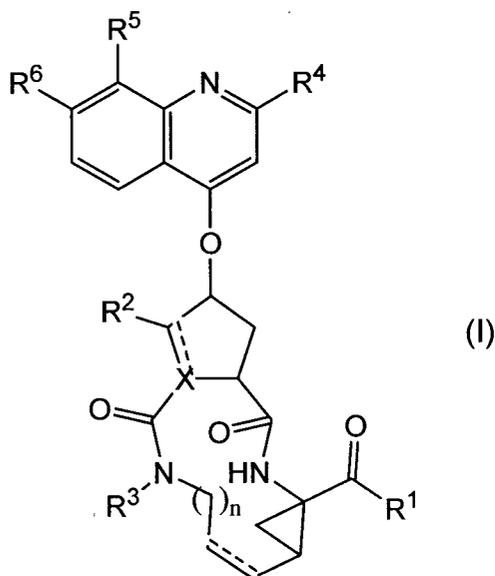


We Claim:

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;

R¹ is -OR⁷, -NH-SO₂R⁸;

R² is hydrogen, and where **X** is C or CH, **R**² may also be C₁₋₆alkyl;

R³ is hydrogen, C₁₋₆alkyl, C₁₋₆alkoxyC₁₋₆alkyl, C₃₋₇cycloalkyl;

R⁴ is aryl or Het;

n is 3, 4, 5, or 6;

R⁵ represents halo, C₁₋₆alkyl, hydroxy, C₁₋₆alkoxy, polyhaloC₁₋₆alkyl, phenyl, or Het;

R⁶ represents C₁₋₆alkoxy, or dimethylamino;

R⁷ is hydrogen; aryl; Het; C₃₋₇cycloalkyl optionally substituted with C₁₋₆alkyl; or

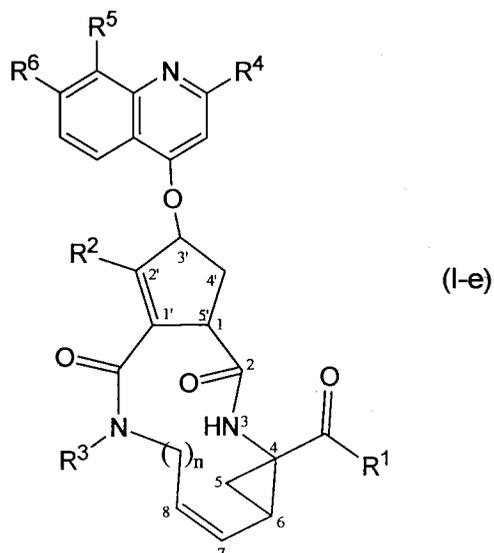
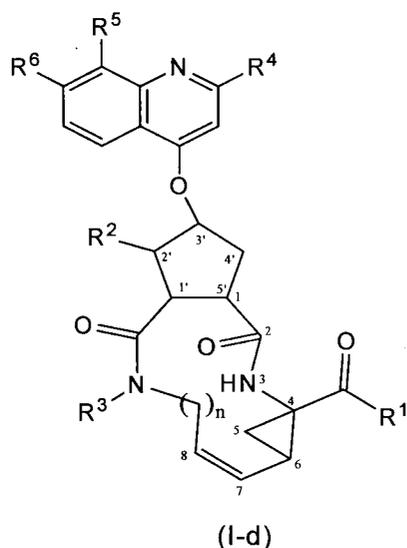
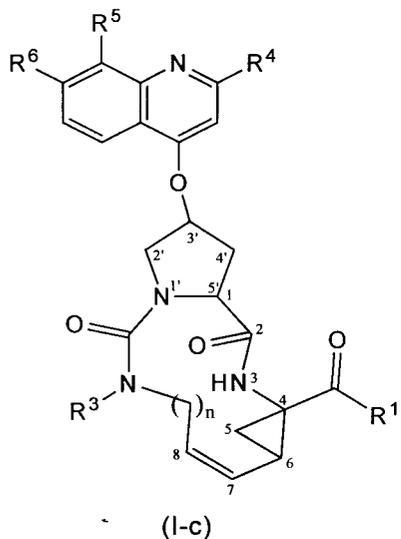
C₁₋₆alkyl optionally substituted with C₃₋₇cycloalkyl, aryl or with Het;

R⁸ is aryl; Het; C₃₋₇cycloalkyl optionally substituted with C₁₋₆alkyl; or C₁₋₆alkyl optionally substituted with C₃₋₇cycloalkyl, aryl or with Het;

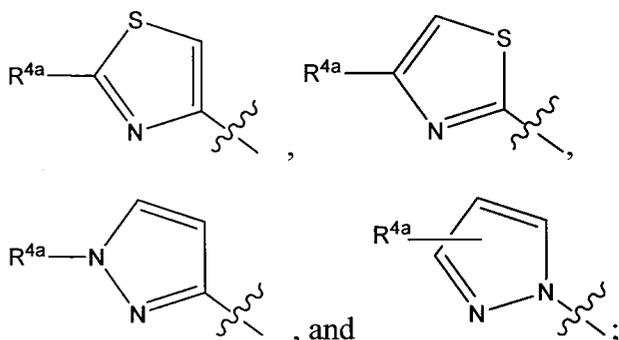
aryl as a group or part of a group is phenyl optionally substituted with one, two or three substituents selected from halo, hydroxy, nitro, cyano, carboxyl, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxyC₁₋₆alkyl, C₁₋₆alkylcarbonyl, amino, mono- or di-C₁₋₆alkylamino, azido, mercapto, polyhaloC₁₋₆alkyl, polyhaloC₁₋₆alkoxy, C₃₋₇cycloalkyl, pyrrolidinyl, piperidinyl, piperazinyl, 4-C₁₋₆alkylpiperazinyl, 4-C₁₋₆alkylcarbonylpiperazinyl, and morpholinyl; wherein the morpholinyl and piperidinyl groups is optionally substituted with one or with two C₁₋₆alkyl 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, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxyC₁₋₆alkyl, C₁₋₆alkylcarbonyl, amino, mono- or di-C₁₋₆alkylamino, azido, mercapto, polyhaloC₁₋₆alkyl, polyhaloC₁₋₆alkoxy, C₃₋₇cycloalkyl, pyrrolidinyl, piperidinyl, piperazinyl, 4-C₁₋₆alkylpiperazinyl, 4-C₁₋₆alkylcarbonylpiperazinyl, and morpholinyl; wherein the morpholinyl and piperidinyl groups is optionally substituted with one or with two C₁₋₆alkyl radicals.

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

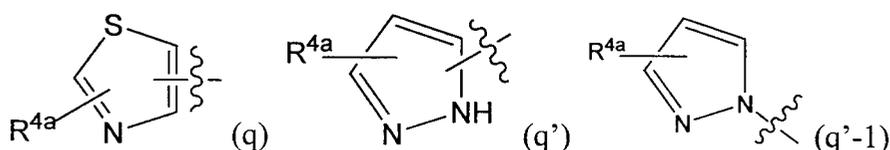


3. A compound as claimed in any one of claims 1-2, wherein R^4 is selected from the group consisting of phenyl, pyridin-4-yl,



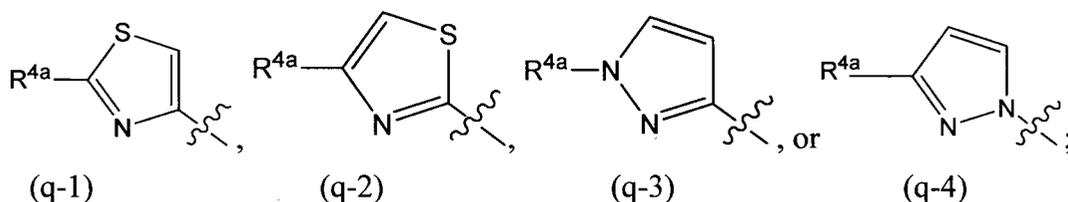
wherein R^{4a} is, each independently, hydrogen, halo, C_{1-6} alkyl, amino, or mono- or di- C_{1-6} alkylamino.

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
- R^1 is $-OR^7$, wherein R^7 is C_{1-6} alkyl or hydrogen;
 - R^1 is $-NHS(=O)_2R^8$, wherein R^8 is methyl, cyclopropyl, or phenyl; or
 - 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.
- 7.6. 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



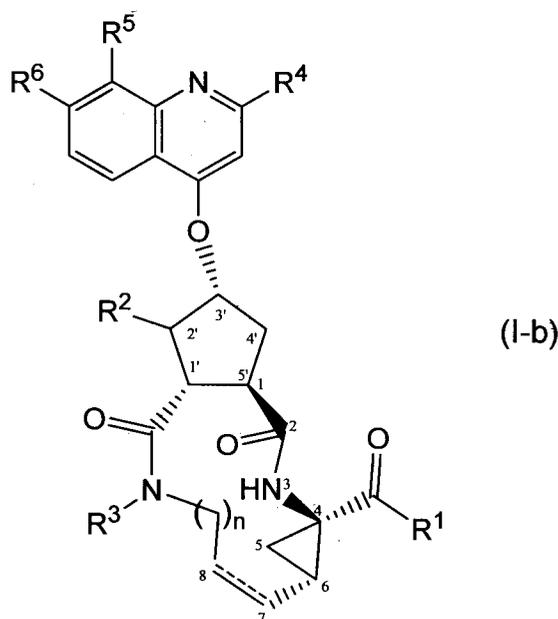
wherein, where possible a nitrogen may bear an R^{4a} substituent or a link to the remainder of the molecule; each R^{4a} in any of the R^4 substituents may be selected from those mentioned as possible substituents on Het, as specified in claim 1.

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



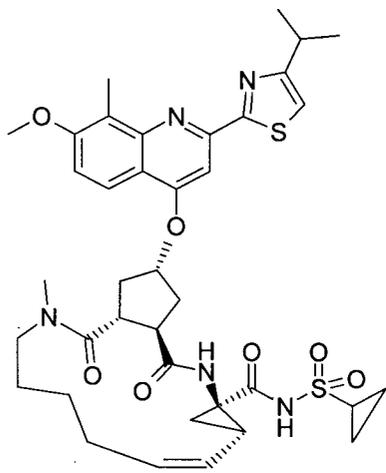
wherein each R^{4a} is hydrogen, halo, C_{1-6} alkyl, amino, or mono- or di- C_{1-6} alkylamino, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, 4- C_{1-6} alkylpiperazinyl; and wherein the morpholinyl and piperidinyl groups may optionally substituted with one or two C_{1-6} alkyl radicals.

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:



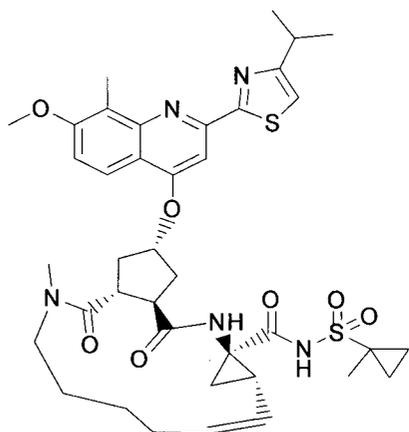
16. A compound as claimed in claim 15 wherein R² is hydrogen and a double bond is present between carbon atoms 7 and 8.

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

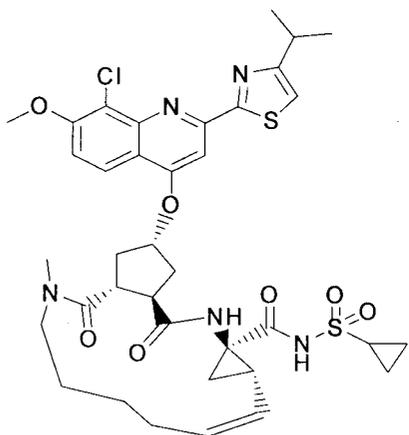


18. A compound as claimed in claim 17, wherein the compound is a white solid.

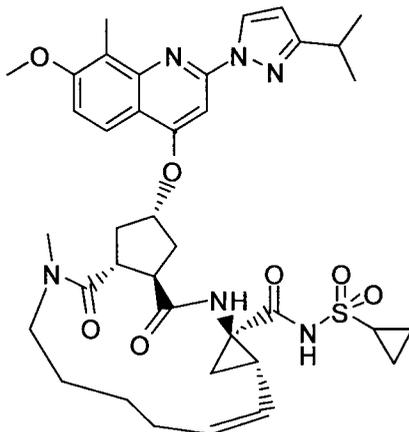
19. A compound as claimed in claim 1 wherein the compound of formula (I) is:



20. 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.

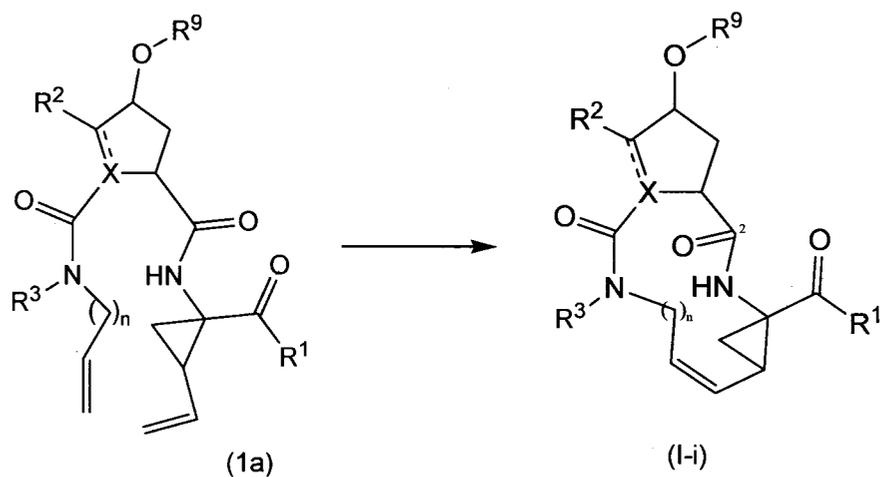
23. A compound as claimed in any of claims 1-21 other than an N-oxide.

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.

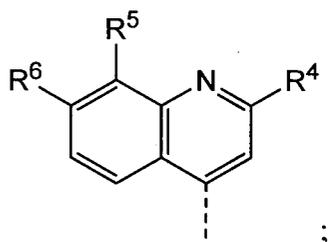
25. A compound according to any of claims 1-23, for use as a medicament and for inhibiting HCV replication.

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

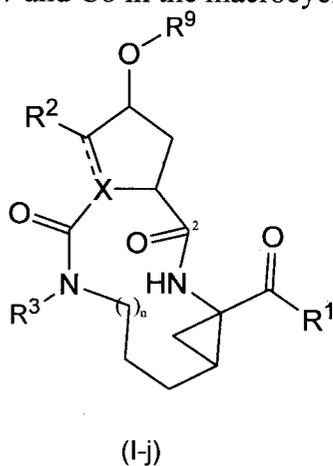
(a) preparing a compound of formula (I) wherein the bond between C₇ and C₈ is a double bond, which is a compound of formula (I-i), by forming a double bond between C₇ and C₈, in particular via an olefin metathesis reaction, with concomitant cyclization to the macrocycle as outlined in the following reaction scheme:



wherein in the above and following reaction schemes R^9 represents a radical



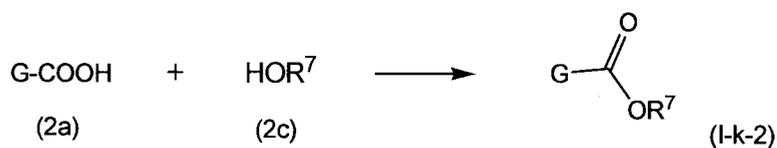
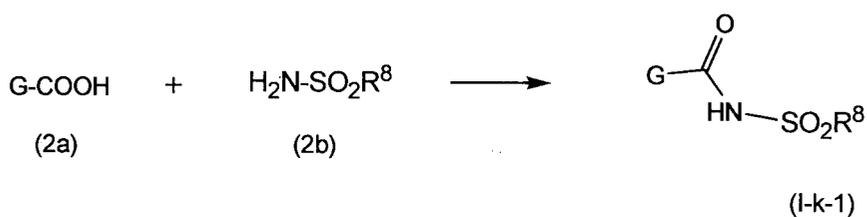
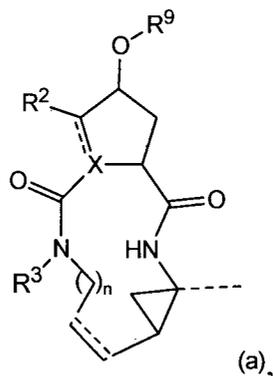
(b) converting a compound of formula (I-i) to a compound of formula (I) wherein the link between C7 and C8 in the macrocycle is a single bond, i.e. a compound of formula (I-j):



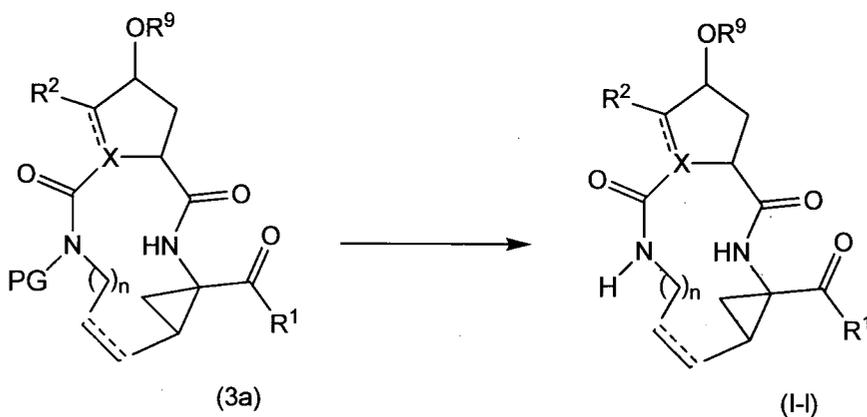
by a reduction of the C7-C8 double bond in the compounds of formula (I-j);

(c) preparing a compound of formula (I) wherein R^1 represents $-NH\text{SO}_2R^8$, said compounds being represented by formula (I-k-1), by forming an amide bond between an intermediate (2a) and an sulfonamide (2b), or preparing a compound of formula (I) wherein R^1 represents $-OR^7$, i.e. a compound (I-k-2), by forming an ester bond between

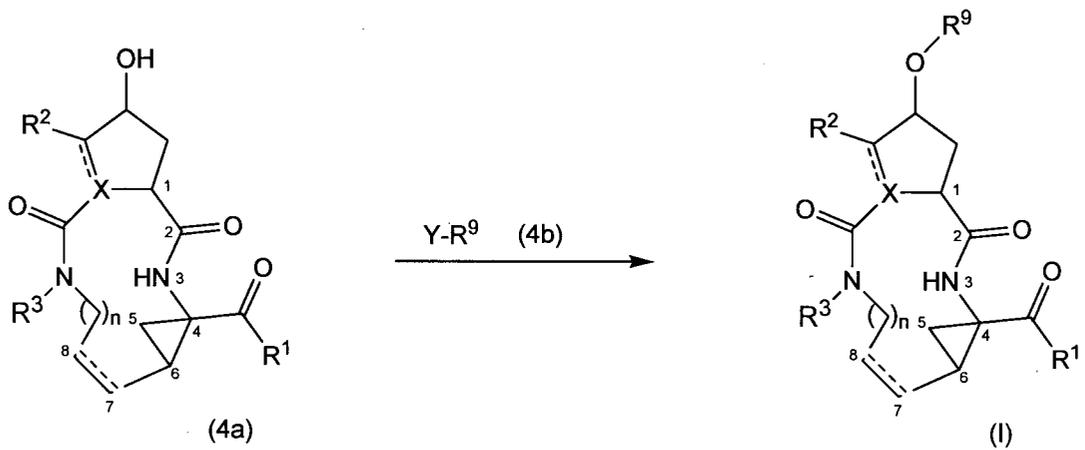
an intermediate (2a) and an alcohol (2c) as outlined in the following scheme wherein G represents a group:



(d) preparing a compound of formula (I) wherein R³ 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


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