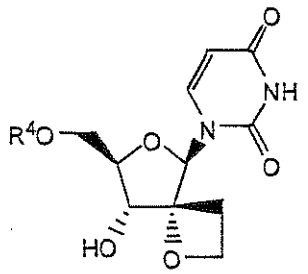
Chem., 2003, 3514-3526. These compounds were tested against HIV, but no activity was found.

Compounds of the invention may also be attractive due to the fact that they lack activity against other viruses, in particular against HIV. HIV-infected patients often suffer from co-infections such as HCV. Treatment of such patients with an HCV inhibitor that also inhibits HIV may lead to the emergence of resistant HIV strains.

Summary

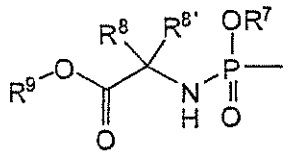
According to the first aspect, there is provided a compound of formula I:



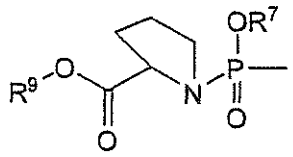
(I)

including any possible stereoisomers thereof, wherein:

R^4 is a group of formula



or



R^7 is phenyl, optionally substituted with 1, 2, or with 3 substituents each independently selected from halo, C_1-C_6alkyl, C_3-C_6alkenyl, C_1-C_6alkoxy, hydroxy, and amino; or R^7 is naphthyl, optionally substituted with 1, 2, or with 3 substituents each independently selected from halo, C_1-C_6alkyl, C_3-C_6alkenyl, C_1-C_6alkoxy, hydroxy, and amino; or R^7 is indolyl, optionally substituted with one C_1-C_6alkyloxy-carbonyl group and optionally further with 1, 2, or with 3 substituents each independently selected from halo, C_1-C_6alkyl, C_3-C_6alkenyl, C_1-C_6alkoxy, hydroxy, and amino;

R^8 is hydrogen, C_1-C_6alkyl, benzyl, or phenyl;

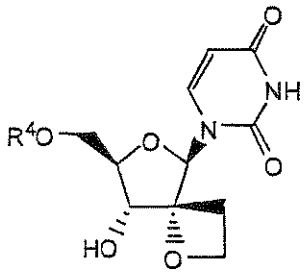
$R^{8'}$ is hydrogen, C_1-C_6alkyl, benzyl, or phenyl; or

R^8 and $R^{8'}$ together with the carbon atom to which they are attached form C_3-C_7cycloalkyl;

R^9 is C_1-C_{10}alkyl, C_3-C_7cycloalkyl or phenyl-C_1-C_6alkyl, wherein the phenyl moiety in phenyl or phenyl-C_1-C_6alkyl is optionally substituted with 1, 2 or 3 substituents each independently selected from hydroxy, C_1-C_6alkoxy, amino, mono- and diC_1-C_6alkylamino;

or a pharmaceutically acceptable salt or solvate thereof.

According to the second aspect, there is provided a compound of formula I:



(I)

including any possible stereoisomers thereof, wherein:

R^4 is a monophosphate;

R^7 is phenyl, optionally substituted with 1, 2, or with 3 substituents each independently selected from halo, C_1-C_6alkyl, C_3-C_6alkenyl, C_1-C_6alkoxy, hydroxy, and amino; or R^7 is naphthyl, optionally substituted with 1, 2, or with 3 substituents each independently selected from halo, C_1-C_6alkyl, C_3-C_6alkenyl, C_1-C_6alkoxy, hydroxy, and amino; or R^7 is indolyl, optionally substituted with one C_1-C_6alkyloxy-carbonyl group and optionally further with 1, 2, or with 3 substituents each independently selected from halo, C_1-C_6alkyl, C_3-C_6alkenyl, C_1-C_6alkoxy, hydroxy, and amino;

R^8 is hydrogen, C_1-C_6alkyl, benzyl, or phenyl;

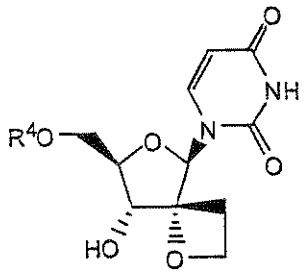
$R^{8'}$ is hydrogen, C_1-C_6alkyl, benzyl, or phenyl; or

R^8 and $R^{8'}$ together with the carbon atom to which they are attached form C_3-C_7cycloalkyl;

R^9 is C_1-C_{10}alkyl, C_3-C_7cycloalkyl or phenyl-C_1-C_6alkyl, wherein the phenyl moiety in phenyl or phenyl-C_1-C_6alkyl is optionally substituted with 1, 2 or 3 substituents each independently selected from hydroxy, C_1-C_6alkoxy, amino, mono- and diC_1-C_6alkylamino;

or a pharmaceutically acceptable salt or solvate thereof.

According to the third aspect, there is provided a compound of formula I:



(I)

including any possible stereoisomers thereof, wherein:

R^4 is a diphosphate;

R^7 is phenyl, optionally substituted with 1, 2, or with 3 substituents each independently selected from halo, C_1-C_6alkyl, C_3-C_6alkenyl, C_1-C_6alkoxy, hydroxy, and amino; or R^7 is naphthyl, optionally substituted with 1, 2, or with 3 substituents each

independently selected from halo, C_1-C_6alkyl, C_3-C_6alkenyl, C_1-C_6alkoxy, hydroxy, and amino; or R^7 is indolyl, optionally substituted with one C_1-C_6alkyloxy-carbonyl group and optionally further with 1, 2, or with 3 substituents each independently selected from halo, C_1-C_6alkyl, C_3-C_6alkenyl, C_1-C_6alkoxy, hydroxy, and amino;

R^8 is hydrogen, C_1-C_6alkyl, benzyl, or phenyl;

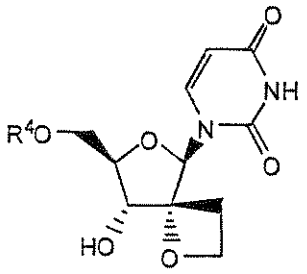
$R^{8'}$ is hydrogen, C_1-C_6alkyl, benzyl, or phenyl; or

R^8 and $R^{8'}$ together with the carbon atom to which they are attached form C_3-C_7cycloalkyl;

R^9 is C_1-C_{10}alkyl, C_3-C_7cycloalkyl or phenyl-C_1-C_6alkyl, wherein the phenyl moiety in phenyl or phenyl-C_1-C_6alkyl is optionally substituted with 1, 2 or 3 substituents each independently selected from hydroxy, C_1-C_6alkoxy, amino, mono- and diC_1-C_6alkylamino;

or a pharmaceutically acceptable salt or solvate thereof.

According to the fourth aspect, there is provided a compound of formula I:



(I)

including any possible stereoisomers thereof, wherein:

R^4 is a triphosphate;

R^7 is phenyl, optionally substituted with 1, 2, or with 3 substituents each independently selected from halo, C_1-C_6alkyl, C_3-C_6alkenyl, C_1-C_6alkoxy, hydroxy, and amino; or R^7 is naphthyl, optionally substituted with 1, 2, or with 3 substituents each independently selected from halo, C_1-C_6alkyl, C_3-C_6alkenyl, C_1-C_6alkoxy, hydroxy, and amino; or R^7 is indolyl, optionally substituted with one C_1-C_6alkyloxy-carbonyl group and optionally further with 1, 2, or with 3 substituents each independently selected from halo, C_1-C_6alkyl, C_3-C_6alkenyl, C_1-C_6alkoxy, hydroxy, and amino;

R^8 is hydrogen, C_1-C_6alkyl, benzyl, or phenyl;

$R^{8'}$ is hydrogen, C_1-C_6alkyl, benzyl, or phenyl; or

R^8 and $R^{8'}$ together with the carbon atom to which they are attached form C_3-C_7cycloalkyl;

R^9 is C_1-C_{10}alkyl, C_3-C_7cycloalkyl or phenyl-C_1-C_6alkyl, wherein the phenyl moiety in phenyl or phenyl-C_1-C_6alkyl is optionally substituted with 1, 2 or 3 substituents each independently selected from hydroxy, C_1-C_6alkoxy, amino, mono- and diC_1-C_6alkylamino;

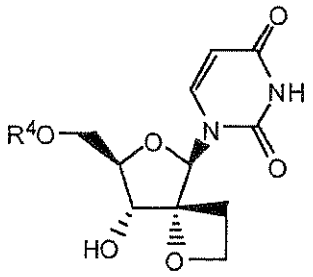
or a pharmaceutically acceptable salt or solvate thereof.

According to the fifth aspect, there is provided a pharmaceutical composition comprising an anti-virally effective amount of a compound of formula I as defined above and a pharmaceutically acceptable carrier.

According to the sixth aspect, there is provided a compound as defined above for use as an HCV inhibitor.

Description of the Invention

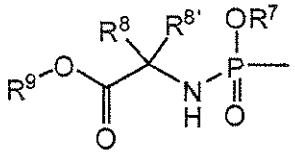
In one aspect the present invention provides compounds that can be represented by the formula I:



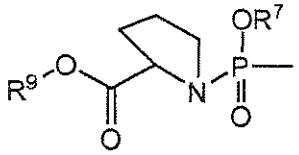
(I)

including any possible stereoisomers thereof, wherein:

R^4 is a monophosphate, diphosphate or triphosphate ester; or R^4 is a group of formula



or



R^7 is phenyl, optionally substituted with 1, 2, or with 3 substituents each independently selected from halo, C_1-C_6alkyl, C_3-C_6alkenyl, C_1-C_6alkoxy, hydroxy, and amino; or R^7 is naphthyl, optionally substituted with 1, 2, or with 3 substituents each independently selected from halo, C_1-C_6alkyl, C_3-C_6alkenyl, C_1-C_6alkoxy, hydroxy, and amino; or R^7 is indolyl, optionally substituted with one C_1-C_6alkyloxycarbonyl group and optionally further with 1, 2, or with 3 substituents each independently selected from halo, C_1-C_6alkyl, C_3-C_6alkenyl, C_1-C_6alkoxy, hydroxy, and amino;

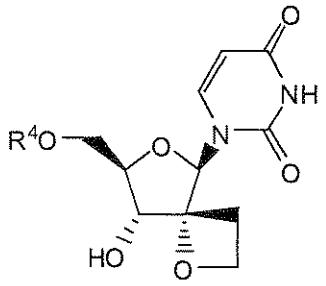
R^8 is hydrogen, C_1-C_6alkyl, benzyl, or phenyl;

$R^{8'}$ is hydrogen, C_1-C_6alkyl, benzyl, or phenyl; or

R^8 and $R^{8'}$ together with the carbon atom to which they are attached form C_3-C_7cycloalkyl;

Claims

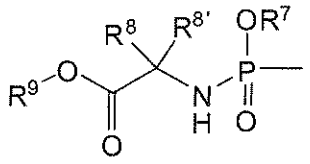
1. A compound of formula I:



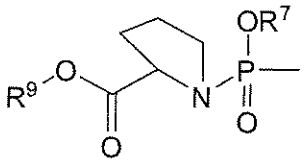
(I)

including any possible stereoisomers thereof, wherein:

~~R^4 is a monophosphate, diphosphate or triphosphate ester; or~~ R^4 is a group of formula



or



R^7 is phenyl, optionally substituted with 1, 2, or with 3 substituents each independently selected from halo, C_1-C_6alkyl, C_3-C_6alkenyl, C_1-C_6alkoxy, hydroxy, and amino; or R^7 is naphthyl, optionally substituted with 1, 2, or with 3 substituents each independently selected from halo, C_1-C_6alkyl, C_3-C_6alkenyl, C_1-C_6alkoxy, hydroxy, and amino; or R^7 is indolyl, optionally substituted with one C_1-C_6alkyloxy-carbonyl group and optionally further with 1, 2, or with 3 substituents each independently selected from halo, C_1-C_6alkyl, C_3-C_6alkenyl, C_1-C_6alkoxy, hydroxy, and amino;

R^8 is hydrogen, C_1-C_6alkyl, benzyl, or phenyl;

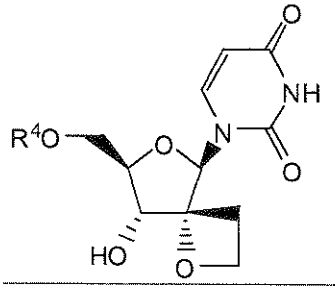
$R^{8'}$ is hydrogen, C_1-C_6alkyl, benzyl, or phenyl; or

R^8 and $R^{8'}$ together with the carbon atom to which they are attached form C_3-C_7cycloalkyl;

R^9 is C_1-C_{10}alkyl, C_3-C_7cycloalkyl or phenyl-C_1-C_6alkyl, wherein the phenyl moiety in phenyl or phenyl-C_1-C_6alkyl is optionally substituted with 1, 2 or 3 substituents each independently selected from hydroxy, C_1-C_6alkoxy, amino, mono- and diC_1-C_6alkylamino;

or a pharmaceutically acceptable salt or solvate thereof.

2. A compound of formula I:



(I)

including any possible stereoisomers thereof, wherein:

R^4 is a monophosphate;

R^7 is phenyl, optionally substituted with 1, 2, or with 3 substituents each independently selected from halo, C_1-C_6alkyl, C_3-C_6alkenyl, C_1-C_6alkoxy, hydroxy, and amino; or R^7 is naphthyl, optionally substituted with 1, 2, or with 3 substituents each independently selected from halo, C_1-C_6alkyl, C_3-C_6alkenyl, C_1-C_6alkoxy, hydroxy, and amino; or R^7 is indolyl, optionally substituted with one C_1-C_6alkyloxy-carbonyl group and optionally further with 1, 2, or with 3 substituents each independently selected from halo, C_1-C_6alkyl, C_3-C_6alkenyl, C_1-C_6alkoxy, hydroxy, and amino;

R^8 is hydrogen, C_1-C_6alkyl, benzyl, or phenyl;

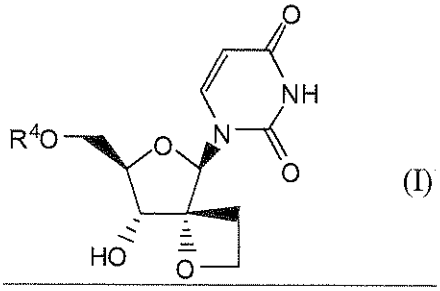
$R^{8'}$ is hydrogen, C_1-C_6alkyl, benzyl, or phenyl; or

R^8 and $R^{8'}$ together with the carbon atom to which they are attached form C_3-C_7cycloalkyl;

R^9 is C_1-C_{10}alkyl, C_3-C_7cycloalkyl or phenyl-C_1-C_6alkyl, wherein the phenyl moiety in phenyl or phenyl-C_1-C_6alkyl is optionally substituted with 1, 2 or 3 substituents each independently selected from hydroxy, C_1-C_6alkoxy, amino, mono- and diC_1-C_6alkylamino;

or a pharmaceutically acceptable salt or solvate thereof.

3. A compound of formula I:



(I)

including any possible stereoisomers thereof, wherein:

R^4 is a diphosphate;

R^7 is phenyl, optionally substituted with 1, 2, or with 3 substituents each independently selected from halo, C_1-C_6alkyl, C_3-C_6alkenyl, C_1-C_6alkoxy, hydroxy, and amino; or R^7 is naphthyl, optionally substituted with 1, 2, or with 3 substituents each independently selected from halo, C_1-C_6alkyl, C_3-C_6alkenyl, C_1-C_6alkoxy, hydroxy, and amino; or R^7 is indolyl, optionally substituted with one C_1-C_6alkyloxy-carbonyl group and optionally further with 1, 2, or with 3 substituents each independently selected from halo, C_1-C_6alkyl, C_3-C_6alkenyl, C_1-C_6alkoxy, hydroxy, and amino;

R^8 is hydrogen, C_1-C_6alkyl, benzyl, or phenyl;

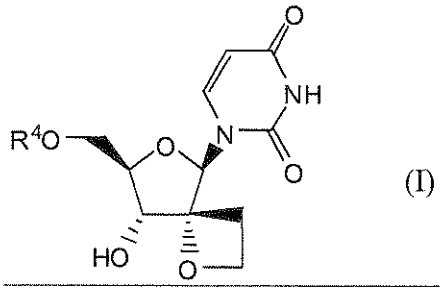
$R^{8'}$ is hydrogen, C_1-C_6alkyl, benzyl, or phenyl; or

R^8 and $R^{8'}$ together with the carbon atom to which they are attached form C_3-C_7cycloalkyl;

R^9 is C_1-C_{10}alkyl, C_3-C_7cycloalkyl or phenyl-C_1-C_6alkyl, wherein the phenyl moiety in phenyl or phenyl-C_1-C_6alkyl is optionally substituted with 1, 2 or 3 substituents each independently selected from hydroxy, C_1-C_6alkoxy, amino, mono- and diC_1-C_6alkylamino;

or a pharmaceutically acceptable salt or solvate thereof.

4. A compound of formula I:



(I)

including any possible stereoisomers thereof, wherein:

R^4 is a triphosphate;

R^7 is phenyl, optionally substituted with 1, 2, or with 3 substituents each independently selected from halo, C_1-C_6alkyl, C_3-C_6alkenyl, C_1-C_6alkoxy, hydroxy, and amino; or R^7 is naphthyl, optionally substituted with 1, 2, or with 3 substituents each independently selected from halo, C_1-C_6alkyl, C_3-C_6alkenyl, C_1-C_6alkoxy, hydroxy, and amino; or R^7 is indolyl, optionally substituted with one C_1-C_6alkyloxy-carbonyl group and optionally further with 1, 2, or with 3 substituents each independently selected from halo, C_1-C_6alkyl, C_3-C_6alkenyl, C_1-C_6alkoxy, hydroxy, and amino;

R^8 is hydrogen, C_1-C_6alkyl, benzyl, or phenyl;

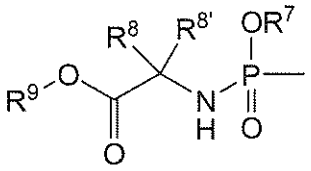
$R^{8'}$ is hydrogen, C_1-C_6alkyl, benzyl, or phenyl; or

R^8 and $R^{8'}$ together with the carbon atom to which they are attached form C_3-C_7cycloalkyl;

R^9 is C_1-C_{10}alkyl, C_3-C_7cycloalkyl or phenyl-C_1-C_6alkyl, wherein the phenyl moiety in phenyl or phenyl-C_1-C_6alkyl is optionally substituted with 1, 2 or 3 substituents each independently selected from hydroxy, C_1-C_6alkoxy, amino, mono- and diC_1-C_6alkylamino;

or a pharmaceutically acceptable salt or solvate thereof.

25. A compound according to claim 1, wherein R^4 is a group of formula



36. A compound according to any of claims 1 - 25, wherein R^7 is phenyl, optionally substituted with halo or with one or two C_1-C_6alkyl groups, or R^7 is naphthyl or indolyl.

47. A compound according to any of claims 1 - 25, wherein R^7 is phenyl, optionally substituted with halo, or with two C_1-C_6alkyl groups, or R^7 is naphthyl.

58. A compound according to any of claims 1 - 25, wherein R^7 is phenyl or naphtyl.

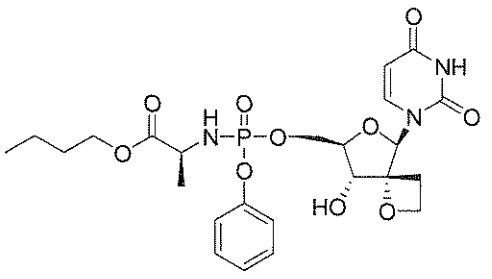
69. A compound according to any of claims 1 - 58, wherein R^8 is hydrogen, and $R^{8'}$ is hydrogen or C_1-C_6alkyl.

710. A compound according to any of claims 1-69, wherein R^8 is hydrogen and $R^{8'}$ is methyl or ethyl.

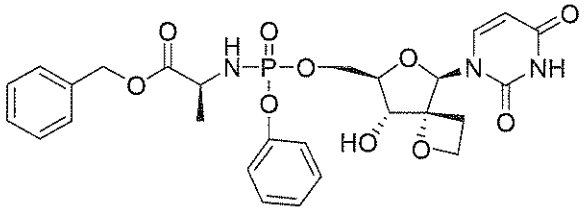
811. A compound according to any of claims 1 - 710, wherein R^9 is C_1-C_6alkyl or benzyl.

912. A compound according to any of claims 1 - 710, wherein R^9 is n.butyl or benzyl.

1013. A compound according to claim 1, wherein the compound of formula I is :



12a ,



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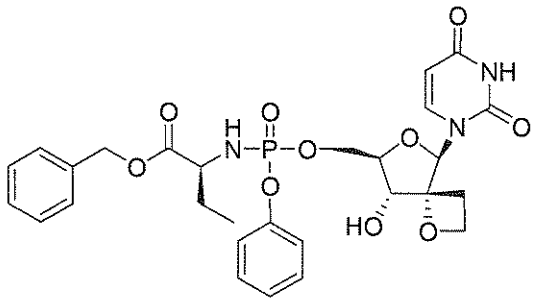
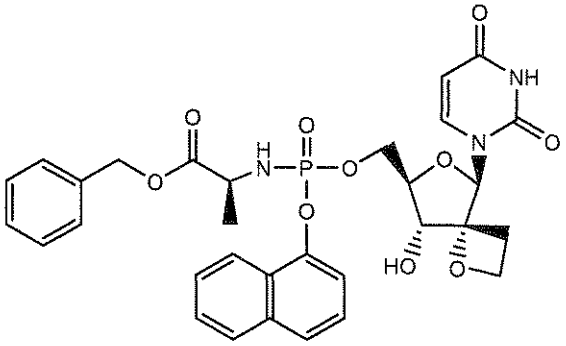


12d

, or



12k

~~11~~14. A pharmaceutical composition comprising an anti-virally effective amount of a compound of formula I as defined in any of claims 1-~~10~~13 and a pharmaceutically acceptable carrier.

~~12~~15. A compound according to any of claims 1-~~10~~13 for use as an HCV inhibitor.