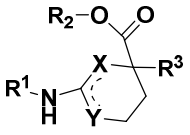


(Ic)

or

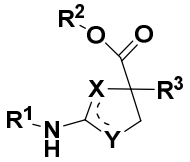


(Id)

or stereoisomers, racemic mixtures, tautomers, pharmaceutically acceptable salts, prodrugs, hydrates, or solvates thereof

wherein ⋯, **X, Y, R**[1], **R**[2] and **R**[3] are as defined in clause 1.

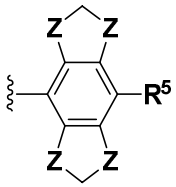
A3. The compound of formula (I) according to clause A2 which is a compound of formula (Ic)



(Ic)

wherein ⋯, **X, Y, R**[1], **R**[2] and **R**[3] are as defined in clause 1.

A4. The compound of formula (I) according to clause A3, wherein

R[1] is 

wherein

Z is CH_2;

R[5] is hydrogen;

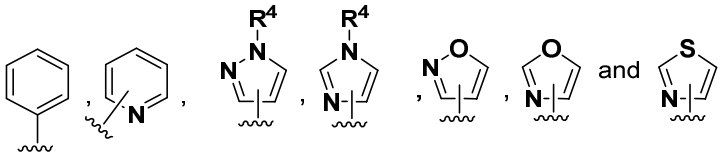
X is O;

Y is N;

as valency permits, ⋯ is the combination of a single bond and a double bond;

R[2] is ethyl;

R[3] is independently selected from the group consisting of



wherein

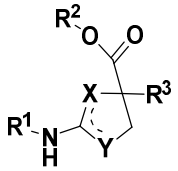
other than at the position of **R**[4], **R**[3] can be optionally substituted with Cl, isopropyl or -OMe, wherein isopropyl can be optionally substituted with –OH; and

R[4] is methyl or ethyl.

atherosclerosis, asthma, allergic inflammation, cryopyrin-associated periodic syndromes (CAPS), Muckle-Wells syndrome (MWS), familial cold autoinflammatory syndrome (FCAS), neonatal-onset multisystem inflammatory disease (NOMID), gout, pseudo-gout, inflammatory bowel disease, non-alcoholic fatty liver disease, non-alcoholic steatohepatitis, hypertension, myocardial infarction, oxalate-induced nephropathy, graft-versus host disease, type 1 diabetes, type 2 diabetes, rheumatoid arthritis, myelodysplastic syndrome, familial Mediterranean fever (FMF), TNF receptor associated periodic syndrome (TRAPS), mevalonate kinase deficiency (MKD), hyperimmunoglobulinemia D, periodic fever syndrome (HIDS), deficiency of interleukin 1 receptor (DIRA) antagonist, Majeed syndrome, acne, pyogenic arthritis pyoderma gangrenosum and acne (PAPA), haploinsufficiency of A20 (HA20), PLCG2-associated antibody deficiency and immune dysregulation (PLAID), pediatric granulomatous arthritis (PGA), PLCG2-associated autoinflammation, antibody deficiency and immune dysregulation (APLAID), sideroblastic anemia with B-cell immunodeficiency, periodic fevers, developmental delay (SIFD), chronic nonbacterial osteomyelitis (CNO), Sweet's syndrome, chronic recurrent multifocal osteomyelitis (CRMO), synovitis, pustulosis, acne, hyperostosis, osteitis syndrome (SAPHO), multiple sclerosis (MS), psoriasis, Behcet's disease, Sjogren's syndrome, Schnitzler syndrome, chronic obstructive pulmonary disorder (COPD), steroid-resistant asthma, asbestosis, silicosis, cystic fibrosis, motor neuron disease, Huntington's disease, cerebral malaria, brain injury from pneumococcal meningitis, obesity, age-related macular degeneration (AMD), corneal infection, uveitis, dry eye, chronic kidney disease, diabetic nephropathy, alcoholic liver disease, skin contact hypersensitivity, sunburn, osteoarthritis, systemic juvenile idiopathic arthritis, adult-onset Still's disease, relapsing polychondritis, Chikungunya virus, Ross River virus, influenza, HIV, Coronaviruses, Dengue, Zika virus, hidradenitis suppurativa (HS), lung cancer metastasis, pancreatic cancers, gastric cancers, myelodisplastic syndrome, leukemia; polymyositis, colitis, helminth infection, bacterial infection, abdominal aortic aneurism, wound healing, depression, psychological stress, pericarditis including Dressler's syndrome, ischaemia reperfusion injury, frontotemporal dementia, HIV-associated neurocognitive disorder, Coronavirus-associated inflammatory pathologies, and traumatic brain injury; preferably the disorder is selected from Alzheimer’s disease, Parkinson’s disease, amyotrophic lateral sclerosis, demyelination, viral encephalitis, epilepsy, stroke, atherosclerosis, asthma, allergic inflammation, cryopyrin-associated periodic syndromes (CAPS), gout, inflammatory bowel disease, non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), hypertension, myocardial infarction, oxalate-induced nephropathy, graft-versus host disease, type 1 diabetes, type 2 diabetes, rheumatoid arthritis, myelodysplastic syndrome, anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV), lupus nephritis, anti-glomerular basement membrane (GBM) disease, IgA nephropathy,

wherein ⟨, **X, Y, R**[1], **R**[2] and **R**[3] are as defined in clause B1.

B3. The compound according to clause B2, which is a compound of formula (Ic)

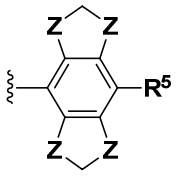


(Ic)

wherein ⟨, **X, Y, R**[1], **R**[2] and **R**[3] are as defined in clause B1.

B4. The compound according to any of the preceding clauses, wherein **R**[2] is hydrogen or ethyl.

B5. The compound according to any of the preceding clauses, wherein

R[1] is 

wherein

Z is CH_2;

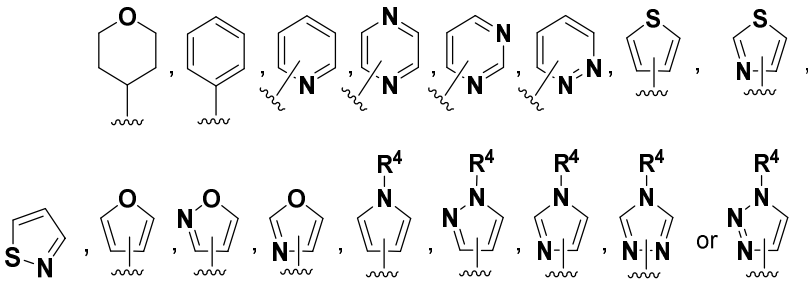
R[5] is hydrogen;

X is O;

Y is N;

as valency permits, ⟨ is the combination of a single bond and a double bond; and

R[3] is



; each of them can be optionally substituted, and **R**[4] is independently selected from the group consisting of hydrogen, C_1-C_6alkyl and C_3-C_6cycloalkyl.

B6. The compound according to any of the preceding clauses, which is selected from

Dengue, Zika virus, hidradenitis suppurativa (HS), lung cancer metastasis, pancreatic cancers, gastric cancers, myelodisplastic syndrome, leukemia; polymyositis, colitis, helminth infection, bacterial infection, abdominal aortic aneurism, wound healing, depression, psychological stress, pericarditis including Dressler's syndrome, ischaemia reperfusion injury, frontotemporal dementia, HIV-associated neurocognitive disorder, Coronavirus-associated inflammatory pathologies, and traumatic brain injury; preferably the disorder is selected from Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, demyelination, viral encephalitis, epilepsy, stroke, atherosclerosis, asthma, allergic inflammation, cryopyrin-associated periodic syndromes (CAPS), gout, inflammatory bowel disease, nonalcoholic fatty liver disease, nonalcoholic steatohepatitis (NASH), hypertension, myocardial infarction, oxalate-induced nephropathy, graft-versus host disease, type 1 diabetes, type 2 diabetes, rheumatoid arthritis, myelodysplastic syndrome, anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV), lupus nephritis, anti-glomerular basement membrane (GBM) disease, IgA nephropathy, glomerulonephritis (GN), systemic lupus erythematosus (SLE), Focal Segmental Glomerulosclerosis , Minimal change disease (MCD), Psoriatic Arthritis, and Hereditary Recurrent Fevers (HRFs).

B17. The compound for use according to clause B16, wherein the disease, the disorder or the abnormality is selected from Alzheimer's disease, Parkinson's disease, cryopyrin-associated periodic syndromes (CAPS), nonalcoholic fatty liver disease, NASH and gout.

B18. The compound for use according to any one of clauses B13 to B15, wherein the disease, the disorder or the abnormality is a disease, disorder or abnormality of the immune system.

B19. The compound for use according to any one of clauses B13 to B15, wherein the disease, the disorder or the abnormality is an inflammatory disease, disorder or abnormality.

B20. The compound for use according to any one of clauses B13 to B15, wherein the disease, the disorder or the abnormality is an autoimmune disease, disorder or abnormality.

B21. The compound for use according to any one of clauses B13 to B15, wherein the disease, the disorder or the abnormality is a disease, disorder or abnormality of the skin.

B22. The compound for use according to clause B21, wherein the disease, disorder or abnormality of the skin is selected from psoriasis, acne, eczema, alopecia areata, or actinic keratosis.

B23. The compound for use according to any one of clauses B13 to B15, wherein the disease, the disorder or the abnormality is a disease, disorder or abnormality of the cardiovascular system.

B24. The compound for use according to any one of clauses B13 to B15, wherein the disease, the disorder or the abnormality is a cancer, a tumor or a malignancy.

B25. The compound for use according to any one of clauses B13 to B15, wherein the disease, the disorder or the abnormality is a disease, disorder or abnormality of the renal system.

B26. The compound for use according to any one of clauses B13 to B15, wherein the disease, the disorder or the abnormality is a disease, disorder or abnormality of the gastrointestinal tract.

B27. The compound for use according to any one of clauses B13 to B15, wherein the disease, the disorder or the abnormality is a disease, disorder or abnormality of the respiratory system.

B28. The compound for use according to any one of clauses B13 to B15, wherein the disease, the disorder or the abnormality is a disease, disorder or abnormality of the endocrine system.

B29. The compound for use according to any one of clauses B13 to B15, wherein the disease, the disorder or the abnormality is a disease, disorder or abnormality of the central nervous system (CNS).

B30. The compound for use according to any one of clauses B13 to B15, wherein the disease, the disorder or the abnormality is a disease, disorder or abnormality of the liver.

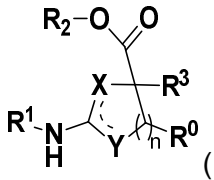
B31. A pharmaceutical composition comprising a combination of a compound according to any one of clauses B1 to B10, or a stereoisomer, a racemic mixture, a tautomer, a polymorph, a pharmaceutically acceptable salt, a prodrug, a hydrate, or a solvate thereof, and at least one further biologically active compound differing from the compound of formula (I) and optionally comprising at least one pharmaceutically acceptable carrier, diluent, adjuvant or excipient.

B32. A combination comprising a therapeutically effective amount of a compound according to any one of clauses B1 to B10, or a stereoisomer, a racemic mixture, a tautomer, a polymorph, a pharmaceutically acceptable salt, a prodrug, a hydrate, or a solvate thereof, and at least one further biologically active compound differing from the compound of formula (I) or the compound of formula (II), and optionally at least one pharmaceutically acceptable carrier, diluent, adjuvant or excipient.

B33. A pharmaceutical composition according to clause B31, or the combination according to clause B32, for use as a medicament.

B34. Use of a compound of formula (I) according to any one of clauses B1 to B10, or a stereoisomer, a racemic mixture, a tautomer, a polymorph, a pharmaceutically acceptable salt, a prodrug, a hydrate, or a solvate thereof, as an analytical reference or an *in vitro* screening tool.

In one example, the present disclosure relates to a compound of formula (I')



(I'),

or a stereoisomer, a racemic mixture, a tautomer, a polymorph, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof;

wherein

X is independently selected from the group consisting of O, N and S;

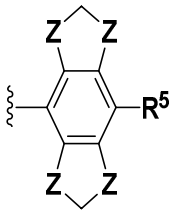
Y is independently selected from the group consisting of N and O;

as valency permits, ⟨ is a combination of a single bond and a double bond or is two single bonds;

n is 1 or 2;

R^0 is H or C_1-C_3alkyl;

R^1 is



wherein

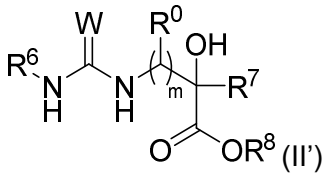
Z is independently selected from the group consisting of CH_2 and O provided that no more than two of **Z** are O;

R^5 is independently selected from the group consisting of hydrogen and halogen;

R^2 is independently selected from the group consisting of hydrogen, C_1-C_6alkyl, C_3-C_6cycloalkyl; and

R^3 is independently selected from the group consisting of heteroC_3-C_6cycloalkyl, aryl or heteroaryl, wherein each of them can be optionally substituted with –C_1-C_6alkyl, –O–C_1-C_6alkyl, –Hal, or –C_1-C_6alkyl-OH.

In another example, the present disclosure relates to a compound of formula (II')



(II')

or a stereoisomer, a racemic mixture, a tautomer, a polymorph, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof,

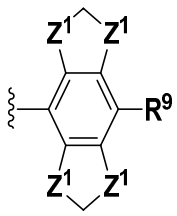
wherein

W is independently selected from the group consisting of O and S;

m is 1 or 2;

R^0 is H or C_1-C_3alkyl;

R^6 is



wherein

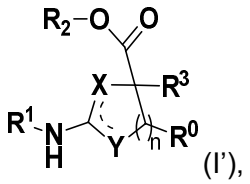
$\mathbf{Z^1}$ is independently selected from the group consisting of CH_2 and O provided that no more than two of $\mathbf{Z^1}$ are O;

$\mathbf{R^9}$ is independently selected from the group consisting of hydrogen and halogen;

$\mathbf{R^8}$ is independently selected from the group consisting of hydrogen, C_1-C_6alkyl, C_3-C_6 cycloalkyl; and

$\mathbf{R^7}$ is independently selected from the group consisting of heteroC_3-C_6cycloalkyl, aryl or heteroaryl wherein each of them can be optionally substituted.

In one aspect, the present disclosure relates to a compound of formula (I')



(I'),

or a stereoisomer, a racemic mixture, a tautomer, a polymorph, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof;

wherein

X is O;

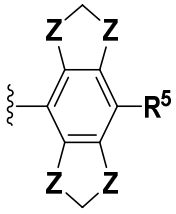
Y is N;

as valency permits, ⁀ is a combination of a single bond and a double bond;

n is 1;

$\mathbf{R^0}$ is H or C_1-C_3alkyl;

$\mathbf{R^1}$ is



wherein

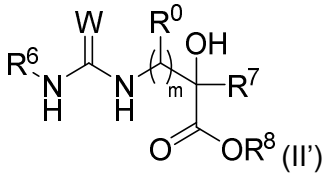
Z is independently selected from the group consisting of CH_2 and O provided that no more than two of **Z** are O;

$\mathbf{R^5}$ is independently selected from the group consisting of hydrogen and halogen;

$\mathbf{R^2}$ is independently selected from the group consisting of hydrogen, C_1-C_6alkyl, C_3-C_6cycloalkyl; and

$\mathbf{R^3}$ is independently selected from the group consisting of heteroC_3-C_6cycloalkyl, aryl or heteroaryl, wherein each of them can be optionally substituted with –C_1-C_6alkyl, –O–C_1-C_6alkyl, –Hal, or –C_1-C_6alkyl-OH.

In another aspect, the present disclosure relates to a compound of formula (II')



(II')

or a stereoisomer, a racemic mixture, a tautomer, a polymorph, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof,

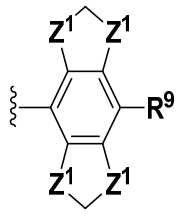
wherein

W is independently selected from the group consisting of O and S;

m is 1;

R^0 is H or C_1-C_3alkyl;

R^6 is



wherein

Z^1 is independently selected from the group consisting of CH_2 and O provided that no more than two of **Z^1** are O;

R^9 is independently selected from the group consisting of hydrogen and halogen;

R^8 is independently selected from the group consisting of hydrogen, C_1-C_6alkyl, C_3-C_6 cycloalkyl; and

R^7 is independently selected from the group consisting of heteroC_3-C_6cycloalkyl, aryl or heteroaryl wherein each of them can be optionally substituted with –C_1-C_6alkyl, –O–C_1-C_6alkyl, –Hal, or –C_1-C_6alkyl-OH.

In another aspect, the present disclosure relates to a pharmaceutical composition comprising a compound as defined herein, or a stereoisomer, a racemic mixture, a tautomer, a polymorph, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof, and optionally comprising at least one pharmaceutically acceptable carrier, diluent, adjuvant or excipient.

In another aspect, the present disclosure relates to a compound as defined herein, or a stereoisomer, a racemic mixture, a tautomer, a polymorph, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof, for use as a medicament.

In another example, the present disclosure relates to use of the compound as defined herein, or a stereoisomer, a racemic mixture, a tautomer, a polymorph, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof, in the manufacture of a medicament for treating, alleviating or preventing a disease, or a disorder or an abnormality which is responsive to the modulation of a

component of the NLRP3 inflammasome pathway and/or which is responsive to the modulation of IL-1 beta and/or IL-18 levels.

In another aspect, the present disclosure relates to use of the compound according to any one of claims 1 to 9, or a stereoisomer, a racemic mixture, a tautomer, a polymorph, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof, in the manufacture of a medicament for treating, alleviating or preventing a disease, or a disorder or an abnormality which is responsive to the modulation of a component of the NLRP3 inflammasome pathway and/or which is responsive to the modulation of IL-1 beta and/or IL-18 levels; wherein the disease, the disorder or the abnormality is selected from Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, demyelination, viral encephalitis, epilepsy, stroke, atherosclerosis, asthma, allergic inflammation, cryopyrin-associated periodic syndromes (CAPS), Muckle-Wells syndrome (MWS), familial cold autoinflammatory syndrome (FCAS), neonatal-onset multisystem inflammatory disease (NOMID), gout, pseudo-gout, inflammatory bowel disease, nonalcoholic fatty liver disease, nonalcoholic steatohepatitis, hypertension, myocardial infarction, oxalate-induced nephropathy, graft-versus host disease, type 1 diabetes, type 2 diabetes, rheumatoid arthritis, myelodysplastic syndrome, familial Mediterranean fever (FMF), TNF receptor associated periodic syndrome (TRAPS), mevalonate kinase deficiency (MKD), hyperimmunoglobulinemia D, periodic fever syndrome (HIDS), deficiency of interleukin 1 receptor (DIRA) antagonist, Majeed syndrome, acne, pyogenic arthritis pyoderma gangrenosum and acne (PAPA), haploinsufficiency of A20 (HA20), PLCG2-associated antibody deficiency and immune dysregulation (PLAID), pediatric granulomatous arthritis (PGA), PLCG2-associated autoinflammation, antibody deficiency and immune dysregulation (APLAID), sideroblastic anemia with B-cell immunodeficiency, periodic fevers, developmental delay (SIFD), chronic nonbacterial osteomyelitis (CNO), Sweet's syndrome, chronic recurrent multifocal osteomyelitis (CRMO), synovitis, pustulosis, eczema, alopecia areata, actinic keratosis, hyperostosis, osteitis syndrome (SAPHO), multiple sclerosis (MS), psoriasis, Behcet's disease, Sjogren's syndrome, Schnitzler syndrome, chronic obstructive pulmonary disorder (COPD), steroid-resistant asthma, asbestosis, silicosis, cystic fibrosis, motor neuron disease, Huntington's disease, cerebral malaria, brain injury from pneumococcal meningitis, obesity, age-related macular degeneration (AMD), corneal infection, uveitis, dry eye, chronic kidney disease, diabetic nephropathy, alcoholic liver disease, skin contact hypersensitivity, sunburn, osteoarthritis, systemic juvenile idiopathic arthritis, adult-onset Still's disease, relapsing polychondritis, Chikungunya virus, Ross River virus, influenza, HIV, Coronaviruses, Dengue, Zika virus, hidradenitis suppurativa (HS), lung cancer metastasis, pancreatic cancers, gastric cancers, leukemia; polymyositis, colitis, helminth infection, bacterial infection, abdominal aortic aneurism, wound healing, depression, psychological stress, pericarditis including Dressler's syndrome, ischaemia reperfusion injury, frontotemporal dementia, HIV-associated neurocognitive disorder, Coronavirus-associated inflammatory pathologies, traumatic

brain injury, dermatitis, anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV), lupus nephritis, anti-glomerular basement membrane (GBM) disease, IgA nephropathy, glomerulonephritis (GN), systemic lupus erythematosus (SLE), Focal Segmental Glomerulosclerosis, Minimal change disease (MCD), Psoriatic Arthritis, and Hereditary Recurrent Fevers (HRFs); preferably the disorder is selected from Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, demyelination, viral encephalitis, epilepsy, stroke, atherosclerosis, asthma, allergic inflammation, cryopyrin-associated periodic syndromes (CAPS), gout, inflammatory bowel disease, non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), hypertension, myocardial infarction, oxalate-induced nephropathy, graft-versus host disease, type 1 diabetes, type 2 diabetes, rheumatoid arthritis, myelodysplastic syndrome, anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV), lupus nephritis, anti-glomerular basement membrane (GBM) disease, IgA nephropathy, glomerulonephritis (GN), systemic lupus erythematosus (SLE), Focal Segmental Glomerulosclerosis , Minimal change disease (MCD), Psoriatic Arthritis, and Hereditary Recurrent Fevers (HRFs).

In another aspect, the present disclosure relates to use of a compound as defined herein, or a stereoisomer, a racemic mixture, a tautomer, a polymorph, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof, as an analytical reference or an *in vitro* screening tool.

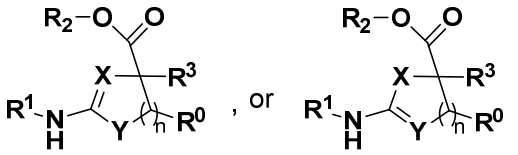
The present disclosure is described hereinafter.

BRIEF DESCRIPTION OF THE FIGURE

Figure 1 shows IL-1β release in peritoneal lavage samples from mice dosed with (1mg/kg or 3 mg/kg) Example 16 and Example 23 by intraperitoneal injection in an LPS-ATP induced peritonitis model.

Preferably, in any of the instances of C_3-C_6cycloalkyl, C_3-C_6 cycloalkyl can be optionally substituted with -OH.

In a further embodiment, the present invention relates to compounds of formula (I') whereas as valency permits, ⟨ is the combination of a single bond and a double bond as described in formulae (Ia') or (Ib')

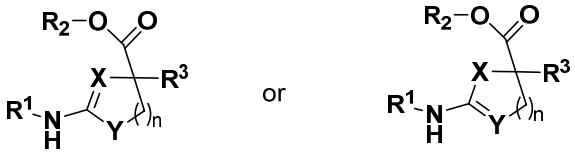


(Ia') , or (Ib') ,

or stereoisomers, or racemic mixtures, or tautomers, or polymorphs, or pharmaceutically acceptable salts, or hydrates, or solvates thereof,

wherein **X, Y, n, R^0**, **R^1**, **R^2** and **R^3** are as defined above. Embodiments as defined for compounds of formula (I') apply here.

In a further embodiment, the present invention relates to compounds of formula (I'), in particular it relates to a compound of formula (I), whereas as valency permits, ⟨ is the combination of a single bond and a double bond as described in formula (Ia) or (Ib)

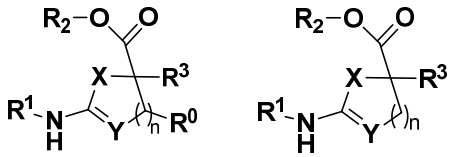


(Ia) or (Ib)

or stereoisomers, or racemic mixtures, or tautomers, or polymorphs, or pharmaceutically acceptable salts, or hydrates, or solvates thereof,

wherein **X, Y, n, R^1**, **R^2** and **R^3** are as defined above. Embodiments as defined for compounds of formula (I') wherein **R^0** is H, or of formula (I) apply here.

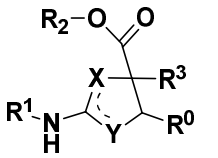
Preferably, the combination of a single bond and double bond is as described in compounds of formula (Ib') or (Ib)

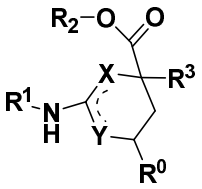


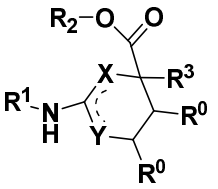
(Ib') , or (Ib) ,

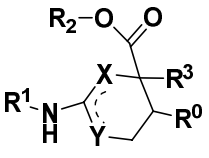
or stereoisomers, or racemic mixtures, or tautomers, or polymorphs, or pharmaceutically acceptable salts, or hydrates, or solvates thereof, wherein **X, Y, n, R^0**, **R^1**, **R^2** and **R^3** are as defined above.

In yet another embodiment, the present invention relates to a compound of formula (I') defined as compounds of formula (Ic'), (Id'), (Id'') or (Id''')


(Ic')

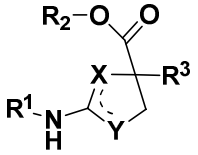

(Id')

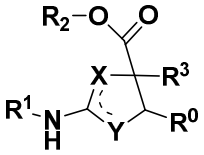

(Id'')

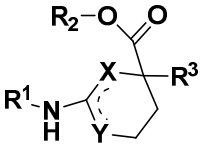

(Id''')

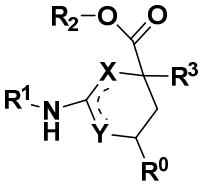
or stereoisomers, or racemic mixtures, or tautomers, or polymorphs, or pharmaceutically acceptable salts, or hydrates, or solvates thereof, wherein **X, Y, n, R^0**, **R^1**, **R^2** and **R^3** are as defined above.

In a preferred embodiment, the present invention relates to a compound of formula (I') defined as compounds of formula (Ic), (Ic'), (Id), or (Id')


(Ic)

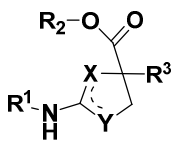

(Ic')


(Id)

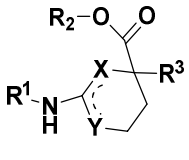

(Id')

or stereoisomers, or racemic mixtures, or tautomers, or polymorphs, or pharmaceutically acceptable salts, or hydrates, or solvates thereof, wherein **X, Y, R^1**, **R^2** and **R^3** are defined as above; and wherein **R^0** is C_1-C_3alkyl.

In a more preferred embodiment, the present invention relates to a compound of formula (I'), in particular it relates to a compound of formula (I), defined as compounds of formula (Ic) or (Id)


(Ic)

or


(Id)

or stereoisomers, or racemic mixtures, or tautomers, or polymorphs, or pharmaceutically acceptable salts, or hydrates, or solvates thereof,
wherein **X, Y, R^1**, **R^2** and **R^3** are defined as above. Embodiments as defined for compounds of formula (I') or (I) apply here.

steatohepatitis (NASH), hypertension, myocardial infarction, oxalate-induced nephropathy, graft-versus host disease, type 1 diabetes, type 2 diabetes, rheumatoid arthritis, myelodysplastic syndrome, anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV), lupus nephritis, anti-glomerular basement membrane (GBM) disease, IgA nephropathy, glomerulonephritis (GN), systemic lupus erythematosus (SLE), Focal Segmental Glomerulosclerosis, Minimal change disease (MCD), Psoriatic Arthritis, and Hereditary Recurrent Fevers (HRFs).

More preferably, the diseases, the disorders or the abnormalities are selected from Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, demyelination, viral encephalitis, epilepsy, stroke, atherosclerosis, asthma and allergic inflammation, cryopyrin-associated periodic syndromes (CAPS), gout, inflammatory bowel disease, non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), hypertension, myocardial infarction, oxalate-induced nephropathy, graft-versus host disease, type 1 and type 2 diabetes, rheumatoid arthritis, and myelodysplastic syndrome.

Even more preferably, the diseases, the disorders or the abnormalities are selected from Alzheimer's disease, Parkinson's disease, cryopyrin-associated periodic syndromes (CAPS), non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), rheumatoid arthritis and gout. Even more preferably, the diseases, the disorders or the abnormalities are selected from Alzheimer's disease, Parkinson's disease, cryopyrin-associated periodic syndromes (CAPS), rheumatoid arthritis and gout.

In one embodiment, the present invention relates to a compound of formula (I'), (I), (II'), or (II) as defined in the present invention, or a stereoisomer, a racemic mixture, a tautomer, a polymorph, a pharmaceutically acceptable salt, a prodrug, a hydrate, or a solvate thereof, for use in the treatment, alleviation or prevention of a IL-18 and/or IL-1 beta related disease by modulating a component of the NLRP3 inflammasome pathway, in particular, by modulating NLRP3 inflammasome pathway. The IL-18 and/or IL-1 beta levels in a subject are decreased as a result of the administration of a compound of formula (I'), (I), (II'), or (II) as defined in the present invention, or a stereoisomer, a racemic mixture, a tautomer, a polymorph, a pharmaceutically acceptable salt, a prodrug, a hydrate, or a solvate thereof.

IL-18 and/or IL-1 beta related diseases, disorders or abnormalities are selected from chronic obstructive pulmonary disease (COPD), transfusion-related lung injury, bronchopulmonary dysplasia (BPD), acute respiratory distress syndrome (ARDS), pediatric autoinflammatory disease or condition, Still's disease, particularly Adult Still's disease or juvenile Still's disease, juvenile rheumatoid arthritis

osteomyelitis (CRMO), synovitis, pustulosis, acne, eczema, alopecia areata, actinic keratosis, hyperostosis, osteitis syndrome (SAPHO), multiple sclerosis (MS), psoriasis, Behcet's disease, Sjogren's syndrome, Schnitzler syndrome, chronic obstructive pulmonary disorder (COPD), steroid-resistant asthma, asbestosis, silicosis, cystic fibrosis, motor neuron disease, Huntington's disease, cerebral malaria, brain injury from pneumococcal meningitis, obesity, age-related macular degeneration (AMD), corneal infection, uveitis, dry eye, chronic kidney disease, diabetic nephropathy, alcoholic liver disease, skin contact hypersensitivity, sunburn, osteoarthritis, systemic juvenile idiopathic arthritis, adult-onset Still's disease, relapsing polychondritis, Chikungunya virus, Ross River virus, influenza, HIV, Coronaviruses, Dengue, Zika virus, hidradenitis suppurativa (HS), lung cancer metastasis, pancreatic cancers, gastric cancers, myelodisplastic syndrome, leukemia; polymyositis, colitis, helminth infection, bacterial infection, abdominal aortic aneurism, wound healing, depression, psychological stress, pericarditis including Dressler's syndrome, ischaemia reperfusion injury, frontotemporal dementia, HIV-associated neurocognitive disorder, Coronavirus-associated inflammatory pathologies, and traumatic brain injury; preferably the disorder is selected from Alzheimer’s disease, Parkinson’s disease, amyotrophic lateral sclerosis, demyelination, viral encephalitis, epilepsy, stroke, atherosclerosis, asthma, allergic inflammation, cryopyrin-associated periodic syndromes (CAPS), gout, inflammatory bowel disease, non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), hypertension, myocardial infarction, oxalate-induced nephropathy, graft-versus host disease, type 1 diabetes, type 2 diabetes, rheumatoid arthritis, myelodysplastic syndrome, anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV), lupus nephritis, anti-glomerular basement membrane (GBM) disease, IgA nephropathy, glomerulonephritis (GN), systemic lupus erythematosus (SLE), Focal Segmental Glomerulosclerosis , Minimal change disease (MCD), Psoriatic Arthritis, and Hereditary Recurrent Fevers (HRFs), comprising administering to the subject a therapeutically effective amount of a compound of formula (I’), (I), (II’) or (II), as defined herein, or stereoisomers, or racemic mixtures, or tautomers, or polymorph, or pharmaceutically acceptable salts, or hydrates, or solvates thereof.

In another embodiment, the present invention also provides a method of inhibiting IL-1 beta in a subject in need, the method comprising administering to a subject in need thereof a therapeutically effective amount of a compound of formula (I’), (I), (II’) or (II), or a stereoisomer, a racemic mixture, a tautomer, a polymorph, a pharmaceutically acceptable salt, a prodrug, a hydrate, or a solvate thereof.

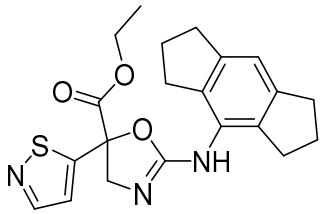
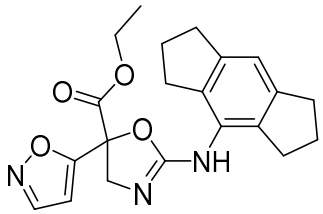
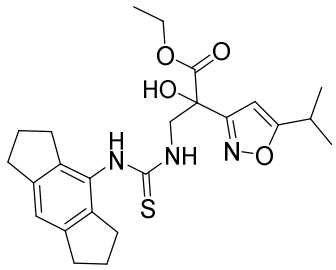
In particular, the disease, disorder or abnormality is one which is responsive to the inhibition of activation of the NLRP3 inflammasome pathway. More particularly, the disease, disorder or abnormality is responsive to the modulation of one or more of, for example, but not limited to, IL-1 β

Schnitzler syndrome, chronic obstructive pulmonary disorder (COPD), steroid-resistant asthma, asbestosis, silicosis, cystic fibrosis, motor neuron disease, Huntington's disease, cerebral malaria, brain injury from pneumococcal meningitis, obesity, age-related macular degeneration (AMD), corneal infection, uveitis, dry eye, chronic kidney disease, diabetic nephropathy, alcoholic liver disease, skin contact hypersensitivity, sunburn, osteoarthritis, systemic juvenile idiopathic arthritis, adult-onset Still's disease, relapsing polychondritis, Chikungunya virus, Ross River virus, influenza, HIV, Coronaviruses, Dengue, Zika virus, hidradenitis suppurativa (HS), lung cancer metastasis, pancreatic cancers, gastric cancers, myelodisplastic syndrome, leukemia; polymyositis, colitis, helminth infection, bacterial infection, abdominal aortic aneurism, wound healing, depression, psychological stress, pericarditis including Dressler's syndrome, ischaemia reperfusion injury, frontotemporal dementia, HIV-associated neurocognitive disorder, Coronavirus-associated inflammatory pathologies, and traumatic brain injury; preferably the disorder is selected from Alzheimer’s disease, Parkinson’s disease, amyotrophic lateral sclerosis, demyelination, viral encephalitis, epilepsy, stroke, atherosclerosis, asthma, allergic inflammation, cryopyrin-associated periodic syndromes (CAPS), gout, inflammatory bowel disease, non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), hypertension, myocardial infarction, oxalate-induced nephropathy, graft-versus host disease, type 1 diabetes, type 2 diabetes, rheumatoid arthritis, myelodysplastic syndrome, anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV), lupus nephritis, anti-glomerular basement membrane (GBM) disease, IgA nephropathy, glomerulonephritis (GN), systemic lupus erythematosus (SLE), Focal Segmental Glomerulosclerosis , Minimal change disease (MCD), Psoriatic Arthritis, and Hereditary Recurrent Fevers (HRFs).

In yet another embodiment, the disease, disorder or abnormality is preferably an inflammatory disease, disorder or abnormality; or an autoimmune disease, disorder or abnormality; or a disease, disorder or abnormality of the skin (such as, for example, but not limited to, psoriasis, acne, eczema, alopecia areata, or actinic keratosis); or a disease, disorder or abnormality of the cardiovascular system; or a disease, disorder, or abnormality such as a cancer, a tumor or a malignancy; or a disease, disorder or abnormality of the renal system; a disease, disorder or abnormality of the gastrointestinal tract; a disease, disorder or abnormality of the respiratory system; or a disease, disorder or abnormality of the endocrine system; or a disease, disorder or abnormality of the central nervous system (CNS); or a disease, disorder or abnormality of the liver.

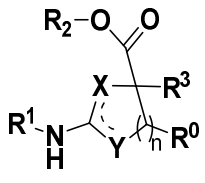
DEFINITIONS

Within the meaning of the present application the following definitions apply unless specified otherwise, and when appropriate, terms used in the singular will also include the plural and vice versa:

Example 43 **Enantiopure ethyl 2-((1,2,3,5,6,7-hexahydro-s-indacen-4-yl)amino)-5-(isothiazol-5-yl)-4,5-dihydrooxazole-5-carboxylate** (second eluting peak)		1. ^{1}H-NMR (500 MHz, DMSO-d6) δ 8.80 (s, 1H), 8.57 (s, 1H), 7.46 (s, 1H), 6.90 (s, 1H), 4.38 – 3.86 (m, 4H), 2.91 – 2.67 (m, 8H), 2.04 – 1.88 (m, 4H), 1.25 (t, 3H). 2. 398.4
Example 44 **ethyl 2-((1,2,3,5,6,7-hexahydro-s-indacen-4-yl)amino)-5-(isoxazol-5-yl)-4,5-dihydrooxazole-5-carboxylate** Racemic		1. ^{1}H-NMR (500 MHz, DMSO-d6) δ 8.83 – 8.56 (m, 2H), 6.91 (s, 1H), 6.84 (s, 1H), 4.37 – 4.22 (m, 4H), 2.86 – 2.67 (m, 8H), 2.03 – 1.86 (m, 4H), 1.21 (t, 3H). 2. 382.2
Example 45 Enantiopure 44 (second eluting peak)		1. ^{1}H-NMR (500 MHz, DMSO-d6) δ 8.68 (d, 1H), 6.96 – 6.77 (m, 2H), 4.34 – 4.08 (m, 4H), 2.87 – 2.56 (m, 8H), 2.04 – 1.82 (m, 4H), 1.21 (t, 3H). 2. 382.0
Example 46 **ethyl 3-(3-(1,2,3,5,6,7-hexahydro-s-indacen-4-yl)thioureido)-2-hydroxy-2-(5-isopropylisoxazol-3-yl)propanoate** Racemic		1. ^{1}H-NMR (500 MHz, DMSO-d6) δ 9.33 (s, 1H), 7.00 (s, 1H), 6.77 (s, 1H), 6.26 (s, 1H), 4.47 – 4.28 (m, 1H), 4.21 – 4.05 (m, 2H), 3.99 (dd, 1H), 3.14 – 2.97 (m, 1H), 2.81 (t, 4H), 2.74 – 2.58 (m, 4H), 2.01 – 1.88 (m, 4H), 1.23 (d, 6H), 1.16 (t, 3H). 2. 458.2

CLAIMS

1. A compound of formula (I')


(I'),

or a stereoisomer, a racemic mixture, a tautomer, a polymorph, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof;

wherein

X is O;

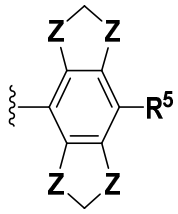
Y is N;

as valency permits, ⟨ is a combination of a single bond and a double bond;

n is 1;

$\mathbf{R^0}$ is H or C_1-C_3alkyl;

$\mathbf{R^1}$ is



wherein

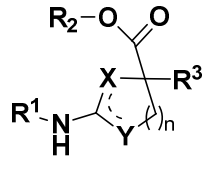
Z is independently selected from the group consisting of CH_2 and O provided that no more than two of **Z** are O;

$\mathbf{R^5}$ is independently selected from the group consisting of hydrogen and halogen;

$\mathbf{R^2}$ is independently selected from the group consisting of hydrogen, C_1-C_6alkyl, C_3-C_6cycloalkyl; and

$\mathbf{R^3}$ is independently selected from the group consisting of heteroC_3-C_6cycloalkyl, aryl or heteroaryl, wherein each of them can be optionally substituted with –C_1-C_6alkyl, –O–C_1-C_6alkyl, –Hal, or –C_1-C_6alkyl-OH.

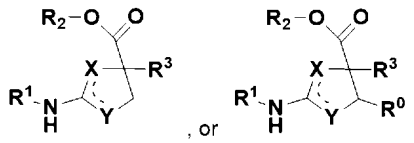
2. The compound according to claim 1, having a formula (I)


(I),

or a stereoisomer, a racemic mixture, a tautomer, a polymorph, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof;

wherein ⋯, **X, Y, n, R^1**, **R^2** and **R^3** are as defined in claim 1 and wherein **R^0** is H.

3. The compound according to claim 1 or 2, which is a compound of formula (Ic) or a compound of formula (Ic')

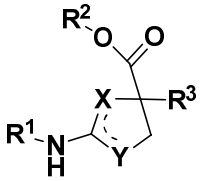


(Ic) , or (Ic')

or a stereoisomer, a racemic mixture, a tautomer, a polymorph, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof,

wherein ⋯, **X, Y, R^1**, **R^2** and **R^3** are as defined in claim 1, and wherein **R^0** is C_1-C_3alkyl.

4. The compound according to claim 3, which is a compound of formula (Ic)

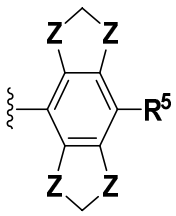


(Ic)

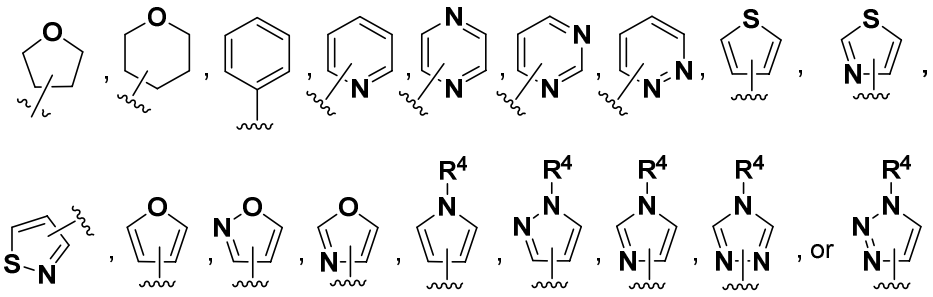
wherein ⋯, **X, Y, R^1**, **R^2** and **R^3** are as defined in claim 1.

5. The compound according to any of the preceding claims, wherein

as valency permits, ⋯ is the combination of a single bond and a double bond;

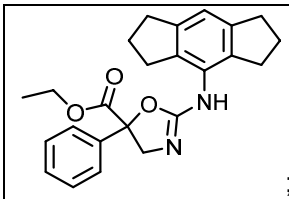
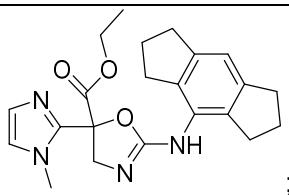
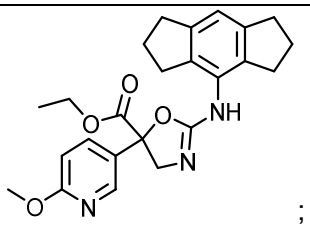
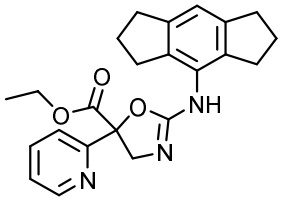
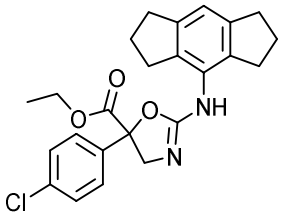
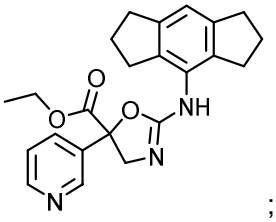
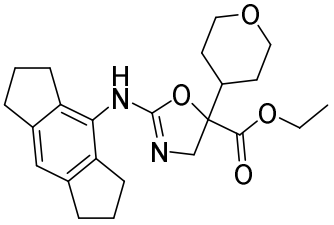
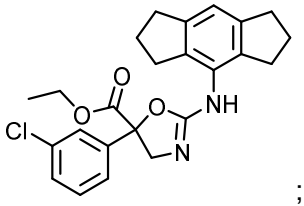
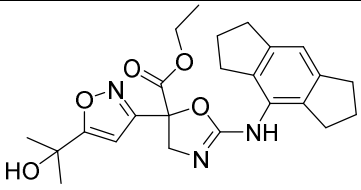
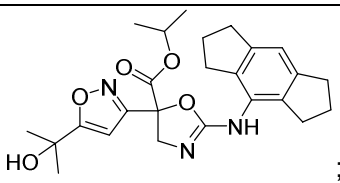
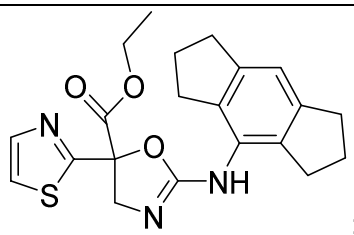
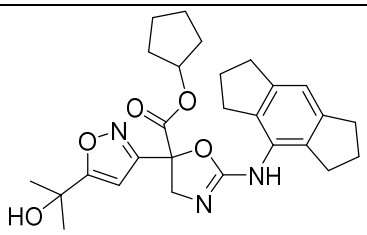
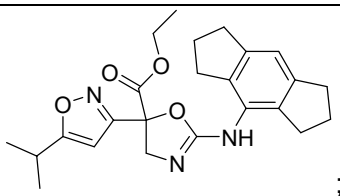
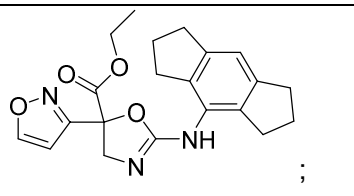
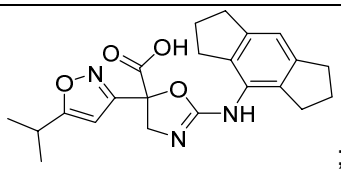
R^1 is  , wherein **Z** is CH_2; **R^5** is hydrogen;

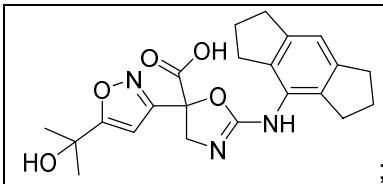
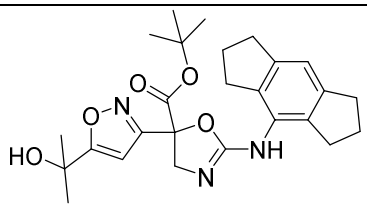
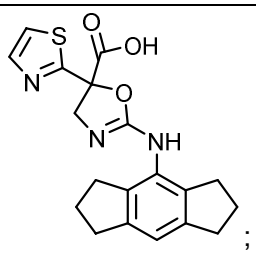
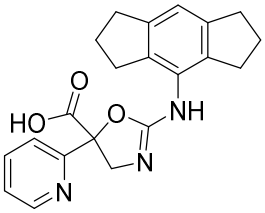
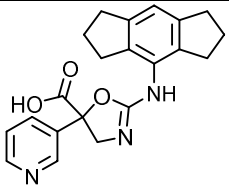
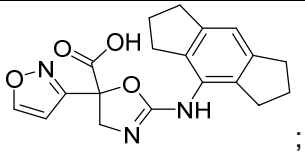
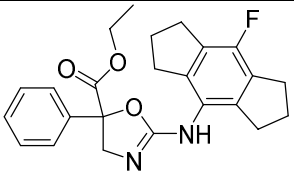
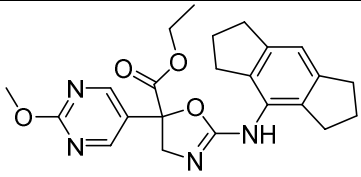
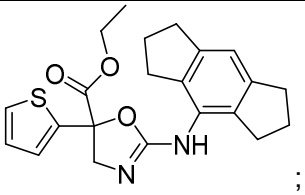
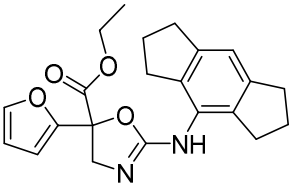
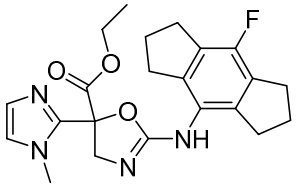
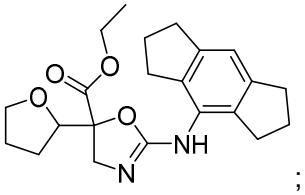
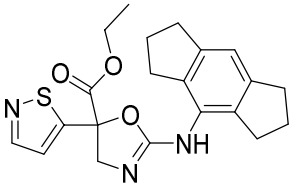
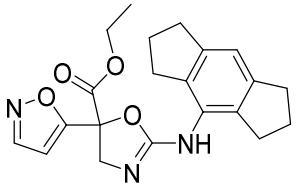
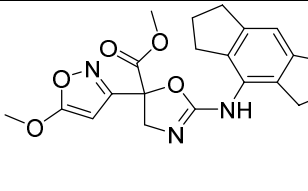
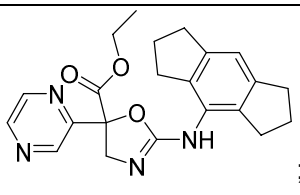
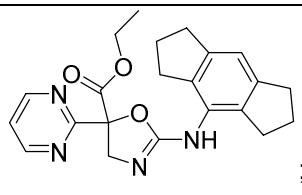
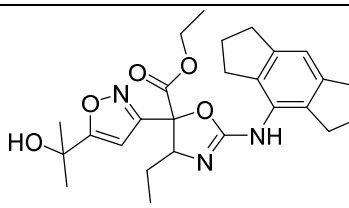
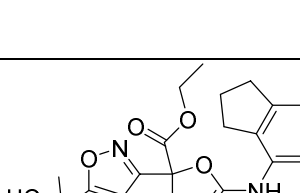
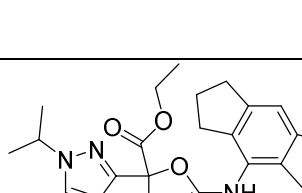
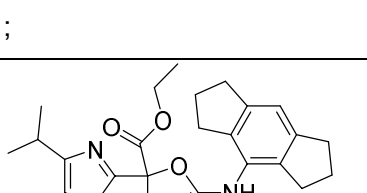
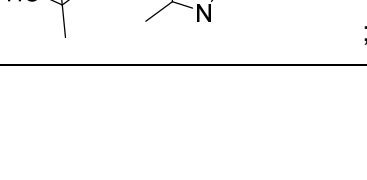
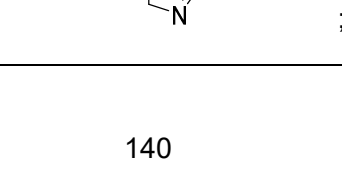
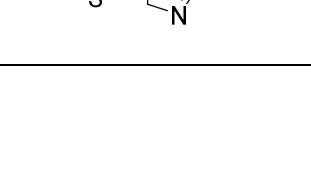
R^3 is

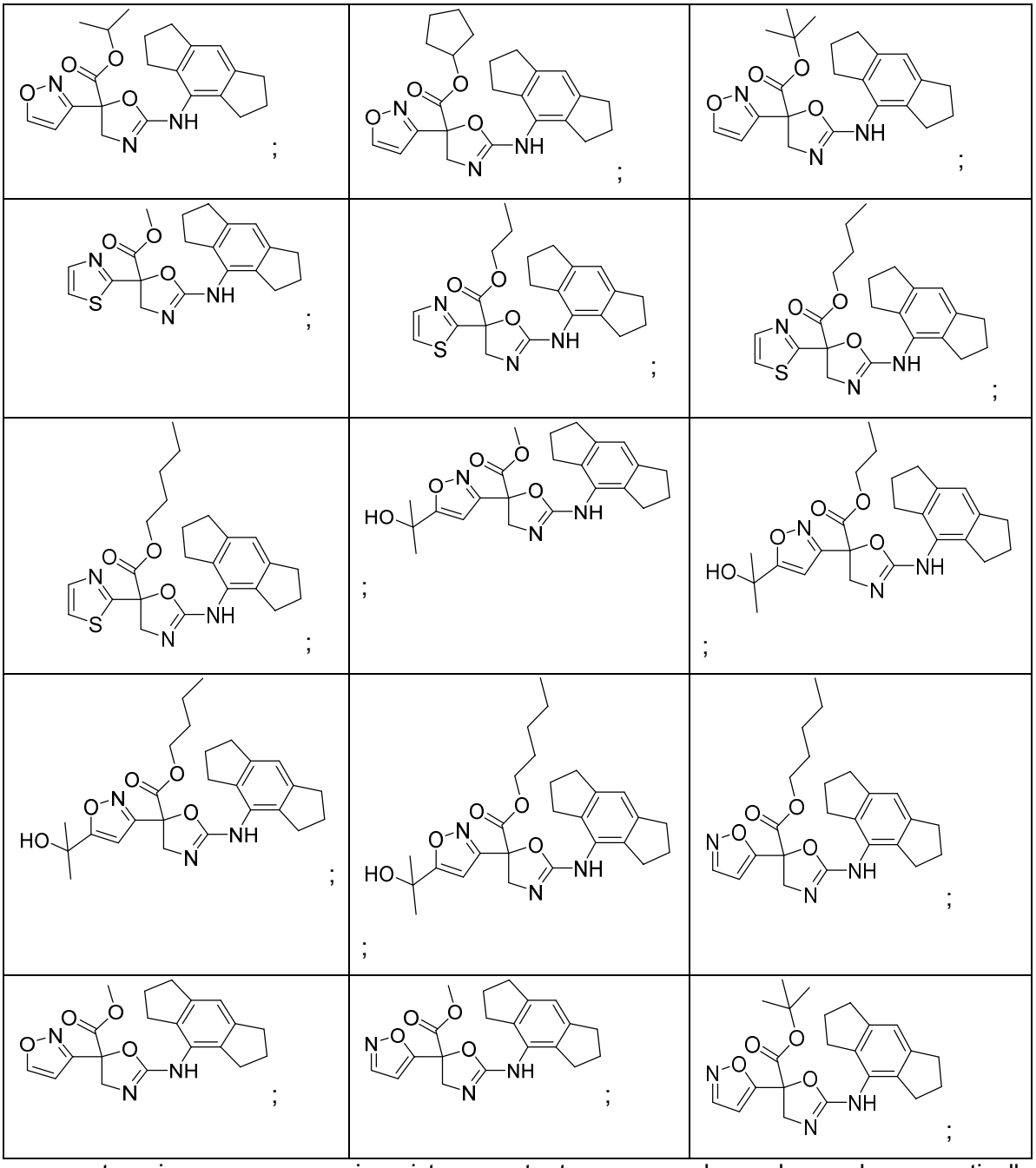


; each of them can be optionally substituted, and **R⁴** is independently selected from the group consisting of hydrogen, and C_1-C_6alkyl.

6. The compound according to any of the preceding claims, which is selected from

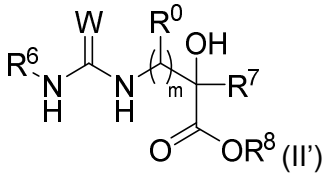
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or a stereoisomer, a racemic mixture, a tautomer, a polymorph, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof.

7. A compound of formula (II')



or a stereoisomer, a racemic mixture, a tautomer, a polymorph, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof,

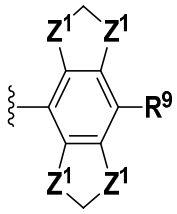
wherein

W is independently selected from the group consisting of O and S;

m is 1;

$\mathbf{R^0}$ is H or C_1-C_3alkyl;

$\mathbf{R^6}$ is



wherein

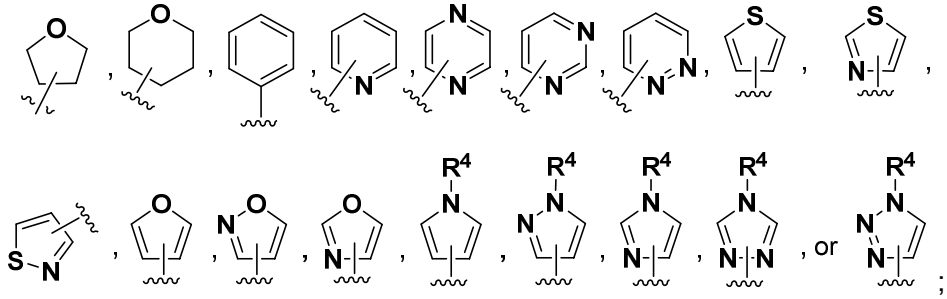
$\mathbf{Z^1}$ is independently selected from the group consisting of CH_2 and O provided that no more than two of $\mathbf{Z^1}$ are O;

$\mathbf{R^9}$ is independently selected from the group consisting of hydrogen and halogen;

$\mathbf{R^8}$ is independently selected from the group consisting of hydrogen, C_1-C_6alkyl, C_3-C_6 cycloalkyl; and

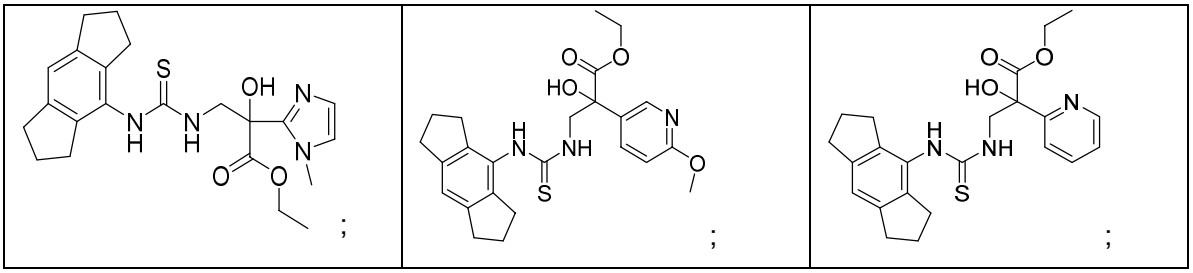
$\mathbf{R^7}$ is independently selected from the group consisting of heteroC_3-C_6cycloalkyl, aryl or heteroaryl wherein each of them can be optionally substituted with –C_1-C_6alkyl, –O–C_1-C_6alkyl, –Hal, or –C_1-C_6alkyl-OH.

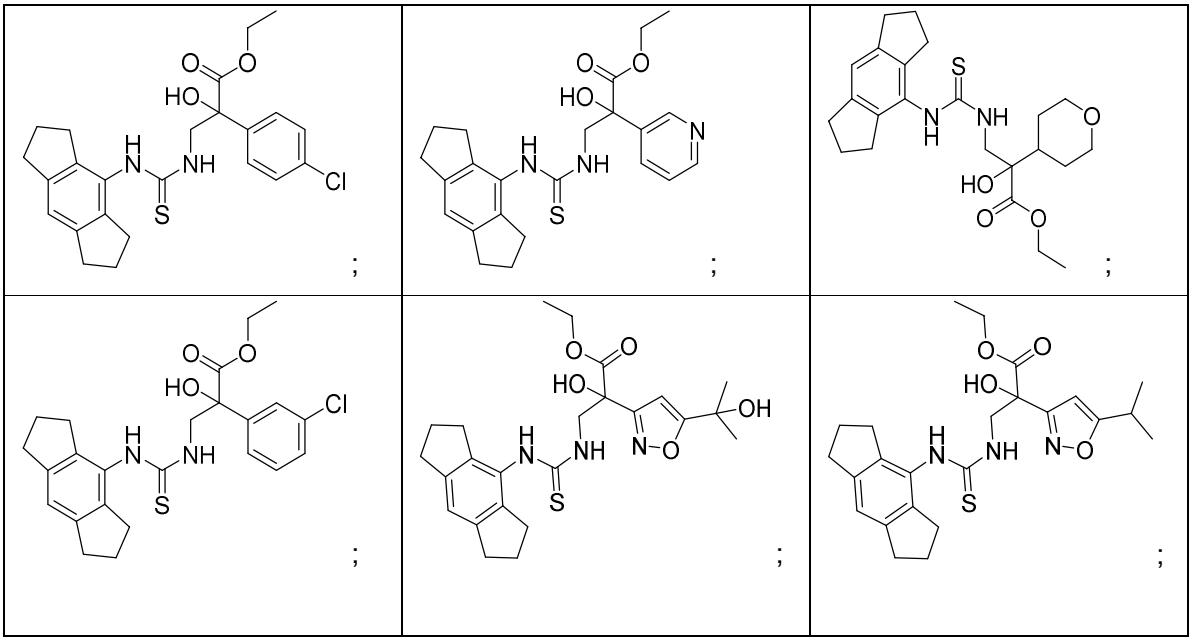
8. The compound according to claim 7, wherein $\mathbf{R^7}$ is



each of them can be optionally substituted and $\mathbf{R^4}$ is independently selected from the group consisting of hydrogen, C_1-C_6alkyl and C_3-C_6cycloalkyl.

9. The compound according to claim 7 or 8, which is





or a stereoisomer, a racemic mixture, a tautomer, a polymorph, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof.

10. A pharmaceutical composition comprising a compound as defined in any one of claims 1 to 9, or a stereoisomer, a racemic mixture, a tautomer, a polymorph, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof, and optionally comprising at least one pharmaceutically acceptable carrier, diluent, adjuvant or excipient.

11. The compound according to any one of claims 1 to 9, or a stereoisomer, a racemic mixture, a tautomer, a polymorph, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof, for use as a medicament.

12. Use of the compound according to any one of claims 1 to 9, or a stereoisomer, a racemic mixture, a tautomer, a polymorph, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof, in the manufacture of a medicament for treating, alleviating or preventing a disease, or a disorder or an abnormality which is responsive to the modulation of a component of the NLRP3 inflammasome pathway and/or which is responsive to the modulation of IL-1 beta and/or IL-18 levels;

wherein the disease, the disorder or the abnormality is selected from Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, demyelination, viral encephalitis, epilepsy, stroke, atherosclerosis, asthma, allergic inflammation, cryopyrin-associated periodic syndromes (CAPS), Muckle-Wells syndrome (MWS), familial cold autoinflammatory syndrome (FCAS), neonatal-onset multisystem inflammatory disease (NOMID), gout, pseudo-gout, inflammatory bowel disease, non-alcoholic fatty liver disease, non-alcoholic steatohepatitis, hypertension, myocardial infarction, oxalate-induced nephropathy, graft-versus host disease, type 1 diabetes, type 2 diabetes, rheumatoid arthritis, myelodysplastic syndrome, familial

Mediterranean fever (FMF), TNF receptor associated periodic syndrome (TRAPS), mevalonate kinase deficiency (MKD), hyperimmunoglobulinemia D, periodic fever syndrome (HIDS), deficiency of interleukin 1 receptor (DIRA) antagonist, Majeed syndrome, acne, pyogenic arthritis pyoderma gangrenosum and acne (PAPA), haploinsufficiency of A20 (HA20), PLCG2-associated antibody deficiency and immune dysregulation (PLAID), pediatric granulomatous arthritis (PGA), PLCG2-associated autoinflammation, antibody deficiency and immune dysregulation (APLAID), sideroblastic anemia with B-cell immunodeficiency, periodic fevers, developmental delay (SIFD), chronic nonbacterial osteomyelitis (CNO), Sweet's syndrome, chronic recurrent multifocal osteomyelitis (CRMO), synovitis, pustulosis, eczema, alopecia areata, actinic keratosis, hyperostosis, osteitis syndrome (SAPHO), multiple sclerosis (MS), psoriasis, Behcet's disease, Sjogren's syndrome, Schnitzler syndrome, chronic obstructive pulmonary disorder (COPD), steroid-resistant asthma, asbestosis, silicosis, cystic fibrosis, motor neuron disease, Huntington's disease, cerebral malaria, brain injury from pneumococcal meningitis, obesity, age-related macular degeneration (AMD), corneal infection, uveitis, dry eye, chronic kidney disease, diabetic nephropathy, alcoholic liver disease, skin contact hypersensitivity, sunburn, osteoarthritis, systemic juvenile idiopathic arthritis, adult-onset Still's disease, relapsing polychondritis, Chikungunya virus, Ross River virus, influenza, HIV, Coronaviruses, Dengue, Zika virus, hidradenitis suppurativa (HS), lung cancer metastasis, pancreatic cancers, gastric cancers, leukemia; polymyositis, colitis, helminth infection, bacterial infection, abdominal aortic aneurism, wound healing, depression, psychological stress, pericarditis including Dressler's syndrome, ischaemia reperfusion injury, frontotemporal dementia, HIV-associated neurocognitive disorder, Coronavirus-associated inflammatory pathologies, traumatic brain injury, dermatitis, anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV), lupus nephritis, anti-glomerular basement membrane (GBM) disease, IgA nephropathy, glomerulonephritis (GN), systemic lupus erythematosus (SLE), Focal Segmental Glomerulosclerosis, Minimal change disease (MCD), Psoriatic Arthritis, and Hereditary Recurrent Fevers (HRFs); preferably the disorder is selected from Alzheimer’s disease, Parkinson’s disease, amyotrophic lateral sclerosis, demyelination, viral encephalitis, epilepsy, stroke, atherosclerosis, asthma, allergic inflammation, cryopyrin-associated periodic syndromes (CAPS), gout, inflammatory bowel disease, non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), hypertension, myocardial infarction, oxalate-induced nephropathy, graft-versus host disease, type 1 diabetes, type 2 diabetes, rheumatoid arthritis, myelodysplastic syndrome, anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV), lupus nephritis, anti-glomerular basement membrane (GBM) disease, IgA nephropathy, glomerulonephritis (GN), systemic lupus erythematosus (SLE), Focal Segmental

Glomerulosclerosis , Minimal change disease (MCD), Psoriatic Arthritis, and Hereditary Recurrent Fevers (HRFs).

13. The use according to claim 12, wherein the disease, the disorder or the abnormality is selected from Alzheimer's disease, Parkinson's disease, cryopyrin-associated periodic syndromes (CAPS), non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH) and gout.

14. Use of a compound according to any one of claims 1 to 9, or a stereoisomer, a racemic mixture, a tautomer, a polymorph, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof, as an analytical reference or an *in vitro* screening tool.