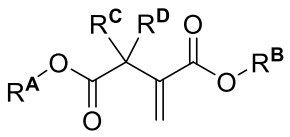
NRF2 activation, as well as GAPDH inhibition (Liao S.-T. *et al*., 2019), 4OI has been demonstrated to produce a wide range of interesting biological effects, including: 1) protection of neuronal cells from hydrogen peroxide (Liu H. *et al.*, 2018); 2) inhibition of proinflammatory cytokine production in peripheral blood mononuclear cells of SLE patients (Tang C. *et al.*, 2018); and 3) protection of human umbilical vein endothelial cells from high glucose (Tang C. *et al.*, 2019); 4) inhibition of osteoclastogenesis by suppressing the E3 ubiquitin ligase Hrd1 and activating NRF2 signaling (Sun X. *et al.*, 2019); 5) induction of repression of STING by NRF2 and type I IFN production in cells from patients with STING-dependent interferonopathies (Olagnier D. *et al.*, 2018); 6) protection against renal fibrosis via inhibiting the TGF-beta/Smad pathway, autophagy and reducing generation of reactive oxygen species (Tian F. *et al.*, 2020); 7) reduction of brain viral burden in mice intracranially injected with Zika virus (Daniels B. P. *et al.* 2019); and 8) protection against liver ischemia–reperfusion injury (Yi F. *et al.* 2020). Furthermore, itaconate has been reported to modulate tricarboxylic acid and redox metabolism to mitigate reperfusion injury (Cordes T. *et al.*, 2020). In addition, raised plasma itaconate levels demonstrate a clear correlation with reduction in rheumatoid arthritis disease activity scores following commencement of therapy with conventional disease modifying anti-rheumatic drug (cDMARD) therapy (Daly R. *et al.* 2019).

Artyomov et al. (WO2017/142855; WO2019/036509) disclose the use of itaconate, malonate or a derivative thereof as an immunomodulatory agent.

In spite of the above findings, there remains a need to identify and develop new itaconate derivatives possessing enhanced properties compared to currently marketed anti-inflammatory agents, such as DMF. The present inventors have now discovered, surprisingly, that certain itaconate diesters are highly effective at reducing cytokine release in cells and/or in activating NRF2-driven effects. These properties, amongst others, make them potentially more effective than DMI and/or dimethyl fumarate. Such compounds therefore possess excellent anti-inflammatory properties.

Summary

The present disclosure provides a compound of formula (IW-1):



(IW-1)

wherein,

$SiR^{4B}R^{5B}R^{6B}$, C_{3-8} cycloalkyl, 4–7 membered heterocyclyl, phenyl and 5-6 membered heteroaryl; wherein methyl, C_{3-8} cycloalkyl, 4–7 membered heterocyclyl, phenyl and 5-6 membered heteroaryl are optionally substituted by R^{7B} and/or R^{8B};

R^{4B}, R^{5B} and R^{6B} are independently selected from the group consisting of C_{1-4} alkyl and phenyl; wherein phenyl is optionally substituted by one or more substituents selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, hydroxy, CO_2H, cyano, methanesulfonyl and halo;

R^{7B} and R^{8B} are independently selected from the group consisting of oxo, C_{1-4} alkyl, C_{1-4} alkoxy, hydroxy, CO_2H, $CO_2(C_{1-6}$ alkyl), cyano, methanesulfonyl and halo;

or, taken together, R^{7B} and R^{8B} form a C_{3-8} cycloalkyl or 4–7 membered heterocyclic ring;

R^{2B} and R^{3B} are independently H, C_{1-8} alkyl, C_{3-8} cycloalkyl or phenyl; wherein R^{2B} and R^{3B} are independently optionally substituted by one or more substituents selected from the group consisting of C_{1-8} alkyl, C_{1-4} alkoxy, fluoro, hydroxy, oxo and $-(CH_2)_{qB}W^B$;

or, taken together, R^{2B} and R^{3B} form a 4–7 membered heterocyclic ring optionally independently substituted by one or more substituents selected from the group consisting of C_{1-2} alkyl, hydroxy and oxo;

R^{9B} is C_{1-8} alkyl, C_{3-8} cycloalkyl or phenyl; wherein R^{9B} is optionally substituted by one or more substituents selected from the group consisting of C_{1-8} alkyl, C_{1-4} alkoxy, halo, CO_2H, hydroxy, oxo and $–(CH_2)_{qB}W^B$;

q**B** is 0 or 1;

W^B is selected from the group consisting of C_{3-8} cycloalkyl, phenyl and 5–6 membered heteroaryl; wherein W^B is optionally substituted by one or more substituents selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, hydroxy, CO_2H, cyano, methanesulfonyl and halo;

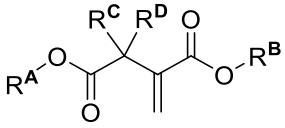
R^C and R^D are independently selected from the group consisting of H, C_{1-2} alkyl, hydroxy, methoxy and fluoro;

and wherein,

when neither R^A nor R^B contain heteroatoms, the total number of carbon atoms in groups R^A and R^B taken together is at least 6;

or a pharmaceutically acceptable salt and/or solvate thereof.

The present disclosure, in one aspect, provides a compound which is a compound of formula (IW-1):



(IW-1)

wherein,

R^A is selected from the group consisting of $C_{1–8}$ alkyl, $C_{3–8}$ cycloalkyl, $C_{5–10}$ spirocycloalkyl and 4–7 membered heterocyclyl; wherein R^A is optionally substituted by one or more substituents selected from the group consisting of oxo, R^{1A}, OR^{2A}, $NR^{2A}R^{3A}$, SR^{2A}, SOR^{9A}, SO_2R^{9A}, $SO_2NR^{2A}R^{3A}$, $C(O)R^{2A}$ and $CONR^{2A}R^{3A}$;

R^{1A} is selected from the group consisting of fluoro, methyl, cyano, $SiR^{4A}R^{5A}R^{6A}$, $C_{3–8}$ cycloalkyl, phenyl and 5-6 membered heteroaryl; wherein methyl, $C_{3–8}$ cycloalkyl, phenyl and 5-6 membered heteroaryl are optionally substituted by R^{7A} and/or R^{8A};

R^{4A}, R^{5A} and R^{6A} are independently selected from the group consisting of $C_{1–4}$ alkyl and phenyl; wherein phenyl is optionally substituted by one or more substituents selected from the group consisting of $C_{1–4}$ alkyl, $C_{1–4}$ alkoxy, hydroxy, CO_2H, cyano, methanesulfonyl and halo;

R^{7A} and R^{8A} are independently selected from the group consisting of oxo, $C_{1–4}$ alkyl, $C_{1–4}$ alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, hydroxy, CO_2H, cyano, methanesulfonyl and halo;

or, taken together, R^{7A} and R^{8A} form a $C_{3–8}$ cycloalkyl or 4–7 membered heterocyclic ring;

R^{2A} and R^{3A} are independently H, $C_{1–8}$ alkyl, $C_{3–8}$ cycloalkyl or phenyl; wherein R^{2A} and R^{3A} are independently optionally substituted by one or more substituents selected from the group consisting of C_{1-8} alkyl, $C_{1–4}$ alkoxy, fluoro, hydroxy, oxo and $-(CH_2)_{qA}W^A$;

or, taken together, R^{2A} and R^{3A} form a 4–7 membered heterocyclic ring optionally independently substituted by one or more substituents selected from the group consisting of $C_{1–2}$ alkyl, hydroxy and oxo;

R^{9A} is $C_{1–8}$ alkyl, $C_{3–8}$ cycloalkyl or phenyl; wherein R^{9A} is optionally substituted by one or more substituents selected from the group consisting of C_{1-8} alkyl, $C_{1–4}$ alkoxy, fluoro, hydroxy, oxo and $–(CH_2)_{qA}W^A$;

q**A** is 0 or 1;

W^A is selected from the group consisting of $C_{3–8}$ cycloalkyl, phenyl and 5–6 membered heteroaryl; wherein W^A is optionally substituted by one or more substituents selected from the group consisting of $C_{1–4}$ alkyl, $C_{1–4}$ alkoxy, hydroxy, CO_2H, cyano, methanesulfonyl and halo;

wherein

R^B is $C_{1–2}$ alkyl substituted by CO_2H optionally substituted by at least one other substituent selected from the group consisting of halo, trifluoromethyl and methyl;

R^C and R^D are independently selected from the group consisting of H, C_{1-2} alkyl, hydroxy, methoxy

and fluoro;

and wherein,

when neither R^A nor R^B contain heteroatoms, the total number of carbon atoms in groups R^A and R^B taken together is at least 6;

or a pharmaceutically acceptable salt and/or solvate thereof;

or a compound selected from the group consisting of:

1-(2-cyanoethyl) 4-octyl 2-methylenesuccinate;

1-(2-(methylsulfonyl)ethyl) 4-octyl 2-methylenesuccinate;

4-octyl 1-(3,3,3-trifluoropropyl) 2-methylenesuccinate;

4-octyl 1-(oxetan-3-yl) 2-methylenesuccinate;

4-octyl 1-(2-(2-oxopyrrolidin-1-yl)ethyl) 2-methylenesuccinate;

1-(3-(dimethylamino)-3-oxopropyl) 4-octyl 2-methylenesuccinate;

4-butyl 1-(2-(methylsulfonyl)ethyl) 2-methylenesuccinate;

1-(2-cyanoethyl) 4-butyl 2-methylenesuccinate;

1-(2-(2,5-dioxopyrrolidin-1-yl)ethyl) 4-octyl 2-methylenesuccinate;

1-(2-cyanoethyl) 4-methyl 2-methylenesuccinate;

1-(2-cyanoethyl) 4-hexyl 2-methylenesuccinate;

4-methyl 1-(2-(methylsulfonyl)ethyl) 2-methylenesuccinate;

4-octyl 1-(2-(trifluoromethoxy)ethyl) 2-methylenesuccinate;

4-hexyl 1-(2-(methylsulfonyl)ethyl) 2-methylenesuccinate;

4-methyl 1-(oxetan-3-yl) 2-methylenesuccinate;

1-(2-(N,N-dimethylsulfamoyl)ethyl) 4-octyl 2-methylenesuccinate;

1-(2-(dimethylamino)ethyl) 4-octyl 2-methylenesuccinate;

1-(3-(methylsulfonyl)propyl) 4-octyl 2-methylenesuccinate;

1-(1-(methylsulfonyl)propan-2-yl) 4-octyl 2-methylenesuccinate;

1-(2-(methylsulfonyl)ethyl) 4-(3-phenoxypropyl) 2-methylenesuccinate;

1-(2-(dimethylamino)-2-oxoethyl) 4-octyl 2-methylenesuccinate;

4-isopropyl 1-(2-(methylsulfonyl)ethyl) 2-methylenesuccinate;

(S)-4-octyl 1-(tetrahydrofuran-3-yl) 2-methylenesuccinate;

(R)-4-octyl 1-(tetrahydrofuran-3-yl) 2-methylenesuccinate;

4-cyclooctyl 1-(2-(methylsulfonyl)ethyl) 2-methylenesuccinate;

4-octyl 1-(tetrahydro-2H-pyran-4-yl) 2-methylenesuccinate;

1-(1-cyanopropan-2-yl) 4-octyl 2-methylenesuccinate;

1-(1-(methylsulfonyl)piperidin-4-yl) 4-octyl 2-methylenesuccinate;

1-(2-methoxyethyl) 4-octyl 2-methylenesuccinate;

1-(2-cyano-2-methylpropyl) 4-octyl 2-methylenesuccinate;

1-(1-methoxypropan-2-yl) 4-octyl 2-methylenesuccinate;

1-((1-cyanocyclopropyl)methyl) 4-octyl 2-methylenesuccinate;

1-(2-methoxypropyl) 4-octyl 2-methylenesuccinate;
1-(2-methoxy-2-methylpropyl) 4-octyl 2-methylenesuccinate;
1-(2-morpholinoethyl) 4-octyl 2-methylenesuccinate;
4-(2-(2-ethoxyethoxy)ethyl) 1-(2-(methylsulfonyl)ethyl) 2-methylenesuccinate;
4-butyl 1-(oxetan-3-yl) 2-methylenesuccinate;
4-hexyl 1-(oxetan-3-yl) 2-methylenesuccinate;
4-butyl 1-(2-tosylethyl) 2-methylenesuccinate;
4-octyl 1-(2-tosylethyl) 2-methylenesuccinate;
4-cyclooctyl 1-methyl 2-methylenesuccinate;
1-methyl 4-octyl 2-methylenesuccinate;
dicyclobutyl 2-methylenesuccinate;
di(oxetan-3-yl) 2-methylenesuccinate;
1-cyclobutyl 4-octyl 2-methylenesuccinate;
1-(1-acetoxyethyl) 4-octyl 2-methylenesuccinate;
1-(1,1-dioxidothietan-3-yl) 4-octyl 2-methylenesuccinate;
1-(2-(tert-butoxy)-2-oxoethyl) 4-octyl 2-methylenesuccinate;
1-(1-acetylazetidin-3-yl) 4-octyl 2-methylenesuccinate;
1-(2-(4-methylpiperazin-1-yl)ethyl) 4-octyl 2-methylenesuccinate;
1-(2-(1,1-dioxidothiomorpholino)ethyl) 4-octyl 2-methylenesuccinate;
1-(2-(methylsulfonamido)ethyl) 4-octyl 2-methylenesuccinate;
4-cyclooctyl 1-(1,1-dioxidothietan-3-yl) 2-methylenesuccinate;
(R)-1-(2-(methylsulfonyl)ethyl) 4-(octan-2-yl) 2-methylenesuccinate;
1-(1-(methylsulfonyl)propan-2-yl) 4-((R)-octan-2-yl) 2-methylenesuccinate;
(R)-1-(1,1-dioxidothietan-3-yl) 4-(octan-2-yl) 2-methylenesuccinate;
(R)-1-(1-acetylazetidin-3-yl) 4-(octan-2-yl) 2-methylenesuccinate;
4-cyclohexyl 1-(1-(methylsulfonyl)propan-2-yl) 2-methylenesuccinate;
4-cyclohexyl 1-(1,1-dioxidothietan-3-yl) 2-methylenesuccinate;
4-cyclohexyl 1-(2-(methylsulfonyl)ethyl) 2-methylenesuccinate;
4-cyclooctyl 1-(1-(methylsulfonyl)propan-2-yl) 2-methylenesuccinate;
1-(1-acetylazetidin-3-yl) 4-cyclooctyl 2-methylenesuccinate;
4-cyclohexyl 1-(tetrahydro-2H-pyran-4-yl) 2-methylenesuccinate;
4-cyclohexyl 1-(2-(2-oxopyrrolidin-1-yl)ethyl) 2-methylenesuccinate;
(S)-1-(1-acetylazetidin-3-yl) 4-(octan-2-yl) 2-methylenesuccinate;
(S)-1-(1,1-dioxidothietan-3-yl) 4-(octan-2-yl) 2-methylenesuccinate;
1-(3-methyloxetan-3-yl) 4-octyl 2-methylenesuccinate;
4-cyclooctyl 1-(1-(methylsulfonyl)piperidin-4-yl) 2-methylenesuccinate;
4-cyclooctyl 1-(tetrahydro-2H-pyran-4-yl) 2-methylenesuccinate;
4-cyclooctyl 1-(2-(2-oxopyrrolidin-1-yl)ethyl) 2-methylenesuccinate;

(R)-4-(octan-2-yl) 1-(2-(2-oxopyrrolidin-1-yl)ethyl) 2-methylenesuccinate;
(R)-4-(octan-2-yl) 1-(tetrahydro-2H-pyran-4-yl) 2-methylenesuccinate;
1-(1-acetylazetidin-3-yl) 4-cyclohexyl 2-methylenesuccinate;
4-cyclohexyl 1-(1-(methylsulfonyl)piperidin-4-yl) 2-methylenesuccinate;
4-hexyl 1-(1-(methylsulfonyl)piperidin-4-yl) 2-methylenesuccinate;
4-hexyl 1-(2-(2-oxopyrrolidin-1-yl)ethyl) 2-methylenesuccinate;
1-(2-(1H-tetrazol-5-yl)ethyl) 4-hexyl 2-methylenesuccinate;
2-(N-methyl-2-((2-methylene-4-(octyloxy)-4-oxobutanoyl)oxy)acetamido)acetic acid;
(2-((2-methylene-4-(octyloxy)-4-oxobutanoyl)oxy)acetyl)-L-proline;
N-methyl-N-(2-((2-methylene-4-(octyloxy)-4-oxobutanoyl)oxy)propanoyl)glycine;
(2-((2-methylene-4-(octyloxy)-4-oxobutanoyl)oxy)propanoyl)-L-proline;
(2-((2-methylene-4-(octyloxy)-4-oxobutanoyl)oxy)propanoyl)glycine;
N-(2-((4-(cyclooctyloxy)-2-methylene-4-oxobutanoyl)oxy)acetyl)-N-methylglycine;
(2-((4-(cyclooctyloxy)-2-methylene-4-oxobutanoyl)oxy)acetyl)-L-proline;
(S)-N-methyl-N-(2-((2-methylene-4-(octan-2-yloxy)-4-oxobutanoyl)oxy)acetyl)glycine;
(S)-(2-((2-methylene-4-(octan-2-yloxy)-4-oxobutanoyl)oxy)acetyl)glycine;
1-(2-(4-methylpiperazin-1-yl)-2-oxoethyl) 4-octyl 2-methylenesuccinate;
1-(3-morpholino-3-oxopropyl) 4-octyl 2-methylenesuccinate;
1-(3-(diethylamino)-3-oxopropyl) 4-octyl 2-methylenesuccinate;
1-(3-(methylamino)-3-oxopropyl) 4-octyl 2-methylenesuccinate;
1-(2-((N,N-dimethylsulfamoyl)amino)-2-oxoethyl) 4-hexyl 2-methylenesuccinate;
4-hexyl 1-(2-(methylsulfonamido)-2-oxoethyl) 2-methylenesuccinate;
4-hexyl 1-(3-(methylsulfonamido)-2-oxoethyl) 2-methylenesuccinate;
(E)-4-((4-(cyclohexyloxy)-2-methylene-4-oxobutanoyl)oxy)but-2-enoic acid;
3-((2-((4-(cyclohexyloxy)-2-methylene-4-oxobutanoyl)oxy)ethyl)sulfonyl)propanoic acid;
1-((2H-tetrazol-5-yl)methyl) 4-cyclohexyl 2-methylenesuccinate;
2-((3-((2-((3-chlorophenyl)sulfonyl)ethoxy)carbonyl)but-3-enoyl)oxy)acetic acid;
(R)-2-((4-(cyclohexyloxy)-2-methylene-4-oxobutanoyl)oxy)-2-phenylacetic acid;
1-(2-(1H-tetrazol-5-yl)ethyl) 4-cyclohexyl 2-methylenesuccinate;
(S)-1-(2-(1H-tetrazol-5-yl)ethyl) 4-octan-2-yl 2-methylenesuccinate;
1-(2-(1H-tetrazol-5-yl)ethyl) 4-cyclooctyl 2-methylenesuccinate;
1-(2-((3-chlorophenyl)sulfonyl)-2-methylpropyl) 4-cyclooctyl 2-methylenesuccinate;
4-cyclooctyl 1-(2-methyl-2-(methylsulfonyl)propyl) 2-methylenesuccinate;
1-(1-(1H-tetrazol-5-yl)ethyl) 4-cyclooctyl 2-methylenesuccinate;
1-((1H-tetrazol-5-yl)methyl) 4-cyclooctyl 2-methylenesuccinate;
(R)-1-(2-(1H-tetrazol-5-yl)ethyl) 4-octan-2-yl 2-methylenesuccinate;
(2R,3S)-2-acetamido-3-((4-(cyclooctyloxy)-2-methylene-4-oxobutanoyl)oxy)butanoic acid;
4-cyclooctyl 1-(3-(2-ethoxy-2-oxoethyl)oxetan-3-yl) 2-methylenesuccinate;

4-(2-(methylsulfonyl)ethyl) 1-octyl 2-methyl-3-methylenesuccinate;
1-octyl 4-((S)-tetrahydrofuran-3-yl) 2-methyl-3-methylenesuccinate;
1-(1-(1H-tetrazol-5-yl)propan-2-yl) 4-((R)-octan-2-yl) 2-methylenesuccinate;
1-(1-(1H-tetrazol-5-yl)propan-2-yl) 4-((S)-octan-2-yl) 2-methylenesuccinate;
4-cyclohexyl 1-((2-methyl-2H-tetrazol-5-yl)methyl) 2-methylenesuccinate;
4-cyclohexyl 1-((1-methyl-1H-tetrazol-5-yl)methyl) 2-methylenesuccinate;
2-((4-((adamantan-2-yl)oxy)-2-methylene-4-oxobutanoyl)oxy)acetic acid;
bis((endo)-3-(methylsulfonyl)-3-azabicyclo[3.2.1]octan-8-yl) 2-methylenesuccinate;
1-((endo)-3-(methylsulfonyl)-3-azabicyclo[3.2.1]octan-8-yl) 4-(2-oxaspiro[3.3]heptan-6-yl) 2-methylenesuccinate;
1-((endo)-3-(methylsulfonyl)-3-azabicyclo[3.2.1]octan-8-yl) 4-(oxepan-4-yl) 2-methylenesuccinate;
4-(1-butoxypropan-2-yl) 1-((endo)-3-(methylsulfonyl)-3-azabicyclo[3.2.1]octan-8-yl) 2-methylenesuccinate;
4-spiro[3.3]heptan-2-yl 1-(3,3,3-trifluoro-2,2-dihydroxypropyl) 2-methylenesuccinate hydrate;(*R*)-1-((2H-tetrazol-5-yl)methyl) 4-(octan-2-yl) 2-methylenesuccinate;
1-(2H-tetrazol-5-yl)methyl 4-cycloheptyl 2-methylenesuccinate;
1-(2H-tetrazol-5-yl)methyl 4-spiro[3.3]heptan-2-yl 2-methylenesuccinate;
(*S*)-1-(2H-tetrazol-5-yl)methyl 4-octan-2-yl 2-methylenesuccinate;
1-(1-(1H-tetrazol-5-yl)ethyl) 4-((S)-octan-2-yl) 2-methylenesuccinate;
1-(cyclopropyl(1H-tetrazol-5-yl)methyl) 4-((S)-octan-2-yl) 2-methylenesuccinate;
dicyclohexyl 2-methylenesuccinate; 2-((4-((-adamantan-1-yl)oxy)-2-methylene-4-oxobutanoyl)oxy)acetic acid;2-((4-(bicyclo[3.3.1]nonan-9-yloxy)-2-methylene-4-oxobutanoyl)oxy)acetic acid;
1-(3,3-difluorocyclobutyl) 4-octyl 2-methylenesuccinate;
1-((endo)-3-(methylsulfonyl)-3-azabicyclo[3.2.1]octan-8-yl) 4-((R)-octan-2-yl) 2-methylenesuccinate; and
(*R*)-4-(octan-2-yl) 1-((3-oxo-2,3-dihydroisoxazol-5-yl)methyl) 2-methylenesuccinate;
or a pharmaceutically acceptable salt and/or solvate thereof.

The present disclosure, in another aspect, provides a pharmaceutical composition comprising a compound of formula (IW-1) or a pharmaceutically acceptable salt and/or solvate thereof.

The present disclosure, in another aspect, provides a compound of formula (IW-1) or a pharmaceutically acceptable

salt and/or solvate thereof for use as a medicament.

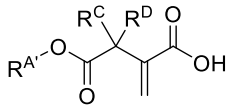
The present disclosure, in another aspect, provides a compound of formula (IW-1) or a pharmaceutically acceptable salt and/or solvate thereof for use in treating or preventing an inflammatory disease or a disease associated with an undesirable immune response.

The present disclosure, in another aspect, provides the use of a compound of formula (IW-1) or a pharmaceutically acceptable salt and/or solvate thereof in the manufacture of a medicament for treating or preventing an inflammatory disease or a disease associated with an immune response.

The present disclosure provides a method of treating or preventing an inflammatory disease or a disease associated with an undesirable immune response, which comprises administering a compound of formula (IW-1) or a pharmaceutically acceptable salt and/or solvate thereof.

Also provided are intermediate compounds of use in the preparation of compounds of formula (IW-1).

The present disclosure, in another aspect, provides a compound which is:



(III)

wherein:

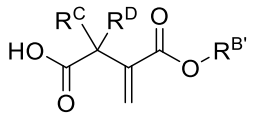
$R^{A'}$ is R^{A} or a protected derivative thereof;

wherein R^{A} is as defined herein;

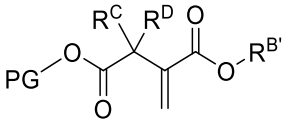
R^{C} and R^{D} are as defined herein;

or a salt thereof

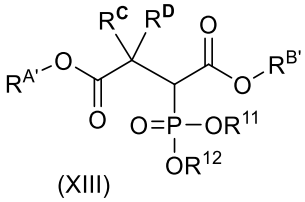
The present disclosure, in another aspect, provides a compound which is selected from the group consisting of:



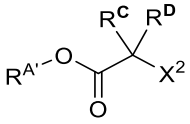
(IX) ;



(VIII) ;



(XIII) ; and



(XI) ;

wherein:

$R^{A'}$ is R^A or a protected derivative thereof;

wherein R^A is as defined herein;

$R^{B'}$ is R^B or a protected derivative thereof;

wherein R^B is as defined herein;

R^C and R^D are as defined herein; and

PG is an oxygen protecting group;

R^{11} is $C_{1–4}$ alkyl optionally substituted with halo;

R^{12} is $C_{1–4}$ alkyl optionally substituted with halo; and

X^2 is a leaving group such as halo e.g., chloro, bromo or iodo;

or a salt thereof.

Detailed description of the invention

Compounds of formula (IW-1)

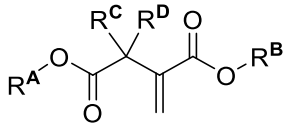
Embodiments and preferences set out herein with respect to the compound of formula (IW-1) apply equally to the pharmaceutical composition, compound for use, use and method aspects of the invention.

The term "C_{1-10} alkyl" refers to a straight or branched fully saturated hydrocarbon group having from 1 to 10 carbon atoms. The term encompasses methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, n-pentyl, n-heptyl, n-hexyl and n-octyl. Other branched variants such as heptyl-$CH(CH_3)$– and hexyl-$CH(CH_3)$– are also included. Further branched variants include n-pentyl–$CH(CH_2CH_3)$– and $(n\text{-}Bu)_2CH$–. Other branched variants include n-pentyl-$C(CH_3)_2$– or n-

hexyl-$C(CH_3)_2$–. Another branched variant is -CH(*t*-Bu)$_2$. Other alkyl groups, for example C_{1-9} alkyl, C_{1-8} alkyl, C_{1-7} alkyl, C_{1-6} alkyl, C_{1-5} alkyl, C_{1-4} alkyl, C_{1-3} alkyl, C_{1-2} alkyl, C_{2-10} alkyl, C_{2-9} alkyl, C_{2-8} alkyl, C_{2-7} alkyl, C_{2-6} alkyl, C_{2-5} alkyl, C_{2-4} alkyl, C_{2-3} alkyl, C_{3-10} alkyl, C_{3-9} alkyl, C_{3-8} alkyl, C_{3-7} alkyl, C_{3-6} alkyl, C_{3-5} alkyl, C_{3-4} alkyl, C_{4-10} alkyl, C_{4-9} alkyl, C_{4-8} alkyl, C_{4-7} alkyl, C_{4-6} alkyl, C_{4-5} alkyl, C_{5-10} alkyl, C_{5-9} alkyl, C_{5-8} alkyl, C_{5-7} alkyl, C_{5-6} alkyl, C_{6-10} alkyl, C_{6-9} alkyl, C_{6-8} alkyl, C_{7-10} alkyl, C_{7-9} alkyl, C_{7-8} alkyl, C_{8-10} alkyl, C_{8-9} alkyl and C_{9-10} alkyl are as defined above but contain different numbers of carbon atoms. The term “C_{1-10} alkyl” also encompasses “C_{1-10} alkylene” which is a

CLAIMS

1. A compound which is a compound of formula (IW-1):



(IW-1)

wherein,

R^A is selected from the group consisting of $C_{1–8}$ alkyl, $C_{3–8}$ cycloalkyl, $C_{5–10}$ spirocycloalkyl and 4–7 membered heterocyclyl; wherein R^A is optionally substituted by one or more substituents selected from the group consisting of oxo, R^{1A}, OR^{2A}, $NR^{2A}R^{3A}$, SR^{2A}, SOR^{9A}, SO_2R^{9A}, $SO_2NR^{2A}R^{3A}$, $C(O)R^{2A}$ and $CONR^{2A}R^{3A}$;

R^{1A} is selected from the group consisting of fluoro, methyl, cyano, $SiR^{4A}R^{5A}R^{6A}$, $C_{3–8}$ cycloalkyl, phenyl and 5-6 membered heteroaryl; wherein methyl, $C_{3–8}$ cycloalkyl, phenyl and 5-6 membered heteroaryl are optionally substituted by R^{7A} and/or R^{8A};

R^{4A}, R^{5A} and R^{6A} are independently selected from the group consisting of $C_{1–4}$ alkyl and phenyl; wherein phenyl is optionally substituted by one or more substituents selected from the group consisting of $C_{1–4}$ alkyl, $C_{1–4}$ alkoxy, hydroxy, CO_2H, cyano, methanesulfonyl and halo;

R^{7A} and R^{8A} are independently selected from the group consisting of oxo, $C_{1–4}$ alkyl, $C_{1–4}$ alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, hydroxy, CO_2H, cyano, methanesulfonyl and halo;

or, taken together, R^{7A} and R^{8A} form a $C_{3–8}$ cycloalkyl or 4–7 membered heterocyclic ring;

R^{2A} and R^{3A} are independently H, $C_{1–8}$ alkyl, $C_{3–8}$ cycloalkyl or phenyl; wherein R^{2A} and R^{3A} are independently optionally substituted by one or more substituents selected from the group consisting of C_{1-8} alkyl, $C_{1–4}$ alkoxy, fluoro, hydroxy, oxo and $-(CH_2)_{qA}W^A$;

or, taken together, R^{2A} and R^{3A} form a 4–7 membered heterocyclic ring optionally independently substituted by one or more substituents selected from the group consisting of $C_{1–2}$ alkyl, hydroxy and oxo;

R^{9A} is $C_{1–8}$ alkyl, $C_{3–8}$ cycloalkyl or phenyl; wherein R^{9A} is optionally substituted by one or more substituents selected from the group consisting of C_{1-8} alkyl, $C_{1–4}$ alkoxy, fluoro, hydroxy, oxo and $–(CH_2)_{qA}W^A$;

q**A** is 0 or 1;

W^A is selected from the group consisting of $C_{3–8}$ cycloalkyl, phenyl and 5–6 membered heteroaryl; wherein W^A is optionally substituted by one or more substituents selected from the group consisting of $C_{1–4}$ alkyl, $C_{1–4}$ alkoxy, hydroxy, CO_2H, cyano, methanesulfonyl and halo;

wherein

R^B is C_{1-2} alkyl substituted by CO_2H optionally substituted by at least one other substituent selected from the group consisting of halo, trifluoromethyl and methyl;

R^C and R^D are independently selected from the group consisting of H, C_{1-2} alkyl, hydroxy, methoxy and fluoro;

and wherein,

when neither R^A nor R^B contain heteroatoms, the total number of carbon atoms in groups R^A and R^B taken together is at least 6;

or a pharmaceutically acceptable salt and/or solvate thereof;

or a compound selected from the group consisting of:

1-(2-cyanoethyl) 4-octyl 2-methylenesuccinate;

1-(2-(methylsulfonyl)ethyl) 4-octyl 2-methylenesuccinate;

4-octyl 1-(3,3,3-trifluoropropyl) 2-methylenesuccinate;

4-octyl 1-(oxetan-3-yl) 2-methylenesuccinate;

4-octyl 1-(2-(2-oxopyrrolidin-1-yl)ethyl) 2-methylenesuccinate;

1-(3-(dimethylamino)-3-oxopropyl) 4-octyl 2-methylenesuccinate;

4-butyl 1-(2-(methylsulfonyl)ethyl) 2-methylenesuccinate;

1-(2-cyanoethyl) 4-butyl 2-methylenesuccinate;

1-(2-(2,5-dioxopyrrolidin-1-yl)ethyl) 4-octyl 2-methylenesuccinate;

1-(2-cyanoethyl) 4-methyl 2-methylenesuccinate;

1-(2-cyanoethyl) 4-hexyl 2-methylenesuccinate;

4-methyl 1-(2-(methylsulfonyl)ethyl) 2-methylenesuccinate;

4-octyl 1-(2-(trifluoromethoxy)ethyl) 2-methylenesuccinate;

4-hexyl 1-(2-(methylsulfonyl)ethyl) 2-methylenesuccinate;

4-methyl 1-(oxetan-3-yl) 2-methylenesuccinate;

1-(2-(N,N-dimethylsulfamoyl)ethyl) 4-octyl 2-methylenesuccinate;

1-(2-(dimethylamino)ethyl) 4-octyl 2-methylenesuccinate;

1-(3-(methylsulfonyl)propyl) 4-octyl 2-methylenesuccinate;

1-(1-(methylsulfonyl)propan-2-yl) 4-octyl 2-methylenesuccinate;

1-(2-(methylsulfonyl)ethyl) 4-(3-phenoxypropyl) 2-methylenesuccinate;

1-(2-(dimethylamino)-2-oxoethyl) 4-octyl 2-methylenesuccinate;

4-isopropyl 1-(2-(methylsulfonyl)ethyl) 2-methylenesuccinate;

(S)-4-octyl 1-(tetrahydrofuran-3-yl) 2-methylenesuccinate;

(R)-4-octyl 1-(tetrahydrofuran-3-yl) 2-methylenesuccinate;

4-cyclooctyl 1-(2-(methylsulfonyl)ethyl) 2-methylenesuccinate;

4-octyl 1-(tetrahydro-2H-pyran-4-yl) 2-methylenesuccinate;

1-(1-cyanopropan-2-yl) 4-octyl 2-methylenesuccinate;

1-(1-(methylsulfonyl)piperidin-4-yl) 4-octyl 2-methylenesuccinate;

1-(2-methoxyethyl) 4-octyl 2-methylenesuccinate;
1-(2-cyano-2-methylpropyl) 4-octyl 2-methylenesuccinate;
1-(1-methoxypropan-2-yl) 4-octyl 2-methylenesuccinate;
1-((1-cyanocyclopropyl)methyl) 4-octyl 2-methylenesuccinate;
1-(2-methoxypropyl) 4-octyl 2-methylenesuccinate;
1-(2-methoxy-2-methylpropyl) 4-octyl 2-methylenesuccinate;
1-(2-morpholinoethyl) 4-octyl 2-methylenesuccinate;
4-(2-(2-ethoxyethoxy)ethyl) 1-(2-(methylsulfonyl)ethyl) 2-methylenesuccinate;
4-butyl 1-(oxetan-3-yl) 2-methylenesuccinate;
4-hexyl 1-(oxetan-3-yl) 2-methylenesuccinate;
4-butyl 1-(2-tosylethyl) 2-methylenesuccinate;
4-octyl 1-(2-tosylethyl) 2-methylenesuccinate;
4-cyclooctyl 1-methyl 2-methylenesuccinate;
1-methyl 4-octyl 2-methylenesuccinate;
dicyclobutyl 2-methylenesuccinate;
di(oxetan-3-yl) 2-methylenesuccinate;
1-cyclobutyl 4-octyl 2-methylenesuccinate;
1-(1-acetoxyethyl) 4-octyl 2-methylenesuccinate;
1-(1,1-dioxidothietan-3-yl) 4-octyl 2-methylenesuccinate;
1-(2-(tert-butoxy)-2-oxoethyl) 4-octyl 2-methylenesuccinate;
1-(1-acetylazetidin-3-yl) 4-octyl 2-methylenesuccinate;
1-(2-(4-methylpiperazin-1-yl)ethyl) 4-octyl 2-methylenesuccinate;
1-(2-(1,1-dioxidothiomorpholino)ethyl) 4-octyl 2-methylenesuccinate;
1-(2-(methylsulfonamido)ethyl) 4-octyl 2-methylenesuccinate;
4-cyclooctyl 1-(1,1-dioxidothietan-3-yl) 2-methylenesuccinate;
(R)-1-(2-(methylsulfonyl)ethyl) 4-(octan-2-yl) 2-methylenesuccinate;
1-(1-(methylsulfonyl)propan-2-yl) 4-((R)-octan-2-yl) 2-methylenesuccinate;
(R)-1-(1,1-dioxidothietan-3-yl) 4-(octan-2-yl) 2-methylenesuccinate;
(R)-1-(1-acetylazetidin-3-yl) 4-(octan-2-yl) 2-methylenesuccinate;
4-cyclohexyl 1-(1-(methylsulfonyl)propan-2-yl) 2-methylenesuccinate;
4-cyclohexyl 1-(1,1-dioxidothietan-3-yl) 2-methylenesuccinate;
4-cyclohexyl 1-(2-(methylsulfonyl)ethyl) 2-methylenesuccinate;
4-cyclooctyl 1-(1-(methylsulfonyl)propan-2-yl) 2-methylenesuccinate;
1-(1-acetylazetidin-3-yl) 4-cyclooctyl 2-methylenesuccinate;
4-cyclohexyl 1-(tetrahydro-2H-pyran-4-yl) 2-methylenesuccinate;
4-cyclohexyl 1-(2-(2-oxopyrrolidin-1-yl)ethyl) 2-methylenesuccinate;
(S)-1-(1-acetylazetidin-3-yl) 4-(octan-2-yl) 2-methylenesuccinate;
(S)-1-(1,1-dioxidothietan-3-yl) 4-(octan-2-yl) 2-methylenesuccinate;

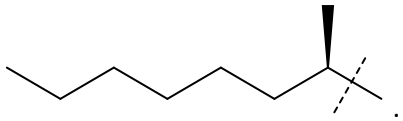
1-(3-methyloxetan-3-yl) 4-octyl 2-methylenesuccinate;
4-cyclooctyl 1-(1-(methylsulfonyl)piperidin-4-yl) 2-methylenesuccinate;
4-cyclooctyl 1-(tetrahydro-2H-pyran-4-yl) 2-methylenesuccinate;
4-cyclooctyl 1-(2-(2-oxopyrrolidin-1-yl)ethyl) 2-methylenesuccinate;
(R)-4-(octan-2-yl) 1-(2-(2-oxopyrrolidin-1-yl)ethyl) 2-methylenesuccinate;
(R)-4-(octan-2-yl) 1-(tetrahydro-2H-pyran-4-yl) 2-methylenesuccinate;
1-(1-acetylazetidin-3-yl) 4-cyclohexyl 2-methylenesuccinate;
4-cyclohexyl 1-(1-(methylsulfonyl)piperidin-4-yl) 2-methylenesuccinate;
4-hexyl 1-(1-(methylsulfonyl)piperidin-4-yl) 2-methylenesuccinate;
4-hexyl 1-(2-(2-oxopyrrolidin-1-yl)ethyl) 2-methylenesuccinate;
1-(2-(1H-tetrazol-5-yl)ethyl) 4-hexyl 2-methylenesuccinate;
2-(N-methyl-2-((2-methylene-4-(octyloxy)-4-oxobutanoyl)oxy)acetamido)acetic acid;
(2-((2-methylene-4-(octyloxy)-4-oxobutanoyl)oxy)acetyl)-L-proline;
N-methyl-N-(2-((2-methylene-4-(octyloxy)-4-oxobutanoyl)oxy)propanoyl)glycine;
(2-((2-methylene-4-(octyloxy)-4-oxobutanoyl)oxy)propanoyl)-L-proline;
(2-((2-methylene-4-(octyloxy)-4-oxobutanoyl)oxy)propanoyl)glycine;
N-(2-((4-(cyclooctyloxy)-2-methylene-4-oxobutanoyl)oxy)acetyl)-N-methylglycine;
(2-((4-(cyclooctyloxy)-2-methylene-4-oxobutanoyl)oxy)acetyl)-L-proline;
(S)-N-methyl-N-(2-((2-methylene-4-(octan-2-yloxy)-4-oxobutanoyl)oxy)acetyl)glycine;
(S)-(2-((2-methylene-4-(octan-2-yloxy)-4-oxobutanoyl)oxy)acetyl)glycine;
1-(2-(4-methylpiperazin-1-yl)-2-oxoethyl) 4-octyl 2-methylenesuccinate;
1-(3-morpholino-3-oxopropyl) 4-octyl 2-methylenesuccinate;
1-(3-(diethylamino)-3-oxopropyl) 4-octyl 2-methylenesuccinate;
1-(3-(methylamino)-3-oxopropyl) 4-octyl 2-methylenesuccinate;
1-(2-((N,N-dimethylsulfamoyl)amino)-2-oxoethyl) 4-hexyl 2-methylenesuccinate;
4-hexyl 1-(2-(methylsulfonamido)-2-oxoethyl) 2-methylenesuccinate;
4-hexyl 1-(3-(methylsulfonamido)-2-oxoethyl) 2-methylenesuccinate;
(E)-4-((4-(cyclohexyloxy)-2-methylene-4-oxobutanoyl)oxy)but-2-enoic acid;
3-((2-((4-(cyclohexyloxy)-2-methylene-4-oxobutanoyl)oxy)ethyl)sulfonyl)propanoic acid;
1-((2H-tetrazol-5-yl)methyl) 4-cyclohexyl 2-methylenesuccinate;
2-((3-((2-((3-chlorophenyl)sulfonyl)ethoxy)carbonyl)but-3-enoyl)oxy)acetic acid;
(R)-2-((4-(cyclohexyloxy)-2-methylene-4-oxobutanoyl)oxy)-2-phenylacetic acid;
1-(2-(1H-tetrazol-5-yl)ethyl) 4-cyclohexyl 2-methylenesuccinate;
(S)-1-(2-(1H-tetrazol-5-yl)ethyl) 4-octan-2-yl 2-methylenesuccinate;
1-(2-(1H-tetrazol-5-yl)ethyl) 4-cyclooctyl 2-methylenesuccinate;
1-(2-((3-chlorophenyl)sulfonyl)-2-methylpropyl) 4-cyclooctyl 2-methylenesuccinate;
4-cyclooctyl 1-(2-methyl-2-(methylsulfonyl)propyl) 2-methylenesuccinate;
1-(1-(1H-tetrazol-5-yl)ethyl) 4-cyclooctyl 2-methylenesuccinate;

1-((1H-tetrazol-5-yl)methyl) 4-cyclooctyl 2-methylenesuccinate;
(R)-1-(2-(1H-tetrazol-5-yl)ethyl) 4-octan-2-yl 2-methylenesuccinate;
(2R,3S)-2-acetamido-3-((4-(cyclooctyloxy)-2-methylene-4-oxobutanoyl)oxy)butanoic acid;
4-cyclooctyl 1-(3-(2-ethoxy-2-oxoethyl)oxetan-3-yl) 2-methylenesuccinate;
4-(2-(methylsulfonyl)ethyl) 1-octyl 2-methyl-3-methylenesuccinate;
1-octyl 4-((S)-tetrahydrofuran-3-yl) 2-methyl-3-methylenesuccinate;
1-(1-(1H-tetrazol-5-yl)propan-2-yl) 4-((R)-octan-2-yl) 2-methylenesuccinate;
1-(1-(1H-tetrazol-5-yl)propan-2-yl) 4-((S)-octan-2-yl) 2-methylenesuccinate;
4-cyclohexyl 1-((2-methyl-2H-tetrazol-5-yl)methyl) 2-methylenesuccinate;
4-cyclohexyl 1-((1-methyl-1H-tetrazol-5-yl)methyl) 2-methylenesuccinate;
2-((4-((adamantan-2-yl)oxy)-2-methylene-4-oxobutanoyl)oxy)acetic acid;
bis((endo)-3-(methylsulfonyl)-3-azabicyclo[3.2.1]octan-8-yl) 2-methylenesuccinate;
1-((endo)-3-(methylsulfonyl)-3-azabicyclo[3.2.1]octan-8-yl) 4-(2-oxaspiro[3.3]heptan-6-yl) 2-methylenesuccinate;
1-((endo)-3-(methylsulfonyl)-3-azabicyclo[3.2.1]octan-8-yl) 4-(oxepan-4-yl) 2-methylenesuccinate;
4-(1-butoxypropan-2-yl) 1-((endo)-3-(methylsulfonyl)-3-azabicyclo[3.2.1]octan-8-yl) 2-methylenesuccinate;
4-spiro[3.3]heptan-2-yl 1-(3,3,3-trifluoro-2,2-dihydroxypropyl) 2-methylenesuccinate hydrate;(*R*)-1-((2H-tetrazol-5-yl)methyl) 4-(octan-2-yl) 2-methylenesuccinate;
1-(2H-tetrazol-5-yl)methyl 4-cycloheptyl 2-methylenesuccinate;
1-(2H-tetrazol-5-yl)methyl 4-spiro[3.3]heptan-2-yl 2-methylenesuccinate;
(*S*)-1-(2H-tetrazol-5-yl)methyl 4-octan-2-yl 2-methylenesuccinate;
1-(1-(1H-tetrazol-5-yl)ethyl) 4-((S)-octan-2-yl) 2-methylenesuccinate;
1-(cyclopropyl(1H-tetrazol-5-yl)methyl) 4-((S)-octan-2-yl) 2-methylenesuccinate;
dicyclohexyl 2-methylenesuccinate; 2-((4-((-adamantan-1-yl)oxy)-2-methylene-4-oxobutanoyl)oxy)acetic acid;2-((4-(bicyclo[3.3.1]nonan-9-yloxy)-2-methylene-4-oxobutanoyl)oxy)acetic acid;
1-(3,3-difluorocyclobutyl) 4-octyl 2-methylenesuccinate;
1-((endo)-3-(methylsulfonyl)-3-azabicyclo[3.2.1]octan-8-yl) 4-((R)-octan-2-yl) 2-methylenesuccinate; and
(*R*)-4-(octan-2-yl) 1-((3-oxo-2,3-dihydroisoxazol-5-yl)methyl) 2-methylenesuccinate;
or a pharmaceutically acceptable salt and/or solvate thereof.

2. The compound or a pharmaceutically acceptable salt and/or solvate thereof according to claim 1, which is a compound of formula (IW-1) wherein R^A is selected from the group consisting of $C_{1–8}$ alkyl, $C_{3–8}$ cycloalkyl and 4–7 membered heterocyclyl.

3. The compound or a pharmaceutically acceptable salt and/or solvate thereof according to claim 2, wherein R^{A} is C_{1-8} alkyl.

4. The compound or a pharmaceutically acceptable salt and/or solvate thereof according to claim 3, wherein R^{A} has the following structure:



5. The compound or a pharmaceutically acceptable salt and/or solvate thereof according to claim 1, which is a compound of formula (IW-1) wherein R^{A} is C_{3-8} cycloalkyl.

6. The compound or a pharmaceutically acceptable salt and/or solvate thereof according to claim 5, wherein R^{A} is cyclobutyl or cyclooctyl.

7. The compound or a pharmaceutically acceptable salt and/or solvate thereof according to claim 6, wherein R^{A} is cyclobutyl.

8. The compound or a pharmaceutically acceptable salt and/or solvate thereof according to claim 1, which is a compound of formula (IW-1) wherein R^{A} is 4–7 membered heterocyclyl.

9. The compound or a pharmaceutically acceptable salt and/or solvate thereof according to claim 8, wherein R^{A} is selected from the group consisting of azetidinyl, oxetanyl and thietanyl.

10. The compound or a pharmaceutically acceptable salt and/or solvate thereof according to any one of claims 1 to 9, which is a compound of formula (IW-1) wherein R^{A} is substituted.

11. The compound or a pharmaceutically acceptable salt and/or solvate thereof according to claim 10, wherein R^{A} is substituted by R^{1A}.

12. The compound or a pharmaceutically acceptable salt and/or solvate thereof according to claim 11, wherein R^{A} is substituted by one R^{1A}.

13. The compound or a pharmaceutically acceptable salt and/or solvate thereof according to any one of claims 1 to 12, which is a compound of formula (IW-1) wherein R^{1A} is selected from the group consisting of fluoro, methyl, cyano, $SiR^{4A}R^{5A}R^{6A}$, phenyl and 5-6 membered heteroaryl; and in particular is selected from the group consisting of fluoro, methyl, cyano, $SiR^{4A}R^{5A}R^{6A}$ and

phenyl.

14. The compound or a pharmaceutically acceptable salt and/or solvate thereof according to claim 13, wherein R^{1A} is phenyl.

15. The compound or a pharmaceutically acceptable salt and/or solvate thereof according to any one of claims 1 to 12, which is a compound of formula (IW-1) wherein R^{1A} is substituted by R^{7A} and/or R^{8A} when R^{1A} is methyl, C_{3-8} cycloalkyl, 4–7 membered heterocyclyl, phenyl or 5-6 membered heteroaryl.

16. The compound or a pharmaceutically acceptable salt and/or solvate thereof according to claim 15, wherein R^{1A} is substituted by R^{7A} and R^{8A} is absent.

17. The compound or a pharmaceutically acceptable salt and/or solvate thereof according to any one of claims 1 to 16, which is a compound of formula (IW-1) wherein R^{7A} is C_{1-4} haloalkyl such as CF_3.

18. The compound or a pharmaceutically acceptable salt and/or solvate thereof according to any one of claims 1 to 17, which is a compound of formula (IW-1) wherein R^{B} is C_{1-2} alkyl substituted by CO_2H.

19. The compound or a pharmaceutically acceptable salt and/or solvate thereof according to any one of claims 1 to 17, which is a compound of formula (IW-1) wherein R^{B} is substituted by CO_2H and at least one other substituent selected from the group consisting of halo, trifluoromethyl and methyl.

20. The compound or a pharmaceutically acceptable salt and/or solvate thereof according to any one of claims 1 to 19, which is a compound of formula (IW-1) wherein R^{C} is H.

21. The compound or a pharmaceutically acceptable salt and/or solvate thereof according to any one of claims 1 to 20, which is a compound of formula (IW-1) wherein R^{D} is H.

22. The compound or a pharmaceutically acceptable salt and/or solvate thereof according to claim 1 which is a compound selected from the group consisting of:
1-(2-cyanoethyl) 4-octyl 2-methylenesuccinate;
1-(2-(methylsulfonyl)ethyl) 4-octyl 2-methylenesuccinate;
4-octyl 1-(3,3,3-trifluoropropyl) 2-methylenesuccinate;
4-octyl 1-(oxetan-3-yl) 2-methylenesuccinate;

4-octyl 1-(2-(2-oxopyrrolidin-1-yl)ethyl) 2-methylenesuccinate;

1-(3-(dimethylamino)-3-oxopropyl) 4-octyl 2-methylenesuccinate;

4-butyl 1-(2-(methylsulfonyl)ethyl) 2-methylenesuccinate;

1-(2-cyanoethyl) 4-butyl 2-methylenesuccinate;

1-(2-(2,5-dioxopyrrolidin-1-yl)ethyl) 4-octyl 2-methylenesuccinate;

1-(2-cyanoethyl) 4-methyl 2-methylenesuccinate;

1-(2-cyanoethyl) 4-hexyl 2-methylenesuccinate;

4-methyl 1-(2-(methylsulfonyl)ethyl) 2-methylenesuccinate;

4-octyl 1-(2-(trifluoromethoxy)ethyl) 2-methylenesuccinate;

4-hexyl 1-(2-(methylsulfonyl)ethyl) 2-methylenesuccinate;

4-methyl 1-(oxetan-3-yl) 2-methylenesuccinate;

1-(2-(N,N-dimethylsulfamoyl)ethyl) 4-octyl 2-methylenesuccinate;

1-(2-(dimethylamino)ethyl) 4-octyl 2-methylenesuccinate;

1-(3-(methylsulfonyl)propyl) 4-octyl 2-methylenesuccinate;

1-(1-(methylsulfonyl)propan-2-yl) 4-octyl 2-methylenesuccinate;

1-(2-(methylsulfonyl)ethyl) 4-(3-phenoxypropyl) 2-methylenesuccinate;

1-(2-(dimethylamino)-2-oxoethyl) 4-octyl 2-methylenesuccinate;

4-isopropyl 1-(2-(methylsulfonyl)ethyl) 2-methylenesuccinate;

(S)-4-octyl 1-(tetrahydrofuran-3-yl) 2-methylenesuccinate;

(R)-4-octyl 1-(tetrahydrofuran-3-yl) 2-methylenesuccinate;

4-cyclooctyl 1-(2-(methylsulfonyl)ethyl) 2-methylenesuccinate;

4-octyl 1-(tetrahydro-2H-pyran-4-yl) 2-methylenesuccinate;

1-(1-cyanopropan-2-yl) 4-octyl 2-methylenesuccinate;

1-(1-(methylsulfonyl)piperidin-4-yl) 4-octyl 2-methylenesuccinate;

1-(2-methoxyethyl) 4-octyl 2-methylenesuccinate;

1-(2-cyano-2-methylpropyl) 4-octyl 2-methylenesuccinate;

1-(1-methoxypropan-2-yl) 4-octyl 2-methylenesuccinate;

1-((1-cyanocyclopropyl)methyl) 4-octyl 2-methylenesuccinate;

1-(2-methoxypropyl) 4-octyl 2-methylenesuccinate;

1-(2-methoxy-2-methylpropyl) 4-octyl 2-methylenesuccinate;

1-(2-morpholinoethyl) 4-octyl 2-methylenesuccinate;

4-(2-(2-ethoxyethoxy)ethyl) 1-(2-(methylsulfonyl)ethyl) 2-methylenesuccinate;

4-butyl 1-(oxetan-3-yl) 2-methylenesuccinate;

4-hexyl 1-(oxetan-3-yl) 2-methylenesuccinate;

4-butyl 1-(2-tosylethyl) 2-methylenesuccinate;

4-octyl 1-(2-tosylethyl) 2-methylenesuccinate;

4-cyclooctyl 1-methyl 2-methylenesuccinate;

1-methyl 4-octyl 2-methylenesuccinate;

dicyclobutyl 2-methylenesuccinate;
di(oxetan-3-yl) 2-methylenesuccinate;
1-cyclobutyl 4-octyl 2-methylenesuccinate;
1-(1-acetoxyethyl) 4-octyl 2-methylenesuccinate;
1-(1,1-dioxidothietan-3-yl) 4-octyl 2-methylenesuccinate;
1-(2-(tert-butoxy)-2-oxoethyl) 4-octyl 2-methylenesuccinate;
2-((2-methylene-4-(octyloxy)-4-oxobutanoyl)oxy)acetic acid;
1-(1-acetylazetidin-3-yl) 4-octyl 2-methylenesuccinate;
1-(2-(4-methylpiperazin-1-yl)ethyl) 4-octyl 2-methylenesuccinate;
1-(2-(1,1-dioxidothiomorpholino)ethyl) 4-octyl 2-methylenesuccinate;
1-(2-(methylsulfonamido)ethyl) 4-octyl 2-methylenesuccinate;
4-cyclooctyl 1-(1,1-dioxidothietan-3-yl) 2-methylenesuccinate;
(R)-1-(2-(methylsulfonyl)ethyl) 4-(octan-2-yl) 2-methylenesuccinate;
1-(1-(methylsulfonyl)propan-2-yl) 4-((R)-octan-2-yl) 2-methylenesuccinate;
(R)-1-(1,1-dioxidothietan-3-yl) 4-(octan-2-yl) 2-methylenesuccinate;
(R)-1-(1-acetylazetidin-3-yl) 4-(octan-2-yl) 2-methylenesuccinate;
4-cyclohexyl 1-(1-(methylsulfonyl)propan-2-yl) 2-methylenesuccinate;
4-cyclohexyl 1-(1,1-dioxidothietan-3-yl) 2-methylenesuccinate;
4-cyclohexyl 1-(2-(methylsulfonyl)ethyl) 2-methylenesuccinate;
4-cyclooctyl 1-(1-(methylsulfonyl)propan-2-yl) 2-methylenesuccinate;
1-(1-acetylazetidin-3-yl) 4-cyclooctyl 2-methylenesuccinate;
4-cyclohexyl 1-(tetrahydro-2H-pyran-4-yl) 2-methylenesuccinate;
4-cyclohexyl 1-(2-(2-oxopyrrolidin-1-yl)ethyl) 2-methylenesuccinate;
(S)-1-(1-acetylazetidin-3-yl) 4-(octan-2-yl) 2-methylenesuccinate;
(S)-1-(1,1-dioxidothietan-3-yl) 4-(octan-2-yl) 2-methylenesuccinate;
1-(3-methyloxetan-3-yl) 4-octyl 2-methylenesuccinate;
4-cyclooctyl 1-(1-(methylsulfonyl)piperidin-4-yl) 2-methylenesuccinate;
4-cyclooctyl 1-(tetrahydro-2H-pyran-4-yl) 2-methylenesuccinate;
4-cyclooctyl 1-(2-(2-oxopyrrolidin-1-yl)ethyl) 2-methylenesuccinate;
(R)-4-(octan-2-yl) 1-(2-(2-oxopyrrolidin-1-yl)ethyl) 2-methylenesuccinate;
(R)-4-(octan-2-yl) 1-(tetrahydro-2H-pyran-4-yl) 2-methylenesuccinate;
1-(1-acetylazetidin-3-yl) 4-cyclohexyl 2-methylenesuccinate;
4-cyclohexyl 1-(1-(methylsulfonyl)piperidin-4-yl) 2-methylenesuccinate;
4-hexyl 1-(1-(methylsulfonyl)piperidin-4-yl) 2-methylenesuccinate;
4-hexyl 1-(2-(2-oxopyrrolidin-1-yl)ethyl) 2-methylenesuccinate;
1-(2-(1H-tetrazol-5-yl)ethyl) 4-hexyl 2-methylenesuccinate;
2-((2-methylene-4-(octyloxy)-4-oxobutanoyl)oxy)propanoic acid;
3-((2-methylene-4-(octyloxy)-4-oxobutanoyl)oxy)propanoic acid;

3-((4-((4-fluorobenzyl)oxy)-2-methylene-4-oxobutanoyl)oxy)propanoic acid;
3-((4-(cyclooctyloxy)-2-methylene-4-oxobutanoyl)oxy)propanoic acid;
3-((2-methylene-4-(neopentyloxy)-4-oxobutanoyl)oxy)propanoic acid;
(S)-3-((2-methylene-4-(octan-2-yloxy)-4-oxobutanoyl)oxy)propanoic acid;
3-((4-(hexyloxy)-2-methylene-4-oxobutanoyl)oxy)propanoic acid;
3-((2-methylene-4-oxo-4-(3-phenoxypropoxy)butanoyl)oxy)propanoic acid;
3-((4-(cyclohexyloxy)-2-methylene-4-oxobutanoyl)oxy)propanoic acid;
(R)-3-((2-methylene-4-(octan-2-yloxy)-4-oxobutanoyl)oxy)propanoic acid;
(S)-2-((2-methylene-4-(octan-2-yloxy)-4-oxobutanoyl)oxy)acetic acid;
2-((4-(cyclooctyloxy)-2-methylene-4-oxobutanoyl)oxy)acetic acid;
2-((4-(cyclohexyloxy)-2-methylene-4-oxobutanoyl)oxy)acetic acid;
2-((2-methylene-4-(neopentyloxy)-4-oxobutanoyl)oxy)acetic acid;
2-((4-((4-fluorobenzyl)oxy)-2-methylene-4-oxobutanoyl)oxy)acetic acid;
2-((4-(hexyloxy)-2-methylene-4-oxobutanoyl)oxy)acetic acid;
2-((2-methylene-4-oxo-4-(3-phenoxypropoxy)butanoyl)oxy)acetic acid;
2-((2-methylene-4-oxo-4-(spiro[3.3]heptan-2-yloxy)butanoyl)oxy)acetic acid;
2-((2-methylene-4-oxo-4-(2-tosylethoxy)butanoyl)oxy)acetic acid;
2-(N-methyl-2-((2-methylene-4-(octyloxy)-4-oxobutanoyl)oxy)acetamido)acetic acid;
(2-((2-methylene-4-(octyloxy)-4-oxobutanoyl)oxy)acetyl)-L-proline;
N-methyl-N-(2-((2-methylene-4-(octyloxy)-4-oxobutanoyl)oxy)propanoyl)glycine;
(2-((2-methylene-4-(octyloxy)-4-oxobutanoyl)oxy)propanoyl)-L-proline;
(2-((2-methylene-4-(octyloxy)-4-oxobutanoyl)oxy)propanoyl)glycine;
N-(2-((4-(cyclooctyloxy)-2-methylene-4-oxobutanoyl)oxy)acetyl)-N-methylglycine;
(2-((4-(cyclooctyloxy)-2-methylene-4-oxobutanoyl)oxy)acetyl)-L-proline;
(S)-N-methyl-N-(2-((2-methylene-4-(octan-2-yloxy)-4-oxobutanoyl)oxy)acetyl)glycine;
(S)-(2-((2-methylene-4-(octan-2-yloxy)-4-oxobutanoyl)oxy)acetyl)glycine;
1-(2-(4-methylpiperazin-1-yl)-2-oxoethyl) 4-octyl 2-methylenesuccinate;
1-(3-morpholino-3-oxopropyl) 4-octyl 2-methylenesuccinate;
1-(3-(diethylamino)-3-oxopropyl) 4-octyl 2-methylenesuccinate;
1-(3-(methylamino)-3-oxopropyl) 4-octyl 2-methylenesuccinate;
2-((4-(cyclohexyloxy)-2-methylene-4-oxobutanoyl)oxy)propanoic acid;
(R)-2-((2-methylene-4-(octan-2-yloxy)-4-oxobutanoyl)oxy)acetic acid;
2-((4-((4,4-difluorocyclohexyl)methoxy)-2-methylene-4-oxobutanoyl)oxy)acetic acid;
2-((4-(3-ethoxypropoxy)-2-methylene-4-oxobutanoyl)oxy)acetic acid;
2-((4-(bicyclo[2.2.1]heptan-2-yloxy)-2-methylene-4-oxobutanoyl)oxy)acetic acid;
2-((4-cyclobutoxy-2-methylene-4-oxobutanoyl)oxy)acetic acid;
3-((4-(cyclohexyloxy)-2-methylene-4-oxobutanoyl)oxy)-2,2-dimethylpropanoic acid;
1-(2-((N,N-dimethylsulfamoyl)amino)-2-oxoethyl) 4-hexyl 2-methylenesuccinate;

4-hexyl 1-(2-(methylsulfonamido)-2-oxoethyl) 2-methylenesuccinate;
4-hexyl 1-(3-(methylsulfonamido)-2-oxoethyl) 2-methylenesuccinate;
2-((4-(cyclohexyloxy)-2-methylene-4-oxobutanoyl)oxy)-3,3,3-trifluoropropanoic acid;
2-((4-(cyclooctyloxy)-2-methylene-4-oxobutanoyl)oxy)-3,3,3-trifluoropropanoic acid;
(E)-4-((4-(cyclohexyloxy)-2-methylene-4-oxobutanoyl)oxy)but-2-enoic acid;
3-((2-((4-(cyclohexyloxy)-2-methylene-4-oxobutanoyl)oxy)ethyl)sulfonyl)propanoic acid;
1-((2H-tetrazol-5-yl)methyl) 4-cyclohexyl 2-methylenesuccinate;
2-((3-((2-((3-chlorophenyl)sulfonyl)ethoxy)carbonyl)but-3-enoyl)oxy)acetic acid;
(R)-2-((4-(cyclohexyloxy)-2-methylene-4-oxobutanoyl)oxy)-2-phenylacetic acid;
1-(2-(1H-tetrazol-5-yl)ethyl) 4-cyclohexyl 2-methylenesuccinate;
(S)-1-(2-(1H-tetrazol-5-yl)ethyl) 4-octan-2-yl 2-methylenesuccinate;
1-(2-(1H-tetrazol-5-yl)ethyl) 4-cyclooctyl 2-methylenesuccinate;
1-(2-((3-chlorophenyl)sulfonyl)-2-methylpropyl) 4-cyclooctyl 2-methylenesuccinate;
4-cyclooctyl 1-(2-methyl-2-(methylsulfonyl)propyl) 2-methylenesuccinate;
1-(1-(1H-tetrazol-5-yl)ethyl) 4-cyclooctyl 2-methylenesuccinate;
1-((1H-tetrazol-5-yl)methyl) 4-cyclooctyl 2-methylenesuccinate;
(R)-1-(2-(1H-tetrazol-5-yl)ethyl) 4-octan-2-yl 2-methylenesuccinate;
(2R,3S)-2-acetamido-3-((4-(cyclooctyloxy)-2-methylene-4-oxobutanoyl)oxy)butanoic acid;
4-cyclooctyl 1-(3-(2-ethoxy-2-oxoethyl)oxetan-3-yl) 2-methylenesuccinate;
4-(2-(methylsulfonyl)ethyl) 1-octyl 2-methyl-3-methylenesuccinate;
1-octyl 4-((S)-tetrahydrofuran-3-yl) 2-methyl-3-methylenesuccinate;
1-(1-(1H-tetrazol-5-yl)propan-2-yl) 4-((R)-octan-2-yl) 2-methylenesuccinate;
1-(1-(1H-tetrazol-5-yl)propan-2-yl) 4-((S)-octan-2-yl) 2-methylenesuccinate;
4-cyclohexyl 1-((2-methyl-2H-tetrazol-5-yl)methyl) 2-methylenesuccinate;
4-cyclohexyl 1-((1-methyl-1H-tetrazol-5-yl)methyl) 2-methylenesuccinate;
3-((4-(cyclooctyloxy)-2-methylene-4-oxobutanoyl)oxy)-4,4,4-trifluorobutanoic acid;
2-(4-(cycloheptyloxy)-2-methylene-4-oxobutanoyloxy)acetic acid;
2-(2-methylene-4-(octan-3-yloxy)-4-oxobutanoyloxy)acetic acid;
2-(2-methylene-4-(octan-4-yloxy)-4-oxobutanoyloxy)acetic acid;
2-((4-(heptan-4-yloxy)-2-methylene-4-oxobutanoyl)oxy) acetic acid;
2-((4-((adamantan-2-yl)oxy)-2-methylene-4-oxobutanoyl)oxy)acetic acid;
2-((4-(1-cyclohexylethoxy)-2-methylene-4-oxobutanoyl)oxy) acetic acid;
2-((4-(1-cycloheptylethoxy)-2-methylene-4-oxobutanoyl)oxy)acetic acid;
2-(2-methylene-4-oxo-4-(spiro[3.4]octan-2-yloxy)butanoyloxy)acetic acid;
2-(2-methylene-4-oxo-4-(spiro[3.5]nonan-2-yloxy)butanoyloxy)acetic acid;
2-(2-methylene-4-oxo-4-(spiro[3.5]nonan-7-yloxy)butanoyloxy)acetic acid;
2-((4-((2,2-dimethylcyclohexyl)oxy)-2-methylene-4-oxobutanoyl)oxy)acetic acid;
bis((endo)-3-(methylsulfonyl)-3-azabicyclo[3.2.1]octan-8-yl) 2-methylenesuccinate;

1-((endo)-3-(methylsulfonyl)-3-azabicyclo[3.2.1]octan-8-yl) 4-(2-oxaspiro[3.3]heptan-6-yl) 2-methylenesuccinate;

1-((endo)-3-(methylsulfonyl)-3-azabicyclo[3.2.1]octan-8-yl) 4-(oxepan-4-yl) 2-methylenesuccinate;

4-(1-butoxypropan-2-yl) 1-((endo)-3-(methylsulfonyl)-3-azabicyclo[3.2.1]octan-8-yl) 2-methylenesuccinate;

4-spiro[3.3]heptan-2-yl 1-(3,3,3-trifluoro-2,2-dihydroxypropyl) 2-methylenesuccinate hydrate;

(*R*)-1-((2H-tetrazol-5-yl)methyl) 4-(octan-2-yl) 2-methylenesuccinate;

1-(2H-tetrazol-5-yl)methyl 4-cycloheptyl 2-methylenesuccinate;

1-(2H-tetrazol-5-yl)methyl 4-spiro[3.3]heptan-2-yl 2-methylenesuccinate;

(*S*)-1-(2H-tetrazol-5-yl)methyl 4-octan-2-yl 2-methylenesuccinate;

1-(1-(1H-tetrazol-5-yl)ethyl) 4-((S)-octan-2-yl) 2-methylenesuccinate;

1-(cyclopropyl(1H-tetrazol-5-yl)methyl) 4-((S)-octan-2-yl) 2-methylenesuccinate;

dicyclohexyl 2-methylenesuccinate;

2-((4-(cyclooctyloxy)-3-methyl-2-methylene-4-oxobutanoyl)oxy)acetic acid;

2-((2-methylene-4-oxo-4-(2,2,4,4-tetramethylcyclobutoxy)butanoyl)oxy) acetic acid;

(*S*)-2-(2-methylene-4-(octan-3-yloxy)-4-oxobutanoyloxy)acetic acid;

2-((4-(cyclooctyloxy)-3-methoxy-2-methylene-4-oxobutanoyl)oxy)acetic acid;

2-((4-((-adamantan-1-yl)oxy)-2-methylene-4-oxobutanoyl)oxy)acetic acid;

(*R*)-2-((4-(heptan-2-yloxy)-2-methylene-4-oxobutanoyl)oxy)acetic acid;

2-((2-methylene-4-(nonan-2-yloxy)-4-oxobutanoyl)oxy)acetic acid;

2-((2-methylene-4-(nonan-5-yloxy)-4-oxobutanoyl)oxy)acetic acid;

2-((4-(1-(3,5-dichlorophenyl)ethoxy)-2-methylene-4-oxobutanoyl)oxy)acetic acid;

2-((4-((1-(3,5-dichlorophenyl)propan-2-yl)oxy)-2-methylene-4-oxobutanoyl)oxy)acetic acid;

(*R*)-2-(2-methylene-4-(octan-3-yloxy)-4-oxobutanoyloxy)acetic acid;

2-((2-methylene-4-oxo-4-(((*1R*,*2S*,*4R*)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)oxy)butanoyl)oxy)acetic acid;

2-((4-(1-cyclohexyl-2,2,2-trifluoroethoxy)-2-methylene-4-oxobutanoyl)oxy)acetic acid;

2-((4-(bicyclo[3.3.1]nonan-9-yloxy)-2-methylene-4-oxobutanoyl)oxy)acetic acid;

(*S*)-2-((2-methylene-4-oxo-4-((1,1,1-trifluorooctan-2-yl)oxy)butanoyl)oxy)acetic acid;

(*R*)-2-((2-methylene-4-(nonan-2-yloxy)-4-oxobutanoyl)oxy)acetic acid;

(*R*)-2-((4-(1-cyclohexylethoxy)-2-methylene-4-oxobutanoyl)oxy)acetic acid;

1-(3,3-difluorocyclobutyl) 4-octyl 2-methylenesuccinate;

1-((endo)-3-(methylsulfonyl)-3-azabicyclo[3.2.1]octan-8-yl) 4-((R)-octan-2-yl) 2-methylenesuccinate;

(*R*)-4-(octan-2-yl) 1-((3-oxo-2,3-dihydroisoxazol-5-yl)methyl) 2-methylenesuccinate;

(*R*)-4,4,4-trifluoro-3-((2-methylene-4-(((R)-octan-2-yl)oxy)-4-oxobutanoyl)oxy)butanoic acid;

2-((4-(cyclooctyloxy)-3-hydroxy-2-methylene-4-oxobutanoyl)oxy)acetic acid;

2-(3-methylene-5-(4-methylheptan-4-yloxy)-5-oxopent-1-en-2-yloxy)acetic acid;
2-((4-(1-cyclohexylcyclobutoxy)-2-methylene-4-oxobutanoyl)oxy)acetic acid;
2-((2-methylene-4-((2-methyloctan-2-yl)oxy)-4-oxobutanoyl)oxy)acetic acid;
2-((2-methylene-4-((2-methylheptan-2-yl)oxy)-4-oxobutanoyl)oxy)acetic acid;
2-((2-methylene-4-oxo-4-(1-pentylcyclobutoxy)butanoyl)oxy) acetic acid;
2-((2-methylene-4-((2-methylspiro[3.5]nonan-2-yl)oxy)-4-oxobutanoyl)oxy)acetic acid;
2-((2-methylene-4-oxo-4-(((exo)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)oxy)butanoyl)oxy)acetic acid;
2-((2-methylene-4-oxo-4-((2,2,6,6-tetramethylcyclohexyl)oxy) butanoyl)oxy)acetic acid;
2-((4-(1-(3,5-dichlorophenyl)ethoxy)-2-methylene-4-oxobutanoyl)oxy)acetic acid (Isomer 1);
2-((4-(1-(3,5-dichlorophenyl)ethoxy)-2-methylene-4-oxobutanoyl)oxy)acetic acid (Isomer 2);
(*R*)-2-((2-methylene-4-oxo-4-(1-(4-(trifluoromethyl)phenyl)ethoxy)butanoyl) oxy) acetic acid);
(*S*)-2-((2-methylene-4-oxo-4-(1-(4-(trifluoromethyl)phenyl)ethoxy)butanoyl) oxy) acetic acid);
2-((4-(1-cyclohexylcyclopropoxy)-2-methylene-4-oxobutanoyl)oxy)acetic acid;
(*S*)-2-((4-(1-cyclohexylethoxy)-2-methylene-4-oxobutanoyl)oxy)acetic acid;
2-((2-methylene-4-oxo-4-((2,2,4,4-tetramethylpentan-3-yl)oxy)butanoyl) oxy)acetic acid;
(*S*)-4,4,4-trifluoro-3-((2-methylene-4-(((*R*)-octan-2-yl)oxy)-4-oxobutanoyl)oxy)butanoic acid;
2-((2-methylene-4-oxo-4-(1-pentylcyclopropoxy)butanoyl)oxy) acetic acid; and
3-((2-methylene-4-oxo-4-(2,2,4,4-tetramethylcyclobutoxy)butanoyl)oxy)propanoic acid;
or a pharmaceutically acceptable salt and/or solvate of any one thereof.

23. A pharmaceutical composition comprising a compound or a pharmaceutically acceptable salt and/or solvate thereof according to any one of claims 1 to 22.

24. A compound or a pharmaceutically acceptable salt and/or solvate thereof according to any one of claims 1 to 22 or a pharmaceutical composition according to claim 23 for use as a medicament.

25. A compound or a pharmaceutically acceptable salt and/or solvate thereof according to any one of claims 1 to 22 or a pharmaceutical composition according to claim 23 for use in treating or preventing an inflammatory disease or a disease associated with an undesirable immune response.

26. Use of a compound or a pharmaceutically acceptable salt and/or solvate thereof according to any one of claims 1 to 22 or a pharmaceutical composition according to claim 23 in the manufacture of a medicament for treating or preventing an inflammatory disease or a disease associated with an undesirable immune response.

27. The use according to claim 26, wherein the inflammatory disease or disease associated with an undesirable immune response is, or is associated with, a disease selected from the group consisting of: psoriasis (including chronic plaque, erythrodermic, pustular, guttate, inverse and nail variants), asthma, chronic obstructive pulmonary disease (COPD, including chronic bronchitis and emphysema), heart failure (including left ventricular failure), myocardial infarction, angina pectoris, other atherosclerosis and/or atherothrombosis-related disorders (including peripheral vascular disease and ischaemic stroke), a mitochondrial and neurodegenerative disease (such as Parkinson's disease, Alzheimer's disease, Huntington's disease, amyotrophic lateral sclerosis, retinitis pigmentosa or mitochondrial encephalomyopathy), autoimmune paraneoplastic retinopathy, transplantation rejection (including antibody-mediated and T cell-mediated forms), multiple sclerosis, transverse myelitis, ischaemia-reperfusion injury (e.g. during elective surgery such as cardiopulmonary bypass for coronary artery bypass grafting or other cardiac surgery, following percutaneous coronary intervention, following treatment of acute ST-elevation myocardial infarction or ischaemic stroke, organ transplantation, or acute compartment syndrome), AGE-induced genome damage, an inflammatory bowel disease (e.g. Crohn’s disease or ulcerative colitis), primary sclerosing cholangitis (PSC), PSC-autoimmune hepatitis overlap syndrome, non-alcoholic fatty liver disease (non-alcoholic steatohepatitis), rheumatica, granuloma annulare, cutaneous lupus erythematosus (CLE), systemic lupus erythematosus (SLE), lupus nephritis, drug-induced lupus, autoimmune myocarditis or myopericarditis, Dressler’s syndrome, giant cell myocarditis, post-pericardiotomy syndrome, drug-induced hypersensitivity syndromes (including hypersensitivity myocarditis), eczema, sarcoidosis, erythema nodosum, acute disseminated encephalomyelitis (ADEM), neuromyelitis optica spectrum disorders, MOG (myelin oligodendrocyte glycoprotein) antibody-associated disorders (including MOG-EM), optic neuritis, CLIPPERS (chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids), diffuse myelinoclastic sclerosis, Addison's disease, alopecia areata, ankylosing spondylitis, other spondyloarthritides (including peripheral spondyloarthritis, that is associated with psoriasis, inflammatory bowel disease, reactive arthritis or juvenile onset forms), antiphospholipid antibody syndrome, autoimmune hemolytic anaemia, autoimmune hepatitis, autoimmune inner ear disease, pemphigoid (including bullous pemphigoid, mucous membrane pemphigoid, cicatricial pemphigoid, herpes gestationis or pemphigoid gestationis, ocular cicatricial pemphigoid), linear IgA disease, Behçet's disease, celiac disease, Chagas disease, dermatomyositis, diabetes mellitus type I, endometriosis, Goodpasture's syndrome, Graves' disease, Guillain-Barre syndrome and its subtypes (including acute inflammatory demyelinating polyneuropathy, AIDP, acute motor axonal neuropathy (AMAN), acute motor and sensory axonal neuropathy (AMSAN), pharyngeal-cervical-brachial variant, Miller-Fisher variant and Bickerstaff's brainstem encephalitis), progressive inflammatory neuropathy, Hashimoto's disease, hidradenitis suppurativa, inclusion body myositis, necrotising myopathy, Kawasaki disease, IgA nephropathy, Henoch-Schonlein purpura, idiopathic

thrombocytopenic purpura, thrombotic thrombocytopenic purpura (TTP), Evans' syndrome, interstitial cystitis, mixed connective tissue disease, undifferentiated connective tissue disease, morphea, myasthenia gravis (including MuSK antibody positive and seronegative variants), narcolepsy, neuromyotonia, pemphigus vulgaris, pernicious anaemia, psoriatic arthritis, polymyositis, primary biliary cholangitis (also known as primary biliary cirrhosis), rheumatoid arthritis, palindromic rheumatism, schizophrenia, autoimmune (meningo-)encephalitis syndromes, scleroderma, Sjogren's syndrome, stiff person syndrome, polymylagia rheumatica, giant cell arteritis (temporal arteritis), Takayasu arteritis, polyarteritis nodosa, Kawasaki disease, granulomatosis with polyangitis (GPA; formerly known as Wegener's granulomatosis), eosinophilic granulomatosis with polyangiitis (EGPA; formerly known as Churg-Strauss syndrome), microscopic polyarteritis/polyangiitis, hypocomplementaemic urticarial vasculitis, hypersensitivity vasculitis, cryoglobulinemia, thromboangiitis obliterans (Buerger's disease), vasculitis, leukocytoclastic vasculitis, vitiligo, acute disseminated encephalomyelitis, adrenoleukodystrophy, Alexander's disease, Alper's disease, balo concentric sclerosis or Marburg disease, cryptogenic organising pneumonia (formerly known as bronchiolitis obliterans organizing pneumonia), Canavan disease, central nervous system vasculitic syndrome, Charcot-Marie-Tooth disease, childhood ataxia with central nervous system hypomyelination, chronic inflammatory demyelinating polyneuropathy (CIDP), diabetic retinopathy, globoid cell leukodystrophy (Krabbe disease), graft-versus-host disease (GVHD) (including acute and chronic forms, as well as intestinal GVHD), hepatitis C (HCV) infection or complication, herpes simplex viral infection or complication, human immunodeficiency virus (HIV) infection or complication, lichen planus, monomelic amyotrophy, cystic fibrosis, pulmonary arterial hypertension (PAH, including idiopathic PAH), lung sarcoidosis, idiopathic pulmonary fibrosis, paediatric asthma, atopic dermatitis, allergic dermatitis, contact dermatitis, allergic rhinitis, rhinitis, sinusitis, conjunctivitis, allergic conjunctivitis, keratoconjunctivitis sicca, dry eye, xerophthalmia, glaucoma, macular oedema, diabetic macular oedema, central retinal vein occlusion (CRVO), macular degeneration (including dry and/or wet age related macular degeneration, AMD), post-operative cataract inflammation, uveitis (including posterior, anterior, intermediate and pan uveitis), iridocyclitis, scleritis, corneal graft and limbal cell transplant rejection, gluten sensitive enteropathy (coeliac disease), dermatitis herpetiformis, eosinophilic esophagitis, achalasia, autoimmune dysautonomia, autoimmune encephalomyelitis, autoimmune oophoritis, autoimmune orchitis, autoimmune pancreatitis, aortitis and periaortitis, autoimmune retinopathy, autoimmune urticaria, Behcet's disease, (idiopathic) Castleman's disease, Cogan's syndrome, IgG4-related disease, retroperitoneal fibrosis, juvenile idiopathic arthritis including systemic juvenile idiopathic arthritis (Still's disease), adult-onset Still's disease, ligneous conjunctivitis, Mooren's ulcer, pityriasis lichenoides et varioliformis acuta (PLEVA, also known as Mucha-Habermann disease), multifocal motor neuropathy (MMN), paediatric acute-onset neuropsychiatric syndrome (PANS) (including paediatric autoimmune neuropsychiatric disorders associated with streptococcal infections

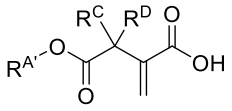
(PANDAS)), paraneoplastic syndromes (including paraneoplastic cerebellar degeneration, Lambert-Eaton myaesthenic syndrome, limbic encephalitis, brainstem encephalitis, opsoclonus myoclonus ataxia syndrome, anti-NMDA receptor encephalitis, thymoma-associated multiorgan autoimmunity), perivenous encephalomyelitis, reflex sympathetic dystrophy, relapsing polychondritis, sperm & testicular autoimmunity, Susac's syndrome, Tolosa-Hunt syndrome, Vogt-Koyanagi-Harada Disease, anti-synthetase syndrome, autoimmune enteropathy, immune dysregulation polyendocrinopathy enteropathy X-linked (IPEX), microscopic colitis, autoimmune lymphoproliferative syndrome (ALPS), autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy syndrome (APEX), gout, pseudogout, amyloid (including AA or secondary amyloidosis), eosinophilic fasciitis (Shulman syndrome) progesterone hypersensitivity (including progesterone dermatitis), amilial Mediterranean fever (FMF), tumour necrosis factor (TNF) receptor-associated periodic fever syndrome (TRAPS), hyperimmunoglobulinaemia D with periodic fever syndrome (HIDS), PAPA (pyogenic arthritis, pyoderma gangrenosum, severe cystic acne) syndrome, deficiency of interleukin-1 receptor antagonist (DIRA), deficiency of the interleukin-36-receptor antagonist (DITRA), cryopyrin-associated periodic syndromes (CAPS) (including familial cold autoinflammatory syndrome [FCAS], Muckle-Wells syndrome, neonatal onset multisystem inflammatory disease [NOMID]), NLRP12-associated autoinflammatory disorders (NLRP12AD), periodic fever aphthous stomatitis (PFAPA), chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature (CANDLE), Majeed syndrome, Blau syndrome (also known as juvenile systemic granulomatosis), macrophage activation syndrome, chronic recurrent multifocal osteomyelitis (CRMO), familial cold autoinflammatory syndrome, mutant adenosine deaminase 2 and monogenic interferonopathies (including Aicardi-Goutières syndrome, retinal vasculopathy with cerebral leukodystrophy, spondyloenchondrodysplasia, STING [stimulator of interferon genes]-associated vasculopathy with onset in infancy, proteasome associated autoinflammatory syndromes, familial chilblain lupus, dyschromatosis symmetrica hereditaria), Schnitzler syndrome; familial cylindromatosis, congenital B cell lymphocytosis, OTULIN-related autoinflammatory syndrome, type 2 diabetes mellitus, insulin resistance and the metabolic syndrome (including obesity-associated inflammation), atherosclerotic disorders (e.g. myocardial infarction, angina, ischaemic heart failure, ischaemic nephropathy, ischaemic stroke, peripheral vascular disease, aortic aneurysm), renal inflammatory disorders (e.g. diabetic nephropathy, membranous nephropathy, minimal change disease, crescentic glomerulonephritis, acute kidney injury, renal transplantation).

28. The compound or pharmaceutical composition according to any one of claims 1 to 23, for use in combination with a further therapeutic agent, such as a corticosteroid (glucocorticoid), retinoid (e.g. acitretin, isotretinoin, tazarotene), anthralin, vitamin D analogue (e.g. cacitriol, calcipotriol), calcineurin inhibitors (e.g. tacrolimus, pimecrolimus), phototherapy or photochemotherapy (e.g. psoralen ultraviolet irradiation, PUVA) or other form of ultraviolet light

irradiation therapy, ciclosporine, a thiopurine (e.g. azathioprine, 6-mercaptopurine), methotrexate, an anti-TNFα agents (e.g. infliximab, etanercept, adalimumab, certolizumab, golimumab or a biosimilar), phosphodiesterase-4 (PDE4) inhibition (e.g. apremilast, crisaborole), anti-IL-17 agent (e.g. brodalumab, ixekizumab, secukinumab), anti-IL12/IL-23 agent (e.g. ustekinumab, briakinumab), anti-IL-23 agent (e.g. guselkumab, tildrakizumab), JAK (Janus Kinase) inhibitor (e.g. tofacitinib, ruxolitinib, baricitinib, filgotinib, upadacitinib), plasma exchange, intravenous immune globulin (IVIG), cyclophosphamide, anti-CD20 B cell depleting agent (e.g. rituximab, ocrelizumab, ofatumumab, obinutuzumab), anthracycline analogue (e.g. mitoxantrone), cladribine, sphingosine 1-phosphate receptor modulator or sphingosine analogue (e.g. fingolimod, siponimod, ozanimod, etrasimod), interferon beta preparation (including interferon beta 1b/1a), glatiramer, anti-CD3 therapy (e.g. OKT3), anti-CD52 targeting agent (e.g. alemtuzumab), leflunomide, teriflunomide, gold compound, laquinimod, potassium channel blocker (e.g. dalfampridine/4-aminopyridine), mycophenolic acid, mycophenolate mofetil, purine analogue (e.g. pentostatin), mTOR (mechanistic target of rapamycin) pathway inhibitor (e.g. sirolimus, everolimus), anti-thymocyte globulin (ATG), IL-2 receptor (CD25) inhibitor (e.g. basiliximab, daclizumab), anti-IL-6 receptor or anti-IL-6 agent (e.g. tocilizumab, siltuximab), Bruton's tyrosine kinase (BTK) inhibitor (e.g. ibrutinib), tyrosine kinase inhibitor (e.g. imatinib), ursodeoxycholic acid, hydroxychloroquine, chloroquine, B cell activating factor (BAFF, also known as BLyS, B lymphocyte stimulator) inhibitor (e.g. belimumab, blisibimod), other B cell targeted therapy including a fusion protein targeting both APRIL (A PRoliferation-Inducing Ligand) and BLyS (e.g. atacicept), PI3K inhibitor including pan-inhibitor or one targeting the p110δ and/or p110γ containing isoforms (e.g. idelalisib, copanlisib, duvelisib), an interferon α receptor inhibitor (e.g. anifrolumab, sifalimumab), T cell co-stimulation blocker (e.g. abatacept, belatacept), thalidomide and its derivatives (e.g. lenalidomide), dapsone, clofazimine, a leukotriene antagonist (e.g. montelukast), theophylline, anti-IgE therapy (e.g. omalizumab), an anti-IL-5 agent (e.g. mepolizumab, reslizumab), a long-acting muscarinic agent (e.g. tiotropium, aclidinium, umeclidinium), a PDE4 inhibitor (e.g. roflumilast), riluzole, a free radical scavenger (e.g. edaravone), a proteasome inhibitor (e.g. bortezomib), a complement cascade inhibitor including one directed against C5 (e.g. eculizumab), immunoadsor, antithymocyte globulin, 5-aminosalicylates and their derivatives (e.g. sulfasalazine, balsalazide, mesalamine), an anti-integrin agent including one targeting α4β1 and/or α4β7 integrins (e.g. natalizumab, vedolizumab), an anti-CD11-α agent (e.g. efalizumab), a non-steroidal anti-inflammatory drug (NSAID) including a salicylate (e.g. aspirin), a propionic acid (e.g. ibuprofen, naproxen), an acetic acid (e.g. indomethacin, diclofenac, etodolac), an oxicam (e.g. meloxicam) a fenamate (e.g. mefenamic acid), a selective or relatively selective COX-2 inhibitor (e.g. celecoxib, etroxicoxib, valdecoxib and etodolac, meloxicam, nabumetone), colchicine, an IL-4 receptor inhibitor (e.g. dupilumab), topical/contact immunotherapy (e.g. diphenylcyclopropenone, squaric acid dibutyl ester), anti-IL-1 receptor therapy (e.g. anakinra), IL-1β inhibitor (e.g. canakinumab), IL-1

neutralising therapy (e.g. rilonacept), chlorambucil, a specific antibiotic with immunomodulatory properties and/or ability to modulate NRF2 (e.g. tetracyclines including minocycline, clindamycin, macrolide antibiotics), anti-androgenic therapy (e.g. cyproterone, spironolactone, finasteride), pentoxifylline, ursodeoxycholic acid, obeticholic acid, fibrate, a cystic fibrosis transmembrane conductance regulator (CFTR) modulator, a VEGF (vascular endothelial growth factor) inhibitor (e.g. bevacizumab, ranibizumab, pegaptanib, aflibercept), pirfenidone or mizoribine.

29. A compound which is:



(III)

wherein:

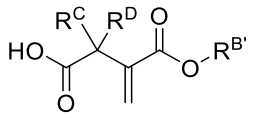
$R^{A'}$ is R^A or a protected derivative thereof;

wherein R^A is as defined in any one of claims 1 to 22;

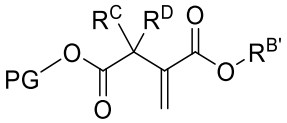
R^C and R^D are as defined in any one of claims 1 to 22;

or a salt thereof.

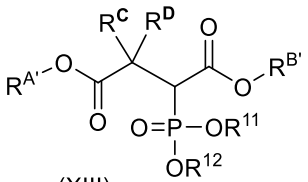
30. A compound which is selected from the group consisting of:



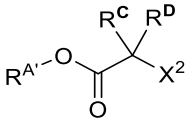
(IX) ;



(VIII) ;



(XIII) ; and



(XI) ;

wherein:

$R^{A'}$ is R^A or a protected derivative thereof;

wherein R^A is as defined in any one of claims 1 to 22;

$R^{B'}$ is R^B or a protected derivative thereof;

wherein R^B is as defined in any one of claims 1 to 22;

R^C and R^D are as defined in any one of claims 1 to 22; and

PG is an oxygen protecting group;

R^{11} is $C_{1–4}$ alkyl optionally substituted with halo;

R^{12} is $C_{1–4}$ alkyl optionally substituted with halo; and

X^2 is a leaving group such as halo e.g., chloro, bromo or iodo;

or a salt thereof.

31. The compound or salt according to claim 29 selected from the group consisting of:
4-(cyclooctyloxy)-2-methylene-4-oxobutanoic acid;
2-methylene-4-oxo-4-(3-phenoxypropoxy)butanoic acid;
4-(2-(2-ethoxyethoxy)ethoxy)-2-methylene-4-oxobutanoic acid;
4-((4-fluorobenzyl)oxy)-2-methylene-4-oxobutanoic acid;
(*R*)-2-methylene-4-(octan-2-yloxy)-4-oxobutanoic acid;
(*S*)-2-methylene-4-(octan-2-yloxy)-4-oxobutanoic acid;
2-methylene-4-(neopentyloxy)-4-oxobutanoic acid;
and
3-methyl-2-methylene-4-(octyloxy)-4-oxobutanoic acid;
or a salt of any one thereof.

32. The compound or salt according to claim 30 which is 3-((2-(tert-butoxy)-2-oxoethoxy)carbonyl)but-3-enoic acid or a salt thereof.