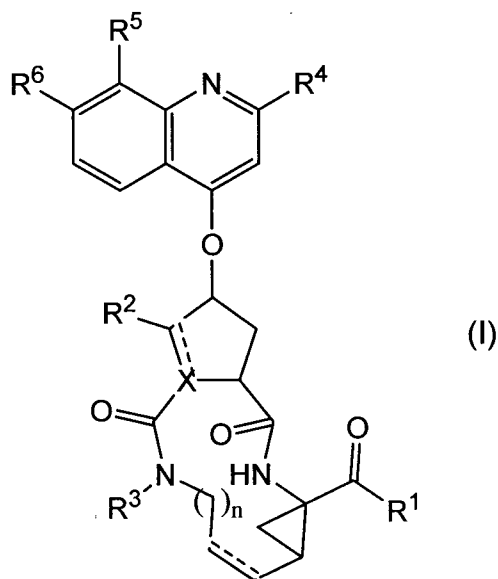


**We Claim:**

1. A compound having the formula



an *N*-oxide, salt, or stereoisomer thereof, wherein

each dashed line (represented by - - - -) represents a double bond;

**X** is N, CH and where **X** bears a double bond it is C;

**R**<sup>1</sup> is -OR<sup>7</sup>, -NH-SO<sub>2</sub>R<sup>8</sup>;

**R**<sup>2</sup> is hydrogen, and where **X** is C or CH, **R**<sup>2</sup> may also be C<sub>1-6</sub>alkyl;

**R**<sup>3</sup> is hydrogen, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxyC<sub>1-6</sub>alkyl, C<sub>3-7</sub>cycloalkyl;

**R**<sup>4</sup> is aryl or Het;

**n** is 3, 4, 5, or 6;

**R**<sup>5</sup> represents halo, C<sub>1-6</sub>alkyl, hydroxy, C<sub>1-6</sub>alkoxy, polyhaloC<sub>1-6</sub>alkyl, phenyl, or Het;

**R**<sup>6</sup> represents C<sub>1-6</sub>alkoxy, or dimethylamino;

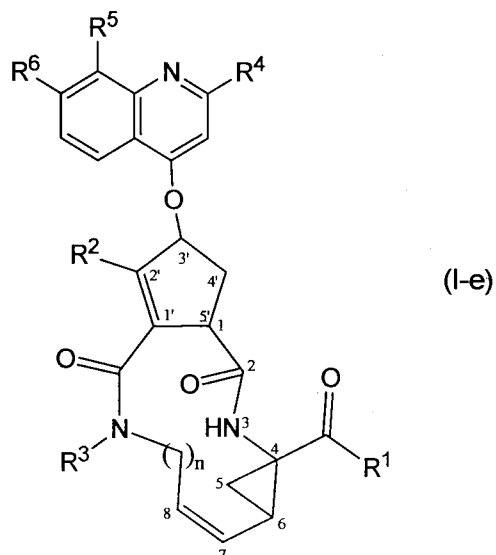
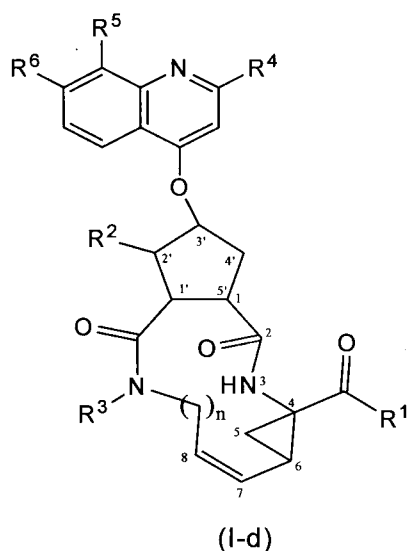
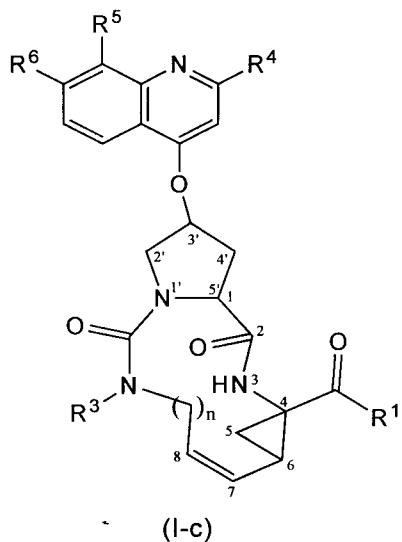
**R**<sup>7</sup> is hydrogen; aryl; Het; C<sub>3-7</sub>cycloalkyl optionally substituted with C<sub>1-6</sub>alkyl; or C<sub>1-6</sub>alkyl optionally substituted with C<sub>3-7</sub>cycloalkyl, aryl or with Het;

**R**<sup>8</sup> is aryl; Het; C<sub>3-7</sub>cycloalkyl optionally substituted with C<sub>1-6</sub>alkyl; or C<sub>1-6</sub>alkyl optionally substituted with C<sub>3-7</sub>cycloalkyl, aryl or with Het;

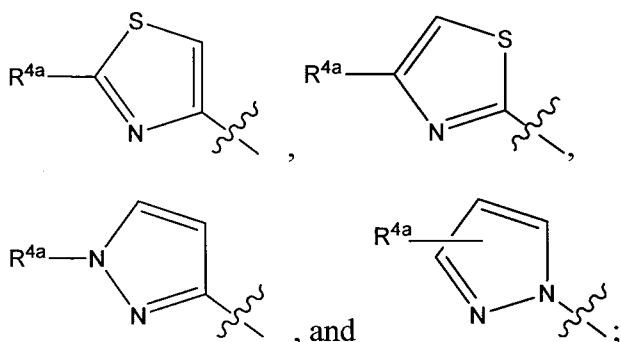
**aryl** as a group or part of a group is phenyl optionally substituted with one, two or three substituents selected from halo, hydroxy, nitro, cyano, carboxyl, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, C<sub>1-6</sub>alkoxyC<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkylcarbonyl, amino, mono- or di-C<sub>1-6</sub>alkylamino, azido, mercapto, polyhaloC<sub>1-6</sub>alkyl, polyhaloC<sub>1-6</sub>alkoxy, C<sub>3-7</sub>cycloalkyl, pyrrolidinyl, piperidinyl, piperazinyl, 4-C<sub>1-6</sub>alkylpiperazinyl, 4-C<sub>1-6</sub>alkylcarbonylpiperazinyl, and morpholinyl; wherein the morpholinyl and piperidinyl groups is optionally substituted with one or with two C<sub>1-6</sub>alkyl radicals;

**Het** as a group or part of a group is a 5 or 6 membered saturated, partially unsaturated or completely unsaturated heterocyclic ring containing 1 to 4 heteroatoms each independently selected from nitrogen, oxygen and sulfur, said heterocyclic ring being optionally condensed with a benzene ring; and wherein said Het as a whole is optionally substituted with one, two or three substituents each independently selected from the group consisting of halo, hydroxy, nitro, cyano, carboxyl, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, C<sub>1-6</sub>alkoxyC<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkylcarbonyl, amino, mono- or di-C<sub>1-6</sub>alkylamino, azido, mercapto, polyhaloC<sub>1-6</sub>alkyl, polyhaloC<sub>1-6</sub>alkoxy, C<sub>3-7</sub>cycloalkyl, pyrrolidinyl, piperidinyl, piperazinyl, 4-C<sub>1-6</sub>alkylpiperazinyl, 4-C<sub>1-6</sub>alkylcarbonylpiperazinyl, and morpholinyl; wherein the morpholinyl and piperidinyl groups is optionally substituted with one or with two C<sub>1-6</sub>alkyl radicals.

2. A compound as claimed in claim 1, wherein the compound has the formula (I-c), (I-d), or (I-e):

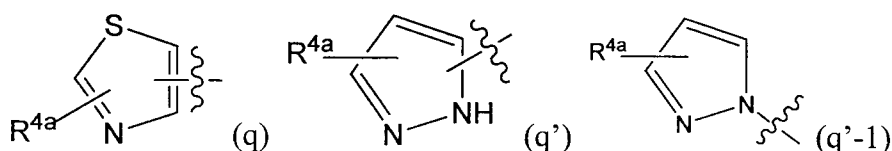


3. A compound as claimed in any one of claims 1-2, wherein  $R^4$  is selected from the group consisting of phenyl, pyridin-4-yl,



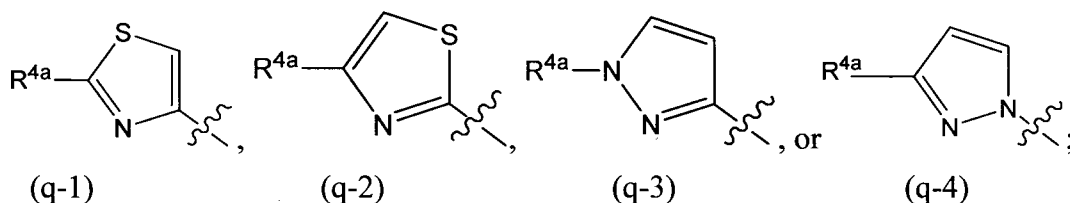
wherein  $R^{4a}$  is, each independently, hydrogen, halo,  $C_{1-6}$ alkyl, amino, or mono- or di- $C_{1-6}$ alkylamino.

4. A compound as claimed in any one of claims 1-3, wherein  $R^5$  is methyl, ethyl, isopropyl, *tert*-butyl, fluoro, chloro, or bromo; and  $R^6$  is methoxy.
5. A compound as claimed in any one of claims 1-4, wherein
- (a)  $R^1$  is  $-OR^7$ , wherein  $R^7$  is  $C_{1-6}$ alkyl or hydrogen;
  - (b)  $R^1$  is  $-NHS(=O)_2R^8$ , wherein  $R^8$  is methyl, cyclopropyl, or phenyl; or
  - (c)  $R^1$  is  $-NHS(=O)_2R^8$ , wherein  $R^8$  is cyclopropyl substituted with methyl.
6. A compound as claimed in claim 5, wherein  $R^1$  is  $-NHS(=O)_2R^8$ , wherein  $R^8$  is methyl, cyclopropyl, or phenyl.
7. A compound as claimed in any one of claims 1-5-6, wherein  $n$  is 4 or 5.
8. A compound as claimed in any one of claims 1-7, wherein  $n$  is 4.
9. A compound as claimed in any one of claims 1-8, wherein  $R^3$  is hydrogen or  $C_{1-6}$ alkyl.
10. A compound as claimed in claim 9, wherein  $R^3$  is hydrogen or methyl.
11. A compound as claimed in any one of claims 1-2, wherein  $R^4$  is a radical



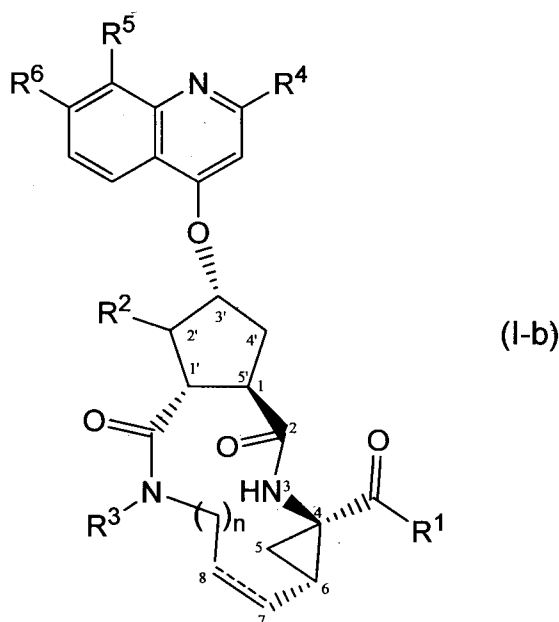
wherein, where possible a nitrogen may bear an  $R^{4a}$  substituent or a link to the remainder of the molecule; each  $R^{4a}$  in any of the  $R^4$  substituents may be selected from those mentioned as possible substituents on Het, as specified in claim 1.

12. A compound as claimed in any one of claims 1-2, wherein  $R^4$  is selected from the group consisting of:



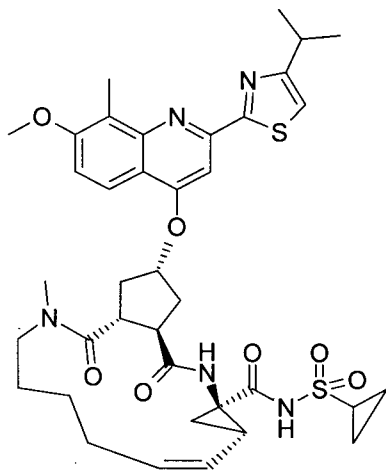
wherein each  $R^{4a}$  is hydrogen, halo,  $C_{1-6}$ alkyl, amino, or mono- or di- $C_{1-6}$ alkylamino, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, 4- $C_{1-6}$ alkylpiperazinyl; and wherein the morpholinyl and piperidinyl groups may optionally substituted with one or two  $C_{1-6}$ alkyl radicals.

13. A compound as claimed in claim 12, wherein in radicals (q-1), (q-2), (q-3), or (q-4) each  $R^{4a}$  is, each independently, hydrogen, halo,  $C_{1-6}$ alkyl, amino, or mono- or di- $C_{1-6}$ alkylamino.
14. A compound as claimed in any one of claims 1-13, wherein  $R^6$  is methoxy.
15. A compound as claimed in claim 1, wherein the compound has the structure:

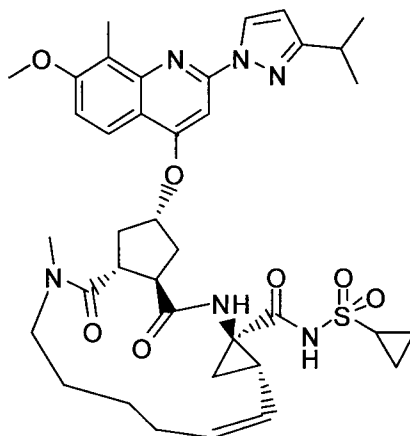


16. A compound as claimed in claim 15 wherein  $R^2$  is hydrogen and a double bond is present between carbon atoms 7 and 8.

17. A compound as claimed in claim 1 wherein the compound of formula (I) is:



21. A compound as claimed in claim 1 wherein the compound of formula (I) is:



22. A compound as claimed in any of claims 1-21 other than an N-oxide, or salt.

23. A compound as claimed in any of claims 1-21 other than an N-oxide.

24. A pharmaceutical composition comprising a carrier, and as active ingredient an anti-virally effective amount of a compound as claimed in any one of claims 1-23.

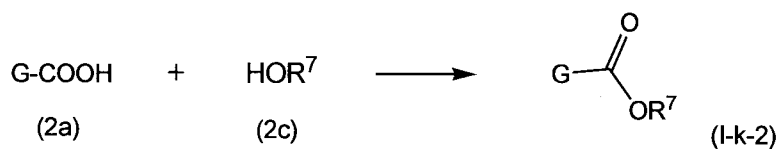
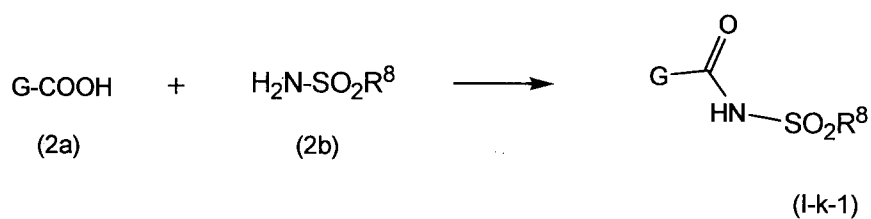
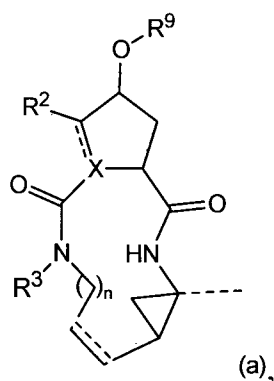
25. A compound according to any of claims 1-23, for use as a medicament and for inhibiting HCV replication.

26. A process for preparing a compound as claimed in any of claims 1 - 23, wherein said process comprises:

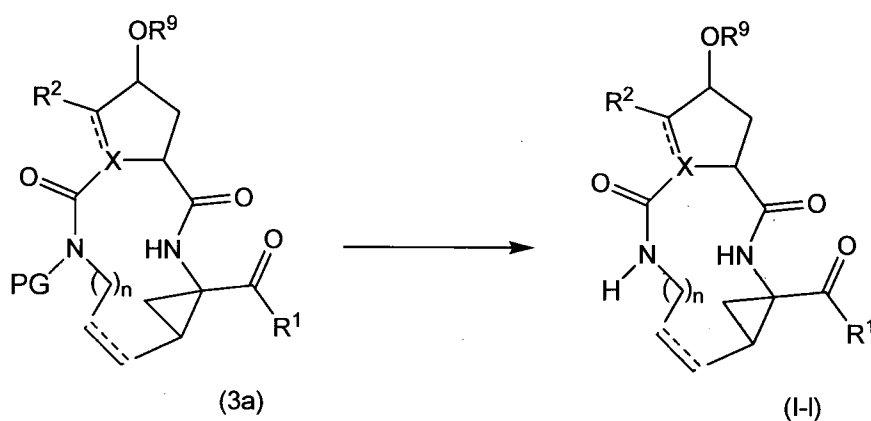
(a) preparing a compound of formula (I) wherein the bond between C<sub>7</sub> and C<sub>8</sub> is a double bond, which is a compound of formula (I-i), by forming a double bond between C<sub>7</sub> and C<sub>8</sub>, in particular via an olefin metathesis reaction, with concomitant cyclization to the macrocycle as outlined in the following reaction scheme:



an intermediate (2a) and an alcohol (2c) as outlined in the following scheme wherein G represents a group:

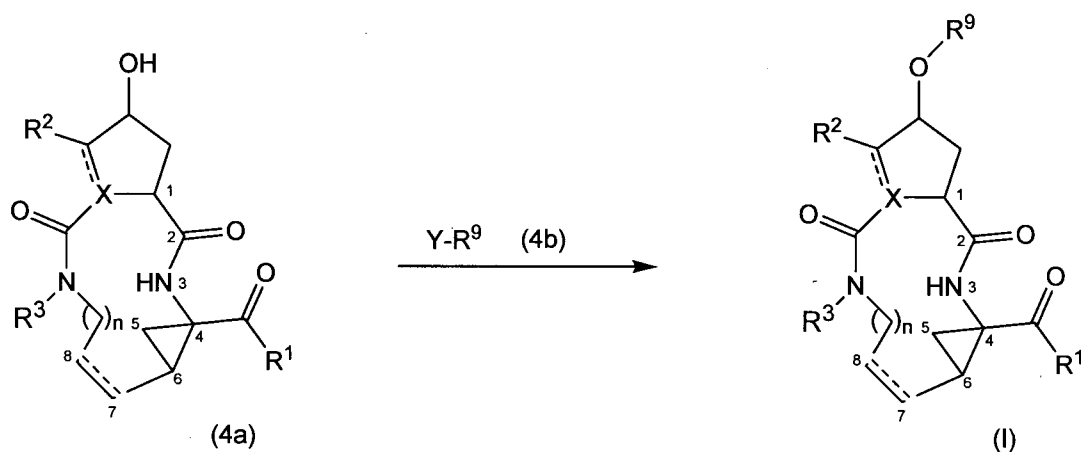


(d) preparing a compound of formula (I) wherein R<sup>3</sup> is hydrogen, said compound being represented by (I-l), from a corresponding nitrogen-protected intermediate (3a), wherein PG represents a nitrogen protecting group:



(e) reacting an intermediate (4a) with intermediate (4b) as outlined in the following reaction scheme:






wherein Y in (4b) represents hydroxy or a leaving group; and where Y represents hydroxy the reaction of (4a) with (4b) is a Mitsunobu reaction; and where Y represents a leaving group the reaction of (4a) with (4b) is a substitution reaction;

(f) converting compounds of formula (I) into each other by a functional group transformation reaction; or

(g) preparing a salt form by reacting the free form of a compound of formula (I) with an acid or a base.

Dated this 28.12.2007

  
 [PAYAL KALRA]  
 OF REMFRY & SAGAR  
 ATTORNEY FOR THE APPLICANT[S]