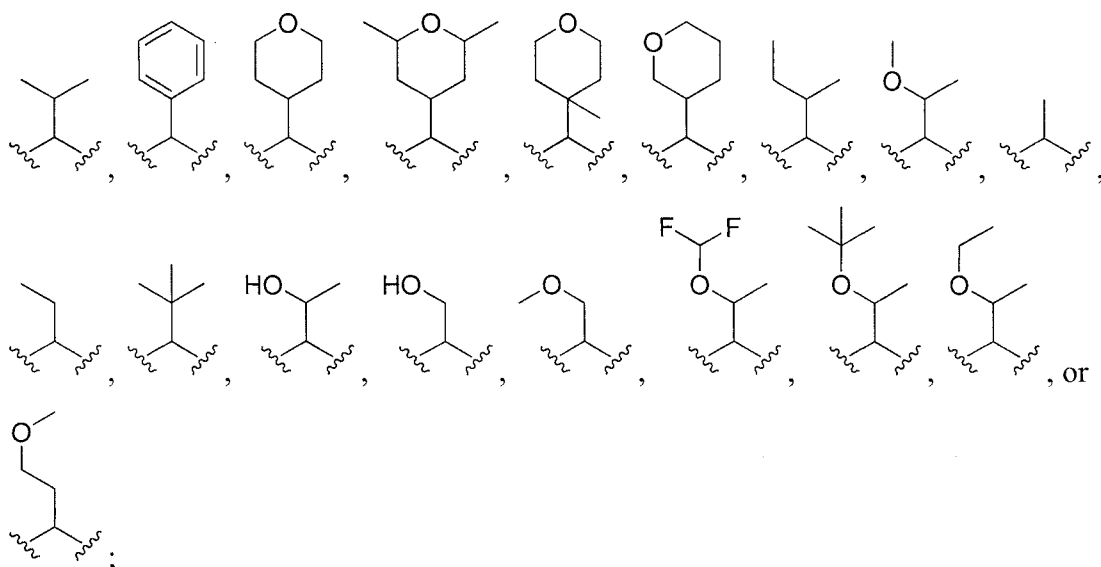
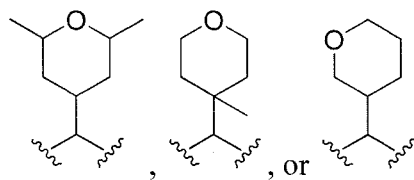


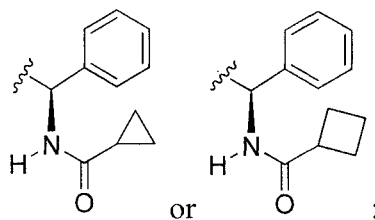


provided that at least one of V^{1a} and V^{1b} is



- 5 E^{1a} and E^{1b} are each independently -N(H)(alkoxycarbonyl), -N(H)(cycloalkylcarbonyl), or -N(H)(cycloalkyloxycarbonyl); or E^{1a} - V^{1a} taken together are R^{9a} ; or E^{1b} - V^{1b} taken together are R^{9b} ; and

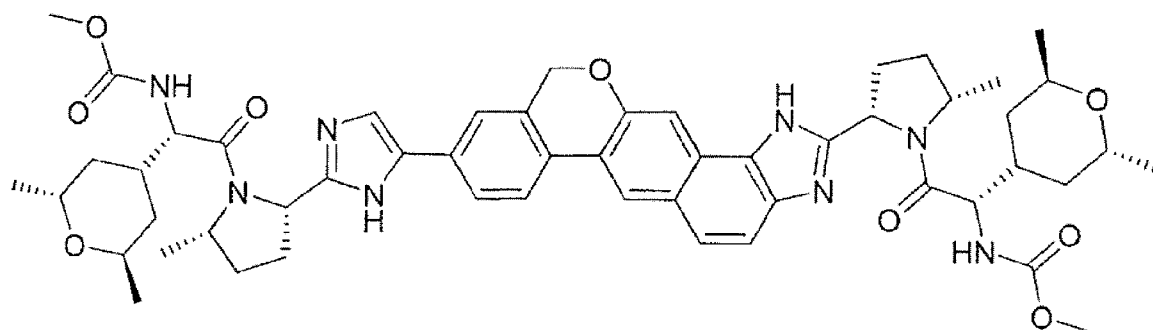
R^{9a} and R^{9b} are each independently:



- 10 or a pharmaceutically acceptable salt or prodrug thereof.

The disclosure also provides isotopically enriched compounds that are compounds of the disclosure that comprise an enriched isotope at one or more positions in the compound.

In one aspect, there is provided compound having the formula:



or a pharmaceutically acceptable salt thereof.

The present disclosure also provides a pharmaceutical composition comprising a compound of the disclosure or a pharmaceutically acceptable salt or prodrug thereof and at least one pharmaceutically acceptable carrier.

In one aspect, there is provided a pharmaceutical composition comprising the compound as described above or a pharmaceutically acceptable salt thereof; and at least one pharmaceutically acceptable carrier.

In one aspect, there is provided a pharmaceutical composition as described above for use in treating hepatitis C (HCV). In one embodiment the composition comprises at least one additional therapeutic agent for treating HCV. In one embodiment, the therapeutic agent is selected

from ribavirin, an NS3 protease inhibitor, a nucleoside or nucleotide inhibitor of HCV NS5B polymerase, an alpha-glucosidase 1 inhibitor, a hepatoprotectant, a non-nucleoside inhibitor of HCV polymerase, or combinations thereof. In one embodiment, the composition further comprises a nucleoside or nucleotide inhibitor of HCV NS5B polymerase. In one
5 embodiment, the nucleoside or nucleotide inhibitor of HCV NS5B polymerase is selected from ribavirin, viramidine, levovirin, a L-nucleoside, or isatoribine.

In one aspect, provided is a pharmaceutical composition comprising a compound as described herein or a pharmaceutically acceptable salt thereof, at least one nucleoside or nucleotide inhibitor of HCV NS5B polymerase, and at least one pharmaceutically acceptable
10 carrier. In one embodiment, the composition further comprises an interferon, a pegylated interferon, ribavirin or combinations thereof. In one embodiment, the nucleoside or nucleotide inhibitor of HCV NS5B polymerase is sofosbuvir. In one aspect, provided is a pharmaceutical composition comprising a compound as described herein or a pharmaceutically acceptable salt thereof, at least one NS3 protease inhibitor, and at least one
15 pharmaceutically acceptable carrier. In one embodiment, the composition further comprises sofosbuvir.

The present disclosure also provides a pharmaceutical composition further comprising an interferon or pegylated interferon.

The present disclosure also provides a pharmaceutical composition further comprising
20 a nucleoside analog.

The present disclosure also provides for a pharmaceutical composition wherein said nucleoside analogue is selected from ribavirin, viramidine, levovirin, an L-nucleoside, and isatoribine and said interferon is α -interferon or pegylated α -interferon.

The present disclosure also provides for a method of treating hepatitis C, said method
25 comprising administering to a human patient a pharmaceutical composition which comprises a therapeutically effective amount of a compound of the disclosure.

The present disclosure also provides a method of inhibiting HCV, comprising administering to a mammal afflicted with a condition associated with HCV activity, an amount of a compound of the disclosure, effective to inhibit HCV.

The present disclosure also provides a compound of the disclosure for use in medical
30 therapy (e.g. for use in inhibiting HCV activity or treating a condition associated with HCV activity), as well as the use of a compound of the disclosure for the manufacture of a

medicament useful for inhibiting HCV or the treatment of a condition associated with HCV activity in a mammal. In one aspect, there is provided a compound as described above or a pharmaceutically acceptable salt thereof for use in medical therapy. In one aspect, there is provided a compound as described above or a pharmaceutically acceptable salt thereof, for use in a method of treating hepatitis C, said method comprising administering to a human patient a pharmaceutical composition which comprises a therapeutically effective amount of the compound or pharmaceutically acceptable salt thereof.

The present disclosure also provides synthetic processes and novel intermediates disclosed herein which are useful for preparing compounds of the disclosure. Some of the compounds of the disclosure are useful to prepare other compounds of the disclosure. In another embodiment the disclosure provides a compound of the disclosure, or a pharmaceutically acceptable salt or prodrug thereof, for use in the prophylactic or therapeutic treatment of hepatitis C or a hepatitis C associated disorder.

In another embodiment the disclosure provides a method of inhibiting HCV activity in a sample comprising treating the sample with a compound of the disclosure.

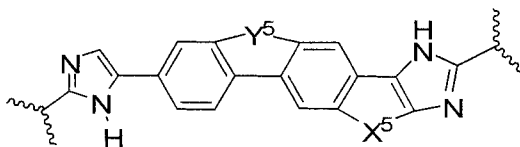
Compounds of formula (I) have been found to possess useful activity against several HCV genotypes. Additionally certain compounds of formula (I) exhibit significant potency against resistant variants in, e.g., GT1.

DETAILED DESCRIPTION

Reference will now be made in detail to certain embodiments of the disclosure, examples of which are illustrated in the accompanying structures and formulas. While the disclosure will be described in conjunction with the enumerated embodiments, it will be understood that they are not intended to limit the disclosure to those embodiments. On the contrary, the disclosure is intended to cover all alternatives, modifications, and equivalents, which may be included within the scope of the present disclosure as defined by the embodiments.

Compounds

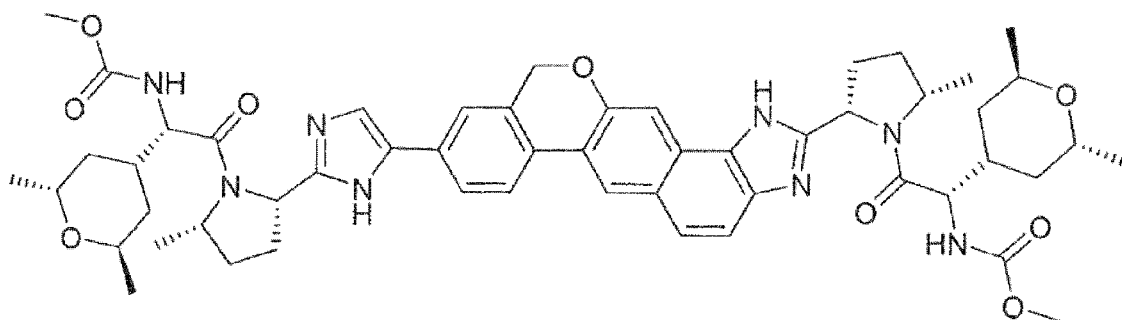
The "P" groups (e.g., P^{1a} and P^{1b}) defined for formula (I) herein have one bond to a -C(=O)- of formula (I) and one bond to a W^{1a} group. It is to be understood that a nitrogen of the P group is connected to the -C(=O)- group of formula (I) and that a carbon of the P group is connected to the W^{1a} group.



In the W^{1a} group, a Y⁵ group is present. When that Y⁵ group is defined as -O-CH₂-, or -CH₂-O- group, those Y⁵ groups have a directionality. The Y⁵ group is connected to the W^{1a}

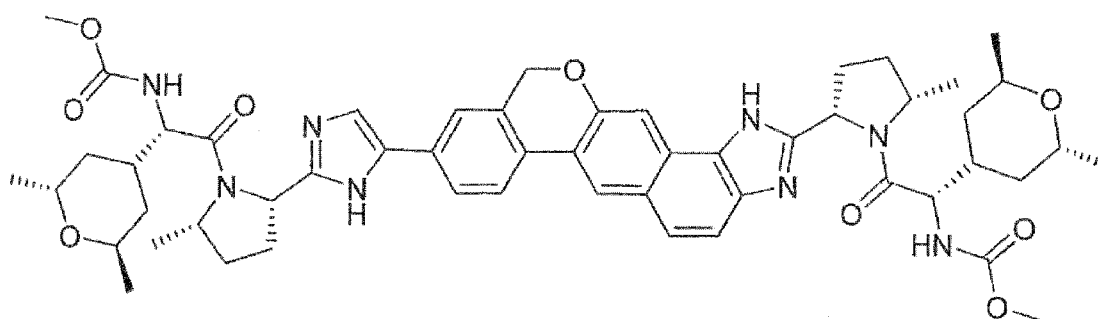
Claims

1. A compound having the formula:



or a pharmaceutically acceptable salt thereof.

2. A compound according to claim 1 having the formula:



3. A pharmaceutical composition comprising the compound as described in claim 1 or claim 2 or a pharmaceutically acceptable salt thereof; and at least one pharmaceutically acceptable carrier.
4. The pharmaceutical composition of claim 3 for use in treating hepatitis C (HCV).
5. The pharmaceutical composition of claim 3, further comprising at least one additional therapeutic agent for treating HCV.
6. The pharmaceutical composition of claim 5, wherein said additional therapeutic agent is selected from ribavirin, an NS3 protease inhibitor, a nucleoside or nucleotide inhibitor of HCV NS5B polymerase, an alpha-glucosidase 1 inhibitor, a hepatoprotectant, a non-nucleoside inhibitor of HCV polymerase, or combinations thereof.

7. The pharmaceutical composition according to claim 3, further comprising a nucleoside or nucleotide inhibitor of HCV NS5B polymerase.
8. The pharmaceutical composition according to claim 7, wherein said nucleoside or nucleotide inhibitor of HCV NS5B polymerase is selected from ribavirin, viremagine, levovirin, a L-nucleoside, or isatoribine.
9. A pharmaceutical composition comprising a compound as described in claim 1 or claim 2 or a pharmaceutically acceptable salt thereof, at least one nucleoside or nucleotide inhibitor of HCV NS5B polymerase, and at least one pharmaceutically acceptable carrier.
10. The pharmaceutical composition according to claim 9, further comprising an interferon, a pegylated interferon, ribavirin or combinations thereof.
11. The pharmaceutical composition of any one of claims 9-10, wherein the nucleoside or nucleotide inhibitor of HCV NS5B polymerase is sofosbuvir.
12. A pharmaceutical composition comprising a compound as described in claim 1 or claim 2 or a pharmaceutically acceptable salt thereof, at least one NS3 protease inhibitor, and at least one pharmaceutically acceptable carrier.
13. The pharmaceutical composition according to claim 12, further comprising sofosbuvir.
14. A compound as described in claim 1 or claim 2 or a pharmaceutically acceptable salt thereof, for use in a method of treating hepatitis C, said method comprising administering to a human patient a pharmaceutical composition which comprises a therapeutically effective amount of the compound or pharmaceutically acceptable salt thereof.
15. The compound or pharmaceutically acceptable salt thereof for the use according to claim 14, wherein the method further comprises administering to the patient an interferon or pegylated interferon.
16. The compound or pharmaceutically acceptable salt thereof for the use of any one of claims 14-15, wherein the method further comprises administering to the patient ribavirin.
17. A compound as described in claim 1 or claim 2 or a pharmaceutically acceptable salt thereof for use in medical therapy.