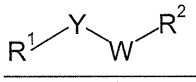
organ fibrosis as well as obesity and/or other metabolic diseases such as diabetes mellitus. Therefore, increased activity of ATX and/or increased levels of LPA, altered LPA receptor expression and altered responses to LPA may contribute to the initiation, progression and/or outcome of a number of different pathophysiological conditions related to the ATX/LPA axis.

In accordance with the invention, the compounds of formula (I) or their pharmaceutically acceptable salts and esters can be used for the treatment or prophylaxis of diseases, disorders or conditions that are associated with the activity of autotaxin and/or the biological activity of lysophosphatidic acid (LPA).

The compounds of formula (I) or their pharmaceutically acceptable salts and esters herein inhibit autotaxin activity and therefore inhibit LPA production and modulate LPA levels and associated signaling. Autotaxin inhibitors described herein are useful as agents for the treatment or prevention of diseases or conditions in which ATX activity and/or LPA signaling participates, is involved in the etiology or pathology of the disease, or is otherwise associated with at least one symptom of the disease. The ATX-LPA axis has been implicated for example in angiogenesis, chronic inflammation, autoimmune diseases, fibrotic diseases, cancer and tumor metastasis and progression, ocular conditions, metabolic conditions such as obesity and/or diabetes mellitus, conditions such as cholestatic or other forms of chronic pruritus as well as acute and chronic organ transplant rejection.

Objects of the ~~present invention~~embodiments disclosed herein are the compounds of formula (I) and their aforementioned salts and esters and their use as therapeutically active substances, a process for the manufacture of the said compounds, intermediates, pharmaceutical compositions, medicaments containing the said compounds, their pharmaceutically acceptable salts or esters, the use of the said compounds, salts or esters for the treatment or prophylaxis of disorders or conditions that are associated with the activity of ATX and/or the biological activity of lysophosphatidic acid (LPA), particularly in the treatment or prophylaxis of renal conditions, liver conditions, inflammatory conditions, conditions of the nervous system, conditions of the respiratory system, vascular and cardiovascular conditions, fibrotic diseases, cancer, ocular conditions, metabolic conditions, cholestatic and other forms of chronic pruritus and acute and chronic organ transplant rejection, and the use of the said compounds, salts or esters for the production of medicaments for the treatment or prophylaxis of renal conditions, liver conditions, inflammatory conditions, conditions of the nervous system, conditions of the respiratory system, vascular and cardiovascular conditions, fibrotic diseases, cancer, ocular conditions, metabolic conditions, cholestatic and other forms of chronic pruritus and acute and chronic organ transplant rejection.

In one aspect, there is provided compounds of formula (I)

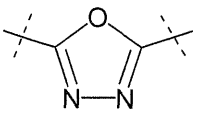
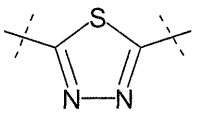


(I)

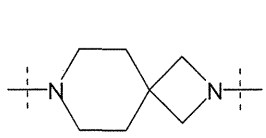
wherein

R^1 is alkyl, haloalkyl, cycloalkyl, substituted phenyl, substituted phenylalkyl, substituted phenoxyalkyl, substituted phenylcycloalkyl, substituted phenylalkenyl, substituted phenylalkynyl, substituted pyridinyl, substituted pyridinylalkyl, substituted pyridinylalkenyl, substituted pyridinylalkynyl, substituted thiophenyl, substituted thiophenylalkyl, substituted thiophenylalkenyl, substituted thiophenylalkynyl, substituted 2,3-dihydro-1H-isoindol-2-yl, substituted 1H-indol-2-yl or substituted benzofuran-2-yl, wherein substituted phenyl, substituted phenylalkyl, substituted phenoxyalkyl, substituted phenylcycloalkyl, substituted phenylalkenyl, substituted phenylalkynyl, substituted pyridinyl, substituted pyridinylalkyl, substituted pyridinylalkenyl, substituted pyridinylalkynyl, substituted thiophenyl, substituted thiophenylalkyl, substituted thiophenylalkenyl, substituted thiophenylalkynyl, substituted 2,3-dihydro-1H-isoindol-2-yl, substituted 1H-indol-2-yl and substituted benzofuran-2-yl are substituted with R^8, R^9 and R^{10};

R^2 is $-(CR^4R^5)_n-R^3$, $-C(O)-R^3$, $-S(O)_2-R^3$ or $-C(O)-NR^6R^3$;

Y is $-OC(O)-$, $-NR^{14}C(O)-$, $-C(O)-$, $-S(O)_2-$,  or , wherein in case R^1 is substituted phenylalkenyl, substituted pyridinylalkenyl or substituted thiophenylalkenyl, then Y is not $-OC(O)-$;

W is selected from one of the following ring systems: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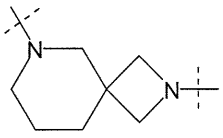
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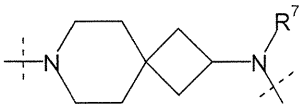
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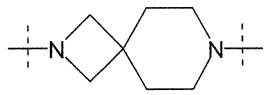
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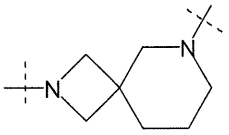
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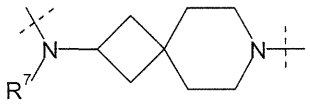
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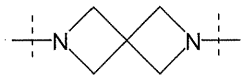
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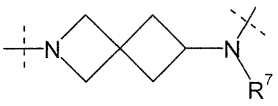
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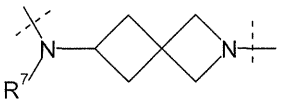
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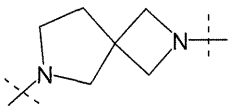
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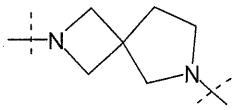
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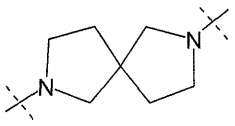
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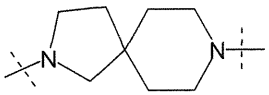
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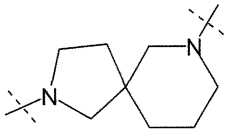
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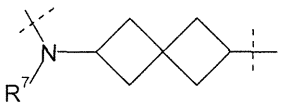
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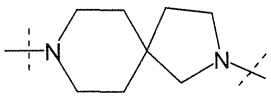
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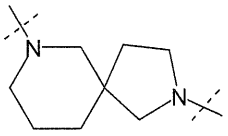
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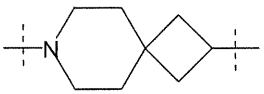
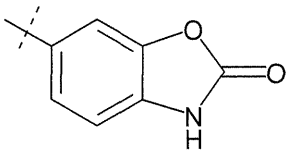

R ;

wherein in case W is the ring system O, then R^2 is $-C(O)-NR^6R^3$;

R^3 is selected from the following groups



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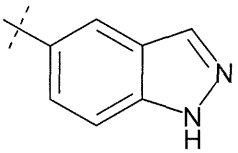

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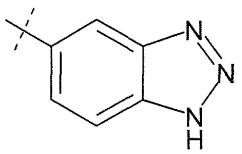

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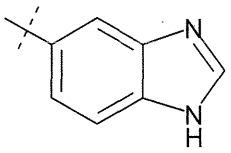

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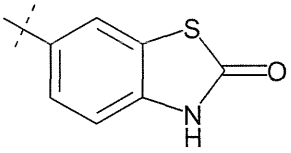

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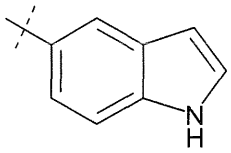

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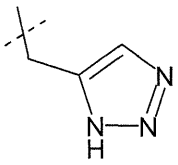

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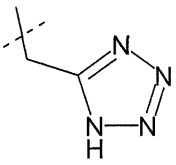

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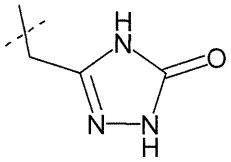

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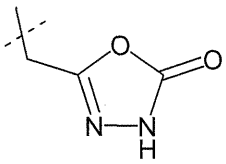

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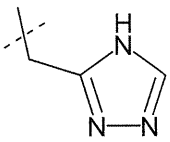

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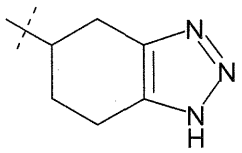

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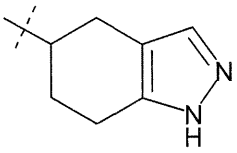

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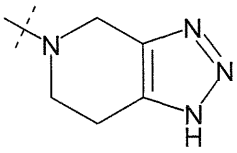

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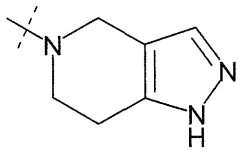

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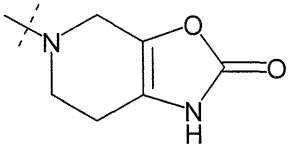

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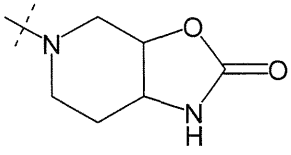

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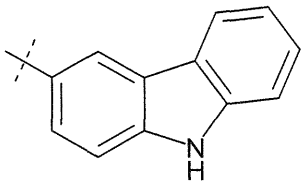


AL ;

R^4 and R^5 are independently selected from H, halogen, alkyl and cycloalkyl;

R^6, R^7 and R^{14} are independently selected from H, alkyl and cycloalkyl;

R^8, R^9, R^{10} are independently selected from H, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, cycloalkylalkoxy, cycloalkoxy, cycloalkoxyalkyl, cycloalkylalkoxyalkyl, alkoxy, alkoxyalkyl, haloalkoxy, haloalkoxyalkyl, alkoxyalkoxy, alkoxyalkoxyalkyl, halogen, hydroxy, cyano, alkylsulfonyl, cycloalkylsulfonyl, substituted aminosulfonyl, substituted amino and substituted aminoalkyl, wherein substituted aminosulfonyl, substituted amino and substituted aminoalkyl are substituted on the nitrogen atom with one to two substituents independently selected from hydrogen, alkyl, cycloalkyl, cycloalkylalkyl, hydroxyalkyl, alkoxyalkyl, alkylcarbonyl and cycloalkylcarbonyl;

n is zero, 1, 2 or 3;

or pharmaceutically acceptable salts.

In another aspect, there is provided a compound selected from

3,5-dichlorobenzyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

benzyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

4-chlorobenzyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

3-chlorobenzyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

1-(2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonan-7-yl)-3-(3,5-dichlorophenyl)propan-1-one;

1-(2-(4-amino-3-hydroxybenzoyl)-2,7-diazaspiro[3.5]nonan-7-yl)-3-(3,5-dichlorophenyl)propan-1-one;

3,5-dichlorobenzyl 2-(4-amino-3-hydroxybenzoyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

6-[(1H-benzotriazole-5-carbonyl)-amino]-2-aza-spiro[3.3]heptane-2-carboxylic acid benzyl ester;

N-(2-(4-phenylbutanoyl)-2-azaspiro[3.3]heptan-6-yl)-1H-benzo[d][1,2,3]triazole-5-carboxamide;

3-chloro-5-(methylsulfonyl)benzyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

[2-(1H-benzotriazole-5-carbonyl)-2-aza-spiro[3.3]hept-6-yl]-carbamic acid benzyl ester;

N-(2-(3-(3,5-dichlorophenyl)propanoyl)-2-azaspiro[3.3]heptan-6-yl)-1H-benzo[d][1,2,3]triazole-5-carboxamide;

[2-(1H-benzotriazole-5-carbonyl)-2-aza-spiro[3.3]hept-6-yl]-carbamic acid 3,5-dichloro-benzyl ester;

6-[(1H-benzotriazole-5-carbonyl)-amino]-2-aza-spiro[3.3]heptane-2-carboxylic acid 3,5-dichloro-benzyl ester;

3,5-dichlorobenzyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,6-diazaspiro[3.4]octane-6-carboxylate;

3,5-dichlorobenzyl 7-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-2-carboxylate;

3,5-dichlorobenzyl 6-(4-amino-3-hydroxybenzamido)-2-azaspiro[3.3]heptane-2-carboxylate;

3-chloro-5-(methylsulfonyl)benzyl 2-(4-sulfamoylbenzoyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

3-chloro-5-(methylsulfonyl)benzyl 2-(3-sulfamoylbenzoyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

3,5-dichlorobenzyl 8-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,8-diazaspiro[4.5]decane-2-carboxylate;

3-fluoro-5-(trifluoromethoxy)benzyl 7-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[4.5]decane-2-carboxylate;

(1H-benzotriazol-5-yl)-{7-[2-(3-chloro-phenyl)-ethanesulfonyl]-2,7-diaza-spiro[3.5]non-2-yl}-methanone;

3,5-dichlorobenzyl 2-(2-oxo-2,3-dihydrobenzo[d]oxazole-6-carbonyl)-2,6-diazaspiro[3.4]octane-6-carboxylate;

3-chloro-5-(methylsulfonyl)benzyl 2-(2-oxo-2,3-dihydrobenzo[d]oxazole-6-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

7-(2-oxo-2,3-dihydro-benzooxazole-6-carbonyl)-2,7-diaza-spiro[3.5]nonane-2-carboxylic acid 3,5-dichloro-benzyl ester;

3,5-dichlorobenzyl 2-(2-oxo-2,3-dihydrobenzo[d]oxazol-6-ylsulfonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

2-oxo-2,3-dihydro-benzooxazole-6-sulfonic acid [2-(4-phenyl-butyryl)-2-aza-spiro[3.3]hept-6-yl]-amide;

benzyl 6-(2-oxo-2,3-dihydrobenzo[d]oxazole-6-sulfonamido)-2-azaspiro[3.3]heptane-2-carboxylate;

2-oxo-2,3-dihydro-benzooxazole-6-sulfonic acid {2-[3-(3,5-dichloro-phenyl)-propionyl]-2-aza-spiro[3.3]hept-6-yl}-amide;

3,5-dichlorobenzyl 6-(2-oxo-2,3-dihydrobenzo[d]oxazole-6-sulfonamido)-2-azaspiro[3.3]heptane-2-carboxylate;

[2-(2-oxo-2,3-dihydro-benzooxazole-6-sulfonyl)-2-aza-spiro[3.3]hept-6-yl]-carbamic acid 3,5-dichloro-benzyl ester;

3-chloro-5-(methylsulfonyl)benzyl 2-(2-oxo-2,3-dihydrobenzo[d]thiazol-6-ylsulfonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

3,5-dichlorobenzyl 2-((2-oxo-2,3-dihydrobenzo[d]oxazol-6-yl)methyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

3,5-dichlorobenzyl 2-(2-oxo-2,3-dihydrobenzo[d]oxazole-6-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

6-(7-(3-(3,5-dichlorophenyl)propanoyl)-2,7-diazaspiro[3.5]nonane-2-carbonyl)benzo[d]oxazol-2(3H)-one;

6-[(2-oxo-2,3-dihydro-benzooxazole-6-carbonyl)-amino]-2-aza-spiro[3.3]heptane-2-carboxylic acid 3,5-dichloro-benzyl ester;

(E)-1-(2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonan-7-yl)-3-(3,5-dichlorophenyl)prop-2-en-1-one;

6-(7-(3-(3,5-dichlorophenyl)propanoyl)-7-azaspiro[3.5]nonan-2-ylamino)benzo[d]oxazol-2(3H)-one;

1-(2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonan-7-yl)-2-(3,5-dichlorophenoxy)ethanone;

(2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonan-7-yl)(3,5-dichlorophenyl)methanone;

6-{7-[(E)-3-(3,5-dichloro-phenyl)-acryloyl]-2,7-diaza-spiro[3.5]nonane-2-carbonyl}-3H-benzooxazol-2-one;

(2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonan-7-yl)(trans-2-(3,5-difluorophenyl)cyclopropyl)methanone;

(7-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[4.4]nonan-2-yl)(5-chloro-1H-indol-2-yl)methanone;

(7-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[4.4]nonan-2-yl)(5-chlorobenzofuran-2-yl)methanone;

(E)-N-((1H-1,2,3-triazol-5-yl)methyl)-7-(3-(4-(trifluoromethoxy)phenyl)acryloyl)-7-azaspiro[3.5]nonane-2-carboxamide;

(1H-benzo[d][1,2,3]triazol-5-yl)(7-(5-(3,5-dichlorophenyl)-1,3,4-oxadiazol-2-yl)-2,7-diazaspiro[3.5]nonan-2-yl)methanone;

(1H-benzo[d][1,2,3]triazol-5-yl)(7-(5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl)-2,7-diazaspiro[3.5]nonan-2-yl)methanone;

(1H-benzo[d][1,2,3]triazol-5-yl)(7-(5-(4-chlorophenyl)-1,3,4-thiadiazol-2-yl)-2,7-diazaspiro[3.5]nonan-2-yl)methanone;

2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-N-(3,5-dichlorobenzyl)-2,7-diazaspiro[3.5]nonane-7-carboxamide;

(2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonan-7-yl)(5-chloroisoindolin-2-yl)methanone;

benzyl 2-(2-oxo-2,3-dihydrobenzo[d]oxazol-6-ylamino)-7-azaspiro[3.5]nonane-7-carboxylate;

4-chloro-3-fluorobenzyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

(2,6-dichloropyridin-4-yl)methyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

3,4-dichlorobenzyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

(5,6-dichloropyridin-3-yl)methyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

2,4-dichlorobenzyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

(6-chloropyridin-3-yl)methyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

4-chloro-3-(methylsulfonyl)benzyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

1-(3,5-dichlorophenyl)ethyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

(5-chloropyridin-3-yl)methyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

(5-bromopyridin-3-yl)methyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

(4,6-dichloropyridin-2-yl)methyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

3-chloro-4-fluorobenzyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

(5-chlorothiophen-3-yl)methyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

thiophen-3-ylmethyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

(5-bromothiophen-3-yl)methyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

4-(trifluoromethyl)benzyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

3,5-dichlorobenzyl 7-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[4.4]nonane-2-carboxylate;

2,4,6-trichlorobenzyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

6-[(1H-benzotriazole-5-carbonyl)-amino]-2-aza-spiro[3.3]heptane-2-carboxylic acid 3-chloro-5-trifluoromethoxy-benzyl ester;

6-[(1H-benzotriazole-5-carbonyl)-amino]-2-aza-spiro[3.3]heptane-2-carboxylic acid 3-trifluoromethyl-benzyl ester;

6-[(1H-benzotriazole-5-carbonyl)-amino]-2-aza-spiro[3.3]heptane-2-carboxylic acid 3-chloro-5-cyano-benzyl ester;

6-[(1H-benzotriazole-5-carbonyl)-amino]-2-aza-spiro[3.3]heptane-2-carboxylic acid 3-chloro-4-fluoro-benzyl ester;

4-(trifluoromethyl)benzyl 2-(2-oxo-2,3-dihydrobenzo[d]oxazole-6-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

6-[(1H-benzotriazole-5-carbonyl)-amino]-2-aza-spiro[3.3]heptane-2-carboxylic acid 3-fluoro-5-trifluoromethyl-benzyl ester;

6-[(1H-benzotriazole-5-carbonyl)-amino]-2-aza-spiro[3.3]heptane-2-carboxylic acid 3-chloro-4-methyl-benzyl ester;

3-(methylsulfonyl)-5-(trifluoromethyl)benzyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

3-(methylsulfonyl)-5-(trifluoromethyl)benzyl 2-(2-oxo-2,3-dihydrobenzo[d]oxazole-6-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

4-chloro-2-(methylsulfonyl)benzyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

2-chloro-4-(methylsulfonyl)benzyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

3,5-dichlorobenzyl 6-(1H-benzo[d][1,2,3]triazol-5-ylcarbamoyl)spiro[3.3]heptan-2-ylcarbamate;

3-fluoro-5-(trifluoromethoxy)benzyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[4.5]decane-7-carboxylate;

3-chloro-5-(methylsulfonyl)benzyl 2-(2-oxo-2,3-dihydrobenzo[d]oxazol-6-ylsulfonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

2-[(3H-[1,2,3]triazol-4-ylmethyl)-carbamoyl]-7-aza-spiro[3.5]nonane-7-carboxylic acid 3,5-dichloro-benzyl ester;

and pharmaceutically acceptable salts thereof.

In another aspect, there is provided a compound selected from

4-(trifluoromethoxy)benzyl 2-(4-sulfamoylbenzoyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

2-fluoro-4-(trifluoromethoxy)benzyl 2-(4-sulfamoylbenzoyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

1-(2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonan-7-yl)-3-(4-(trifluoromethoxy)phenyl)propan-1-one;

3-isopropyl-4-(2-oxo-2-(2-(4,5,6,7-tetrahydro-1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonan-7-yl)ethoxy)benzonitrile;

1-(2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonan-7-yl)-2-(4-chloro-2-isopropylphenoxy)ethanone;

2-(4-chloro-2-isopropylphenoxy)-1-(2-(4,5,6,7-tetrahydro-1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonan-7-yl)ethanone;

1-(2-(4,5,6,7-tetrahydro-1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonan-7-yl)-3-(4-(trifluoromethoxy)phenyl)propan-1-one;

1-(2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonan-7-yl)-3-(3-chlorophenyl)prop-2-yn-1-one;

1-(2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonan-7-yl)-3-(4-chlorophenyl)prop-2-yn-1-one;

3-fluoro-4-(trifluoromethoxy)benzyl 7-(4,5,6,7-tetrahydro-1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-2-carboxylate;

4-(trifluoromethoxy)benzyl 7-(4,5,6,7-tetrahydro-1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-2-carboxylate;

[4-(trifluoromethyl)phenyl]methyl 2-(3a,4,5,6,7,7a-hexahydro-1H-benzotriazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

[2-fluoro-4-(trifluoromethyl)phenyl]methyl 2-(4,5,6,7-tetrahydro-1H-benzotriazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

[2-methyl-4-(trifluoromethoxy)phenyl]methyl 2-(4,5,6,7-tetrahydro-1H-benzotriazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

2-fluoro-4-(2,2,2-trifluoroethoxy)benzyl 2-(4,5,6,7-tetrahydro-1H-benzo[d][1,2,3]triazole-6-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

4-(2,2,2-trifluoroethoxy)benzyl 2-(4,5,6,7-tetrahydro-1H-benzo[d][1,2,3]triazole-6-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

3-fluoro-4-(2,2,2-trifluoroethoxy)benzyl 2-(4,5,6,7-tetrahydro-1H-benzo[d][1,2,3]triazole-6-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

2-fluoro-4-(trifluoromethoxy)benzyl 7-(4,5,6,7-tetrahydro-1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-2-carboxylate;

2-fluoro-4-(trifluoromethoxy)benzyl 2-(4,5,6,7-tetrahydro-1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

4-(trifluoromethoxy)benzyl 2-(4,5,6,7-tetrahydro-1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

3-chloro-5-(trifluoromethyl)benzyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

3-(methylsulfonyl)-5-(trifluoromethyl)benzyl 2-(2-oxo-2,3-dihydrobenzo[d]oxazol-6-ylsulfonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

4-(trifluoromethoxy)benzyl 2-(4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

2-fluoro-4-(trifluoromethoxy)benzyl 2-(4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

[4-(trifluoromethoxy)phenyl]methyl 2-((1H-triazol-4-ylmethyl)carbamoyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

[2-fluoro-4-(trifluoromethoxy)phenyl]methyl 2-((1H-triazol-4-ylmethyl)carbamoyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

(-)-2-fluoro-4-(trifluoromethoxy)benzyl 2-(4,5,6,7-tetrahydro-1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

(+)-2-fluoro-4-(trifluoromethoxy)benzyl 2-(4,5,6,7-tetrahydro-1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

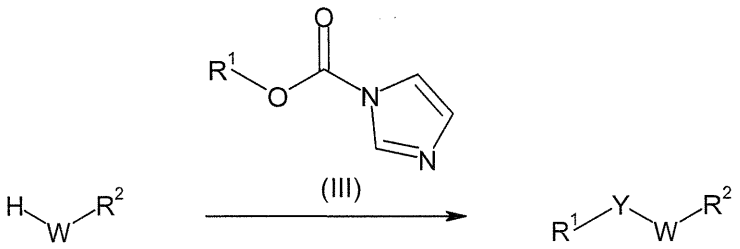
[2-fluoro-4-(trifluoromethyl)phenyl]methyl 2-[4,5,6,7-tetrahydro-1H-benzotriazole-5-carbonyl]-2,7-diazaspiro[3.5]nonane-7-carboxylate (enantiomer A);

[2-fluoro-4-(trifluoromethyl)phenyl]methyl 2-[4,5,6,7-tetrahydro-1H-benzotriazole-5-carbonyl]-2,7-diazaspiro[3.5]nonane-7-carboxylate (enantiomer B);

and pharmaceutically acceptable salts thereof.

In another aspect, there is provided a process to prepare a compound as defined herein comprising

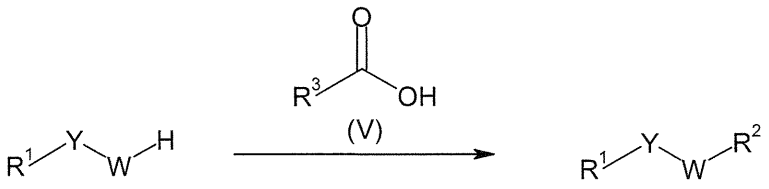
a) the reaction of a compound of formula (II) in the presence of a compound of formula (III);



(II) (III) (I)

or

b) the reaction of a compound of formula (IV) in the presence of a compound of formula (V);



(IV) (V) (I)

wherein in step a) R^1, R^2 and W are as defined herein, Y is -C(O)- and wherein in step b) R^1 and Y are as defined herein, W is A, B, C, D, E, F, G, H, I, J, K, L, M, N, P or Q and R^2 is -C(O)-R^3.

In another aspect, there is provided a compound as defined herein for use as therapeutically active substance.

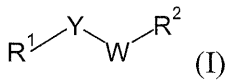
In another aspect, there is provided a pharmaceutical composition comprising a compound as defined herein and a therapeutically inert carrier.

In another aspect, there is provided a compound as defined herein for use in the treatment or prophylaxis of renal conditions, liver conditions, inflammatory conditions, conditions of the nervous system, fibrotic diseases and acute and chronic organ transplant rejection.

In another aspect, there is provided a compound as defined herein, when manufactured according to a process as defined herein.

Claims

1. Compounds of formula (I)

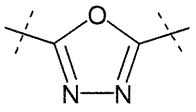
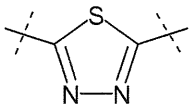


(I)

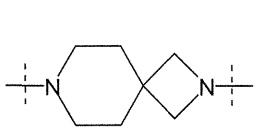
wherein

R^1 is alkyl, haloalkyl, cycloalkyl, substituted phenyl, substituted phenylalkyl, substituted phenoxyalkyl, substituted phenylcycloalkyl, substituted phenylalkenyl, substituted phenylalkynyl, substituted pyridinyl, substituted pyridinylalkyl, substituted pyridinylalkenyl, substituted pyridinylalkynyl, substituted thiophenyl, substituted thiophenylalkyl, substituted thiophenylalkenyl, substituted thiophenylalkynyl, substituted 2,3-dihydro-1H-isoindol-2-yl, substituted 1H-indol-2-yl or substituted benzofuran-2-yl, wherein substituted phenyl, substituted phenylalkyl, substituted phenoxyalkyl, substituted phenylcycloalkyl, substituted phenylalkenyl, substituted phenylalkynyl, substituted pyridinyl, substituted pyridinylalkyl, substituted pyridinylalkenyl, substituted pyridinylalkynyl, substituted thiophenyl, substituted thiophenylalkyl, substituted thiophenylalkenyl, substituted thiophenylalkynyl, substituted 2,3-dihydro-1H-isoindol-2-yl, substituted 1H-indol-2-yl and substituted benzofuran-2-yl are substituted with R^8, R^9 and R^{10}, ~~wherein in case R^1 is alkyl and Y is -C(O)-, then R^3 is selected from the groups S, T, U, V, X, Z, AA, AB, AC, AD, AE, AF, AG, AH, AI, AJ, AK and AL~~;

R^2 is $-(CR^4R^5)_n-R^3$, $-C(O)-R^3$, $-S(O)_2-R^3$ or $-C(O)-NR^6R^3$;

Y is $-OC(O)-$, $-NR^{14}C(O)-$, $-C(O)-$, $-S(O)_2-$,  or , wherein in case R^1 is substituted phenylalkenyl, substituted pyridinylalkenyl or substituted thiophenylalkenyl, then Y is not $-OC(O)-$;

W is selected from one of the following ring systems: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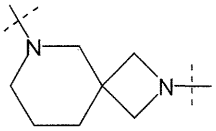
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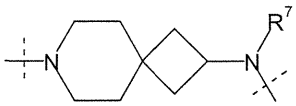
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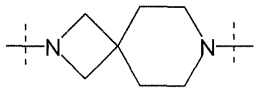
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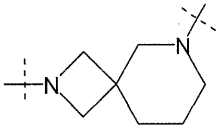
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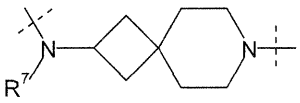
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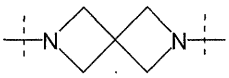
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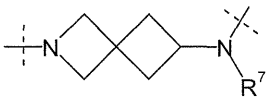
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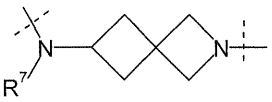
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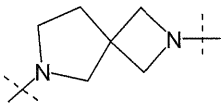
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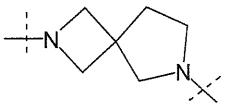
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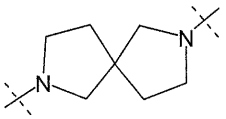
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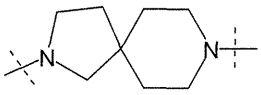
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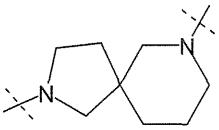
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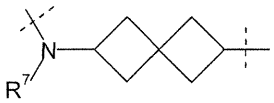
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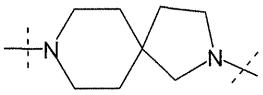
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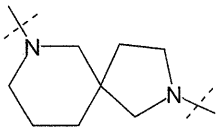
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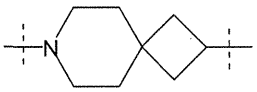

R ;

wherein in case W ~~is one of the ring systems M or N, then R^3 is selected from the groups S, T, U, V, X, Z, AA, AB, AC, AD, AE, AF, AG, AH, AI, AJ, AK and AL and wherein in case W~~ is the ring system O, then R^2 is $-C(O)-NR^6R^3$;

R^3 is selected from the following groups

~~or R^3 is substituted phenyl, substituted pyridinyl or substituted thiophenyl, wherein substituted phenyl, substituted pyridinyl and substituted thiophenyl are substituted with R^{11}, R^{12} and R^{13};~~

R^4 and R^5 are independently selected from H, halogen, alkyl and cycloalkyl;

R^6, R^7 and R^{14} are independently selected from H, alkyl and cycloalkyl;

R^8, R^9, R^{10}~~, R^{11}, R^{12}, and R^{13}~~ are independently selected from H, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, cycloalkylalkoxy, cycloalkoxy, cycloalkoxyalkyl, cycloalkylalkoxyalkyl, alkoxy, alkoxyalkyl, haloalkoxy, haloalkoxyalkyl, alkoxyalkoxy, alkoxyalkoxyalkyl, halogen, hydroxy, cyano, alkylsulfonyl, cycloalkylsulfonyl, substituted aminosulfonyl, substituted amino and substituted aminoalkyl, wherein substituted aminosulfonyl, substituted amino and substituted aminoalkyl are substituted on the nitrogen atom with one to two substituents independently selected from hydrogen, alkyl, cycloalkyl, cycloalkylalkyl, hydroxyalkyl, alkoxyalkyl, alkylcarbonyl and cycloalkylcarbonyl;

n is zero, 1, 2 or 3;

or pharmaceutically acceptable salts.

2. A compound according to claim 1, wherein R^1 is substituted phenyl, substituted phenylalkyl, substituted phenoxyalkyl, substituted phenylcycloalkyl, substituted phenylalkenyl, substituted phenylalkynyl, substituted pyridinylalkyl, substituted thiophenylalkyl, substituted 2,3-dihydro-1H-isoindol-2-yl, substituted 1H-indol-2-yl or substituted benzofuran-2-yl, wherein substituted phenyl, substituted phenylalkyl, substituted phenoxyalkyl, substituted phenylcycloalkyl, substituted phenylalkenyl, substituted pyridinylalkyl, substituted thiophenylalkyl, substituted 2,3-dihydro-1H-isoindol-2-yl, substituted 1H-indol-2-yl and substituted benzofuran-2-yl are substituted with R^8, R^9 and R^{10}.

~~3. A compound according to claim 1 or 2, wherein R^1 is substituted phenyl, substituted phenylalkyl, substituted phenoxyalkyl, substituted phenylcycloalkyl or substituted phenylalkenyl, wherein substituted phenyl, substituted phenylalkyl, substituted phenoxyalkyl, substituted phenylcycloalkyl and substituted phenylalkenyl are substituted with R^8, R^9 and R^{10}.~~

~~4. A compound according to any one of claims 1 to 3, wherein R^1 is phenylalkyl substituted with R^8, R^9 and R^{10}.~~

53. A compound according to any one of claims 1 to 42, wherein R^2 is -C(O)-R^3.

6. A compound according to any one of claims 1 to 5, wherein Y is -OC(O)- or -C(O)-, wherein in case R^1 is substituted phenylalkenyl, substituted pyridinylalkenyl or substituted thiophenylalkenyl, then Y is not -OC(O)-.

74. A compound according to any one of claims 1 to 63, wherein Y is -OC(O)- and R^1 is not substituted phenylalkenyl, substituted pyridinylalkenyl or substituted thiophenylalkenyl.

8. A compound according to any one of claims 1 to 7, wherein W is selected from one of the ring systems A, C, D, H, I, J, L, M, N, O, Q and R, wherein in case W is one of the ring systems M or N, then R^3 is selected from the groups S, T, U, V, X, Z, AA, AB, AC, AD, AE, AF, AG, AH, AI, AJ, AK and AL, and wherein in case W is the ring system O, then R^2 is -C(O)-NR^6R^3.

95. A compound according to any one of claims 1 to 84, wherein W is the ring system A.

10. A compound according to any one of claims 1 to 9, wherein R^3 is substituted phenyl, substituted pyridinyl or substituted thiophenyl, wherein substituted phenyl, substituted pyridinyl and substituted thiophenyl are substituted with R^{11}, R^{12} and R^{13}.

11. A compound according to any one of claims 1 to 9, wherein R^3 is selected from the groups S, T, U, V, X, Z, AA, AB, AC, AD, AE, AF, AG, AH, AI, AJ, AK and AL.

126. A compound according to any one of claims 1 to 9 and 115, wherein R^3 is selected from the groups S, U and AF.

13. A compound according to any one of claims 1 to 12, wherein R^8 is haloalkoxy, halogen or alkylsulfonyl.

14. A compound according to any one of claims 1 to 13, wherein R^9 is alkyl, haloalkyl or halogen.

15. A compound according to any one of claims 1 to 14, wherein R^{10} is H.

167. A compound according to any one of claims 1 to 15, selected from

3,5-dichlorobenzyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

benzyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

4-(trifluoromethyl)benzyl 2-(2-oxo-2,3-dihydrobenzo[d]oxazole-6-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

6-[(1H-benzotriazole-5-carbonyl)-amino]-2-aza-spiro[3.3]heptane-2-carboxylic acid 3-fluoro-5-trifluoromethyl-benzyl ester;

6-[(1H-benzotriazole-5-carbonyl)-amino]-2-aza-spiro[3.3]heptane-2-carboxylic acid 3-chloro-4-methyl-benzyl ester;

3-(methylsulfonyl)-5-(trifluoromethyl)benzyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

3-(methylsulfonyl)-5-(trifluoromethyl)benzyl 2-(2-oxo-2,3-dihydrobenzo[d]oxazole-6-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

4-chloro-2-(methylsulfonyl)benzyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

2-chloro-4-(methylsulfonyl)benzyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

3,5-dichlorobenzyl 6-(1H-benzo[d][1,2,3]triazol-5-ylcarbamoyl)spiro[3.3]heptan-2-ylcarbamate;

3-fluoro-5-(trifluoromethoxy)benzyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[4.5]decane-7-carboxylate;

3-chloro-5-(methylsulfonyl)benzyl 2-(2-oxo-2,3-dihydrobenzo[d]oxazol-6-ylsulfonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

2-[(3H-[1,2,3]triazol-4-ylmethyl)-carbamoyl]-7-aza-spiro[3.5]nonane-7-carboxylic acid 3,5-dichloro-benzyl ester;

and pharmaceutically acceptable salts thereof.

~~17~~8. A compound ~~according to any one of claims 1 to 15,~~ selected from

4-(trifluoromethoxy)benzyl 2-(4-sulfamoylbenzoyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

2-fluoro-4-(trifluoromethoxy)benzyl 2-(4-sulfamoylbenzoyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

~~18~~9. A compound according to any one of claims 1 to ~~16~~8, selected from

3,5-dichlorobenzyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

3-chloro-5-(methylsulfonyl)benzyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

3-chloro-5-(methylsulfonyl)benzyl 2-(2-oxo-2,3-dihydrobenzo[d]oxazole-6-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

3,5-dichlorobenzyl 2-(2-oxo-2,3-dihydrobenzo[d]oxazole-6-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

(E)-1-(2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonan-7-yl)-3-(3,5-dichlorophenyl)prop-2-en-1-one;

3-(methylsulfonyl)-5-(trifluoromethyl)benzyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

[2-methyl-4-(trifluoromethoxy)phenyl]methyl 2-(4,5,6,7-tetrahydro-1H-benzotriazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

(+)-2-fluoro-4-(trifluoromethoxy)benzyl 2-(4,5,6,7-tetrahydro-1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

and pharmaceutically acceptable salts thereof.

~~19~~10. A compound according to any one of claims 1 to ~~15~~ 6 and ~~17~~8, selected from

3,5-dichlorobenzyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

3-chloro-5-(methylsulfonyl)benzyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

3-chloro-5-(methylsulfonyl)benzyl 2-(2-oxo-2,3-dihydrobenzo[d]oxazole-6-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

3,5-dichlorobenzyl 2-(2-oxo-2,3-dihydrobenzo[d]oxazole-6-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

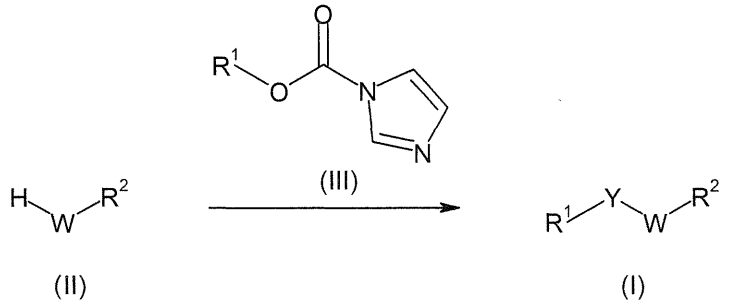
(E)-1-(2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonan-7-yl)-3-(3,5-dichlorophenyl)prop-2-en-1-one;

3-(methylsulfonyl)-5-(trifluoromethyl)benzyl 2-(1H-benzo[d][1,2,3]triazole-5-carbonyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate;

and pharmaceutically acceptable salts thereof.

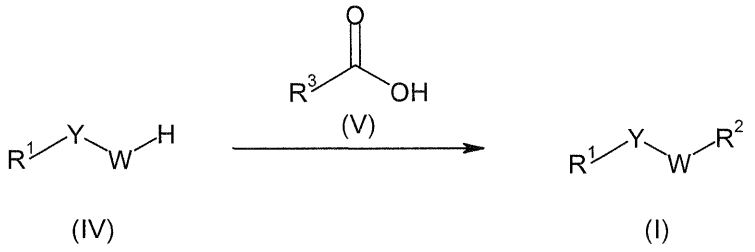
~~20~~11. A process to prepare a compound according to any one of claims 1 to ~~19~~10 comprising

a) the reaction of a compound of formula (II) in the presence of a compound of formula (III);



or

b) the reaction of a compound of formula (IV) in the presence of a compound of formula (V);



wherein in step a) R^1, R^2 and W are as defined in claim 1, Y is -C(O)- and ~~compounds of formula (I) are of formula (In), and~~ wherein in step b) R^1 and Y are as defined in claim 1, W is A, B, C, D, E, F, G, H, I, J, K, L, M, N, P or Q and R^2 is -C(O)-R^3.

~~21~~12. A compound according to any one of claims 1 to ~~19~~10 for use as therapeutically active substance.

~~22~~13. A pharmaceutical composition comprising a compound according to any one of claims 1 to ~~19~~10 and a therapeutically inert carrier.

~~23. The use of a compound according to any one of claims 1 to 19 for the treatment or prophylaxis of renal conditions, liver conditions, inflammatory conditions, conditions of the nervous system, fibrotic diseases and acute and chronic organ transplant rejection.~~

~~24~~14. A compound according to any one of claims 1 to ~~19~~ 10 for use in the treatment or prophylaxis of renal conditions, liver conditions, inflammatory conditions, conditions of the nervous system, fibrotic diseases and acute and chronic organ transplant rejection.

~~25. The use of a compound according to any one of claims 1 to 19 for the preparation of a medicament for the treatment or prophylaxis of renal conditions, liver conditions, inflammatory conditions, conditions of the nervous system, fibrotic diseases and acute and chronic organ transplant rejection.~~

~~26. A method for the treatment or prophylaxis a renal condition selected from the group consisting of renal conditions, liver conditions, inflammatory conditions, conditions of the nervous system, fibrotic diseases and acute and chronic organ transplant rejection, which method comprises administering an effective amount of a compound according to any one of claims 1 to 19.~~

~~27~~15. A compound according to any one of claims 1 to ~~19~~10, when manufactured according to a process of claim ~~20~~11.