Hz, 1H), 5.11 (AB四重峰, Δv = 9.2 Hz, J = 13.2 Hz, 2H)
94A	(2-二氟甲氧苯基)甲基	682.635	E	F, L	683.1	7.37 (d, J = 7.1 Hz, 1H), 7.29 (dd, 清晰的 bt, J = 7 Hz, 1H), 7.16 (dd, 清晰的 bt, J = 7.5 Hz, 1H), 7.10 (m, 1H), 6.72 (t, J = 74 Hz, 1H), 5.54 (d, J = 4.4 Hz, 1H), 5.11 (s, 2H), 4.24 (d, J = 7.9 Hz, 1H)
95A	(3-氟苯基)甲基	634.618	E; 4″位α-立体化学	F; N-1	634.9	7.36 (ddd, 清晰的 td, J = 7.9, 5.9 Hz, 1H), 7.18 (m, 1H), 7.10 (m, 1H), 7.02 (m, 1H), 5.73 (d, J = 4.3 Hz, 1H), 5.12 (s, 2H), 4.79 (d, J = 6.9 Hz, 1H)
96A	(3-氯苯基)甲基	651.073	E; 4″位α-立体化学	F; N-1	650.8	7.32 (bs, 1H), 7.27 (m, 3H), 5.68 (d, J = 4.4 Hz, 1H), 5.05 (s, 2H), 4.74 (d, J = 7.1 Hz, 1H)
97A	(3, 4-二氯苯基)甲基	685.518	E	F, L	684.9; 686.9	7.42 (m, 2H), 7.20 (dd, J = 8.3, 2.1 Hz, 1H), 5.53 (d, J = 4.6 Hz, 1H), 5.00 (s, 2H), 4.23 (d, J = 7.9 Hz, 1H)
98A	(2, 6-二甲基苯基)甲基	644.682	Z	F, L	644.9	7.05 (dd, J = 8.3, 6.4 Hz, 1H) 6.97 (bd, J = 7.5 Hz, 2H), 5.59 (d, J = 4.4 Hz, 1H), 5.11 (AB四重峰, Δv = 18.3 Hz, J = 10.9 Hz, 2H), 5.09 (d, J = 6.4 Hz,

实施例	Y	分子量	立体化学	制备方法	质 谱	1H NMR峰 值 (CD_3OD)
						1H), 2.37 (s, 6H)
99A	(2, 6-二甲基苯基)甲基	644.682	E	F, L	645.1	7.03 (dd, J = 8.1, 6.4 Hz, 1H), 6.95 (bd, J = 7.3, 2H), 5.54 (d, J = 4.6 Hz, 1H), 5.13 (s, 2H), 4.25 (d, J = 7.7 Hz, 1H), 2.33 (s, 6H)
100A	(3-氟苯基)甲基	634.618	Z;4″位α-立体化学	F; N-1	635.1	7.36 (ddd, 清晰的 td, J = 7.9, 5.6 Hz, 1H), 7.16 (m, 1H), 7.13 (m, 1H), 7.02 (bt, J = 8.9 Hz, 1H), 5.80 (d, J = 4.0 Hz, 1H), 5.51 (d, J = 4.9 Hz, 1H), 5.07 (AB 四重峰, Δv = 11.8 Hz, J = 12.8 Hz, 1H)
101A	(3-氯苯基)甲基	651.073	Z; 4″位α-立体化学	F; N-1	650.9; 653.0	7.40 (bs, 1H), 7.29 (m, 3H), 5.80 (d, J = 4.0 Hz, 1H), 5.50 (d, J = 5.3 Hz, 1H), 5.06 (AB 四重峰, Δv = 11.89 Hz, J = 12.8 Hz, 2H)
102A		693.11	Z	E, J	693.1; 695.1	7.37 (d, J = 2.7 Hz, 1H), 7.14 (dd, J = 8.7, 2.7 Hz, 1H), 6.76 (d, J = 8.7 Hz, 1H), 5.63 (d, J = 4.4 Hz, 1H), 5.16 (d, J = 6.6 Hz, 1H), 5.05 (m, 1H), 2.21 (m, 1H), 2.04 (m, 1H)
103A		693.11	E; 非对映体的混合物	E, J	693.1; 695.1	7.24 (m, 1H), 7.11 (m, 1H), 6.73 (d, J = 8.9 Hz, 1H), 5.58 和 5.57 (d, J = 4.2 4.2 Hz, 1H), 5.04 (m, 1H), 4.31 和 4.30 (d, J = 7.7 和 7.7 Hz, 1H), 4.02 (m, 1H), 2.21 (m, 1H), 2.00 (m, 1H)
104A	(4-苯基-2-噻唑基)甲基	699.74	Z	G, L	700.2	7.87 (m, 2H), 7.74 (br s, 1H), 7.38 (m, 2H), 7.30 (m, 1H), 5.85 (d, J = 4.4, 1H), 5.83 (br s, 2H), 5.22 (d, J = 6.2 Hz, 1H)
105A	(4-苯基-2-噻唑基)甲基	699.74	E	G, L	700.2	7.82 (m, 2H), 7.67 (br s, 1H), 7.36 (m, 2H), 7.27 (m, 1H), 5.55 (d, J = 4.6, 1H), 5.84 (br s, 2H),
106A	1-(2, 4-二氟苯基)丙基	680.66	Z; 非对映体的混合物	G, L	681.0	7.48 和 7.32 (2m, 1H), 6.85 (m, 2H), 5.65 (m, 1H), 5.32 和 5.26 (2d, J = 6.4 and 6.2 Hz, 1H), 5.20 (m, 1H), 1.86 和 1.74 (2m,

实施例	Y	分子量	立体化学	制备方法	质 谱	1H NMR 峰 值 (CD_3OD)
			s			2H), 0.89 (m, 3H).
107A	1-(2, 4-二氟苯基) 丙基	680.66	E; 非对映体的混合物	G, L	681.0	7.25 (m, 1H), 6.83 (m, 2H), 5.52 和 5.51 (2d, J = 4.5 和 4.5 Hz, 1H), 5.23 (m, 1H), 1.86 和 1.72 (2m, 2H), 0.86 (m, 3H).
108A	1-(3, 4-二氟苯基) 乙基	666.64	Z; 非对映体的混合物	G, L	667.0, 689.0	7.28 (m, 1H), 7.15 (m, 1H), 5.64 (d, J 4.2 Hz, 1H), 5.29 (d, J = 6.6 Hz, 1H), 5.09 (q, J = 6.6 Hz, 1H), 1.43 (d, J = 6.6 Hz, 3H).
109A	1-(3, 4-二氟苯基) 乙基	666.64	E; 非对映体的混合物	G, L	667.0, 689.0	7.13 (m, 3H), 5.52 (m, 1H), 5.14 (m, 1H), 1.43 和 1.42 (2d, J = 6.4 和 6.6 Hz, 3H).
110A	1-(2, 4-二氟苯基) 乙基	666.64	Z; 非对映体的混合物	G, L	667.1	7.51 and 7.37 (m, 1H), 8.85 (m, 1H), 5.65 (m, 1H), 5.38 (m, 1H), 5.30 和 5.24 (2 d, J = 6.6 和 6.4 Hz, 1H), 1.45 和 1.44(2d, J = 6.6 和 6.6 Hz, 3H).
111A	1-(2, 4-二氟苯基) 乙基	666.64	E; 非对映体的混合物	G, L	667.1	7.29 (m, 1H), 6.85 (m, 2H), 5.52 (m, 1H), 5.40 (m, 1H),1.47 和 1.46 (2 d, J = 6.6 和 6.6 Hz, 3H)
112A	1-(3, 5-二氟苯基) 乙基	666.64	Z; 非对映体的混合物	G, L	667.0	6/97 (m, 2H), 6.76 (m, 1H), 5.65 (d, J 4.2 Hz, 1H), 5.30 (d, J 6.6 Hz, 1H), 5.10 (q, J = 6.6 Hz, 1H), 1.4 (d, J = 6.6 Hz, 3H).
113A	1-(3, 5-二氟苯基) 乙基	666.64	E; 非对映体的混合物	G, L	667.0	6.83 (m., 2H), 6.75 (m, 1H), 5.52 (2 d, J = 4.8 和 4.6 Hz, 1H), 5.15 (m, 1H), 1.43 和 1.42 (2d , J = 6.6 和 6.6 Hz, 3H)
114A	1-(3-氯-2, 6-二氟苯基) 乙基	701.081	Z; 非对映体的混合物	G, L	701.0, 703.0	7.39 (m, 1H), 6.94 (m, 1H), 5.64 (br d, J = 3.9 Hz, 1H), 5.49 (q, 6.8 Hz), 5.18 (m, 1H), 1.60 (d, 6.9 Hz).

实施例	Y	分子量	立体化学	制备方法	质 谱	1H NMR 峰 值(CD_3OD)
115A	1-(3-氯-2,6-二氟苯基)乙基	701.081	E; 非对映体的混合物	G, L	701.0, 703.0	7.35 (m, 1H), 6.89 (m, 1H), 5.58 (m, 1H), 5.49 (m, 1H), 1.56 和 1.55 (2 d, J = 6.8 和 6.8 Hz, 3H).
116A	1-(3-氯苯基)乙基	665.10	E	E, L	665.1, 667.1	7.25 (m, 1H), 7.20 (m, 1H), 5.54 和 5.53 (2d, J = 4.8 和 4.8 Hz, 1H), 5.17 (m, 1H), 1.47 和 1.45 (2d, J = 6.2 和 6.6 Hz, 3H).

表 2



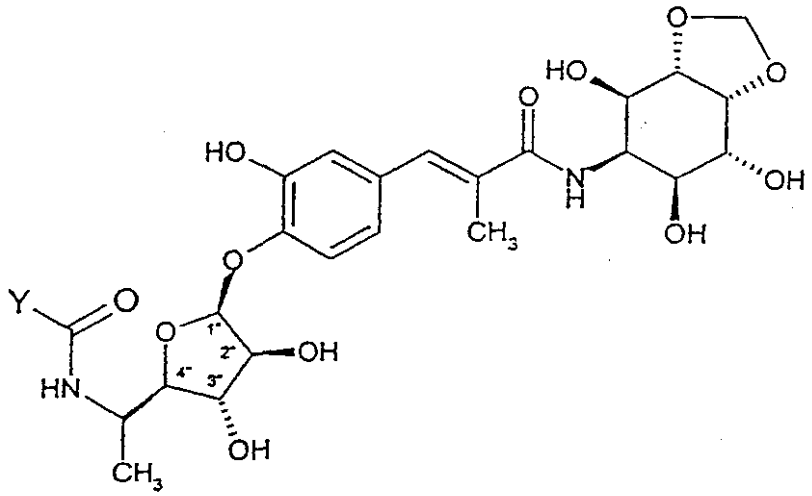
在下表2中列出的实施例中，除了实施例97中的Y^1为甲基以外，其他所有实施例中的Y^1均为H。

实施例	Y	分子量	制备方法	质 谱	1H NMR 峰 值 (CD_3OD)
93	苯甲基	602.64	O	603.2	7.17 (m, 3H), 7.08 (m, 2H), 5.53 (d, J = 4.6 Hz, 1H), 3.87 (dd, J = 7.5, 4.4 Hz, 1H), 3.79 (d, J = 13.1 Hz, 1H), 3.61 (d, J = 13.1 Hz, 1H), 2.90 (m, 1H), 1.09 (d, J = 6.6 Hz, 3H)
94	(3,4-二甲氧苯基)甲基	662.7	O	663.3	7.07 (s, 1H), 6.92 (m, 2H), 5.61 (d, J = 3.7 Hz, 1H), 4.07 (右半部分为 AB 四重峰;左手信号模糊, J = 13.1 Hz, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 3.41 (m, 1H), 1.26 (d,

实施例	Y	分子量	制备方法	质 谱	1H NMR 峰 值 (CD_3OD)
					J = 6.9 Hz, 3H)
95	[2-(三氟甲基)苯基]甲基	670.64	P	671.2	7.56 (bd, J = 7.9 Hz, 1H), 7.41 (m, 2H), 7.33 (bt, J = 7.5 Hz, 1H), 5.53 (d, J = 4.6 Hz, 1H), 3.87 (dd, J = 7.5, 4.4 Hz, 1H), 2.92 (m, 1H), 1.09 (d, J = 6.6 Hz, 3H)
96	(4-叔丁基苯基)甲基	658.75	P	659.3	7.20 (d, J = 8.3 Hz, 2H), 6.97 (d, J = 8.3 Hz, 2H), 5.51 (d, J = 4.6 Hz, 1H), 3.84 (dd, J = 7.5, 4.4 Hz, 1H), 3.73 (d, J = 13.1 Hz, 1H), 3.55 (d, J = 13.1 Hz, 1H), 2.86 (m, 1H), 1.24 (s, 9H), 1.07 (d, J = 6.4 Hz, 3H)
97	苯甲基	616.67	Q (使用实施例93的产物作为起始物)	617.2	7.30 (m, 5H), 5.55 (d, J = 3.9 Hz, 1H), 4.04 (dd, J = 7.1, 4.9 Hz, 1H), 3.54 (AB 四重峰, Δν = 49.0 Hz, J = 13.2 Hz, 2H), 2.88 (m, 1H), 2.16 (s, 3H), 0.91 (d, J = 6.6 Hz, 3H)
98	苯 基	588.62	R	589.2	7.02 (dd, J = 8.6, 7.4 Hz, 2H), 6.58 (dd, J = 8.7, 1.0 Hz, 2H), 6.54 (dd, J = 7.3, 1.0 Hz, 1H), 5.57 (d, J = 4.4 Hz, 1H), 3.86 (dd, J = 6.8, 5.4 Hz, 1H), 3.59 (m, 1H), 1.04 (d, J = 6.4 Hz, 3H)
99	2-苯乙基	616.67	P	617.3	7.19 (m, 2H), 7.08 (m, 3H), 5.52 (d, J = 4.4 Hz, 1H), 3.87 (dd, J = 7.2, 3.8 Hz, 1H), 2.88 (m, 3H), 2.67 (m, 2H), 1.03 (d, J = 6.4 Hz, 3H)
100	4-氟苯基	606.61	R	607.2	6.76 (dd, 清晰的 t, J = 8.8 Hz, 2H), 6.56 (dd, J = 9.0, 4.5 Hz, 2H), 5.58 (d, J = 4.4 Hz, 1H), 3.53 (m, 1H), 1.04 (d, J = 6.4 Hz, 3H)
101	2-(4-氯苯基)乙基	651.12	P	651.2; 653.2	7.19 (d, J = 8.3 Hz, 2H), 7.08 (d, J = 8.3 Hz, 2H), 5.53 (d, J = 4.4 Hz, 1H), 2.9 (m, 3H), 2.7 (m, 2H),

实施例	Y	分子量	制备方法	质 谱	1H NMR 峰 值 (CD_3OD)
					1.07 (d, J = 6.4 Hz, 3H)

表3



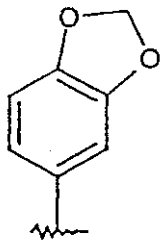
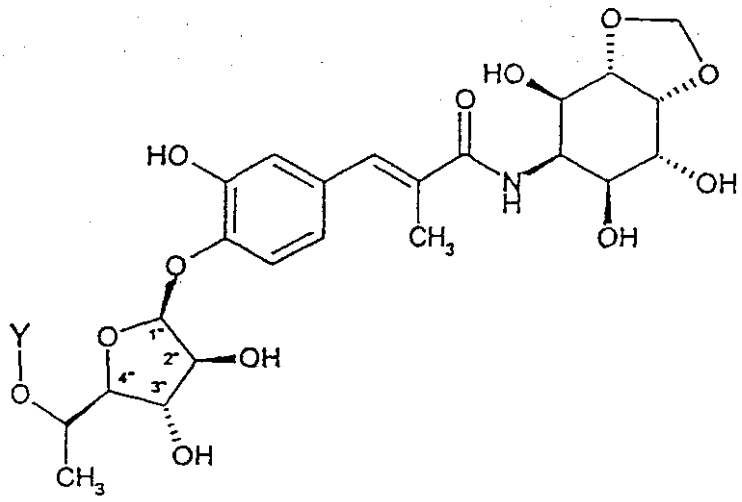
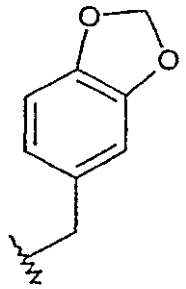
实施例	Y	分子量	制备方法	质 谱	1H NMR 峰 值(CD_3OD)
102	苯甲基	630.67	S	631.1	7.22 (m, 5H), 5.50 (d, J = 4.4 Hz, 1H), 3.39 (左半部分为AB四重峰, 右半部分模糊, J = 14.3 Hz, 1H), 1.03 (d, J = 6.6 Hz, 3H)
103	环丙基	580.59	S	581.3	5.56 (d, J = 3.7 Hz, 1H), 1.47 (m, 1H), 1.06 (d, J = 6.6 Hz, 3H), 0.69 (m, 2H), 0.56 (m, 2H)
104		660.64	T	661.3	7.29 (dd, J = 8.1, 1.9 Hz, 1H), 7.21 (bs, 1H), 6.78 (d, J = 8.1 Hz, 1H), 5.97 (s, 2H), 5.50 (d, J = 4.6 Hz, 1H), 4.29 (m, 1H), 3.86 (dd, 清晰的 t, J = 6.9 Hz, 1H), 1.18 (d, J = 6.8 Hz, 3H)

表4



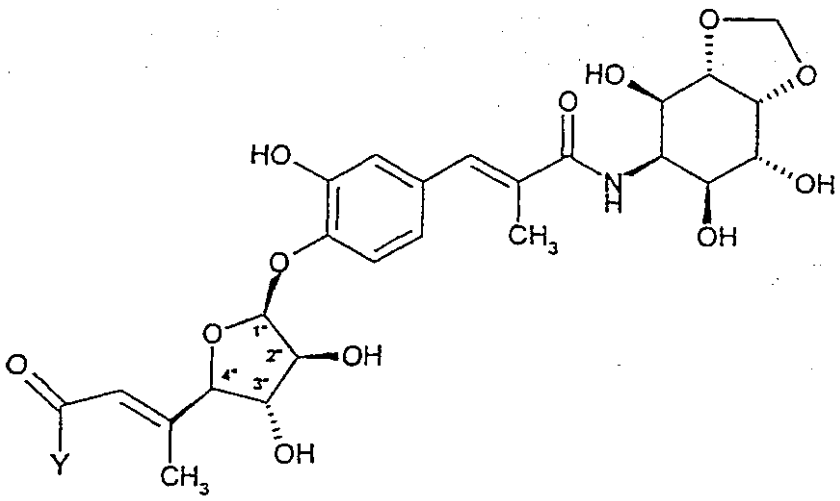
实施例	Y	分子量	制备方法	质 谱	1H NMR 峰 值 (CD_3OD)
105	苯甲基	603.63	U	604.1	7.25 (br s, 1H), 7.2-7.13 (m, 6H), 6.92 (d, J = 1.3 Hz, 1H), 6.84 (dd, J = 8.5 和 1.9 Hz, 1H), 5.56 (d, J = 3.7 Hz, 1H), 4.42 (AB 四重峰, Δv = 16 Hz, J = 11.8 Hz, 2H), 2.08 (d, J = 1.5 Hz, 3H), 1.16 (d, J = 6.4 Hz, 3H).
106	(3, 4-二氯苯基) 甲基	672.52	U	672.1, 674.1	7.30-7.26 (m, 2H); 7.22 (s, 1H); 7.13 (d, J = 8.5 Hz, 1H); 7.03 (dd, J = 8.3 和 2.0 Hz, 1H); 6.89 (d, J = 2 Hz, 1H); 6.85 (dd, J =8.5, 1.9 Hz, 1H); 5.56 (br dd, 1H); 4.34 (AB 四重峰, Δv = 34.7 Hz, J = 12.7 Hz, 12H), 2.05 (d, J = 1.5 Hz, 3H); 1.16, (d, J = 6.2 Hz, 1H).
107	(4-氟苯基) 甲基	621.62	U	622.2	7.22 (br s, 1H), 7.16-7.12 (m, 3H), 6.90-6.81 (m,4H), 5.54 (d, J = 4.0 Hz, 1H), 4.38 (AB四重峰, Δv = 25.1 Hz, J = 11.7 Hz, 2H), 2.06 (d, J = 1.4 Hz, 3H), 1.14 (d, J = 6.2 Hz)
108	(4-甲基苯基) 甲基	617.66	U	618.3	7.25 (s, 1H), 7.17(d, J = 8.3 Hz, 1H), 7.04-6.99 (m, 4H), 6.93 (d, J = 1.8 Hz, 1H), 6.84 (dd, J = 8.5和 2.1 Hz, 1H), 5.55 (d, J = 3.9 Hz, 1H), 4.37(AB 四重峰, Δv = 16.0 Hz, J = 11.7 Hz, 2H), 2.25 (s, 3H), 2.08 (d, J = 2.2 Hz, 3H), 1.15 (d, J = 6.2 Hz, 3H)
109	(3-氟苯基) 甲基	621.62	U	622	7.22 (d, J = 5.4 Hz, 1H), 7.2-7.16 (m, 1H) 7.16 (d, J = 8.5 Hz, 1H),

实施例	Y	分子量	制备方法	质 谱	1H NMR 峰 值 (CD_3OD)
					6.94-6.89 (m, 4H), 6.82 (dd, J = 8.3 和 1.9 Hz, 1H), 5.57 (d, J = 3.5 Hz, 1H), 4.41 (AB 四重峰，Δv = 20.1 Hz, J = 12.5 Hz, 2H), 2.08 (d, J = 1.7 Hz, 3H), 1.18 (d, J = 6.4 Hz).
110		647.64	V	648.1	7.24 (brs, 1H), 7.15 (d, J = 8.3 Hz, 1 Hz), 6.92 (d, J = 2.0 Hz, 1H), 6.84 (dd, J = 8.4 和 2.0 Hz, 1H), 6.65-6.59 (m, 3H), 5.86, (s, 2H), 5.54 (d, J = 3.5 Hz, 1H), 4.30 (AB四重峰，Δv = 23.6 Hz, J = 11.5 Hz, 2 H)，2.08 (d, J = 1.3 Hz, 3H), 1.14 (d, J = 6.4 Hz, 3H).
111	（苯甲基）氧-甲基	633.66	Z	634.2	7.28-7.18 (m, 5H), 7.11 (d, J = 8.5 Hz, 1H), 6.90 (d, J = 2.1 Hz, 1H) 6.78 (dd, J = 8.5 和 2.1 Hz, 1H), 5.54 (d, J = 4.2 Hz, 1H), 4.66 (AB 四重峰，Δv = 57.9, J = 6.8 Hz, 2H), 4.43 (AB四重峰，Δv = 19.8 Hz, J = 11.9 Hz, 2H), 1.20 (d, J = 6.2 Hz, 3H).
112	（4-氯苯基）甲基	638	U	638.1, 640.1	7.25 (s, 1H), 7.19-7.11 (m, 4H), 6.92 (s, 1H), 6.84 (dd, J = 8.5 和 1.9 Hz, 1H), 5.56 (d, J = 3.5 Hz, 1H), 4.40 (AB 四重峰，Δv = 27.2 Hz, J = 12.0, 2H), 1.17 (d, J = 6.4 Hz).
113	（3-氯苯基）甲基	638	U	638.1, 640.1	7.24 (brs, 3H), 7.17-7.16 (m, 4H), 7.06-7.03 (m, 1H), 6.92, (d, J = 1.9 Hz, 1H), 6.83, (dd, J = 8.5 和 1.8 Hz, 1H), 5.58-5.57 (m, 1H), 4.38 (AB四重峰，Δv = 24.0 Hz, J = 12.2 Hz, 2H), 1.18 (d, J = 6.4 Hz, 3H).
114	（4-环己基苯基）甲基	685.8	U	685.9	7.26 (s, 1H), 7.19 (d, J = 8.5 Hz, 1H), 7.03 (AB 四重峰, Δv =13.8 Hz, J = 8.1 Hz, 4H), 6.93 (d, J = 1.8Hz, 1H), 6.86 (dd, J = 8.5 和 1.8 Hz, 1H), 5.55 (d, J = 3.5 Hz, 1H), 4.39 (AB四重峰, Δv = 20.6 Hz, J = 11.6 Hz, 2H) 1.15 (d, J = 6.2 Hz, 3H).
115	（2-甲基苯基）甲基	617.6	U	617.9	7.23 (s, 1H), 7.16 (d, J = 8.3 Hz, 1H), 7.11-7.01 (m, 4H), 6.92 (d, J = 1.9 Hz, 1H), 6.82 (dd, J = 8.3 和 2.0 Hz, 1H), 5.56 (d, J = 3.9 Hz, 1H), 4.39 (brs, 2H), 1.18 (d, J = 6.2 Hz, 3H).

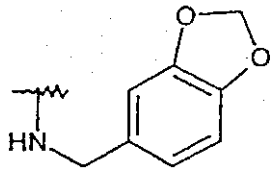
实施例	Y	分子量	制备方法	质 谱	1H NMR 峰 值 (CD_3OD)
116	（2-氟苯基）甲基	621.6	U	621.8	7.28-7.19 (m, 3H), 7.17 (d, J = 8.3 Hz, 1H), 7.01-6.95 (m, 2H), 6.90 (d, J = 1.9 Hz, 1H), 6.81 (dd, J = 8.3 和 1.8 Hz, 1H), 5.54 (d, J = 4.2 Hz, 1H), 4.48 (brs, 2H), 1.19 (d, J = 6.5 Hz, 3H).
117	（4-甲氧基苯基）甲基	633.7	V	634.2	7.25 (s, 1H), 7.17 (d, J = 8.5 Hz, 1H), 7.06 (d, J = 8.5 Hz, 2H), 6.93 (d, J = 1.9 Hz, 1H), 6.85 (dd, J = 8.5 和 2.0 Hz, 1H), 6.73 (d, J = 8.5 Hz, 2H), 5.55 (d, J = 3.3 Hz, 1H), 4.35 (AB 四重峰, Δv = 20.5 Hz, J = 11.4 Hz, 2H), 1.14 (d, J = 6.3 Hz, 3H).
118	（3-氰基苯基）甲基	628.6	W	629.2	7.54 (d, J = 6.2 Hz, 1H), 7.46-7.35 (m, 2H), 7.23 (s, 1H), 7.15 (d, J = 8.3 Hz, 1H), 6.91 (d, J = 2.1 Hz, 1H), 6.84 (dd, J = 8.4 和 1.9 Hz, 1H), 5.6 (d, J = 3.7 Hz, 1H), 4.45 (AB 四重峰, Δv = 42.3, J = 12.3, 2H), 1.20 (d, J = 6.2 Hz, 3H).
119	[（4-三氟甲基）苯基]甲基	671.6	W	672.1	7.47 (d, J = 8.1 Hz, 2H), 7.33 (d, J = 8.1 Hz, 2H), 7.24 (s, 1H), 7.15 (d, J = 8.3 Hz, 1H), 6.91 (d, J = 1.9 Hz, 1H), 6.84 (dd, J = 8.4 和 1.9 Hz, 1H), 5.59 (d, J = 3.7 Hz, 1H), 4.50 (AB 四重峰, Δv = 27.1 Hz, J = 12.7 Hz, 2H), 1.20 (d, J = 6.5 Hz, 3H)
120	（4-氰基苯基）甲基	628.6	W	629.2	7.52 (d, J = 8.1 Hz, 1H), 7.31 (d, J = 8.1, 2H), 7.24 (s, 1H), 7.15 (d, J = 8.5 Hz, 1H), 6.91 (d, J = 1.9 Hz, 1H), 6.83 (dd, J = 8.5 和 1.9 Hz, 1H), 5.59 (d, J = 3.7 Hz, 1H), 4.48 (AB 四重峰, Δv = 32.3 Hz, J = 13.4 Hz, 2H), 1.21 (d, J = 6.4 Hz, 3H).
121	（3-甲基苯基）甲基	617.6	W	618.3	7.25 (s, 1H), 7.18 (d, J = 8.5 Hz, 1H), 7.15-6.95 (3m, 3H), 6.93 (d, J = 2.1 Hz, 1H), 6.85 (dd, J = 8.5 和 2.1 Hz, 1H), 5.55 (d, J = 3.5 Hz, 1H) 4.38 (AB 四重峰, Δv = 14.1 Hz, J = 11.7 Hz, 2H), 2.24 (s, 3H) 1.15 (d, J = 6.4 Hz, 3H).
122	（3，4-二甲基苯基）甲基	631.7	W	632.2	7.25 (s, 1H), 7.18 (d, J = 8.5 Hz, 1H), 6.96-6.93 (m, 2H), 6.87-6.83 (m, 3H), 5.54 (d, J = 3.3 Hz, 1H), 4.34 (AB 四重峰, Δv = 12.9 Hz, J = 11.5 Hz, 2H), 2.17 (s, 3H), 2.15 (s, 3H), 1.13 (d, J = 6.2 Hz, 3H).
123	苯氨基羰基	632.63	X	633.1	7.35-7.19 (2 m, 5H), 7.11 (d, J = 8.6

实施例	Y	分子量	制备方法	质 谱	1H NMR 峰 值 (CD_3OD)
					Hz, 1 H) 6.96 (t, J = 7.4 Hz, 1H) 6.91 (d, J = 2.1 Hz, 1H), 6.73 (dd, J = 8.5 和 2.1 Hz, 1H), 5.56 (d, J = 3.5 Hz, 1H), 1.22 (d, J = 6.4 Hz, 3H).
124	3-氟苯氨基羰基	650.62	X	651.1	7.26-7.20 (m , 3H), 7.15, (d, J = 8.5 Hz, 1H), 7.05 (dd, J = 8.1 和 1.8 Hz, 1H), 6.93 (d, J = 2.1 Hz, 1H), 6.76-6.68 (m, 2H), 5.58 (d, J = 3.5 Hz, 1H), 1.24 (d, J = 6.4 Hz, 3H).
125	3，4-二氯苯氨基羰基	701.52	X	701, 703	7.62 (s, 1H), 7.33 (d, J = 8.9 Hz, 1H), 7.23-7.20 (m, 2H), 7.11 (d, J = 8.5 Hz, 1H), 6.92 (d, J = 2.1 Hz, 1H), 6.74 (dd, J = 8.5 和 2.1 Hz, 1H), 5.56 (d, J = 3.1 Hz, 1H), 4.91-4.8 (m, 1H), 1.25 (d, J = 6.4 Hz, 3H).
126	4-氯苯氨基羰基	667.07	X	667,669	7.35-7.32 (m, 2H), 7.20-7.19 (m, 3H), 7.12 (d, J = 8.5 Hz, 1H), 6.93 (d, J = 2.1 Hz, 1H), 6.75 (dd, J = 8.5 和 2.1 Hz, 1H), 5.57 (d, J = 3.1 Hz, 1H), 1.24 (d, J = 6.4 Hz, 3H).
127	4-甲氧基苯氨基羰基	662.65	X	663	7.23-7.21 (m , 3H), 7.13 (d, J = 8.5 Hz, 1H), 6.93, (d, J = 1.9 Hz, 1H), 6.80-6.76 (m, 3H), 5.58 (brs, 1H), 1.23, (d, J = 6.4 Hz, 3H).
128	[（4-氟苯基）甲基]氨基羰基	664.5	Y	665.1	7.24 (br s, 3H), 7.10 (d, J = 8.3 Hz, 1H), 7.00 (m, 2H), 6.6 (br s, 1H), 6.77 (br d, J = 8.1 Hz, 1H), 5.52 (br s, 1H), 4.9-4.80 (m, 1H), 1.19 (br d, J = 6.4 Hz, 1H).
129	（苯甲基）氨基羰基	646.6	Y	647.2	7.7.3-7.1(m, 6H), 7.5 (d, J = 8.3 Hz 1H), 6.82 (br s, 1H), 6.66 (d, J = 8.3, 1H) , 5.50 (d, J = 5.2 Hz, 1H), 4.83-4.80 (m, 1H), 1.20 (d, J = 6.9 Hz, 3H).
130	[（3，4-二氯苯基）甲基]氨基羰基	715.5	Y	715, 717	7.39 (s, 1H), 7.23 (s, 1H), 7.18-7.01 (m, 3H), 6.86 (d, J = 1.6 Hz. 1H), 6.77-6.72 (m, 1H), 5.52 (d, J = 2.5 Hz, 1H), 4.85-4.82 (m, 1H), 1.20 (d, J = 6.5 Hz, 3H).
131	[（4-氯苯基）甲基]氨基羰基	681.1	Y	681.1, 683.1	7.3-7.2 (m, 4H) 7.11 (d, J = 8.5 Hz, 1H), 6.77 (d, J = 7.7, 1H), 5.5 (br s, 1H), 4.84-4.80 (m, 1H), 1.19 (d, J = 6.4 Hz).

表5



实施例	Y	分子量	制备方法	质 谱	1H NMR 峰值 (CD_3OD)
132	乙氧基	581.58	AA	582.2	5.80 (bs, 1H), 5.59 (d, J = 4.6 Hz, 1H), 4.02 (q, J = 7.1 Hz, 2H), 2.04 (d, J = 1.2 Hz, 3H), 1.15 (t, J = 7.1 Hz, 3H)
133	羟 基	553.52	BB	554.1	5.84 (bs, 1H), 5.56 (d, J = 3.9 Hz, 1H), 1.95 (d, J = 1.2 Hz, 3H)
134	（苯甲基）氨基	642.67	CC	643.3	7.21 (m, 5H), 5.90 (s, 1H), 5.60 (d, J = 2.3 Hz, 1H), 4.32 (s, 2H), 1.99 (s, 3H)
135	[（3-氟苯基）甲基]氨基	660.66	DD	661.2	7.30 (m, 1H), 7.03 (d, J = 7.9 Hz, 1H), 6.94 (m, 2H), 5.93 (s, 1H), 5.61 (d, J = 3.8 Hz, 1H), 4.34 (s, 2H), 2.00 (d, J = 1.3 Hz, 3H)
136	环己氨基	634.69	EE, L	635.1	5.82 (s, 1H), 5.60 (d, J = 3.9 Hz, 1H), 3.59 (m, 1H), 1.95 (d, J = 1.2 Hz, 3H),1.78 (bd, J = 11.8 Hz, 2H), 1.70 (bd, J = 13.3 Hz, 2H), 1.59 (bd, J = 12.7 Hz, 1H), 1.31 (m, 2H), 1.14 (m, 3H)
137	4-吡啶基甲氨基	643.65	EE, J	644.3	8.39 (m, 2H), 7.23 (m, 2H), 5.93 (bs, 1H), 5.60 (d, J = 3.7 Hz, 1H), 4.36 (AB 四重峰, Δν = 20.3 Hz, J = 16.2 Hz, 2H), 1.99 (d, J = 1.2 Hz, 3H)

实施例	Y	分子量	制备方法	质 谱	1H NMR峰 值 (CD_3OD)
138		686.68	EE, L	687.2	6.68 (m, 3H), 5.87 (s, 2H), 5.87 (bs, 1H), 5.59 (d, J = 3.7 Hz, 1H), 1.97 (d, J = 1.2 Hz, 3H)
139	2-（二甲氨基）乙氨基	623.66	EE, N	623.8	5.84 (bs, 1H), 5.57 (d, J = 3.7 Hz, 1H), 3.27 (t, J = 6.8 Hz, 2H), 2.39 (t, J = 6.7 Hz, 2H), 2.21 (s, 6H), 1.96 (d, J = 1.2 Hz, 3H)
140	2-呋喃基甲氨基	632.63	EE, J	632.8	7.35 (dd, J = 1.9, 0.8 Hz, 1H), 6.28 (dd, J = 3.3, 1.9 Hz, 1H), 6.15 (dd, J = 3.2, 0.7 Hz, 1H), 5.85 (bs, 1H), 5.57 (d, J = 3.7 Hz, 1H), 4.29 (s, 2H), 1.96 (d, J = 1.2 Hz, 3H)