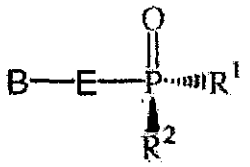
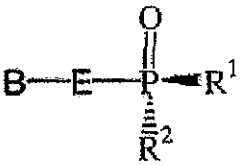
We claim:

1. A methoxyphosphonate nucleotide prodrug having the structure (3)



(3)

which is substantially free of the diastereomer (4)



(4)

wherein

R^1 is an oxyester which is hydrolyzable in vivo, or hydroxyl;

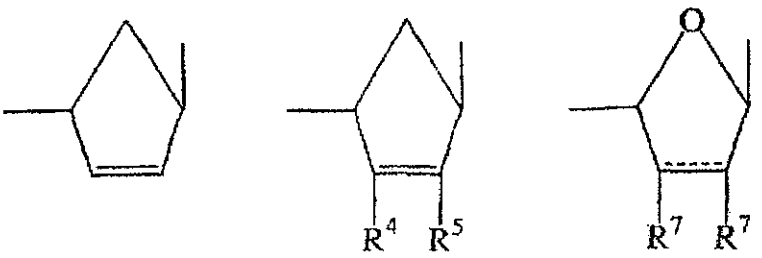
B is a heterocyclic base;

R^2 is hydroxyl, or the residue of an amino acid bonded to the P atom

through an amino group of the amino acid and having each carboxy substituent of the amino acid optionally esterified, but not both of R^1 and R^2 are hydroxyl;

E is $-(CH_2O)_2-$, $-CH(CH_3)CH_2O-$, $-CH(CH_2F)CH_2O-$, $-CH(CH_2OH)CH_2-$, $-CH(CH=CH_2)CH_2O-$,

$-CH(CH=CH)CH_2O-$, $-CH(CH_2N_3)CH_2O-$,



$-CH(R^6)OCH(R^6)-$, $-CH(R^9)CH_2-$ or $-CH(R^8)O-$, wherein the right hand bond is linked to the heterocyclic base;

the broken line represents an optional double bond;

R^4 and R^5 are independently hydrogen, hydroxy, halo, amino or a substituent having 1-5 carbon atoms selected from acyloxy, alkoxy, alkylthio, alkylamino and dialkylamino;

R6 and R6' are independently H, C_1-C_6 alkyl, C_1-C_6 hydroxyalkyl, or C_2-C_7 alkanol;

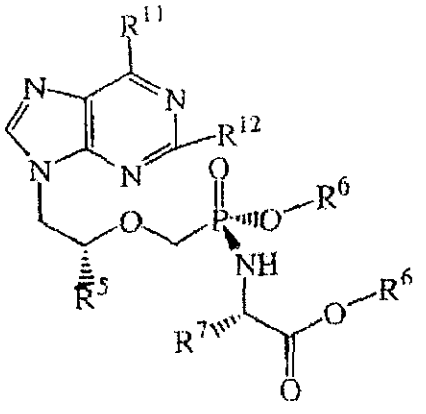
R^7 is independently H, C_1-C_6 alkyl, or are taken together to form -O- or $-CH_2-$;

R^8 is H, C_1-C_6 alkyl, C_1-C_6 hydroxyalkyl or C_1-C_6 haloalkyl; and

R^9 is H, hydroxymethyl or acyloxymethyl;

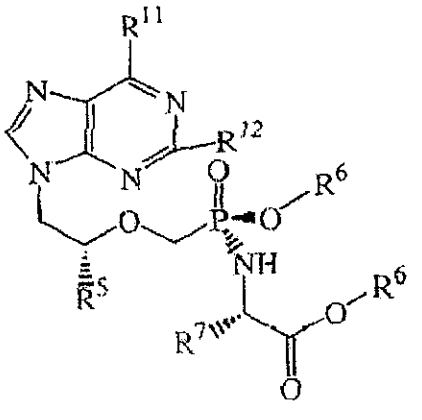
and their salts, free base, and solvates.

2. A methoxyphosphonate nucleotide prodrug as claimed in claim 1 having the structure (5a)



(5a)

which is substantially free of diastereomer (5b)



(5b)

wherein R^5 is methyl or hydrogen;

R^6 independently is H, alkyl, alkenyl, alkynyl, aryl or arylalkyl, or R^6 independently is alkyl, alkenyl, alkynyl aryl or arylalkyl which is substituted with from 1 to 3 substituents selected from alkylamino, alkylaminoalkyl

dialkylaminoalkyl, dialkylamino, hydroxyl, oxo, halo, amino, alkylthio, alkoxy, alkoxyalkyl, aryloxy, aryloxyalkyl, arylalkoxy, arylalkoxyalkyl, haloalkyl, nitro, nitroalkyl, azido, azidoalkyl, alkylacyl, alkylacylalkyl, carboxyl, alkylacylamino;

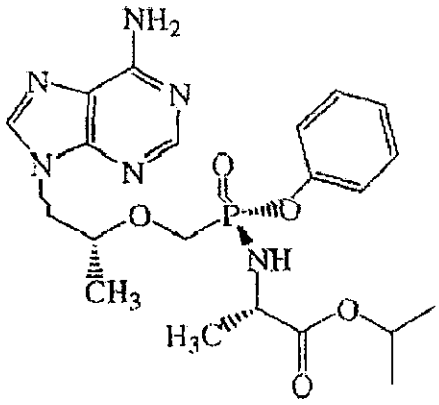
R^7 is the side chain of any naturally-occurring or pharmaceutically acceptable amino acid and which, if the side chain comprises carboxyl, the carboxyl group is optionally esterified with an alkyl or aryl group;

R^{11} is amino, alkylamino, oxo, or dialkylamino; and

R^{12} is amino or H;

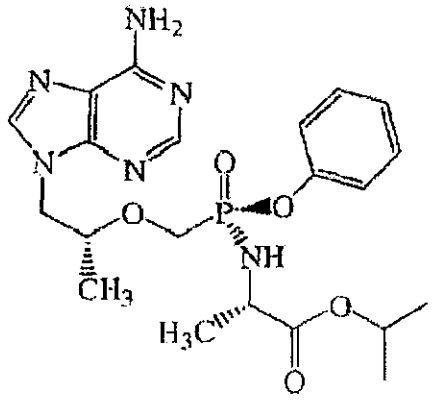
and it salts, tautomers, free base and solvates.

3. A methoxyphosphonate nucleotide prodrug of structure (6a)



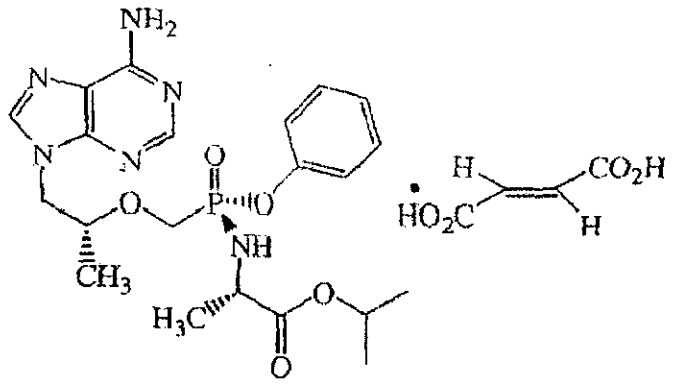
(6a)

which is substantially free of diastereomer (6b)

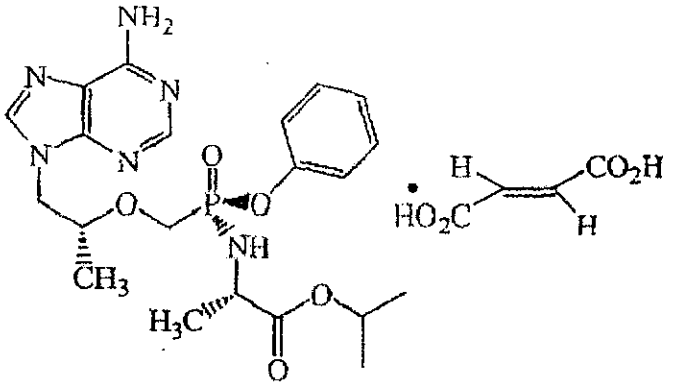


and its salts and solvates.

4. A methoxyphosphonate nucleotide prodrug of structure (7a)



which is substantially free of diastereomer (7b)



(7b)

and its salts and solvates.

Dated this 1st day of May 2006

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