Title: NAPHTHALIMIDE DERIVATIVES AS ANTIVIRAL AGENTS

Abstract: The present invention relates to the use of naphthalimide compounds of formula (I), wherein A, B, R₁, R₂, n and R₈ are defined herein, and pharmaceutically acceptable salts thereof, for the treatment or prevention of infection by hepatitis C virus.
Naphthalimide derivatives as antiviral agents

This invention relates to compounds which can act as inhibitors of viral polymerases, especially the hepatitis C virus (HCV) polymerase, to uses of such compounds in the treatment and prevention of infection by hepatitis C virus, and to their preparation.

The hepatitis C virus (HCV) is the major causative agent of parenterally-transmitted and sporadic non-A, non-B hepatitis (NANB-H). Some 1% of the human population of the planet is believed to be affected. Infection by the virus can result in chronic hepatitis and cirrhosis of the liver, and may lead to hepatocellular carcinoma. Currently no vaccine nor established therapy exists, although partial success has been achieved in a minority of cases by treatment with recombinant interferon-α, either alone or in combination with ribavirin. There is therefore a pressing need for new and broadly-effective therapeutics.

Several virally-encoded enzymes are putative targets for therapeutic intervention, including a metalloprotease (NS2-3), a serine protease (NS3), a helicase (NS3), and an RNA-dependent RNA polymerase (NS5B). Of these, the polymerase plays an essential role in replication of the virus and is therefore an important target in the fight against hepatitis C.

Certain naphthalimide derivatives have been disclosed in the art but none are disclosed as being useful as inhibitors of hepatitis C virus (HCV) polymerase.

Published International application WO 00/32577 (Merck Patent GmbH) discloses the compounds of formula (A):

\[ \text{(A)} \]

where R, R¹ and R² are as defined therein, as glycoprotein IbIX antagonists.

Published International application WO 00/01672 (Taiho Pharmaceutical Co., Ltd.) discloses the compounds of formula (B):

\[ \text{(B)} \]

where X¹, Y, A¹, R¹, R² and e are as defined therein. These compounds are disclosed as being useful as antitumour agents.

However none of these disclosures relate to the treatment of hepatitis C virus infections.

It has now surprisingly been found that certain naphthalimide derivatives, including certain of the known compounds referred to above, act as inhibitors of the hepatitis C virus (HCV) polymerase enzyme.

Thus, in one aspect, there is provided the use of a compound of formula (I):

\[
(R^2)\text{A}N\text{B}R^1
\]

or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment or prevention of infection by hepatitis C virus,

wherein

A and B are each independently CH₂, C=O or C=S, with the proviso that A and B are not both CH₂;

R¹ is C₁₋₄alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, (CH₂)ₐ₋₁₃cycloalkyl, (CH₂)₂₋₁₀Het, (CH₂)₂₋₁₀aryl or (CH₂)₂₋₁₀heteroaryl, optionally substituted by halogen, hydroxy, C₁₋₄alkyl, C₁₋₄alkoxy, C₂₋₆alkenyl, CN, (CH₂)₂₋₁₀O(CH₂)₂₋₁₀aryl, S(C₁₋₄alkyl), S(O)(C₁₋₄alkyl), S(O)₂(C₁₋₄alkyl), S-heteroaryl, S(O)heteroaryl, S(O)₂heteroaryl, S-aryl, S(O)aryl, S(O)₂aryl, SO₂NR¹R², CO₂R¹, CONR¹R², NR¹COR¹, NR¹SO₂R² or NR¹CONR¹ where said C₁₋₄alkyl, (CH₂)₂₋₁₀Het, (CH₂)₂₋₁₀aryl and (CH₂)₂₋₁₀heteroaryl groups, either by themselves or as part of other substituents, may optionally be substituted by 1 to 8 halogen atoms, and where said (CH₂)₂₋₁₀Het, (CH₂)₂₋₁₀aryl and (CH₂)₂₋₁₀heteroaryl groups may optionally be further substituted with one or two groups selected from hydroxy, C₁₋₄alkoxy, C₁₋₄alkyl, (CH₂)₂₋₁₀CO₂H, (CH₂)₂₋₁₀CO₂C₁₋₄alkyl and C(O)NR¹R², and where said (CH₂)₂₋₁₀aryl group may be fused to C₃₋₅cycloalkyl;

R⁴, R⁵ and R²¹ are each independently selected from hydrogen, C₁₋₄alkyl, (CH₂)₂₋₁₀Het, (CH₂)₂₋₁₀aryl, (CH₂)₂₋₁₀heteroaryl and SO₂(C₁₋₄alkyl), optionally substituted by 1 to 5 halogen atoms and/or 1 or 2 groups selected from hydroxy, C₁₋₄alkyl, NH₂ and C₁₋₄alkoxy;

R² is halogen, hydroxy, C₁₋₄alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₄alkoxy, (CH₂)₂₋₁₀C₅₋₆cycloalkyl, (CH₂)₂₋₁₀aryl, CN, NO₂, NR²R³, OR³, CO₂R³, CONR³R⁴, NR³COR³, NR³SO₂R³, NR³CONR³, SR³, SOR³, SO₂R³ or SO₃NR³R⁴, where said C₁₋₄alkyl, C₂₋₆alkenyl, C₁₋₄alkoxy and aryl groups are optionally substituted by 1 to 2 groups selected from halogen, hydroxy, C₁₋₄alkyl, C₁₋₄alkoxy, NH₂, SO₂NR³R⁴, CO₂R³ and CONR³R⁴;

R⁶ and R⁷ are each independently selected from hydrogen, C₁₋₄alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, (CH₂)₂₋₁₀C₅₋₆cycloalkyl, (CH₂)₂₋₁₀Het, (CH₂)₂₋₁₀aryl, (CH₂)₂₋₁₀heteroaryl, (CH₂)₂₋₁₀OR³, (CH₂)₂₋₁₀SR³,
(CH₂)₃NR¹⁰R¹¹, -C(CH₂OH)₂, COR₂², C(O)C(O)OC₁₋₆alkyl, CO₂R₂², CONR²²R²³, SO₂R²² and
SO₂NR²²R²³, where said C₁₋₆alkyl, C₂₋₆alkenyl, C₆₋₁₄alkynyl, cycloalkyl, Het, aryl and heteroaryl groups
are optionally substituted by 1 or 2 groups selected from halogen, hydroxy, C₁₋₆alkyl, CF₃, NH₂,
N(C₁₋₆alkyl)₂, SO₂aryl, SO₂NR₁⁸R₁⁹, (CH₂)₁₋₃aryl, (CH₂)₁₋₃heteroaryl, C(O)C₁₋₆alkyl, C(O)(CH₂)₁₋₃aryl,
(CH₂)₁₋₃CO₂R₁⁸, (CH=CH)CO₂R₁⁸, CONR¹⁸R¹⁹ and O(CH₂)₁₋₃aryl, which optional aryl substituents are
further optionally substituted by CO₂H or Het;
R¹⁸ and R¹⁹ are each independently selected from hydrogen, C₁₋₆alkyl, C₂₋₆alkenyl,
(CH₂)₁₋₃C₃₋₇cycloalkyl, (CH₂)₁₋₃Het, (CH₂)₁₋₃aryl, (CH₂)₁₋₃heteroaryl, (CH₂)₁₋₃OR⁹, (CH₂)₁₋₃SR⁹,
(CH₂)₁₋₃NR¹⁰R¹¹, -C(CH₂OH)₂, where said C₁₋₆alkyl, C₂₋₆alkenyl and C₁₋₆alkoxy groups are optionally
substituted by halogen or hydroxy;
R⁹, R¹⁰ and R¹¹ are each independently selected from hydrogen, C₁₋₆alkyl, C₂₋₆alkenyl,
C(O)C₁₋₆alkyl and aryl;
or R⁸, R⁷ and the nitrogen atom to which they are attached form a heteroaliphatic ring of 4 to 7
ring atoms, which ring optionally contains 1, 2 or 3 additional heteroatoms selected from O and S or a
group S(O), S(O)₂ or NR₁², where R₁² is hydrogen, C₁₋₆alkyl, C₂₋₆alkenyl or aryl, and which ring is
optionally substituted by halogen, hydroxy, C₁₋₆alkyl, C₂₋₆alkenyl, C₁₋₆alkoxy, oxo, SO₂NR₁⁸R¹⁹, COR¹⁸,
CO₂R¹⁸ or CONR¹⁸R¹⁹, and which ring is optionally bridged by –CH₂- or –CH₂CH₂–;
R⁸, R²⁰, R²² and R²³ are each independently selected from hydrogen, C₁₋₆alkyl, (CH₂)₁₋₃OR¹₅,
(CH₂)₁₋₃NR¹⁴R¹⁵, (CH₂)₁₋₃aryl and (CH₂)₁₋₃heteroaryl;
R¹₃, R¹⁴ and R¹⁵ are each independently selected from hydrogen, C₁₋₆alkyl, C₂₋₆alkenyl, aryl,
C(O)R¹⁶ and C(O)OR¹⁷;
R¹⁶, R¹⁷ and R²⁴ are independently selected from hydrogen, C₁₋₆alkyl and aryl;
R²⁵ is hydrogen, C₁₋₆alkyl, (CH₂)₁₋₃CO₂H, (CH₂)₁₋₃C₃₋₇cycloalkyl, (CH₂)₁₋₃phenyl or
SO₂(C₁₋₆alkyl), where C₁₋₆cycloalkyl and phenyl are optionally substituted by 1 to 3 groups selected from
halogen, hydroxy or CO₂H;
n is 0 or 1 or 2,
and when n is 2, the R² groups may be the same or different;
R⁸ is hydrogen,
or R² and R⁸ are joined to form a 5- to 8-membered carbocyclic ring.
In one embodiment of the present invention, there is provided the use of a compound of formula
(ii):
or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment or prevention of infection by hepatitis C virus, wherein

A and B are each independently CH₂, C=O or C=S, with the proviso that A and B are not both CH₂;

R¹ is C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl, (CH₂)₃₋₇ cycloalkyl, (CH₂)₃₋₇ Het, (CH₂)₃₋₇ aryl or (CH₂)₃₋₇ heteroaryl, optionally substituted by halogen, hydroxy, C₁₋₄ alkoxy, C₂₋₄ alkenyl, CN, S(C₁₋₄ alkyl), S(O)(C₁₋₄ alkyl), S(O)₂(C₁₋₄ alkyl), S-heteroaryl, S(O) heteroaryl, S(O)₂ heteroaryl, S-aryl, S(O)aryl, S(O)₂ aryl, SO₂NR⁺R⁺⁵, CO₂R⁺⁴, CONR⁺R⁺⁴, NR⁺COR⁺⁵, NR⁺SO₂R⁺⁵ or NR⁺CONR⁺⁵ where said C₁₋₄ alkyl and (CH₂)₃₋₇ aryl groups, either by themselves or as part of other substituents, may optionally be substituted by 1 to 8 halogen atoms;

R⁺⁴, R⁺⁵ and R⁺⁶ are each independently selected from hydrogen, C₁₋₄ alkyl, (CH₂)₃₋₇ Het, (CH₂)₃₋₇ aryl and (CH₂)₃₋₇ heteroaryl;

R⁺⁷ is halogen, hydroxy, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₁₋₄ alkoxy, CN, NO₂, NR⁺R⁺⁷, OR⁺, CO₂H, CO₂R⁺⁸, CONR⁺⁸R⁺²⁰, NR⁺²¹COR⁺⁸, NR⁺²¹SO₂R⁺⁸, NR⁺²¹CONR⁺²⁰, SR⁺, SOR⁺⁸, SO₂R⁺⁸ or SO₂NR⁺²⁰R⁺²⁰, where said C₁₋₄ alkyl, C₂₋₄ alkenyl and C₁₋₄ alkoxy groups are optionally substituted by halogen, hydroxyl, SO₂NR⁺R⁺⁷, CO₂R⁺⁶ or CONR⁺⁶R⁺⁷;

R⁺⁸ and R⁺⁹ are each independently selected from hydrogen, C₁₋₄ alkyl, C₂₋₄ alkenyl, (CH₂)₃₋₇ cycloalkyl, (CH₂)₃₋₇ Het, (CH₂)₃₋₇ aryl, (CH₂)₃₋₇ heteroaryl, (CH₂)₃₋₇ OR⁺, (CH₂)₃₋₇ SR⁺⁹, (CH₂)₃₋₇ NR⁺¹⁰R⁺¹¹, -C(CH₂OH)₃⁻, COR⁺²², CO₂R⁺²², CONR⁺²²R⁺²³, SO₂R⁺²² and SO₂NR⁺²²R⁺²³, where said C₁₋₄ alkyl, C₂₋₄ alkenyl, cycloalkyl, Het, aryl and heteroaryl groups are optionally substituted by halogen, hydroxy, SO₂NR⁺¹⁸R⁺¹⁹, CO₂R⁺¹⁸ or CONR⁺¹⁸R⁺¹⁹;

R⁺¹⁰ and R⁺¹¹ are each independently selected from hydrogen, C₁₋₄ alkyl, C₂₋₄ alkenyl, (CH₂)₃₋₇ cycloalkyl, (CH₂)₃₋₇ Het, (CH₂)₃₋₇ aryl, (CH₂)₃₋₇ heteroaryl, (CH₂)₃₋₇ OR⁺⁹, (CH₂)₃₋₇ SR⁺⁹, (CH₂)₃₋₇ NR⁺¹⁰R⁺¹¹, -C(CH₂OH)₃⁻, where said C₁₋₄ alkyl, C₂₋₄ alkenyl and C₁₋₄ alkoxy groups are optionally substituted by halogen or hydroxy;

R⁺⁵, R⁺¹⁰ and R⁺¹¹ are each independently selected from hydrogen, C₁₋₄ alkyl, C₂₋₄ alkenyl, C(O)C₁₋₄ alkyl and aryl;

or R⁺⁵, R⁺⁷ and the nitrogen atom to which they are attached form a heteroaliphatic ring of 4 to 7 ring atoms, which ring optionally contains 1, 2 or 3 additional heteroatoms selected from O and S or a group S(O), S(O)₂ or NR⁺¹², where R⁺¹² is hydrogen, C₁₋₄ alkyl, C₂₋₄ alkenyl or aryl, and which ring is optionally substituted by halogen, hydroxy, C₁₋₄ alky1, C₂₋₄ alkenyl or C₁₋₄ alkoxy, carboxy1, SO₂NR⁺¹⁸R⁺¹⁹, COR⁺¹⁸, CO₂R⁺¹⁸ or CONR⁺¹⁸R⁺¹⁹;

R⁺⁸, R⁺²⁰, R⁺²² and R⁺²³ are each independently selected from C₁₋₄ alkyl, (CH₂)₃₋₇ OR⁺¹³, (CH₂)₃₋₇ NR⁺¹⁴R⁺¹⁵, (CH₂)₃₋₇ aryl and (CH₂)₃₋₇ heteroaryl;

R⁺¹³, R⁺¹⁴ and R⁺¹⁵ are each independently selected from hydrogen, C₁₋₄ alkyl, C₂₋₄ alkenyl, aryl, C(O)R⁺¹⁶ and C(O)OR⁺¹⁷;

R⁺¹⁶ and R⁺¹⁷ are independently selected from hydrogen, C₁₋₄ alkyl and aryl;
n is 0 or 1.

In one embodiment of the present invention, one of A or B is C=O and the other is CH₂ or C=O, preferably A is C=O and B is CH₂ or C=O, more preferably A and B are C=O.

In another embodiment, R¹ is (CH₂)₃aryl, preferably (CH₂)₃phenyl, more preferably phenyl or benzyl, most preferably phenyl, optionally substituted by halogen, hydroxy, C₁₋₆alkyl, C₁₋₆alkoxy, C₂₋₆alkenyl, CN, S(C₁₋₆alkyl), S(O)(C₁₋₆alkyl), S(O)₂(C₁₋₆alkyl), SO₂NR²R⁵ where R⁴ and R⁵ are as hereinbefore defined, preferably halogen, C₁₋₆alkyl or C₁₋₆alkoxy, more preferably, fluorine, chlorine, bromine, most preferably bromine.

When R¹ is substituted, it is preferably mono- or di-substituted, more preferably mono-substituted.

When R¹ is phenyl and substituted, preferably it is substituted at the 3-position of the phenyl group, especially when it is mono-substituted.

In another embodiment, R² is NR⁶R⁷ where R⁶ and R⁷ are as hereinbefore defined. Preferably, R⁶ and R⁷ are independently selected from hydrogen, C₁₋₆alkyl, (CH₂)₃₋₅cycloalkyl, (CH₂)₃₋₅OR⁸ where R⁹ is as hereinbefore defined. More preferably, one of R⁶ and R⁷ is hydrogen and the other is selected from C₁₋₆alkyl, (CH₂)₃₋₅cycloalkyl or (CH₂)₃₋₅OR⁸, especially (CH₂)₃OR⁹. Preferably, R⁹ is selected from hydrogen, C₁₋₆alkyl and aryl, more preferably hydrogen.

In another embodiment, when n is 1, preferably the R³ group is at the 4-position of the naphthalimide moiety.

In a further embodiment of the present invention, there is provided the use of a compound of formula (Ia):

![Diagram](image)

or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment or prevention of infection by hepatitis C virus, wherein R¹ and R² are as defined in relation to formula (Ii).

Preferably, R¹ is (CH₂)₃aryl, more preferably phenyl, optionally substituted by halogen, hydroxy, C₁₋₆alkyl, C₁₋₆alkoxy, C₂₋₆alkenyl, CN, S(C₁₋₆alkyl), S(O)(C₁₋₆alkyl), S(O)₂(C₁₋₆alkyl), SO₂NR²R⁵ where R⁴ and R⁵ are as defined in relation to formula (Ii), preferably halogen, C₁₋₆alkyl or C₁₋₆alkoxy, more preferably halogen, especially fluorine, chlorine and bromine.

When R¹ is phenyl, preferably it is mono- or di-substituted, more preferably monosubstituted, especially at the 3-position of the phenyl group.

Preferably, R² is NR⁶R⁷ where R⁶ and R⁷ are as hereinbefore defined. Preferably, one of R⁶ and R⁷ is hydrogen and the other is selected from C₁₋₆alkyl, (CH₂)₃₋₅cycloalkyl or (CH₂)₃₋₅OR⁸, especially
(CH₂)₈₃OR°. Preferably, R° is selected from hydrogen and C₁₄alkyl, more preferably hydrogen. In particular, NR°R° may be NH(CH₂)₂OH.

In a further embodiment, there is provided the use of a compound of formula (Ib):

or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment or prevention of infection by hepatitis C virus, wherein

R² is as defined in relation to formula (I), and
R¹ is phenyl substituted by bromine and/or CO₂H, optionally further substituted by halogen, hydroxy, C₂₋₆alkyl, C₁₋₆alkoxy or CH₂CO₂H.

In a further embodiment, there is provided the use of a compound of formula (Ic):

or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment or prevention of infection by hepatitis C virus, wherein

R¹ is as defined in relation to formula (I), and
R² is C₃₋₅cycloalkyl,
(CH₂)₉₋₁₀OH,
C₂₋₆alkoxy,
phenyl,
NH(CH₂)₉₋₁₀Het substituted by C(O)(CH₂)₉₋₁₀aryl, C(O)(C₁₋₆alkyl), C(O)C₃₋₅cycloalkyl,
SO₂aryl, (CH₂)₁₂₋₁₅aryl (optionally substituted by CO₂C₁₋₆alkyl or (CH₂)₉₋₁₀CO₂H),
(CH₂)₁₂₋₁₅heteroaryl or (CH₂)₁₂₋₁₅C(O)OC₁₋₆alkyl,
NH(CH₂)₉₋₁₀C₁₋₅cycloalkyl substituted by CO₂H or CO₂(C₁₋₆alkyl),
NH(O)(C₁₋₆alkyl),
NHC(O)(CH₂)₉₋₁₀aryl,
NH(CH₂)₉₋₁₀O(CH₂)₁₂₋₁₅aryl,
3-oxo-2-azabicyclo[2.2.2]oct-2-yl,
NH(CH₂)₉₋₁₀aryl substituted by CO₂H, CO₂C₁₋₆alkyl, Het or CH=CHC(O)OC₁₋₆alkyl,
CO₂H, or
C(O)NH(CH₂)₃aryl,

where phenyl is optionally substituted by 1 to 3 groups selected from halogen, C₁₋₄alkyl, NH₂, C₁₋₄alkoxy or CO₂H.

In a further embodiment, there is provided the use of a compound of formula (Id):

![Chemical Structure]

(Id)

or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment or prevention of infection by hepatitis C virus, wherein

R² is as defined in relation to formula (I), and
R¹ is C₅₋₈alkyl substituted by CO₂H, C(O)NH(C₄₋₈alkyl), C(O)NHS(O)₂(C₁₋₄alkyl), C(O)NH(CH₂)₃ heteroaryl, C(O)NH(CH₂)₃Het, C(O)NHCH(CH₃)phenyl or O(CH₂)₉aryl,
(CH₂)₃C₅₋₈cycloalkyl,
(CH₂)₈aryl,
(CH₂)₃Het,
(CH₂)₉heteroaryl,
phenyl substituted by SH, SC₁₋₆alkyl or SO₂C₁₋₄alkyl,
C(O)NH(CH₂)₃aryl,
C(O)NH(CH₂)₃CO₂H, or
C(O)NH(C₃₋₅cycloalkyl) substituted by CO₂H or C(O)NHSO₂(C₁₋₄alkyl),
where the Het groups of (CH₂)₉Het and C(O)NH(CH₂)₃Het are optionally substituted by C₁₋₄alkyl, OH or NH₂, and
where the aryl group of C(O)NH(CH₂)₃aryl is optionally substituted by CO₂H, halogen, C₁₋₄alkyl or C₁₋₄alkoxy, and
where the heteroaryl group of C(O)NH(CH₂)₃heteroaryl is optionally substituted by C₁₋₄alkyl.

When any variable occurs more than one time in formula (I) or in any substituent, its definition on each occurrence is independent of its definition at every other occurrence.

As used herein, the term “alkyl” or “alkoxy” as a group or part of a group means that the group is straight or branched. Examples of suitable alkyl groups include methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl and t-butyl. Examples of suitable alkoxy groups include methoxy, ethoxy, n-propoxy, i-propoxy, n-butoxy, s-butoxy and t-butoxy.
The cycloalkyl groups referred to herein may represent, for example, cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl.

As used herein, the term “alkenyl” and “alkynyl” as a group or part of a group means that the group is straight or branched. Examples of suitable alkenyl groups include vinyl and allyl. Suitable alkynyl groups are ethynyl and propargyl.

When used herein, the term “halogen” means fluorine, chlorine, bromine and iodine.

When used herein, the term “aryl” as a group or part of a group means a carbocyclic aromatic ring. Examples of suitable aryl groups include phenyl and naphthyl.

When used herein, the term “heteroaryl” as a group or part of a group means a 5- to 10-membered heteroaromatic ring system containing 1 to 4 heteroatoms selected from N, O and S. Particular examples of such groups include pyrrolyl, furanyl, thienyl, pyridyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazinyl, pyrimidinyl, pyridazinyl, triazolyl, oxadiazolyl, thiadiazolyl, triazinyl, tetrazolyl, indolyl, benzimidazolyl, benzothienyl and quinolinyl.

When used herein, the term “Het” as a group or part of a group means a heteroaliphatic ring of 4 to 7 ring atoms, which ring may contain 1, 2 or 3 heteroatoms selected from N, O or S or a group S(O), S(O)₂, NH or NC₃₋₄-alkyl.

Where a compound or group is described as “optionally substituted”, one or more substituents may be present. Optional substituents may be attached to the compounds or groups which they substitute in a variety of ways, either directly or through a connecting group of which the following are examples: amine, amide, ester, ether, thioether, sulfonamide, sulfamide, sulfoxide, urea, thiourea and urethane. As appropriate an optional substituent may itself be substituted by another substituent, the latter being connected directly to the former or through a connecting group such as those exemplified above.

Specific compounds within the scope of this invention include those compounds named in the Examples and Tables below and their pharmaceutically acceptable salts. Preferred compounds of the present invention are those of Group (II) as defined below:

**Group (II):**

1H-benz[de]isoquinoline-1,3(2H)-dione, 2-(3-bromophenyl)-6-[(2-hydroxyethyl)amino],
2-(3-chlorophenyl)-6-[(2-hydroxyethyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-butyl-6-[(2-hydroxyethyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-[(2-hydroxyethyl)thio]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-7-[(2-hydroxyethyl)amino]-2,3-dihydro-1H-benzo[de]isoquinolin-1-one,
2-(3-chlorophenyl)-6-(3-hydroxypropyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-chlorophenyl)-6-(1H-pyrazol-3-yl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
3-[6-[(benzylamino)carbonyl]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanoic acid,
6-[(2-hydroxyethyl)amino]-2-[(5-methylisoxazol-3-yl)methyl]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
cis-4-[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl)amino]cyclohexanecarboxylic acid,
2-(3-bromophenyl)-6-[(2-hydroxyethyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-[(2-methoxyethyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-(propylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-[(3-hydroxypropyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
6-amino-2-(3-bromophenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-[(2-hydroxyethyl)thio]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-(methylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-[(2-(dimethylamino)ethyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-(isobutylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-(ethylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
6-(benzylamino)-2-(3-bromophenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-[(2-phenylethyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-[(2-phenoxymethyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-[(2-hydroxyethyl)(methyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-[(tetrahydrofuran-2-ylmethyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-(cyclopentylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-(cyclohexylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-(isopropylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-[(2-(methylthio)ethyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-methoxy-1H-benzo[de]isoquinoline-1,3(2H)-dione,
N-(2-[(2-(3-bromophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl)amino]ethyl)acetamide,
2-(3-bromophenyl)-6-[(2-(methylamino)ethyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-[(2-hydroxyethoxy)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
6-[(2-aminoethyl)amino]-2-(3-bromophenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-[(cyclopropylmethyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-[(pyridin-2-ylmethyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
benzyl (2-[(2-(3-bromophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl)amino]ethyl)carbamate,
6-[(1-benzylpiperidin-4-yl)amino]-2-(3-bromophenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
4-[(2-(3-bromophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl)amino]methylbenzoic acid,
trans-4-[(2-(3-bromophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl)amino]cyclohexanecarboxylic acid,
yl]amino)cyclohexanecarboxylic acid,
4-[[2-(3-bromophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino] piperidinium trifluoroacetate,
6-[[2-hydroxyethyl]amino]-2-phenyl-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-benzyl-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-butyl-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-cyclohexyl-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
6-[[2-hydroxyethyl]amino]-2-isobutyl-1H-benzo[de]isoquinoline-1,3(2H)-dione,
3-6-[[2-hydroxyethyl]amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]benzonitrile,
6-[[2-hydroxyethyl]amino]-2-(3-methoxyphenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
6-[[2-hydroxyethyl]amino]-2-(3-methylphenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
6-[[2-hydroxyethyl]amino]-2-[[3-(methylthio)phenyl]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(4-bromophenyl)-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione
6-[[2-hydroxyethyl]amino]-2-[[3-(trifluoromethyl)phenyl]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-fluorophenyl)-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
6-[[2-hydroxyethyl]amino]-2-(3-methylsulfonyl)phenyl]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(5-bromopyridin-3-yl)-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
3-6-[[2-hydroxyethyl]amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]benzenesulfonamide,
2-(2-bromophenyl)-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3,5-dichlorophenyl)-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(2,3-dichlorophenyl)-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(2,5-dichlorophenyl)-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-chloro-4-fluorophenyl)-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-chloro-4-methoxyphenyl)-6-[[2-hydroxyethyl] amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
6-[[2-aminoethyl]amino]-2-phenyl-1H-benzo[de]isoquinoline-1,3(2H)-dione,
methyl 6-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino] (oxo)acetate,
6-[[1-benzyloxy]piperidin-4-yl]amino]-2-(3-chlorophenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
6-[[1-acetylpiperidin-4-yl]amino]-2-(3-chlorophenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-chlorophenyl)-6-[[1-(cyclohexylocarbonyl)piperidin-4-yl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-chlorophenyl)-6-[[1-(phenylsulfonyl)piperidin-4-yl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
N-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]glycine,
4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino] methyl cyclohexanecarboxylic acid,
2-(3-chlorophenyl)-5-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-[[4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]piperidin-1-yl]carbonyl]benzoic acid,
4-[[4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]piperidin-1-yl]carbonyl]benzoic acid,
N-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-5-yl]acetamide,
4-chloro-2-[[6-[[2-hydroxyethyl]amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]benzoic acid,
N-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]-2-phenylacetamide,
2-(3-chlorophenyl)-5-(methylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-chlorophenyl)-5-(dimethylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-5-yl]amino]methyl)pyridinium trifluoroacetate,
trans-4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino)cyclohexancarboxylic acid,
2-(3-chlorophenyl)-6-(2-oxopyrrolidin-1-yl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
5-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]pentanoic acid,
1-benzyl-4-[[2-(2-carboxy-5-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]piperidinium trifluoroacetate,
(2S)-2-[[2-hydroxyethyl]amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]pentanoic acid,
4-[[2-(3-carboxyphenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]piperidinium trifluoroacetate,
3-[[1-acetyl)piperidin-4-yl]amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-5-bromobenzoic acid,
1-benzyl-4-[[2-[[15]-1-carboxybutyl]-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]piperidinium trifluoroacetate,
ethyl 2-[[6-bromo-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-1,3-thiazole-5-carboxylate,
6-[[2-benzyloxy]ethyl]amino]-2-[[5-methylisoxazol-3-yl]methyl]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
6-[[2-hydroxyethyl]amino]-2-[[5-methylisoxazol-3-yl]methyl]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
3-[[2-(3-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]benzoic acid,
4-[[2-(3-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]benzoic acid,
2-[[2-(3-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-4-methylpentanoic acid,
methyl cis-4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino)cyclohexancarboxylic acid,
2-(3-chlorophenyl)-6-(3-oxo-2-azabicyclo[2.2.2]oct-2-yl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-[[2-(3-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]benzoic acid,
cis-4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino)cyclohexancarboxylic acid,
4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]-1-methylpiperidinium trifluoroacetate,
4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]-1-(2-phenylethyl)piperidinium trifluoroacetate,
4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]-1-propylpiperidinium trifluoroacetate,
4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]-1-(1,3-thiazol-2-ylmethyl)piperidinium trifluoroacetate,
4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]-1-[4-(methoxycarbonyl)benzyl]piperidinium trifluoroacetate,
4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]-1-isopropylpiperidinium trifluoroacetate,
1-benzyl-4-[[2-[3-bromo-5-(ethoxy carbonyl)phenyl]-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]piperidinium trifluoroacetate,
4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]-1-(2-ethoxy-2-oxoethyl)piperidinium trifluoroacetate,
1-(4-carboxybenzyl)-4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]piperidinium trifluoroacetate,
6-anilino-2-(3-chlorophenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-chlorophenyl)-6-(4-methoxyphenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
3-[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]benzoic acid,
4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]benzoic acid,
2-(3-chlorophenyl)-6-(3-fluoro-4-methoxyphenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-chlorophenyl)-6-(2-fluoro-4-methoxyphenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-chlorophenyl)-6-(4-fluoro-3-methylphenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-chlorophenyl)-6-(5-fluoro-2-methoxyphenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
3-[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]-1H-pyrazol-1-ium trifluoroacetate,
2-(3-chlorophenyl)-6-(3-thienyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]pyridinium trifluoroacetate,
2-(3-chlorophenyl)-6-(3-furyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
3-[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]pyridinium trifluoroacetate,
2-(3-chlorophenyl)-6-pyrimidin-5-yl-1H-benzo[de]isoquinoline-1,3(2H)-dione,
3-[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]benzenaminium trifluoroacetate,
2-(3-chlorophenyl)-6-cyclohexyl-1H-benzo[de]isoquinoline-1,3(2H)-dione,
1-(carboxymethyl)-4-[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino)piperidinium trifluoroacetate,
1-benzyl-3-[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino)pyrrolidinium trifluoroacetate,
methyl 4-[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]benzoate,
4-[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]benzoic acid,
2-(3-chlorophenyl)-6-(pyridin-2-ylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-chlorophenyl)-6-(pyridin-3-ylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
3-[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanoic acid,
3-bromo-5-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-N,N-dimethylbenzamide,
3-[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]benzoic acid,
2-(3-chlorophenyl)-6-[(4-morpholin-4-ylphenyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
6-[(3-benzyloxy)phenyl]amino]-2-(3-chlorophenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-chlorophenyl)-6-(quinolin-3-ylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-chlorophenyl)-6-(isoquinolin-7-ylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
ethyl (2E)-3-[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino)phenylacrylate,
2-(3-chlorophenyl)-6-[(3-(trifluoromethyl)phenyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
6-[(4-sec-butylphenyl)amino]-2-(3-chlorophenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-chlorophenyl)-6-[(4-(trifluoromethyl)phenyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
3-bromo-5-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-N-methylbenzamide,
N-[(3-bromo-5-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]benzoyl]-β-alanine,
4-[(3-bromo-5-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]benzoyl]amino)methyl benzoic acid,
cis-4-[(3-bromo-5-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]benzoyl]amino)cyclohexanecarboxylic acid,
3-[(3-bromo-5-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]benzoyl]amino)cyclohexanecarboxylic acid,
3-[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]-N,N-dimethylbenzenaminium trifluoroacetate,
3-bromo-5-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-N-(methylsulfonyl)benzamide,
2-(6-anilino-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)pentanoic acid,
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4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]-2-methylquinolinium trifluoroacetate,
ethyl 3-[(6-anilino-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-5-chlorobenzoate,
3-(6-anilino-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-5-chlorobenzoic acid,
4-[[2-(3-carboxy-5-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]-1-isopropylpiperidinium trifluoroacetate,
4-[[2-(3-carboxy-5-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]-1-{2-phenylethyl}piperidinium trifluoroacetate,
4-[[4-[[2-(3-carboxy-5-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]piperidinium-1-yl]methyl]pyridinium bis(trifluoroacetate),
1-benzyl-4-[[2-(3-bromo-5-[[methylamino]carbonyl]phenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]piperidinium trifluoroacetate,
6-anilino-2-butyl-1H-benzo[de]isoquinoline-1,3(2H)-dione,
4-[[2-butyl-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]-1-isopropylpiperidinium trifluoroacetate,
3-(6-anilino-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)hexanoic acid,
4-[[2-[1-((carboxymethyl)butyl]-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]-1-isopropylpiperidinium trifluoroacetate,
2-(3-bromophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinoline-6-carboxylic acid,
2-[1-((carboxymethyl)butyl]-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinoline-6-carboxylic acid,
3-[6-[(benzylamino)carbonyl]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanoic acid,
2-(5-chloro-2-methoxyphenyl)-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
3-(6-anilino-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-N-(methylsulfonfyl)hexanamide,
1-isopropyl-4-[[3-[6-[[1-isopropylpiperidinium-4-yl]amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanoyl]amino]piperidinium bis(trifluoroacetate),
1-isopropyl-4-[[2-1-[2-(methylamino)-2-oxoethyl]butyl]-1,3-dioxo-2,3-dihydro-1H-
benzo[de]isoquinolin-6-yl]amino]piperidinium trifluoroacetate,
2-(5-chloro-2-hydroxyphenyl)-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(2,3-dihydro-1H-inden-4-yl)-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-chloro-2-fluorophenyl)-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromo-2-methylphenyl)-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
6-[[2-hydroxyethyl]amino]-2-(4-methylpyridin-2-yl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
3-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]methyl)benzoic acid,
3-[6-[[2-hydroxyethyl]amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-N-1,3,4-thiadiazol-2-
ylhexanamide,
2-\{(3-amino-1H-pyrazol-1-yl)-2-oxoethyl\}butyl} - 6-\{(2-hydroxyethyl)amino\}-1H-benzo[de]isouquinoline-1,3(2H)-dione,
2-\{(3-[6-\{(2-hydroxyethyl)amino\}-1,3-dioxo-1H-benzo[de]isouquinolin-2(3H)-yl]hexanoyl\}amino\}-1,3-thiazol-3-ium trifluoroacetate,
3-\{(3-[6-\{(2-hydroxyethyl)amino\}-1,3-dioxo-1H-benzo[de]isouquinolin-2(3H)-yl]hexanoyl\}amino\}methyl\}pyridinium trifluoroacetate,
2-\{(3-[6-\{(2-hydroxyethyl)amino\}-1,3-dioxo-1H-benzo[de]isouquinolin-2(3H)-yl]hexanoyl\}amino\}methyl\}pyridinium trifluoroacetate,
4-\{(3-[6-\{(2-hydroxyethyl)amino\}-1,3-dioxo-1H-benzo[de]isouquinolin-2(3H)-yl]hexanoyl\}amino\}methyl\}pyridinium trifluoroacetate,
3-\{(3-[6-\{(2-hydroxyethyl)amino\}-1,3-dioxo-1H-benzo[de]isouquinolin-2(3H)-yl]hexanoyl\}amino\}ethyl\}pyridinium trifluoroacetate,
5-\{(3-[6-\{(2-hydroxyethyl)amino\}-1,3-dioxo-1H-benzo[de]isouquinolin-2(3H)-yl]hexanoyl\}amino\}ethyl\}1H-imidazol-3-ium trifluoroacetate,
2-(3-chlorophenyl)-6-(3-hydroxypropyl)-1H-benzo[de]isouquinoline-1,3(2H)-dione,
6-[\{(2-hydroxyethyl)amino\}-2-(3-methylcyclohexyl)-1H-benzo[de]isouquinoline-1,3(2H)-dione,
N-(2,6-difluorobenzyl)-3-[6-\{(2-hydroxyethyl)amino\}-1,3-dioxo-1H-benzo[de]isouquinolin-2(3H)-yl]hexanamide,
3-[6-\{(2-hydroxyethyl)amino\}-1,3-dioxo-1H-benzo[de]isouquinolin-2(3H)-yl]-N-[2-(1H-1,2,4-triazol-5-yl)ethoxyethyl]hexanamide,
3-[6-\{(2-hydroxyethyl)amino\}-1,3-dioxo-1H-benzo[de]isouquinolin-2(3H)-yl]-N-(2-pyridin-4-yloxyethyl)hexanamide,
3-[6-\{(2-hydroxyethyl)amino\}-1,3-dioxo-1H-benzo[de]isouquinolin-2(3H)-yl]-N-(1H-indol-6-yl)methyl]hexanamide,
\{N-benzyl-3-[6-\{(2-hydroxyethyl)amino\}-1,3-dioxo-1H-benzo[de]isouquinolin-2(3H)-yl]hexanamide,
N-(2,6-dimethoxybenzyl)-3-[6-\{(2-hydroxyethyl)amino\}-1,3-dioxo-1H-benzo[de]isouquinolin-2(3H)-yl]hexanamide,
N-(2,6-difluorobenzyl)-3-[6-\{(2-hydroxyethyl)amino\}-1,3-dioxo-1H-benzo[de]isouquinolin-2(3H)-yl]hexanamide,
N-(2,6-difluorobenzyl)-3-[6-\{(2-hydroxyethyl)amino\}-1,3-dioxo-1H-benzo[de]isouquinolin-2(3H)-yl]hexanamide,
\{3-bromo-5-[6-\{(2-hydroxyethyl)amino\}-1,3-dioxo-1H-benzo[de]isouquinolin-2(3H)-yl]phenyl\}acetic acid,
3-[6-\{(2-hydroxyethyl)amino\}-1,3-dioxo-1H-benzo[de]isouquinolin-2(3H)-yl]-N\{(1R)-1-phenylethyl\}hexanamide,
3-[6-\{(2-hydroxyethyl)amino\}-1,3-dioxo-1H-benzo[de]isouquinolin-2(3H)-yl]-N\{(1R)-1-}
phenylethyl]hexanamide,
N-[(3R,4R)-4-hydroxy-1,1-dioxidotetrahydro-3-thienyl]-3-[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanamide,
3-[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-N-[(1-methyl-1H-pyrazol-4-yl)methyl]hexanamide,
N-(2-chloro-6-methylbenzyl)-3-[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanamide,
N-(2-fluorobenzyl)-3-[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanamide,
3-[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-N-[(1S)-1-phenylethyl]hexanamide,
3-[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-N-[(1S)-1-phenylethyl]hexanamide,
2-butyl-6-(butylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-[(3-6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanol] amino)methyl]-5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-1-ium trifluoroacetate,
1-benzyl-4-{[1,3-dioxo-2-{[1-(2-oxo-2-[[1(1S)-1-phenylethyl]amino]ethyl]butyl}-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino}piperidinium trifluoroacetate,
1-benzyl-4-{[1,3-dioxo-2-{[1-(2-oxo-2-[[1(1S)-1-phenylethyl]amino]ethyl]butyl}-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino}piperidinium trifluoroacetate,
cis-4-{[1,3-dioxo-2-{[1-(2-oxo-2-[[1(1S)-1-phenylethyl]amino]ethyl]butyl}-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino}cyclohexanecarboxylic acid,
cis-4-{[1,3-dioxo-2-{[1-(2-oxo-2-[[1(1S)-1-phenylethyl]amino]ethyl]butyl}-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino}cyclohexanecarboxylic acid,
2-{1-[(benzylloxy)methyl]butyl}-6-{[(2-hydroxyethyl) amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione, 
trans-1-benzyl-4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino}cyclohexanecarboxylic acid,
2-(3-chlorophenyl)-6-{[1-(phenylacetyl)piperidin-4-yl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
3-bromo-5-6-{[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]benzoic acid,
1-benzyl-4-[[2-(3-bromo-5-carboxyphenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino}piperidinium trifluoroacetate,
4-[[4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino}piperidinium-1-yl]methyl]pyridinium bis(trifluoroacetate),
4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]-1-(3-thienylmethyl)piperidinium trifluoroacetate,
cis-4-[[2-(3-methyl-5-[(methylamino) carbonyl] phenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino}piperidinium trifluoroacetate,
6-yl]amino]cyclohexanecarboxylic acid,
cis-1-benzyl-4- {{2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]cyclohexanecarboxylic acid,
6-bromo-2-butyl-1H-benzo[de]isoquinoline-1,3(2H)-dione,

and their pharmaceutically acceptable salts.

For use in medicine, the salts of the compounds of formula (I) will be non-toxic pharmaceutically acceptable salts. Other salts may, however, be useful in the preparation of the compounds according to the invention or of their non-toxic pharmaceutically acceptable salts. Suitable pharmaceutically acceptable salts of the compounds of this invention include acid addition salts which may, for example, be formed by mixing a solution of the compound according to the invention with a solution of a pharmaceutically acceptable acid such as hydrochloric acid, fumaric acid, p-toluenesulfonic acid, maleic acid, succinic acid, acetic acid, citric acid, tartaric acid, carbonic acid, phosphoric acid or sulfuric acid. Salts of amine groups may also comprise quaternary ammonium salts in which the amino nitrogen atom carries a suitable organic group such as an alkyl, alkenyl, alkynyl or aralkyl moiety. Furthermore, where the compounds of the invention carry an acidic moiety, suitable pharmaceutically acceptable salts thereof may include metal salts such as alkali metal salts, e.g. sodium or potassium salts; and alkaline earth metal salts, e.g. calcium or magnesium salts.

The salts may be formed by conventional means, such as by reacting the free base form of the product with one or more equivalents of the appropriate acid in a solvent or medium in which the salt is insoluble, or in a solvent such as water which is removed in vacuo or by freeze drying or by exchanging the anions of an existing salt for another anion on a suitable ion exchange resin.

The present invention includes within its scope prodrugs of the compounds of formula (I) above. In general, such prodrugs will be functional derivatives of the compounds of formula (I) which are readily convertible in vivo into the required compound of formula (I). Conventional procedures for the selection and preparation of suitable prodrug derivatives are described, for example, in "Design of Prodrugs", ed. H. Bundgaard, Elsevier, 1985.

A prodrug may be a pharmacologically inactive derivative of a biologically active substance (the "parent drug" or "parent molecule") that requires transformation within the body in order to release the active drug, and that has improved delivery properties over the parent drug molecule. The transformation in vivo may be, for example, as the result of some metabolic process, such as chemical or enzymatic hydrolysis of a carboxylic, phosphoric or sulfate ester, or reduction or oxidation of a susceptible functionality.

The present invention includes within its scope solvates of the compounds of formula (I) and salts thereof, for example, hydrates.
The present invention also includes within its scope any enantiomers, diastereomers, geometric isomers and tautomers of the compounds of formula (I). It is to be understood that all such isomers and mixtures thereof are encompassed within the scope of the invention.

In another aspect of the invention, there is provided a method of inhibiting hepatitis C virus polymerase and/or of treating or preventing an illness due to hepatitis C virus, the method involving administering to a human or animal (preferably mammalian) subject suffering from the condition a therapeutically or prophylactically effective amount of the pharmaceutical composition described above or of a compound of formula (I) as defined above, or a pharmaceutically acceptable salt thereof. "Effective amount" means an amount sufficient to cause a benefit to the subject or at least to cause a change in the subject's condition.

In a further embodiment of the present invention, there is provided the use of a compound of formula (I), or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment or prevention of infection by hepatitis C virus, in combination with one or more other agents for the treatment of viral infections such as an antiviral agent, and/or an immunomodulatory agent such as α-, β- or γ-interferon, particularly α-interferon. Suitable antiviral agents include ribavirin and inhibitors of hepatitis C virus (HCV) polymerase, such as inhibitors of metalloprotease (NS2-3), serine protease (NS3), helicase (NS3) and RNA-dependent RNA polymerase (NS5B).

A further aspect of the invention provides a pharmaceutical composition comprising a compound of formula (Ic) or (Id) as defined above or a compound selected from Group (II) as defined above, or a pharmaceutically acceptable salt thereof, in association with a pharmaceutically acceptable carrier. The composition may be in any suitable form, depending on the intended method of administration. It may for example be in the form of a tablet, capsule or liquid for oral administration, or of a solution or suspension for administration parenterally. The composition may be prepared by admixing at least one active ingredient, or a pharmaceutically acceptable salt thereof, with one or more pharmaceutically acceptable adjuvants, diluents or carriers and/or with one or more other therapeutically or prophylactically active agents.

A further aspect of the invention provides a compound of formula (Ic) or (Id) as defined above or a compound selected from Group (II) as defined above, or a pharmaceutically acceptable salt thereof for use in therapy.

A further aspect of the invention provides a compound of formula (Ic) or (Id) as defined above or a compound selected from Group (II) as defined above, or a pharmaceutically acceptable salt thereof.

The dosage rate at which the compound is administered will depend on a variety of factors including the activity of the specific compound employed, the metabolic stability and length of action of that compound, the age of the patient, body weight, general health, sex, diet, mode and time of administration, rate of excretion, drug combination, the severity of the particular condition and the host undergoing therapy. For the treatment or prevention of infection by hepatitis C virus, suitable dosage levels may be of the order of 0.02 to 5 or 10 g per day, with oral dosages two to five times higher. For
instance, administration of from 10 to 50 mg of the compound per kg of body weight from one to three times per day may be in order. Appropriate values are selectable by routine testing. The compound may be administered alone or in combination with other treatments, either simultaneously or sequentially. For instance, it may be administered in combination with effective amounts of antiviral agents, immunomodulators, anti-infectives or vaccines known to those of ordinary skill in the art. It may be administered by any suitable route, including orally, intravenously, cutaneously and subcutaneously. It may be administered directly to a suitable site or in a manner in which it targets a particular site, such as a certain type of cell. Suitable targeting methods are already known.

Compounds of general formula (I) may be prepared by methods disclosed in the documents hereinbefore referred to and by methods known in the art of organic synthesis as set forth below.

According to a general process (a), compounds of formula (I) may be prepared by the reaction of a compound of formula (II) with a compound of formula (III):

$$\begin{align*}
\text{(II)} & \quad \text{R}^3\text{NH}_2 \\
\text{(III)} & \quad 
\end{align*}$$

where $\text{R}^1$, $\text{R}^2$, $\Lambda$, $B$ and $n$ are as defined for formula (I). The reaction is conveniently performed in the presence of a suitable solvent, such as NMP, ethanol or DMF, at a raised temperature, such as the reflux temperature of the solvent, and optionally under microwave irradiation.

Compounds of formula (I) may also be prepared by the reaction of a compound of formula (IV) with a compound of formula (V):

$$\begin{align*}
\text{(IV)} & \quad \text{R}^3\text{NH}_2 \\
\text{(V)} & \quad 
\end{align*}$$

where $\text{R}^1$, $\text{R}^2$, $\Lambda$ and $B$ are as defined for formula (I), and $L$ is a suitable leaving group such as chlorine, bromine or nitro. The reaction is conveniently performed in the presence of a suitable solvent, such as NMP, at a raised temperature, optionally under microwave irradiation.

Alternatively, the compounds of formula (I) may be prepared by the reaction of the compound of formula (IV) with a compound of formula (VI):

$$\begin{align*}
\text{(VI)} & \quad 
\end{align*}$$
\[ R^2 - \text{B(OH)}_2 \] (VI)

where \( R^2 \) is as defined for formula (I). The reaction is conveniently performed in the presence of a suitable catalyst, such as palladium triphenylphosphine, in a suitable solvent, such as a dimethyl ether/ethanol mixture, at raised temperature.

Where they are not commercially available, the starting material of formulae (II), (III), (IV) and (V) may be prepared by methods analogous to those described in the accompanying Examples, or by standard methods well known from the art.

It will be understood that any compound of formula (I) initially obtained from any of the above processes may, where appropriate, subsequently be elaborated into a further compound of formula (I) by techniques known from the art.

For instance, a compound of formula (I) where \( B = \text{C=O} \) may be transformed into a compound of formula (I) where \( B = \text{CH}_2 \) by reduction with a suitable reducing agent, such as sodium borohydride, in a suitable solvent, such as an ethanol/water mixture.

Many of the compounds of the present invention were prepared using the general method (A):

**Method A**

1,8-naphthalimides were prepared by condensation reaction of naphthalic anhydrides with primary amines under microwave irradiation. The 6-amino analogues were synthesised by treatment of 6-bromo-1,8-naphthalimides with primary or secondary amines under microwave irradiation. General method (A) is illustrated by Example 1 below.

Where a mixture of products is obtained from any of the processes described above for the preparation of compounds according to the invention, the desired product can be separated therefrom at an appropriate stage by conventional methods such as preparative HPLC; or column chromatography utilising, for example, silica and/or alumina in conjunction with an appropriate solvent system.

During any of the above synthetic sequences it may be necessary and/or desirable to protect sensitive or reactive groups on any of the molecules concerned. This may be achieved by means of conventional protecting groups, such as those described in *Protective Groups in Organic Chemistry*, ed. J.F.W. McOmie, Plenum Press, 1973; and T.W. Greene & P.G.M. Wuts, *Protective Groups in Organic Synthesis*, John Wiley & Sons, 3rd edition, 1999. The protecting groups may be removed at a convenient subsequent stage using methods known from the art.
The following Examples are illustrative of the invention. The compounds of the invention were tested for inhibitory activity against the HCV RNA dependent RNA polymerase (NS5B) in an enzyme inhibition assay (example i)). The compounds have IC50's below 30μM in the enzyme assay.

i) In-vitro HCV NS5B Enzyme Inhibition Assay

The HCV-BK cDNA sequence coding for the NS5B protein lacking of the 21 C-terminal residues (residues 1-570) was cloned in the pT7.7 vector downstream of the T7 promoter and in frame with the first ATG of the gene 10 protein of the T7 phage. A C-terminal HisTag was added to simplify purification procedure. Expression in *E.coli* BL21(DE3) was performed as described (Tomei *et al.*, JGV (2000), 81, 759). Bacteria were grown at 37°C in standard LB medium up to an absorbance of 0.8 at 600 nm. The temperature of the culture was then lowered to 18°C and expression induced with 0.4 mM IPTG for further 23 hrs. All the subsequent purification steps were performed at 4°C. Cells were harvested, washed with PBS (20 mM Na-phosphate [pH 7.5], 150 mM NaCl), resuspend in 100 ml of lysis buffer/liter of culture, and disrupted with a model 110S Microfluidizer. Lysis buffer contained 10 mM Tris [pH 8.0], 1 mM EDTA, 0.5 M NaCl, 50% glycerol, 10 mM β-mercaptoethanol, 0.1% n-octyl-β-D-glucopyranoside (Inalco; n-OG), Complete™ protease inhibitor cocktail (Roche). After addition of 10 mM MgCl₂, the extract was incubated with 0.5 units/ml of DNase I for 30 min. The insoluble material was pelleted by centrifugation for 60 min at 15,000 rpm in a Sorvall SS34 rotor. The clarified supernatant was incubated batchwise for 45 min with 50 ml/liter of culture of DEAE-Sepharose FF resin equilibrated in lysis buffer lacking glycerol. The flow-through from the DEAE-Sepharose was diluted to 0.3 M NaCl and loaded on a Ni-NTA Superflow column (Qiagen; 3 ml/liter of culture) equilibrated with A buffer + 10 mM Imidazole (A buffer: 10 mM Tris [pH 8.0], 20% glycerol, 0.3 M NaCl, 0.1% n-OG, 10 mM β-mercaptoethanol) and eluted with a 50 to 500 mM imidazole gradient in A buffer. Peak fraction were collected, dialysed vs D buffer (10 mM Hepes [pH 8.0], 20% glycerol, 0.2% n-OG, 1 mM EDTA, 5 mM DTT) containing 0.15 M NaCl and loaded on HiTrap Heparin column (Amersham) equilibrated with D buffer and eluted with a 0.15 to 0.8M NaCl gradient in D buffer. The protein was stored in aliquots in liquid nitrogen. The purified enzyme was shown to possess in vitro RNA polymerase activity using RNA as template according to a description in Journal of General Virology 81:759-767 (2000). The reference describes a polymerisation assay using poly(A) and oligo(U) as a template/primer. Incorporation of tritiated UTP is quantified by measuring acid-insoluble radioactivity. The present inventors have employed this assay to screen the various compounds described above as inhibitors of HCV RdRp.

Incorporation of radioactive UMP was measured as follows. The standard reaction (50 μl) was carried out in a buffer containing 20 mM Tris/HCl pH 7.5, 5 mM MgCl₂, 1 mM DTT, 10 mM NaCl, 0.01% Triton X-100, 1 μCi [³H]-UTP (40 Ci/mmol, NEN), 10 μM UTP and 10 μg/ml poly(A)/Oligo(U)₁₂ (1 μg/ml, Genset) as a template/primer. The final NS5B_AC21 enzyme concentration was 5 nM. The
order of assembly was: 1) compound, 2) enzyme, 3) template/primer, 4) NTP. After 1 h. incubation at 22°C the reaction was stopped by adding 50 µl of 20% TCA and applying samples to DE81 filters. The filters were washed thoroughly with 5% TCA containing 1M Na₂HPO₄/NaH₂PO₄, pH 7.0, rinsed with water and then ethanol, air dried, and the filter-bound radioactivity was measured in the scintillation counter. Carrying out this reaction in the presence of various concentrations of each compound set out above allowed determination of IC₅₀ values by utilising the formula:

\[ \% \text{ Residual activity} = \frac{100}{1 + [I]/IC_{50}}^S \]

where [I] is the inhibitor concentration and "s" is the slope of the inhibition curve.

ii) General Procedures

All solvents were obtained from commercial sources (Fluka, puriss.) and were used without further purification. With the exception of routine deprotection and coupling steps, reactions were carried out under an atmosphere of nitrogen in oven dried (110 °C) glassware. Organic extracts were dried over sodium sulfate, and were concentrated (after filtration of the drying agent) on rotary evaporators operating under reduced pressure. Flash chromatography was carried out on silica gel following published procedure (W.C. Still et al., J. Org. Chem. 1978, 43, 2923) or on semi-automated flash chromatography systems utilising pre-packed columns.

Reagents were usually obtained directly from commercial suppliers (and used as supplied) but a limited number of compounds from in-house corporate collections were utilised. In the latter case the reagents are readily accessible using routine synthetic steps that are either reported in the scientific literature or are known to those skilled in the art.

¹H nmr spectra were recorded on Bruker AM series spectrometers operating at (reported) frequencies between 300 and 600 MHz. Chemical shifts (δ) for signals corresponding to non-exchangeable protons (and exchangeable protons where visible) are recorded in parts per million (ppm) relative to tetramethylsilane and are measured using the residual solvent peak as reference. Signals are tabulated in the order: multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad, and combinations thereof); coupling constant(s) in hertz; number of protons. Mass spectral (MS) data were obtained on a Perkin Elmer API 100 operating in negative (ES⁻) or positive (ES⁺) ionization mode and results are reported as the ratio of mass over charge (m/z) for the parent ion only. Preparative scale HPLC separations were carried out on a Waters Delta Prep 4000 separation module, equipped with a Waters 486 absorption detector or on a Gilson preparative system. In all cases compounds were eluted with linear gradients of water and acetonitrile both containing 0.1% TFA using flow rates between 15 and 25 mL/min.

The following abbreviations are used in the examples:
AcOH: acetic acid; BINAP: 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl; Boc₂O: di-tert-butyl dicarbonate; DIPEA: N,N-diisopropylethylamine; DMAP: 4-(dimethylamino)pyridine; DME: 1,2-dimethoxyethane; DMF: dimethylformamide; DMSO: dimethylsulfoxide; eq.: equivalent(s); EtOH: ethanol; H₂O: water; Et₂O: ethyl ether; EtOAc: ethyl acetate; h: hour(s); HCl: hydrogen chloride; M: molar; MeCN: acetonitrile; MeOH: methanol; min: minutes; NMP: 1-methyl-2-pyrrolidinone; RP-HPLC: reversed phase high-pressure liquid chromatography; RT: room temperature; TFA: trifluoroacetic acid.

**Example 1:** 1H-benz[de]isoquinoline-1,3(2H)-dione, 2-(3-bromophenyl)-6-[(2-hydroxyethyl)amino]

**Step 1:** 6-bromo-2-(3-bromophenyl)-1H-benz[de]isoquinoline-1,3(2H)-dione

3-bromoaniline (1.3 eq.) was added to a solution (0.3 M) of 4-bromo-1,8-naphthalic anhydride in NMP. The reaction mixture was heated at 145°C for 24 h and then cooled at RT. The resulting precipitate was filtered, washed subsequently with EtOH and Et₂O and dried to afford the title compound (42%) as a pale brown solid; MS (ES⁺) m/z 430, 432 (M+H)⁺.

**Step 2:** 2-(3-bromophenyl)-6-[(2-hydroxyethyl)amino]-1H-benz[de]isoquinoline-1,3(2H)-dione

A solution (0.2 M) of 6-bromo-2-(3-bromophenyl)-1H-benz[de]isoquinoline-1,3(2H)-dione (from Step 1) and ethanolamine (10 eq.) in NMP was heated at 200°C under microwave irradiation for 30 min. After addition of water the resulting precipitate was filtered and washed subsequently with EtOH and Et₂O. Crystallization from acetone afforded the title compound (27%) as a yellow solid.

[^1]H NMR (400 MHz, DMSO-d₆, 400 K) δ 3.51 (m, 2H), 3.73 (m, 2H), 4.91 (t, J 5.19, 1H), 6.87 (d, J 8.57, 1H), 7.38 (d, J 7.67, 1H), 7.48 (t, J 7.75, 1H), 7.65 (m, 2H), 7.73 (t, J 7.76, 1H), 8.27 (d, J 8.48, 1H), 8.45 (d, J 7.13, 1H), 8.77 (d, J 8.30, 1H); MS (ES⁺) m/z 411, 413 (M+H)⁺.

Example 2: 2-(3-chlorophenyl)-6-[(2-hydroxyethyl)amino]-1H-benz[de]isoquinoline-1,3(2H)-dione

A solution (0.09 M) of 4-bromo-1,8-naphthalic anhydride in EtOH was treated with 3-chloroaniline (1.5 eq.). The reaction mixture was heated to reflux for 15 h. After cooling down, filtration and washing with EtOH afforded a solid that was a mixture (1.2:1) of starting material and 6-bromo-2-(3-chlorophenyl)-1H-benz[de]isoquinoline-1,3(2H)-dione (MS (ES⁺) m/z 386, 388, 390 (M+H)⁺). This crude was dissolved in NMP. The resulting solution (0.15 M) was treated with 2-aminoethanol (2.0 eq.). The reaction mixture was heated at 200°C under microwave irradiation for 30 min. After cooling down, the reaction mixture was diluted with MeCN/DMSO (3:1) and it was purified by RP-HPLC (Conditions: Waters X-TERRA MS C18, 5 micron, 19 x 150 mm; flow: 20 mL/min; Gradient: A: H₂O + 0.1% TFA; B: MeCN + 0.1% TFA; 99% A isocratic for 2 min, linear to 1% A in 10 min, 1% A isocratic for 5 min) to afford the title compound (20%) as a solid.
Example 3: 2-butyl-6-[(2-hydroxyethyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione

Step 1: 6-bromo-2-butyl-1H-benzo[de]isoquinoline-1,3(2H)-dione
A solution (0.32 M) of 4-bromo-1,8-naphthalic anhydride in EtOH was treated with n-butylamine (1.1 eq.). The reaction mixture was heated at 150°C under microwave irradiation for 1 h. After addition of MeOH the resulting precipitate was filtered and dried to afford a first crop of the title compound (62%) as a solid. The filtrate was concentrated, and the residue was treated with EtOH/H2O (1:4) to afford a second crop of the title compound (35%). This compound was used as such in the next step; MS (ES+) m/z 332, 334 (M+H)+.

Step 2: 2-butyl-6-[(2-hydroxyethyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione
A solution (0.15 M) of 6-bromo-2-butyl-1H-benzo[de]isoquinoline-1,3(2H)-dione (from Step 1) in NMP was treated with 2-aminoethanol (1.2 eq.). The reaction mixture was heated at 200°C under microwave irradiation for 30 min. After cooling down, the reaction mixture was diluted with EtOAc and water was added. The organic layer was separated and the aqueous layer was extracted with EtOAc. The combined organic layers were dried and evaporated to give a residue that was purified by RP-HPLC (Conditions: Waters X-TERRA MS C18, 5 micron, 19 x 150 mm; flow: 20 mL/min; Gradient: A: H2O + 0.1% TFA; B: MeCN + 0.1% TFA; 99% A isocratic for 2 min, linear to 1% A in 10 min, 1% A isocratic for 5 min) to afford the title compound (53%) as a solid.

1H NMR (400 MHz, DMSO-d6, 300 K) δ 9.11 (t, 3H, J 7.2), 1.33 (m, 2H), 1.58 (m, 2H), 3.46 (m, 2H), 3.70 (t, 2H, J 6.1), 4.04 (t, 2H, J 7.4), 6.81 (d, 1H, J 8.8), 7.67 (dd, 1H, J 7.4, 8.3), 7.70 (bs, 1H), 8.25 (d, 1H, J 8.6), 8.42 (d, 1H, J 6.8), 8.68 (d, 1H, J 7.6); MS (ES+) m/z 313 (M+H)+.

Example 4: 2-(3-bromophenyl)-6-[(2-hydroxyethyl)thio]-1H-benzo[de]isoquinoline-1,3(2H)-dione
A solution (1.0 M) of 6-[(2-hydroxyethyl)thio]-1H, 3H-benzo[de]isochromene-1,3-dione in NMP was treated with 3-bromoaniline (1.5 eq.). The reaction mixture was heated at 200°C under microwave irradiation for 30 min. Then more 3-bromoaniline (0.75 eq) was added, and the reaction was heated under microwave irradiation for another 15 min. After cooling down, water and EtOAc were added. The layers were separated, and the aqueous layer was extracted with EtOAc. The gummy residue that remained on the reaction vessel gave a solid after addition of EtOH. This solid was filtered off and washed with EtOH to afford 39% of recovered starting material. After drying, combined EtOAc layers were joint with the EtOH filtrate and evaporated. The residue was purified by RP-HPLC (Conditions: Waters X-TERRA MS C18, 5 micron, 19 x 150 mm; flow: 20 mL/min; Gradient: A: H2O + 0.1% TFA;
B: MeCN + 0.1% TFA; 99% A isocratic for 2 min, linear to 1% A in 10 min, 1% A isocratic for 5 min) to afford the title compound (11%) as a solid.

$^1$H NMR (400 MHz, DMSO-d$_6$, 300 K) δ 3.39 (t, 2H, J 6.4), 3.77 (t, 2H, J 6.4), 5.14 (bs, 1H), 7.43 (d, 1H, J 7.9), 7.50 (t, 1H, J 7.9), 7.68 (d, 1H, J 7.9), 7.70 (d, 1H, J 1.5), 7.85 (d, 1H, J 8.1), 7.93 (dd, 1H, J 7.4, 8.3), 8.38 (d, 1H, J 7.9), 8.55 (d, 1H, J 7.2), 8.65 (d, 1H, J 8.5); MS (ES$^+$) m/z 428, 430 (M+H)$^+$.  

Example 5: 2-(3-bromophenyl)-7-[(2-hydroxyethyl)amino]-2,3-dihydro-1H-benzo[de]isoquinolin-1-one

A solution (0.02 M) of 2-(3-bromophenyl)-6-[(2-hydroxyethyl)amino]-1H-benz[de]isoquinoline-1,3(2H)-dione (from Example 1) in EtOH/water (10:1) was treated with sodium borohydride (5 eq.). The reaction was stirred overnight at RT. After quenching with aqueous HCl (1 N), the reaction mixture was extracted with EtOAc and the combined organic layers were dried and concentrated. The residue was purified by RP-HPLC (Conditions: Waters X-TERRA MS C18, 5 micron, 19 x 150 mm; flow: 20 mL/min; Gradient: A: H$_2$O + 0.1% TFA; B: MeCN + 0.1% TFA; 90% A isocratic for 2 min, linear to 30% A in 10 min, then linear to 0% A in 2 min) to afford the title compound (26%) as a solid.

$^1$H NMR (300 MHz, DMSO-d$_6$, 300 K) δ 3.41 (m, 2H), 3.70 (m, 2H), 4.83 (t, J 5.53, 1H), 5.29 (s, 2H), 6.68 (d, J 8.40, 1H), 6.91 (m, 1H), 7.35-7.55 (m, 5H), 7.74 (s, 1H), 8.06 (d, J 8.41, 1H), 8.15 (m, 1H); MS (ES$^+$) m/z 397, 399 (M+H)$^+$.  

Example 6: 2-(3-chlorophenyl)-6-(3-hydroxypropyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione

Step 1: 2-(3-chlorophenyl)-6-[(1E)-3-hydroxyprop-1-en-1-yl]-1H-benzo[de]isoquinoline-1,3(2H)-dione

A solution (0.1 M) of 6-bromo-2-(3-chlorophenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione (prepared as in Example 2) in DMF was treated with prop-2-en-1-ol (10 eq.), palladium acetate (0.05 eq.), triphenylphosphine (0.1 eq.) and silver acetate (1.0 eq.). The reaction mixture was heated at 80°C for 12 h. After cooling down, the reaction mixture was diluted with EtOAc and aqueous HCl (1N) was added. The organic layer was separated and the aqueous layer was extracted with EtOAc. The combined organic layers were dried and evaporated to give a yellow solid as residue that was used as such in the next step; MS (ES$^+$) m/z 364, 366 (M+H)$^+$.  

Step 2: 2-(3-chlorophenyl)-6-(3-hydroxypropyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione

A solution (0.1 M) of 2-(3-chlorophenyl)-6-[(1E)-3-hydroxyprop-1-en-1-yl]-1H-benzo[de]isoquinoline-1,3(2H)-dione (from step 1) in MeOH/EtOAc (1:1) was treated with ZnBr$_2$ (0.2 eq.), 10% Pd on carbon (50% w/w) and stirred under H$_2$ (g) for 12 h. The catalyst was then deactivate by bubbling N$_2$ for 10 min, filtered off and washed with hot MeOH and EtOAc. The solution was evaporated to give a residue that was purified by RP-HPLC (Conditions: Waters Symmetry C18, 5 micron, 19x300 mm; flow: 20 mL/min;
Gradient: A: H₂O + 0.1 %TFA; B: MeCN + 0.1% TFA; 60 % A isocratic for 3 min, linear to 10 % A in 23 min, 10 % A isocratic for 2 min) to afford the title compound (6% over two steps) as a solid.


Example 7: 2-(3-chlorophenyl)-6-(1H-pyrazol-3-yl)-1H-benzo[de]isoquinoline-1,3(2H)-dione

A solution (0.1 M) of 6-bromo-2-(3-chlorophenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione (prepared as in Example 2) in DME/EtOH (2.6/1) was treated with 1H-pyrazol-3-yl boronic acid (1.2 eq.), aqueous Na₂CO₃ (2M solution) and Pd(PPH₃)₄ (0.1 eq.). The reaction mixture was heated at 80°C for 2 h. After cooling down, the reaction mixture was acidified with aqueous HCl (1N) and filtered. The precipitate was washed sequentially with water, a small portion of Et₂O and dried to give a residue that was purified by RP-HPLC (Conditions: Waters X-TERRA C18, 5 micron, 19x100 mm; flow: 20 mL/min; Gradient: A: H₂O + 0.1 %TFA; B: MeCN + 0.1% TFA; 50 % A isocratic for 1 min, linear to 0 % A in 9 min, 0 % A isocratic for 2 min) to afford the title compound (25%) as a solid.


Example 8: 3-[6-[(benzylamino)carbonyl]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanoic acid

**Step 1:** 1,3-dioxo-1H,3H-benzo[de]isochromene-6-carboxylic acid

A solution (0.4 M) of 1,2-dihydroacenaphthylene-5-carboxylic acid in glacial AcOH was treated with Na₂Cr₂O₇ (4.0 eq.). After the spontaneous exothermic reaction was finished the reaction mixture was heated at reflux for 10 min. The reaction mixture was then cooled down, acidified with aqueous HCl (1N) and the precipitate formed was filtered, washed with water and dried to give the title compound (50%) as a solid; MS (ES⁺) m/z 243 (M+H)⁺.

**Step 2:** 3-[6-[(benzylamino)carbonyl]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanoic acid

A solution (0.4 M) of 1,3-dioxo-1H,3H-benzo[de]isochromene-6-carboxylic acid (from step 1) in CH₂Cl₂ was treated with DMF (0.05 eq.) and cooled to 0°C. Oxaly chloride (2M solution in CH₂Cl₂, 2.0 eq.) was added and the reaction mixture was stirred at 0°C for 1 h., then at 25°C for 1 h. The solvent was removed *in vacuo* and the residue was dissolved in toluene/DMF (1/1). The resulting solution (0.1 M) was treated with benzylamine (0.98 eq.) and a catalytic amount of DMAP. The reaction mixture was stirred at 25°C for 1 h., then at 60°C for 6 h. After cooling down, the reaction mixture was diluted with EtOAc and aqueous HCl (1N) was added. The organic layer was separated and the aqueous layer was
extracted with EtOAc. The combined organic layers were washed with brine, dried and evaporated to give a brown solid as residue that was used as such after dilution in EtOH. The resulting solution (0.14 M) was treated with β-norvaline (3.0 eq.). The reaction mixture was heated at 150°C under microwave irradiation for 30 min. After cooling down, the solvent was evaporated and the residue was purified by RP-HPLC (Conditions: Waters X-TERRA C18, 5 micron, 19x100 mm; flow: 20 mL/min; Gradient: A: H₂O + 0.1 %TFA; B: MeCN + 0.1% TFA; 50 % A isocratic for 1 min, linear to 0 % A in 9 min, 0 % A isocratic for 2 min) to afford the title compound (22%) as a solid.

⁴H NMR (400 MHz, DMSO-d₆, 300 K) δ 0.86 (t, J 7.32, 3H), 1.19-1.31 (m, 2H), 1.69-1.81 (m, 1H), 2.10-2.22 (m, 1H), 2.90 (dd, J 6.9, 16.0, 1H), 3.08 (dd, J 7.7, 16.0, 1H), 4.59 (d, J 5.9, 2H), 5.42-5.53 (m, 1H), 7.27-7.33 (m, 1H), 7.36-7.46 (m, 4H), 7.92 (t, J 7.9, 1H), 7.97 (d, J 7.5, 1H), 8.49-8.57 (m, 2H), 8.59 (d, J 8.4, 1H), 9.37 (bt, J 5.94, 1H), 12.0-12.4 (bs, 1H); MS (ES⁺) m/z 445 (M+H)⁺.

Example 9: 6-[(2-hydroxyethyl)amino]-2-[(5-methylisoxazol-3-yl)methyl]-1H-benzo[de]isoquinoline-1,3(2H)-dione

**Step 1: tert-butyl 6-bromo-1,3-dioxo-1H-benzo[de]isoquinoline-2(3H)-carboxylate**

A solution (0.9 M) of 6-bromo-1H,3H-benzo[de]isochromene-1,3-dione in EtOH and ammonia (32% aqueous solution, 1 eq.) were mixed in an Ace tube. The tube was well closed and heated at 80°C for 3 h. After cooling down, a precipitate was formed. The precipitate was isolated by filtration and washed with small portions of EtOH. The resulting solid was dissolved in dioxane. The resulting solution (0.2 M) was treated with Boc₂O (1.2 eq.) and catalytic amount of DMAP. The reaction mixture was stirred at RT for 1 h. Then, the solvent was evaporated and the residue was diluted with EtOAc and washed with aqueous HCl (1N), NaHCO₃ (saturated solution), brine and dried. Evaporation of the solvent afforded the title compound (85%) as pale yellow powder; m/z 276,278 (M+H)⁺.

**Step 2: 6-[(2-(benzoyloxy)ethyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione**

A solution (0.5 M) of tert-butyl 6-bromo-1,3-dioxo-1H-benzo[de]isoquinoline-2(3H)-carboxylate (from step 1) and 2-(benzoyloxy)ethanamine (3 eq.) in NMP (0.5 M) was heated at 180°C under microwave irradiation for 30 min. Then, the reaction was treated with water and kept at 4°C overnight. The resulting precipitate was isolated by filtration giving the title compound (70%) as a solid; m/z 347 (M+H)⁺.

**Step 3: 6-[(2-hydroxyethyl)amino]-2-[(5-methylisoxazol-3-yl)methyl]-1H-benzo[de]isoquinolone-1,3(2H)-dione**

A solution (0.4 M) of 6-[(2-benzoyloxy)ethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione in DMF was treated with KOH (1.1 eq.) and stirred for 30 min at 0°C. Then, 3-(chloromethyl)-5-methylisoxazole (1.2 eq.) was added and the reaction was stirred overnight. The reaction was treated with NH₄Cl (saturated solution) and extracted with EtOAc. The recombined organic layers were washed with NH₄Cl
(saturated solution), water, brine and dried. Evaporation of the solvent afforded a crude that was dissolved in MeOH. 10% Pd on carbon (50% w/w) was added to the resulting solution (0.1 M). The reaction was stirred under H₂ for 2 h. at RT. Then, the catalyst was filtered off and washed with EtOAc. After evaporation of the solvent the resulting residue was diluted with MeCN/DMSO (3:1) and purified by RP-HPLC (Conditions: Waters X-TERRA MS C18, 5 micron, 19 x 100 mm; flow: 20 mL/min; Gradient: A: H₂O + 0.1% TFA; B: MeCN + 0.1% TFA; 80% A isocratic for 1 min, linear to 20% A in 9 min, 20% A isocratic for 2 min) affording the title compound (37%) as a solid.

¹H NMR (300 MHz, DMSO-d₆, 300 K) δ 2.32 (s, 3H), 3.50 (m, 2H), 3.70 (m, 2H), 4.88 (t, J 5.5, 1H), 5.21 (s, 2H), 6.85 (d, J 8.6, 1H), 7.70 (t, J 8.0, 1H), 7.80 (m, 1H), 7.99 (m, 1H), 8.29 (d, J 8.6, 1H), 8.46 (d, J 7.1, 1H), 8.74 (d, J 8.2, 1H); m/z 353 (M+H)⁺.

Example 10: cis-4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]cyclohexanecarboxylic acid

**Step 1:** methyl cis-4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]cyclohexanecarboxylate

A solution (0.1 M) of 6-bromo-2-(3-chlorophenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione (prepared as in Example 2), methyl cis-4-aminocyclohexanecarboxylate hydrochloride (1.2 eq.) and DIPEA (1.5 eq.) in dry and degassed toluene was treated sequentially with BINAP (0.03 eq.), Pd(OAc)₂ (0.02 eq.), and NaOt-Bu (1.4 eq.). The reaction was stirred at 80°C for 2 h., then additional amounts of reagents: BINAP (0.06 eq.), Pd(OAc)₂ (0.08 eq.), and NaOt-Bu (1.4 eq.) were added. The reaction was stirred for another 3 h. and then diluted with EtOAc and water. The layers were separated and the aqueous layer was extracted with EtOAc. The combined organic layers were dried and concentrated to give a residue that was purified by chromatography on silica gel (petroleum ether/EtOAc (7:3) to EtOAc) to afford the title compound (43%) as a solid; MS (ES⁻) m/z 463, 465 (M+H)⁺.

**Step 2:** cis-4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]cyclohexanecarboxylic acid

A solution (0.075 M) of methyl cis-4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]cyclohexanecarboxylate in MeOH was treated with NaOH (2M aqueous solution, 2 eq.). The reaction mixture was heated at 60°C for 8 h. Then the solvent was evaporated under reduced pressure and the residue was taken up with EtOAc and aqueous HCl (1N) was added. The layers were separated and the aqueous layer was extracted with EtOAc. The combined organic layers were dried and concentrated. The residue was purified by RP-HPLC (Conditions: Waters Symmetry Prep C18, 7 micron, 19 x 300 mm; flow: 15 mL/min; Gradient: A: H₂O + 0.1% TFA; B: MeCN + 0.1% TFA; 90% A to 0% A linear in 15 min) to afford the title compound (47%) as a solid.
The following table shows additional examples which were prepared using procedures analogous to the general methods or specific examples described above, or which are commercially available, as indicated in the final column.

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Table 2
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<td>3-{6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]benzenesulfonamide</td>
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<td>2-(2-bromophenyl)-6-{(2-hydroxyethyl)amino}-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
<td>411, 413</td>
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<td>2-(3,5-dichlorophenyl)-6-{(2-hydroxyethyl)amino}-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
<td>401, 403</td>
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<td>2-(2,3-dichlorophenyl)-6-{(2-hydroxyethyl)amino}-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
<td>401, 403</td>
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<td>401, 403</td>
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<td>2-(3-chloro-4-fluorophenyl)-6-{(2-hydroxyethyl)amino}-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
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<td>2-(3-chloro-4-methoxyphenyl)-6-{(2-hydroxyethyl)amino}-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
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<td>227</td>
<td>6-{(2-aminoethyl)amino}-2-phenyl-1H-benzo[de]isoquinolin-1,3(2H)-dione</td>
<td>333, 335</td>
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<td>2-(3-methylphenyl)-6-piperazin-1-yl-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
<td>333, 335</td>
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<td>229</td>
<td>methyl {{[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino}(oxo)acetate}</td>
<td>409, 411</td>
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<td>230</td>
<td>6-{{(1-benzyloxy)piperidin-4-yl}amino}-2-(3-chlorophenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
<td>510, 512</td>
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<td>6-{{(1-acetyl)piperidin-4-yl}amino}-2-(3-chlorophenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
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<td>2-(3-chlorophenyl)-6-{{[1-(cyclohexylcarbonyl)piperidin-4-yl]amino}-1H-benzo[de]isoquinolin-1,3(2H)-dione</td>
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<td>2-(3-chlorophenyl)-6-{{[1-(phenylsulfonfyl)piperidin-4-yl]amino}-1H-benzo[de]isoquinolin-1,3(2H)-dione</td>
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<td>N-[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]glycine</td>
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235 4-\{[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl)amino]methyl\}cyclohexanecarboxylic acid 463, 465 10

236 2-(3-chlorophenyl)-5-{[(2-hydroxyethyl)amino]-1H-benzo[de]isoquinoline-3(2H)-dione} 367, 369 A

237 2-\{[(4-\{[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl)amino]piperidin-1-yl\}carbonyl]benzoic acid\} 554, 556 10

238 4-\{[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl)amino]piperidin-1-yl\}carbonyl]benzoic acid 552, 554 10

239 N-\{[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-5-yl)acetamide\} 365, 367 A

240 4-chloro-2-\{6-\{[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl\}benzoic acid\} 411, 413 A

241 N-\{[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl\}2-phenylacetamide 441, 443 A

242 2-(3-chlorophenyl)-5-(methylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione 337, 339 A

243 2-(3-chlorophenyl)-5-(dimethylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione 351, 353 A

244 2-\{[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-5-yl)amino]methyl\}pyridinium trifluoroacetate 414, 416 A

245 trans-4-\{[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl)amino\}cyclohexanecarboxylic acid 447, 449 10

246 2-(3-chlorophenyl)-6-(2-oxopyrrolidin-1-yl)-1H-benzo[de]isoquinoline-1,3(2H)-dione 391, 393 10

247 5-\{[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl)amino\}pentanoic acid 437, 439 10

248 1-benzyl-4-\{[(2-(2-carboxy-5-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl)amino\}piperidinium trifluoroacetate 411, 413 A

249 (2S)-2-\{6-\{[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl\}pentanoic acid\} 357 A

250 4-\{[(2-(3-carboxyphenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl)amino\}piperidinium trifluoroacetate 416 A

251 3-\{6-\{[(1-acetylpiperidin-4-yl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl\}5-bromobenzoic acid\} 494, 496 A

252 1-benzyl-4-\{[(2\{[(1S)-1-carboxybutyl]-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl\}amino\}piperidinium trifluoroacetate 486 A

253 ethyl 2-\{6-bromo-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl\}1,3-thiazole-5-carboxylate 431, 433 A

254 6-\{[(2-(benzyl oxy)ethyl)amino]-2-\{[(5-methylisoxazol-3-yl)methyl]-1H-benzo[de]isoquinoline-1,3(2H)-dione\} 441 9

255 6-\{[(2-hydroxyethyl)amino]-2-\{[(5-methylisoxazol-3-yl)methyl]-1H-benzo[de]isoquinoline-1,3(2H)-dione\} 453 9

256 3-\{6-\{[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl\}benzoic acid\} 378 A

257 4-\{[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl\}benzoic acid 378 A

258 2-\{[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl\}4-methylpentanoic acid 371 A

259 methyl cis-4-\{[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl)amino\}cyclohexanecarboxylate 463, 465 10
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<p>| 260 | 2-(3-chlorophenyl)-6-(3-oxo-2-azabicyclo[2.2.2]oct-2-yl)-1H-benzo[de]isoquinoline-1,3(2H)-dione | 431, 433 | 10 |
| 261 | 2-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]benzoic acid | 377 | A |
| 262 | cis-4-[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino)cyclohexanecarboxylic acid | 449, 451 | 10 |
| 263 | 4-[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]-1-methylpiperidinium trifluoroacetate | 420, 422 | 2 |
| 264 | 4-[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]-1-(2-phenylethyl)piperidinium trifluoroacetate | 510, 512 | 10 |
| 265 | 4-[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]-1-propylpiperidinium trifluoroacetate | 448, 450 | 10 |
| 266 | 4-[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]-1-(1,3-thiazol-2-ylmethyl)piperidinium trifluoroacetate | 503, 505 | 9 |
| 267 | 4-[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]-1-[4-(methoxycarbonyl)benzyl]piperidinium trifluoroacetate | 554, 556 | 9 |
| 268 | 4-[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]-1-isopropylpiperidinium trifluoroacetate | 448, 450 | 10 |
| 269 | 1-benzyl-4-[(2-[3-bromo-5(ethoxycarbonyl)phenyl]-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino)piperidinium trifluoroacetate | 613, 615 | A |
| 270 | 4-[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]-1-(2-ethoxy-2-oxoethyl)piperidinium trifluoroacetate | 492, 494 | 10 |
| 271 | 1-(4-carboxybenzyl)-4-[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino)piperidinium trifluoroacetate | 540, 542 | 10 |
| 272 | 6-anilino-2-(3-chlorophenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione | 399, 401 | 10 |
| 273 | 2-(3-chlorophenyl)-6-(4-methoxyphenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione | 414, 416 | 7 |
| 274 | 3-[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]benzoic acid | 428, 430 | 7 |
| 275 | 4-[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]benzoic acid | 428, 430 | 7 |
| 276 | 2-(3-chlorophenyl)-6-(3-fluoro-4-methoxyphenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione | 432, 434 | 7 |
| 277 | 2-(3-chlorophenyl)-6-(2-fluoro-4-methoxyphenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione | 432, 434 | 7 |
| 278 | 2-(3-chlorophenyl)-6-(4-fluoro-3-methylphenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione | 416, 418 | 7 |
| 279 | 2-(3-chlorophenyl)-6-(5-fluoro-2-methoxyphenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione | 432, 434 | 7 |
| 280 | 3-[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]-1H-pyrazol-1-ium trifluoroacetate | 374, 376 | 7 |
| 281 | 4-[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]pyridinium trifluoroacetate | 385, 387 | 7 |</p>
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<td>2-(3-chlorophenyl)-6-(3-furyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
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<td>3-[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]pyrrolidinum trifluoroacetate</td>
<td>385, 387</td>
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<td>284</td>
<td>2-(3-chlorophenyl)-6-pyrimidin-5-yl-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
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<td>3-[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]benzenaminium trifluoroacetate</td>
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<td>286</td>
<td>2-(3-chlorophenyl)-6-cyclohexyl-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
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<td>1-(carboxymethyl)-4-{[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino} piperidinium trifluoroacetate</td>
<td>464, 466</td>
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<td>288</td>
<td>6-amino-2-(3-methylphenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
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<td>289</td>
<td>2-(3,4-dimethylphenyl)-6,7-dihydro-1H-indeno[6,7,1-de]isoquinoline-1,3(2H)-dione</td>
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<td>2-(3-methylphenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinoline-6-carboxylic acid</td>
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<td>2-(2,3-dimethylcyclohexyl)-6,7-dihydro-1H-indeno[6,7,1-de]isoquinoline-1,3(2H)-dione</td>
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<td>6-bromo-2-(3,5-dimethyl-1H-phenazol-4-yl)-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
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<td>5-amino-2-butyl-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
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<td>294</td>
<td>3-(6-nitro-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)propanoic acid</td>
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<td>6-chloro-2-(6-methylpyridin-2-yl)-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
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<td>6-acetyl-2-(5-chloro-2-hydroxyphenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
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<td>2-butyl-5-hydroxy-6-nitro-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
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<td>298</td>
<td>1-benzyl-3-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino] pyrrolidinum trifluoroacetate</td>
<td>484, 486</td>
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<td>methyl 4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino] benzoate</td>
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<td>4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino] benzoic acid</td>
<td>443, 445</td>
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<td>301</td>
<td>2-(3-chlorophenyl)-6-(pyridin-2-ylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
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<td>2-(3-chlorophenyl)-6-(pyridin-3-ylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
<td>400, 402</td>
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<td>303</td>
<td>3-[6-[[2-hydroxyethyl]amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanoic acid</td>
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<td>304</td>
<td>3-bromo-5-[[2-hydroxyethyl]amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-N,N-dimethylbenzamide</td>
<td>482, 484</td>
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<td>305</td>
<td>3-[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino] benzoic acid</td>
<td>443, 445</td>
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<td>2-(3-chlorophenyl)-6-[4-morpholin-4-ylphosphoryl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
<td>484, 486</td>
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<td>307</td>
<td>6-[[3-(benzoxolyl)phenyl]amino]-2-(3-chlorophenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
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<td>308</td>
<td>2-(3-chlorophenyl)-6-(quolinin-3-ylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
<td>450, 452</td>
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<td>2-(3-chlorophenyl)-6-(isooquinolin-7-ylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
<td>450, 452</td>
<td>10</td>
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<td>310</td>
<td>Ethyl (2E)-3-(4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]phenyl]acrylate</td>
<td>497, 499</td>
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<td>311</td>
<td>2-(3-chlorophenyl)-6-[[3-(trifluoromethyl)phenyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
<td>467, 469</td>
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<td>6-[[4-sec-butylyphenyl]amino]-2-(3-chlorophenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
<td>455, 457</td>
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<td>314</td>
<td>3-bromo-5-[[2-(hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-N-methylbenzamide</td>
<td>468, 470</td>
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<td>N-[[3-bromo-5-[[2-(hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]benzoyl]-β-alanine</td>
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<td>316</td>
<td>4-[[3-bromo-5-[[2-(hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]benzoyl]-amino)methyl]benzoic acid</td>
<td>588, 590</td>
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<td>317</td>
<td>cis-4-[[3-bromo-5-[[2-(hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]benzoyl]-amino)cyclohexanecarboxylic acid</td>
<td>580, 582</td>
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<td>318</td>
<td>3-[[3-bromo-5-[[2-(hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]benzoyl]-amino)cyclohexanecarboxylic acid</td>
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<td>3-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]-N,N-dimethylbenzenaminium trifluoroacetate</td>
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<td>3-bromo-5-[[2-(hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-N-(methylsulfonyl)benzamide</td>
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<td>2-[6-anilino-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]pentanoic acid</td>
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<td>322</td>
<td>4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]-2-methylquinolinium trifluoroacetate</td>
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<td>323</td>
<td>ethyl 3-[6-anilino-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-5-chlorobenzoate</td>
<td>471, 473</td>
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<td>324</td>
<td>3-[6-anilino-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-5-chlorobenzoic acid</td>
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<td>4-[[2-(3-carboxy-5-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]-1-isopropylpiperidinium trifluoroacetate</td>
<td>492, 494</td>
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<td>326</td>
<td>4-[[2-(3-carboxy-5-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]-1-(2-phenylethyl)piperidinium trifluoroacetate</td>
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<td>4-[[2-(3-carboxy-5-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]piperidinium-1-yl)methyl)pypyridinium bis(trifluoroacetate)</td>
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<td>1-benzyl-4-[[2-(3-bromo-5-[[methylamino]carbonyl] phenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]piperidinium trifluoroacetate</td>
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<td>4-[[2-{1-(carboxymethyl)butyl}-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]-1-isopropylpiperidinium trifluoroacetate</td>
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<td>2-(3-bromophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinoline-6-carboxylic acid</td>
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<td>2-(5-chloro-2-methoxyphenyl)-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
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<td>3-(6-anilino-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-N-(methylsulfonyl)hexanamide</td>
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<td>1-isopropyl-4-[[3-[[6-[[1-isopropylpiperidinium-4-yl]amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanoyl]amino]piperidinium bis(trifluoroacetate)</td>
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<td>1-isopropyl-4-[[2-{1-[[2-((methylamino)-2-oxoethyl)butyl]-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]piperidinium trifluoroacetate</td>
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<td>2-(5-chloro-2-hydroxyphenyl)-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
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<td>2-(3-bromo-2-methylphenyl)-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
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<td>6-[[2-hydroxyethyl]amino]-2-(4-methylpyridin-2-yl)-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
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<td>3-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]methylbenzoic acid</td>
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<td>3-[[2-(hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-N-1,3,4-thiadiazol-2-ylhexanamide</td>
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<td>2-{1-[[2-(3-amino-1H-pyrazol-1-yl)-2-oxoethyl]butyl]-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
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<td>2-[[3-[[6-[[2-(hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanoyl]amino]-1,3-thiazol-3-ium trifluoroacetate</td>
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<td>3-[[3-[[6-[[2-(hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanoyl]amino]methyl]pyridinium trifluoroacetate</td>
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<td>4-[[3-[[6-[[2-(hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanoyl]amino]methyl]pyridinium trifluoroacetate</td>
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<td>5-{2-[(3-[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanoyl]amino)ethyl]-1H-imidazol-3-ium trifluoroacetate}</td>
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<td>2-(3-chlorophenyl)-6-(3-hydroxypropyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
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<td>6-[[2-hydroxyethyl]amino]-2-(3-methylcyclohexyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione</td>
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<td>N-(2,6-difluorobenzyl)-3-[[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanamide}</td>
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<td>3-[[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]N-[2-(1H-1,2,4-triazol-5-yl)ethyl]hexanamide}</td>
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<td>3-[[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]N-(2-pyridin-4-ylhexyl)hexanamide}</td>
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<td>3-[[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]N-(1H-indol-6-ylmethyl)hexanamide}</td>
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<td>N-benzyl-3-[[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanamide}</td>
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<td>N-(2,6-dimethoxybenzyl)-3-[[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanamide}</td>
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<td>N-(2,6-difluorobenzyl)-3-[[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanamide}</td>
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<td>{3-bromo-5-[[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]phenyl}acetic acid}</td>
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<td>3-[[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]N-[(1R)-1-phenylethyl]hexanamide}</td>
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<td>3-[[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]N-[(1R)-1-phenylethyl]hexanamide}</td>
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<td>N-[[3R,4R]-4-hydroxy-1,1-dioxido-tetrahydro-3-thienyl]3-[[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanamide}</td>
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<td>3-[[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]N-[(1-methyl-1H-pyrazol-4-yl)methyl]hexanamide}</td>
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<td>N-[(2-chloro-6-methylbenzyl)-3-[[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanamide}</td>
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<td>N-[(2-fluorobenzyl)-3-[[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanamide}</td>
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<td>3-[[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]N-[(1S)-1-phenylethyl]hexanamide}</td>
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<td>3-[[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]N-[(1S)-1-phenylethyl]hexanamide}</td>
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<td>2-buty1-6-(butylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione}</td>
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<td>2-[(3-[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanoyl]amino)methyl]-5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-1-ium trifluoroacetate}</td>
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<td>1-benzyl-4-[[1,3-dioxo-2-[[1-(2-oxo-2-[[1(S)-1-phenylethyl]amino]ethyl]butyl]-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]piperidinium trifluoroacetate}</td>
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<td>1-benzyl-4-{1,3-dioxo-2-{1-(2-oxo-2-{[(1S)-1-phenylethyl]amino}ethyl}butyl}-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl}amino)piperidinium trifluoroacetate</td>
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<td>cis-4-{1,3-dioxo-2-{1-(2-oxo-2-{[(1S)-1-phenylethyl]amino}ethyl}butyl}-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl}amino)cyclohexanecarboxylic acid</td>
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<td>2-{1-{(benzylxoy)methyl}butyl}-6-{(2-hydroxyethyl)amino}-1H-benzo[de]isoquinoline-1,3-(2H)-dione</td>
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<td>trans-1-benzyl-4-{2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl}amino)cyclohexanecarboxylic acid</td>
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<td>2-(3-chlorophenyl)-6-{1-(phenylacetyl)piperidin-4-yl}amino}-1H-benzo[de]isoquinoline-1,3-(2H)-dione</td>
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<td>3-bromo-5-{6-{(2-hydroxyethyl)amino}-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl}benzoic acid</td>
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<td>1-benzyl-4-{2-(3-bromo-5-carboxyphenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl}amino)piperidinium trifluoroacetate</td>
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<td>4-({2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl}amino)piperidinium-1-yl)methylpyridinium bis(trifluoroacetate)</td>
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<td>4-{2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl}amino}-1-(3-thienylmethyl)piperidinium trifluoroacetate</td>
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<td>cis-4-{2-(3-methyl-5-{(methylamino)carbonyl}phenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl}amino)cyclohexanecarboxylic acid</td>
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<td>cis-1-benzyl-4-{2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl}amino)cyclohexanecarboxylic acid</td>
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<td>2-(5-ethyl-1,3,4-thiadiazol-2-yl)-6-nitro-1H-benzo[de]isoquinoline-1,3-(2H)-dione</td>
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<td>2-allyl-1H-benzo[de]isoquinoline-1,3-(2H)-dione</td>
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<td>2-butyl-5-hydroxy-1H-benzo[de]isoquinoline-1,3-(2H)-dione</td>
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<td>6-amino-2-(1,3-dimethyl-1H-pyrazol-4-yl)-1H-benzo[de]isoquinoline-1,3-(2H)-dione</td>
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<td>2-(1H-benzimidazol-1-yl)ethyl]-1H-benzo[de]isoquinoline-1,3-(2H)-dione</td>
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<td>6-amino-2-(3-morpholin-4-ylpropyl)-1H-benzo[de]isoquinoline-1,3-(2H)-dione</td>
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<td>394</td>
<td>6-{2-hydroxy-1,1-bis(hydroxymethyl)ethyl}amino}-2-(3-methylphenyl)-1H-benzo[de]isoquinoline-1,3-(2H)-dione</td>
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<td>6-bromo-2-butyl-1H-benzo[de]isoquinoline-1,3-(2H)-dione</td>
<td>332, 334</td>
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Sources of commercially available compounds:

comm\textsuperscript{1}: Asinex (Russia); comm\textsuperscript{2}: Interchim Intermediates (France); comm\textsuperscript{3}: Maybridge (UK); comm\textsuperscript{4}: Labotest (Germany); comm\textsuperscript{5}: Chembridge (San Diego, USA).
Claims

1. Use of a compound of formula (I):

\[ R^2 \]

\[ R^1 \]

or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment or prevention of infection by hepatitis C virus,

wherein

A and B are each independently CH\(_2\), C=O or C=S, with the proviso that A and B are not both CH\(_2\);

R\(^1\) is C\(_1\)-aryl, C\(_2\)-alkenyl, C\(_2\)-alkynyl, (CH\(_2\))\(_{0,3}\)C\(_{3-7}\)cycloalkyl, (CH\(_2\))\(_{0,3}\)Het, (CH\(_2\))\(_{0,3}\)aryl or (CH\(_2\))\(_{0,3}\)heteroaryl, optionally substituted by halogen, hydroxy, C\(_1\)-alkyl, C\(_1\)-alkoxy, C\(_2\)-alkenyl, CN, (CH\(_2\))\(_{0,3}\)O(CH\(_2\))\(_{0,3}\)aryl, S(C\(_1\)-alkyl), S(O)(C\(_1\)-alkyl), S(O)\(_2\)(C\(_1\)-alkyl), S-heteroaryl, S(O)heteroaryl, S(O)\(_2\)heteroaryl, S-aryl, S(O)aryl, S(O)\(_2\)aryl, SO\(_2\)NR\(^R^5\)\(^R^5\), CO\(_2\)R\(^4\), CONR\(^R^6\)\(^R^6\), NR\(^4\)COR\(^5\), NR\(^4\)SO\(_2\)R\(^3\) or NR\(^4\)CONR\(^5\) where said C\(_1\)-alkyl, (CH\(_2\))\(_{0,3}\)Het, (CH\(_2\))\(_{0,3}\)aryl and (CH\(_2\))\(_{0,3}\)heteroaryl groups, either by themselves or as part of other substituents, may optionally be substituted by 1 to 8 halogen atoms, and where said (CH\(_2\))\(_{0,3}\)Het, (CH\(_2\))\(_{0,3}\)aryl and (CH\(_2\))\(_{0,3}\)heteroaryl groups may optionally be further substituted with one or two groups selected from hydroxy, C\(_1\)-alkoxy, C\(_1\)-alkyl, (CH\(_2\))\(_{0,3}\)CO\(_2\)H, (CH\(_2\))\(_{0,3}\)CO\(_2\)C\(_1\)-alkyl and C(O)NR\(^R^4\)R\(^5\), and where said (CH\(_2\))\(_{0,3}\)aryl group may be fused to C\(_3\)-cycloalkyl;

R\(^4\), R\(^3\) and R\(^3\)\(^1\) are each independently selected from hydrogen, C\(_1\)-alkyl, (CH\(_2\))\(_{0,3}\)Het, (CH\(_2\))\(_{0,3}\)aryl, (CH\(_2\))\(_{0,3}\)heteroaryl and SO\(_2\)(C\(_1\)-alkyl), optionally substituted by 1 to 5 halogen atoms and/or 1 or 2 groups selected from hydroxy, C\(_1\)-alkyl, NH\(_2\) and C\(_1\)-alkoxy;

R\(^2\) is halogen, hydroxy, C\(_1\)-alkyl, C\(_2\)-alkenyl, C\(_2\)-alkynyl, C\(_1\)-alkoxy, (CH\(_2\))\(_{0,3}\)C\(_3\)-cycloalkyl, (CH\(_2\))\(_{0,3}\)aryl, CN, NO\(_2\), NR\(^R^7\), OR\(^6\), C(O)C\(_1\)-alkyl, CO\(_2\)H, CO\(_2\)R\(^8\), CONR\(^R^8\)R\(^8\), NR\(^2\)COR\(^8\), NR\(^2\)SO\(_2\)R\(^8\), NR\(^2\)CONR\(^R^8\), SR\(^8\), SOR\(^8\), SO\(_2\)R\(^8\) or SO\(_2\)NR\(^R^2\)R\(^8\), where said C\(_1\)-alkyl, C\(_2\)-alkenyl, C\(_1\)-alkoxy and aryl groups are optionally substituted by 1 or 2 groups selected from halogen, hydroxy, C\(_1\)-alkyl, C\(_1\)-alkoxy, NH\(_2\), SO\(_2\)NR\(^R^6\)R\(^7\), CO\(_2\)R\(^8\) and CONR\(^R^8\)R\(^7\);

R\(^8\) and R\(^7\) are each independently selected from hydrogen, C\(_1\)-alkyl, C\(_2\)-alkenyl, C\(_2\)-alkynyl, (CH\(_2\))\(_{0,3}\)C\(_3\)-cycloalkyl, (CH\(_2\))\(_{0,3}\)Het, (CH\(_2\))\(_{0,3}\)aryl, (CH\(_2\))\(_{0,3}\)heteroaryl, (CH\(_2\))\(_{0,3}\)OR\(^9\), (CH\(_2\))\(_{0,3}\)SR\(^9\), (CH\(_2\))\(_{0,3}\)NR\(^R^1\)R\(^1\)\(^{11}\), -C(CH\(_2\)OH)\(_{3}\), COR\(^{22}\), C(O)C(O)OC\(_1\)-alkyl, CO\(_2\)R\(^{22}\), CONR\(^{22}\)R\(^{22}\), SO\(_2\)R\(^{22}\) and SO\(_2\)NR\(^R^2\)R\(^{23}\), where said C\(_1\)-alkyl, C\(_2\)-alkenyl, C\(_2\)-alkynyl, cycloalkyl, Het, aryl and heteroaryl groups are optionally substituted by 1 or 2 groups selected from halogen, hydroxy, C\(_1\)-alkyl, CF\(_3\), NH\(_2\), N(C\(_1\)-alkyl)\(_2\), SO\(_2\)aryl, SO\(_2\)NR\(^R^1\)R\(^1\)\(^{15}\), (CH\(_2\))\(_{0,3}\)aryl, (CH\(_2\))\(_{0,3}\)heteroaryl, C(O)C\(_1\)-alkyl, C(O)(CH\(_2\))\(_{0,3}\)aryl,
(CH₂)₃CO₂R¹⁸, (CH=CH)CO₂R¹⁸, CONR¹⁸R¹⁹ and O(CH₂)₃aryl, which optional aryl substituents are further optionally substituted by CO₂H or Het;

R¹⁸ and R¹⁹ are each independently selected from hydrogen, C₁₋₆alkyl, C₂₋₆alkenyl, (CH₂)₃₋₅cycloalkyl, (CH₂)₃₋₅Het, (CH₂)₃₋₅aryl, (CH₂)₅₋₇heteroaryl, (CH₂)₃₋₅OR⁹, (CH₂)₅₋₇SR⁹, (CH₂)₃₋₅NR¹⁰R¹¹, -C(CH₂OH)₂, where said C₁₋₆alkyl, C₂₋₆alkenyl and C₁₋₆alkoxy groups are optionally substituted by halogen or hydroxy;

R², R¹⁰ and R¹¹ are each independently selected from hydrogen, C₁₋₆alkyl, C₂₋₆alkenyl, C(O)C₁₋₆alkyl and aryl;

or R⁶, R⁷ and the nitrogen atom to which they are attached form a heteroaliphatic ring of 4 to 7 ring atoms, which ring optionally contains 1, 2 or 3 additional heteroatoms selected from O and S or a group S(O)₂, S(O)₂ or NR¹², where R¹² is hydrogen, C₁₋₆alkyl, C₂₋₆alkenyl or aryl, and which ring is optionally substituted by halogen, hydroxy, C₁₋₆alkyl, C₂₋₆alkenyl, C₁₋₆alkoxy, oxo, SO₂NR¹⁸R¹⁹, COR¹⁸, CO₂R¹⁸ or CONR¹⁸R¹⁹, and which ring is optionally bridged by –CH₂– or –CH₂CH₂–;

R⁸, R¹⁰, R²² and R²³ are each independently selected from hydrogen, C₁₋₆alkyl, (CH₂)₃₋₅OR¹³, (CH₂)₃₋₅NR¹⁴R¹⁵, (CH₂)₃₋₅aryl and (CH₂)₅₋₇heteroaryl;

R¹³, R¹⁴ and R¹⁵ are each independently selected from hydrogen, C₁₋₆alkyl, C₂₋₆alkenyl, aryl, C(O)R¹⁶ and C(O)OR¹⁷;

R¹⁶, R¹⁷ and R²⁴ are independently selected from hydrogen, C₁₋₆alkyl and aryl;

R²⁵ is hydrogen, C₁₋₆alkyl, (CH₂)₃₋₅CO₂H, (CH₂)₅₋₇C₃₋₅cycloalkyl, (CH₂)₅₋₇phenyl or SO₂(C₁₋₆alkyl), where C₃₋₅cycloalkyl and phenyl are optionally substituted by 1 to 3 groups selected from halogen, hydroxy or CO₂H;

n is 0 or 1 or 2,

and when n is 2, the R² groups may be the same or different;

R⁷ is hydrogen,

or R² and R⁴ are joined to form a 5- to 8-membered carbocyclic ring.

2. Use as claimed in Claim 1 of a compound of formula (ii):

![Formula (ii)](attachment:formula.png)

or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment or prevention of infection by hepatitis C virus, wherein

A and B are each independently CH₃, C=O or C=S, with the proviso that A and B are not both CH₂;
R¹ is C₁₋₄ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, (CH₂)₃C₃₋₅ cycloalkyl, (CH₂)₃Het, (CH₂)₃aryl or
(CH₂)₃heteroaryl, optionally substituted by halogen, hydroxy, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₂₋₆ alkenyl, CN,
S(C₁₋₄ alkyl), S(O)(C₁₋₄ alkyl), S(O₂)(C₁₋₄ alkyl), S-heteroaryl, S(O)heteroaryl, S(O₂)heteroaryl, S-aryl,
S(O)aryl, S(O₂)aryl, SO₂NR⁺R⁻, CO₂R⁺, CONR⁺R⁻, NR⁺COR⁻, NR⁺SO₂R⁻ or NR⁺CONR⁻ where said
C₁₋₄ alkyl and (CH₂)₃aryl groups, either by themselves or as part of other substituents, may optionally be
substituted by 1 to 8 halogen atoms;

R², R³ and R⁴ are each independently selected from hydrogen, C₁₋₄ alkyl, (CH₂)₃Het,
(CH₂)₃aryl and (CH₂)₃heteroaryl;

R⁵ is halogen, hydroxy, C₁₋₄ alkyl, C₂₋₆ alkenyl, C₁₋₄ alkoxy, CN, NO₂, NR⁺R⁻, OR⁺, CO₂H, CO₂R⁺,
CONR⁺R⁻, NR⁺COR⁻, NR⁺SO₂R⁻, NR⁺CONR⁻, SR⁺, SOR⁺, SO₂R⁺ or SO₂NR⁺R⁻, where said
C₁₋₄ alkyl, C₂₋₆ alkenyl and C₁₋₄ alkoxy groups are optionally substituted by halogen, hydroxyl, SO₂NR⁺R⁻,
CO₂R⁺ or CONR⁺R⁻;

R⁶ and R⁷ are each independently selected from hydrogen, C₁₋₄ alkyl, C₂₋₆ alkenyl,
(CH₂)₃C₃₋₅ cycloalkyl, (CH₂)₃Het, (CH₂)₃aryl, (CH₂)₃heteroaryl, (CH₂)₃OR⁺, (CH₂)₃SR⁺,
(CH₂)₃NR⁺R¹¹, -C(CH₂OH)₃, COR⁺, CO₂R⁺, CONR⁺R¹¹, SO₂R⁺ and SO₂NR⁺R¹¹, where said
C₁₋₄ alkyl, C₂₋₆ alkenyl, cycloalkyl, Het, aryl and heteroaryl groups are optionally substituted by halogen,
hydroxy, SO₂NR⁺R¹¹, CO₂R⁺ or CONR⁺R¹¹;

R⁸ and R⁹ are each independently selected from hydrogen, C₁₋₄ alkyl, C₂₋₆ alkenyl,
(CH₂)₃C₃₋₅ cycloalkyl, (CH₂)₃Het, (CH₂)₃aryl, (CH₂)₃heteroaryl, (CH₂)₃OR⁺, (CH₂)₃SR⁺,
(CH₂)₃NR⁺R¹¹, -C(CH₂OH)₃, where said C₁₋₄ alkyl, C₂₋₆ alkenyl and C₁₋₄ alkoxy groups are optionally
substituted by halogen or hydroxy;

R⁰, R¹⁰ and R¹¹ are each independently selected from hydrogen, C₁₋₄ alkyl, C₂₋₆ alkenyl,
C(O)C₁₋₆ alkyl and aryl;

or R⁵, R⁷ and the nitrogen atom to which they are attached form a heteroaliphatic ring of 4 to 7
ring atoms, which ring optionally contains 1, 2 or 3 additional heteroatoms selected from O and S or a
group S(O), S(O₂) or NR⁺, where R¹² is hydrogen, C₁₋₄ alkyl, C₂₋₆ alkenyl or aryl, and which ring is
optionally substituted by halogen, hydroxy, C₁₋₄ alkyl, C₂₋₆ alkenyl or C₁₋₄ alkoxy, carboxyl, SO₂NR⁺R¹¹,
COR⁺, CO₂R⁺ or CONR⁺R¹¹;

R⁸, R¹⁰ and R¹¹ are each independently selected from C₁₋₄ alkyl, (CH₂)₁₋₃ OR⁺¹³,
(CH₂)₁₋₃ NR⁺R¹¹, (CH₂)₁₋₃ aryl and (CH₂)₁₋₃ heteroaryl;

R¹³, R¹⁴ and R¹⁵ are each independently selected from hydrogen, C₁₋₄ alkyl, C₂₋₆ alkenyl, aryl,
C(O)R⁺ and C(O)OR⁺;

R¹⁵ and R¹⁷ are independently selected from hydrogen, C₁₋₄ alkyl and aryl;

n is 0 or 1.

3. Use as claimed in Claim 1 or Claim 2 wherein one of A or B is C=O and the other is CH₂ or
C=O.
4. Use as claimed in Claim 3 wherein A is C=O and B is CH₂ or C=O.

5. Use as claimed in Claim 4 wherein A and B are C=O.

6. Use as claimed in any one of Claims 1 to 5 wherein R¹ is (CH₂)₃aryl, optionally substituted by halogen, hydroxy, C₁-alkyl, C₁-alkoxy, C₂-alkenyl, CN, S(C₁-alkyl), S(O)(C₁-alkyl), S(O)₂(C₁-alkyl), SO₂NR⁴R⁵ where R⁴ and R⁵ are as defined in Claim 1.

7. Use as claimed in any one of Claims 1 to 6 wherein R² is NR⁶R⁷ where R⁶ and R⁷ are as defined in Claim 1.

8. Use as claimed in Claim 7 wherein R⁶ and R⁷ are independently selected from hydrogen, C₁-alkyl, (CH₂)₃C₆-cycloalkyl, (CH₂)₃OR where R⁹ is as defined in Claim 1.

9. Use as claimed in Claim 1 of a compound of formula (Ia):

   ![Formula (Ia)](image-link)

or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment or prevention of infection by hepatitis C virus, wherein R¹ and R² are as defined in Claim 1.

10. Use as claimed in Claim 9 wherein R¹ is (CH₂)₃aryl, optionally substituted by halogen, hydroxy, C₁-alkyl, C₁-alkoxy, C₂-alkenyl, CN, S(C₁-alkyl), S(O)(C₁-alkyl), S(O)₂(C₁-alkyl), SO₂NR⁴R⁵ where R⁴ and R⁵ are as defined in Claim 1.

11. Use as claimed in Claim 9 or Claim 10 wherein R² is NR⁶R⁷ where R⁶ and R⁷ are as defined in Claim 1.

12. Use as claimed in Claim 11 wherein one of R⁶ and R⁷ is hydrogen and the other is selected from C₁-alkyl, (CH₂)₃C₆-cycloalkyl or (CH₂)₃OR where R⁹ is as defined in Claim 1.

13. Use as claimed in Claim 1 of a compound of formula (Ib):
or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment or prevention of infection by hepatitis C virus, wherein

\[ R^2 \text{ is as defined in Claim 1, and} \]

\[ R^1 \text{ is phenyl substituted by bromine and/or } \text{CO}_2\text{H, optionally further substituted by halogen, hydroxy, } C_{2-6}\text{alkyl, } C_{1-6}\text{alkoxy or } \text{CH}_2\text{CO}_2\text{H.} \]

14. Use as claimed in Claim 1 of a compound of formula (Ic):

\[ \text{or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment or prevention of infection by hepatitis C virus, wherein} \]

\[ R^1 \text{ is as defined in Claim 1, and} \]

\[ R^2 \text{ is } C_{5,6}\text{cycloalkyl,} \]

\[ (\text{CH}_2)_{1-4}\text{alkyl,} \]

\[ C_{2,8}\text{alkoxy,} \]

\[ \text{phenyl,} \]

\[ \text{NH}(\text{CH}_2)_{2-3}\text{Het substituted by } \text{C}(\text{O})(\text{CH}_2)_{2-3}\text{aryl, } \text{C}(\text{O})(\text{C}_{1-6}\text{alkyl), } \text{C}(\text{O})C_{2,3}\text{cycloalkyl,} \]

\[ \text{SO}_2\text{aryl, } (\text{CH}_2)_{1,3}\text{aryl (optionally substituted by } \text{CO}_2\text{C}_{1,4}\text{alkyl or } (\text{CH}_2)_{2,3}\text{CO}_2\text{H,} \]

\[ (\text{CH}_2)_{1,3}\text{heteroaryl or } (\text{CH}_2)_{1,3}\text{C}(\text{O})OC_{1,4}\text{alkyl,} \]

\[ \text{NH}(\text{CH}_2)_{2,3}\text{cycloalkyl substituted by } \text{CO}_2\text{H or } \text{CO}_2\text{C}_{1,4}\text{alkyl,} \]

\[ \text{NHC}(\text{O})C_{1,4}\text{alkyl,} \]

\[ \text{NHC}(\text{O})(\text{CH}_2)_{2,3}\text{aryl,} \]

\[ \text{NH}(\text{CH}_2)_{2,3}\text{O}(\text{CH}_2)_{1,3}\text{aryl,} \]

\[ 3\text{-oxo-2-azabicyclo[2.2.2]oct-2-yl,} \]

\[ \text{NH}(\text{CH}_2)_{2,3}\text{aryl substituted by } \text{CO}_2\text{H, } \text{CO}_2\text{C}_{1,4}\text{alkyl, Het or CH=CHC}(\text{O})OC_{1,4}\text{alkyl,} \]

\[ \text{CO}_2\text{H, or} \]

\[ \text{C}(\text{O})\text{NH}(\text{CH}_2)_{2,3}\text{aryl,} \]
where phenyl is optionally substituted by 1 to 3 groups selected from halogen, C₁₋₄ alkyl, NH₂, C₁₋₄ alkoxy or CO₂H.

15. Use as claimed in Claim 1 of a compound of formula (Id):

![Chemical structure diagram](image)

(Id)

or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment or prevention of infection by hepatitis C virus, wherein

R² is as defined in Claim 1, and

R¹ is C₃₋₅ alkyl substituted by CO₂H, C(O)NHС₁₋₄ alkyl, C(O)NHS(O)₂(C₁₋₄ alkyl),
C(O)NH(CH₂)₅ heteroaryl, C(O)NH(CH₂)₃ Het, C(O)NHCH(CH₃)phenyl or
O(CH₂)₃ ary1,
(CH₂)₃ C₃₋₅ cycloalkyl,
(CH₂)₃ aryl,
(CH₂)₃ Het,
(CH₂)₃ heteroaryl,
phenyl substituted by SH, SC₁₋₄ alkyl or SO₂C₂₋₆ alkyl,
C(O)NH(CH₂)₃ aryl,
C(O)NH(CH₂)₅ CO₂H, or
C(O)NH(CH₂)₅ cycloalkyl) substituted by CO₂H or C(O)NHS(O)₂(C₁₋₄ alkyl),
where the Het groups of (CH₂)₃ Het and C(O)NH(CH₂)₅ Het are optionally substituted by
C₁₋₄ alkyl, OH or NH₂, and
where the aryl group of C(O)NH(CH₂)₃ aryl is optionally substituted by CO₂H, halogen,
C₁₋₄ alkyl or C₁₋₄ alkoxy, and
where the heteroaryl group of C(O)NH(CH₂)₅ heteroaryl is optionally substituted by
C₁₋₄ alkyl.

16. Use as claimed in Claim 1 of a compound of Group II or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment or prevention of infection by hepatitis C virus, wherein Group II is defined as:

1H-benz[d]isoquinoline-1,3(2H)-dione, 2-(3-bromophenyl)-6-[(2-hydroxyethyl)amino],
2-(3-chlorophenyl)-6-[(2-hydroxyethyl)amino]-1H-benz[d]isoquinoline-1,3(2H)-dione,
2-buty1-6-[(2-hydroxyethyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-[(2-hydroxyethyl)thiao]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-7-[(2-hydroxyethyl)amino]-2,3-dihydro-1H-benzo[de]isoquinolin-1-one,
2-(3-chlorophenyl)-6-(3-hydroxypropy1)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-chlorophenyl)-6-(1H-pyrazol-3-yl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
3-[6-[(benzylamino)carbonyl]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanoic acid,
6-[(2-hydroxyethyl)amino]-2-[[5-methylisoxazol-3-yl)methyl]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
cis-4-[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-
yl)amino]cyclohexanecarboxylic acid,
2-(3-bromophenyl)-6-[(2-hydroxyethyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-[(2-methoxyethyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-[(propylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-[(3-hydroxypropyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
6-amino-2-(3-bromophenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-[(2-hydroxyethyl)thio]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-(methylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-[(2-(dimethylamino)ethyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-[(isobutylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-(ethylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
6-(benzylamino)-2-(3-bromophenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-[(2-phenylethyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-[(2-phenoxoethyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-[(2-hydroxyethyl)(methyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-[(tetrahydrofuran-2-yl)methyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-(cyclopentylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-(cyclohexylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-(isopropylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-[(2-(methylthio)ethyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-methoxy-1H-benzo[de]isoquinoline-1,3(2H)-dione,
N-(2-[(2-(3-bromophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl)amino)ethyl]acetamide,
2-(3-bromophenyl)-6-[(2-(methylamino)ethyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-(2-hydroxyethoxy)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
6-[(2-aminomethyl)amino]-2-(3-bromophenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-[(cyclopropylmethyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromophenyl)-6-[(pyrind-2-yl)thio)methyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
benzyl (2-[(2-(3-bromophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-
yl]amino)ethyl)carbamate,
6-(1-benzylpiperidin-4-yl)amino]-2-(3-bromophenyl)-1H-benzolo[de]isoquinoline-1,3(2H)-dione, 4-[[2-(3-bromophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]methyl)benzoic acid,
trans-4-[[2-(3-bromophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino)cyclohexanecarboxylic acid,
cis-4-[[2-(3-bromophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino)cyclohexanecarboxylic acid,
4-[[2-(3-bromophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]piperidinium trifluoroacetate,
6-[[2-hydroxyethyl]amino]-2-phenyl-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-benzyl-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-butyl-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-cyclohexyl-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
6-[[2-hydroxyethyl]amino]-2-isobutyl-1H-benzo[de]isoquinoline-1,3(2H)-dione,
3-[[2-hydroxyethyl]amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]benzonitrile,
6-[[2-hydroxyethyl]amino]-2-(3-methoxyphenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
6-[[2-hydroxyethyl]amino]-2-(3-methylphenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
6-[[2-hydroxyethyl]amino]-2-[3-(methylthio)phenyl]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(4-bromophenyl)-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione
6-[[2-hydroxyethyl]amino]-2-[3-(trifluoromethyl)phenyl]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-fluorophenyl)-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
6-[[2-hydroxyethyl]amino]-2-[3-(methylsulfonyl)phenyl]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(5-bromopyridin-3-yl)-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
3-[[2-hydroxyethyl]amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]benzenesulfonamide,
2-(2-bromophenyl)-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3,5-dichlorophenyl)-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(2,3-dichlorophenyl)-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(2,5-dichlorophenyl)-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-chloro-4-fluorophenyl)-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-chloro-4-methoxyphenyl)-6-[[2-hydroxyethyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
6-[[2-aminoethyl]amino]-2-phenyl-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-chlorophenyl)-6-[[1-(cyclohexylcarbonyl)piperidin-4-yl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-
dione,
2-(3-chlorophenyl)-6-{{1-(phenylsulfonfonyl)piperidin-4-yl}amino}-1H-benzo[de]isoquinoline-1,3(2H)-dione,
N-[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]glycine,
4-{{[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino}methyl}cyclohexanecarboxylic acid,
2-(3-chlorophenyl)-5-{{2-(hydroxyethyl)amino}-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-{{4-{{[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino}piperidin-1-yl}carbonyl}benzoic acid,
4-{{4-{{[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino}piperidin-1-yl}carbonyl}benzoic acid,
N-[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-5-yl]acetamide,
4-chloro-2-{{[2-hydroxyethyl]amino}-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl}benzoic acid,
N-[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]-2-phenylacetamide,
2-(3-chlorophenyl)-5-{{methylamino}-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-chlorophenyl)-5-{{dimethylamino}-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-{{[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-5-yl]amino}methyl}pyridinium trifluoroacetate,
trans-4-{{[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino}cyclohexanecarboxylic acid,
2-(3-chlorophenyl)-6-{{2-oxopyrrolidin-1-yl}-1H-benzo[de]isoquinoline-1,3(2H)-dione,
5-{{2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino}pentanoic acid,
1-benzyl-4-{{[2-(2-carboxy-5-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino}piperidinium trifluoroacetate,
(2S)-2-{{[2-hydroxyethyl]amino}-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl}pentanoic acid,
4-{{[2-(carboxyphenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino}piperidinium trifluoroacetate,
3-{{[1-acetyl]piperidin-4-yl]amino}-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-5-bromobenzoic acid,
1-benzyl-4-{{[2-(1H)-1-carboxybutyl]-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino}piperidinium trifluoroacetate,
ethyl 2-{{6-bromo-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl}-1,3-thiazole-5-carboxylate,
6-{{[benzyloxy]ethyl}amino}-2-{{[5-methylisoxazol-3-yl]methyl}-1H-benzo[de]isoquinoline-1,3(2H)-dione,
6-{{[2-hydroxyethyl]amino}-2-{{[5-methylisoxazol-3-yl]methyl}-1H-benzo[de]isoquinoline-1,3(2H)-dione,
3-{{[2-hydroxyethyl]amino}-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl}benzoic acid,
4-{{[2-hydroxyethyl]amino}-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl}benzoic acid,
2-[6-((2-hydroxyethyl)amino)-1,3-dioxo-1H-benzo[d]isoquinolin-2(3H)-yl]-4-methylpentanoic acid, methyl cis-4-[1-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[d]isoquinolin-6-yl] amino)cyclohexanecarboxylate, 
2-(3-chlorophenyl)-6-(3-oxo-2-azabicyclo[2.2.2]oct-2-yl)-1H-benzo[d]isoquinoline-1,3(2H)-dione, 
2-[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[d]isoquinolin-2(3H)-yl]benzoic acid, 
cis-4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[d]isoquinolin-6-yl] amino)cyclohexanecarboxylic acid, 
4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[d]isoquinolin-6-yl] amino]-1-methylpiperidinium trifluoroacetate, 
4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[d]isoquinolin-6-yl] amino]-1-(2-phenylethyl)piperidinium trifluoroacetate, 
4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[d]isoquinolin-6-yl] amino]-1-propylpiperidinium trifluoroacetate, 
4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[d]isoquinolin-6-yl] amino]-1-(1,3-thiazol-2-ylmethyl)piperidinium trifluoroacetate, 
4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[d]isoquinolin-6-yl] amino]-1-[4-(methoxycarbonyl)benzyl]piperidinium trifluoroacetate, 
4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[d]isoquinolin-6-yl] amino]-1-isopropylpiperidinium trifluoroacetate, 
1-benzyl-4-[[2-(3-bromo-5-(ethoxycarbonyl)phenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[d]isoquinolin-6-yl] amino)piperidinium trifluoroacetate, 
4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[d]isoquinolin-6-yl] amino)piperidinium trifluoroacetate, 
1-(4-carboxybenzyl)-4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[d]isoquinolin-6-yl] amino)piperidinium trifluoroacetate, 
6-anilino-2-(3-chlorophenyl)-1H-benzo[d]isoquinoline-1,3(2H)-dione, 
2-(3-chlorophenyl)-6-(4-methoxyphenyl)-1H-benzo[d]isoquinoline-1,3(2H)-dione, 
3-(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[d]isoquinolin-6-yl] benzoic acid, 
4-(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[d]isoquinolin-6-yl] benzoic acid, 
2-(3-chlorophenyl)-6-(3-fluoro-4-methoxyphenyl)-1H-benzo[d]isoquinoline-1,3(2H)-dione, 
2-(3-chlorophenyl)-6-(2-fluoro-4-methoxyphenyl)-1H-benzo[d]isoquinoline-1,3(2H)-dione, 
2-(3-chlorophenyl)-6-(4-fluoro-3-methylphenyl)-1H-benzo[d]isoquinoline-1,3(2H)-dione, 
2-(3-chlorophenyl)-6-(5-fluoro-2-methoxyphenyl)-1H-benzo[d]isoquinoline-1,3(2H)-dione, 
3-(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[d]isoquinolin-6-yl]-1H-pyrazol-1-ium trifluoroacetate, 
2-(3-chlorophenyl)-6-(3-thienyl)-1H-benzo[d]isoquinoline-1,3(2H)-dione,
4-[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]pyridinium trifluoroacetate,
2-(3-chlorophenyl)-6-(3-furyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
3-[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]pyridinium trifluoroacetate,
2-(3-chlorophenyl)-6-pyrimidin-5-yl-1H-benzo[de]isoquinoline-1,3(2H)-dione,
3-[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]benzenaminium trifluoroacetate,
2-(3-chlorophenyl)-6-cyclohexyl-1H-benzo[de]isoquinoline-1,3(2H)-dione,
1-(carboxymethyl)-4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-y1]amino]piperidinium trifluoroacetate,
1-benzyl-3-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-y1]amino]pyrrolidinium trifluoroacetate,
methyl 4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-y1]amino]benzoate,
4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-y1]amino]benzoic acid,
2-(3-chlorophenyl)-6-(pyridin-2-ylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-chlorophenyl)-6-(pyridin-3-ylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
3-[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanoic acid,
3-bromo-5-[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-N,N-dimethylbenzamide,
3-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-y1]amino]benzoic acid,
2-(3-chlorophenyl)-6-[[4-morpholin-4-ylphenyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
6-[[3-(benzyloxy)phenyl]amino]-2-(3-chlorophenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-chlorophenyl)-6-(quinolin-3-ylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-chlorophenyl)-6-(isoquinolin-7-ylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
ethyl (2E)-3-(4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-y1]amino]phenyl)acrylate,
2-(3-chlorophenyl)-6-[[3-(trifluoromethyl)phenyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
6-[[4-sec-butylphenyl]amino]-2-(3-chlorophenyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-chlorophenyl)-6-[[4-(trifluoromethyl)phenyl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
3-bromo-5-[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-N-methylbenzamide,
N-3-bromo-5-[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]benzoyl]-β-alanine,
4-[[3-bromo-5-[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]benzoyl]amino]methyl benzoic acid,
cis-4-[[3-bromo-5-[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]benzoyl]amino]cyclohexanecarboxylic acid,
3-[(3-bromo-5-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)]-ylnyl]benzoyl]amino)cyclohexanecarboxylic acid,

3-[(2-[(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino)-N,N-dimethylbenzenaminium trifluoroacetate,

3-bromo-5-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-N-(methylsulfonyl)benzamide,

2-(6-anilino-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)pentanoic acid,

4-[(2-[(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino)-2-methylquinolinium trifluoroacetate,

ethyl 3-(6-anilino-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-5-chlorobenzoate,

3-(6-anilino-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-5-chlorobenzoic acid,

4-[(2-[(3-carboxy-5-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino)-1-isopropyl]piperidinium trifluoroacetate,

4-[(2-[(3-carboxy-5-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino)-1-(2-phenylethyl) piperidinium trifluoroacetate,

4-[(4-[(2-[(3-carboxy-5-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino) piperidinium-1-yl] methyl]pyridinium bis(trifluoroacetate),

1-benzyl-4-[(2-[(3-bromo-5-[(methylamino)carbonyl]phenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino] piperidinium trifluoroacetate,

6-anilino-2-butyl-1H-benzo[de]isoquinoline-1,3(2H)-dione,

4-[(2-butyl-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino)-1-isopropyl]piperidinium trifluoroacetate,

3-(6-anilino-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)hexanoic acid,

4-[(2-[(1-carboxymethyl)butyl]-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino)-1-isopropyl]piperidinium trifluoroacetate,

2-(3-bromophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinoline-6-carboxylic acid,

2-[(carboxymethyl)butyl]-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinoline-6-carboxylic acid,

3-[(6-[(benzylamino)carbonyl]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanoic acid,

2-(5-chloro-2-methoxyphenyl)-6-[(2-hydroxyethyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,

3-(6-anilino-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-N-(methylsulfonyl)hexanamide,

1-isopropyl-4-[(3-6-[(1-isopropyl]piperidinium-4-yl]amino)-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanoyl]amino)piperidinium bis(trifluoroacetate),

1-isopropyl-4-[(2-[(1-[2-(methylamino)-2-oxoethyl]butyl]-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino)piperidinium trifluoroacetate,

2-(5-chloro-2-hydroxyphenyl)-6-[(2-hydroxyethyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,

2-(2,3-dihydro-1h-inden-4-yl)-6-[(2-hydroxyethyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-chloro-2-fluorophenyl)-6-[(2-hydroxyethyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-(3-bromo-2-methylphenyl)-6-[(2-hydroxyethyl)amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
6-[(2-hydroxyethyl)amino]-2-(4-methylpyridin-2-yl)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
3-[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino)methyl]benzoic acid,
3-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]N-1,3,4-thiadiazol-2-ylhexanamide,
2-[(2-(3-amino-1H-pyrazol-1-yl)-2-oxoethyl)butyl]-6-[(2-hydroxyethyl)amino]-1H-
benzo[de]isoquinoline-1,3(2H)-dione,
2-[(2-(3-amino-1H-pyrazol-1-yl)-2-oxoethyl)butyl]-6-[(2-hydroxyethyl)amino]-1H-
benzo[de]isoquinoline-1,3(2H)-dione,
3-[(2-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanoyl]amino)-1,3-
thiazol-3-ium trifluoroacetate,
3-[(2-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanoyl]amino)methyl]pyridinium trifluoroacetate,
2-[(3-amino-1H-pyrazol-1-yl)-2-oxoethyl]butyl]-6-[(2-hydroxyethyl)amino]-1H-
benzo[de]isoquinoline-1,3(2H)-dione,
3-[(2-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanoyl]amino)methyl]pyridinium trifluoroacetate,
3-[(2-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanoyl]amino)methyl]pyridinium trifluoroacetate,
2-[(3-amino-1H-pyrazol-1-yl)-2-oxoethyl]butyl]-6-[(2-hydroxyethyl)amino]-1H-
benzo[de]isoquinoline-1,3(2H)-dione,
2-[(3-amino-1H-pyrazol-1-yl)-2-oxoethyl]butyl]-6-[(2-hydroxyethyl)amino]-1H-
benzo[de]isoquinoline-1,3(2H)-dione,
3-[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino)methyl]benzoic acid,
N-(2,6-difluorobenzyl)-3-[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanamide,
{3-bromo-5-[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]phenyl} acetic acid,
3-[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-N-{[(1R)-1-phenylethyl]hexanamide,
3-[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-N-{[(1R)-1-phenylethyl]hexanamide,
N-{[3R,4R]-4-hydroxy-1,1-dioxidotetrahydro-3-thienyl]-3-[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanamide,
3-[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-N-{[1-methyl-1H-pyrazol-4-yl]methyl}hexanamide,
N-(2-chloro-6-methylbenzyl)-3-[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanamide,
N-(2-fluorobenzyl)-3-[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanamide,
3-[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-N-{[(1S)-1-phenylethyl]hexanamide,
3-[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-N-{[(1S)-1-phenylethyl]hexanamide,
2-butyl-6-(butylamino)-1H-benzo[de]isoquinoline-1,3(2H)-dione,
2-[[3-[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]hexanoyl]amino]methyl]-5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-1-ium trifluoroacetate,
1-benzyl-4-[[1,3-dioxo-2-[1-(2-oxo-2-[[1(5S)-1-phenylethyl]amino]ethyl]butyl]-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]piperidinium trifluoroacetate,
1-benzyl-4-[[1,3-dioxo-2-[1-(2-oxo-2-[[1(5S)-1-phenylethyl]amino]ethyl]butyl]-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]piperidinium trifluoroacetate,
cis-4-[[1,3-dioxo-2-[1-(2-oxo-2-[[1(5S)-1-phenylethyl]amino]ethyl]butyl]-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]cyclohexanecarboxylic acid,
cis-4-[[1,3-dioxo-2-[1-(2-oxo-2-[[1(5S)-1-phenylethyl]amino]ethyl]butyl]-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]cyclohexanecarboxylic acid,
2-[1-[(benzoxyl)methyl]butyl]-6-[2-(hydroxyethyl) amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
trans-1-benzyl-4-[[2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl]amino]cyclohexanecarboxylic acid,
2-(3-chlorophenyl)-6-[1-(phenylacetyl)piperidin-4-yl]amino]-1H-benzo[de]isoquinoline-1,3(2H)-dione,
3-bromo-5-[6-[(2-hydroxyethyl)amino]-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]benzoic acid,
1-benzyl-4-[(2-(3-bromo-5-carboxyphenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl)amino]piperidinium trifluoroacetate,
4-[(4-[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl)amino]piperidinium-1-yl)methyl]pyridinium bis(trifluoroacetate),
4-[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl)amino]-1-(3-thienylmethyl)piperidinium trifluoroacetate,
cis-4-[(2-(3-methyl-5-[(methylamino)carbonyl]phenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl)amino]cyclohexanecarboxylic acid,
cis-1-benzyl-4-[(2-(3-chlorophenyl)-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl)amino]cyclohexanecarboxylic acid,
6-bromo-2-butyl-1H-benzo[de]isoquinoline-1,3(2H)-dione.

17. A method of inhibiting hepatitis C virus polymerase and/or of treating or preventing an illness due to hepatitis C virus, the method involving administering to a human or animal subject suffering from the condition a therapeutically or prophylactically effective amount of a compound of any one of Claims 1 to 16, or a pharmaceutically acceptable salt thereof.

18. Use of a compound of any one of Claims 1 to 16, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment or prevention of infection by hepatitis C virus, in combination with one or more other agents for the treatment of viral infections.

19. A pharmaceutical composition comprising a compound of formula (Ic) as defined in Claim 14, or a compound of formula (Id) as defined in Claim 15, or a compound selected from Group (II) as defined in Claim 16, or a pharmaceutically acceptable salt thereof, in association with a pharmaceutically acceptable carrier.

20. A compound of formula (Ic) as defined in Claim 14, or a compound of formula (Id) as defined in Claim 15, or a compound selected from Group (II) as defined in Claim 16, or a pharmaceutically acceptable salt thereof for use in therapy.

21. A compound of formula (Ic) as defined in Claim 14, or a compound of formula (Id) as defined in Claim 15, or a compound selected from Group (II) as defined in Claim 16, or a pharmaceutically acceptable salt thereof.

22. A process for preparing a compound of formula (I) as defined in Claim 1 by the reaction of either
(a) a compound of formula (II) with a compound of formula (III):
where $R^1$, $R^2$, A, B and $n$ are as defined in Claim 1; or

(b) a compound of formula (IV) with a compound of formula (V):

where $R^1$, $R^2$, A and B are as defined in Claim 1, and $L$ is a suitable leaving group such as chlorine, bromine or nitro; or

(c) the compound of formula (IV) with a compound of formula (VI):

where $R^2$ is as defined in Claim 1.