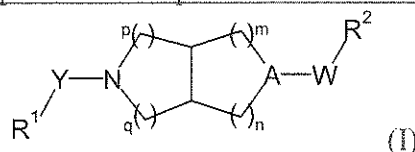


one symptom of the disease. The ATX-LPA axis has been implicated for example in angiogenesis, chronic inflammation, autoimmune diseases, fibrotic diseases, cancer and tumor metastasis and progression, ocular conditions, metabolic conditions such as obesity and/or diabetes mellitus, conditions such as 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.

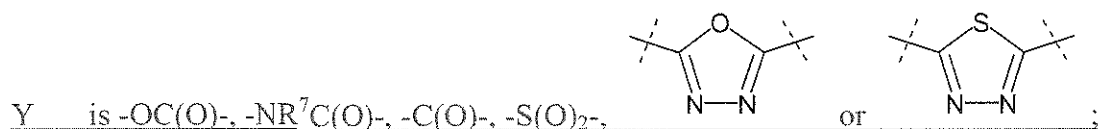
In a first aspect, there is provided compounds of formula (I)



wherein

R¹ is alkyl, haloalkyl, substituted cycloalkyl, substituted cycloalkylalkyl, substituted piperazinyl, substituted piperidinyl, substituted indanyloxyalkyl, 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, naphthyl, substituted naphthyl,

- quinolyl, substituted quinolynyl, isoquinolyl, substituted isoquinolynyl, substituted 2,3-dihydro-1H-isoindol-2-yl, substituted 1H-indol-2-yl or substituted benzofuran-2-yl wherein substituted cycloalkyl, substituted cycloalkylalkyl, substituted piperazinyl, substituted piperidinyl, substituted indanyloxyalkyl, substituted phenyl, substituted phenylalkyl, substituted phenylalkynyl, substituted phenoxyalkyl, substituted phenylcycloalkyl, substituted phenylalkenyl, substituted pyridinyl, substituted pyridinylalkyl, substituted pyridinylalkenyl, substituted pyridinylalkynyl, substituted thiophenyl, substituted thiophenylalkyl, substituted thiophenylalkenyl, substituted thiophenylalkynyl, substituted naphthyl, substituted quinolynyl, substituted isoquinolynyl, 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} ;



A is $-N-$ or CR^5- ;

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

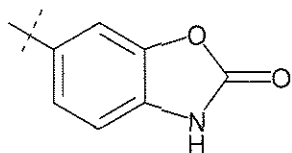
R^3 and R^4 are independently selected from H, halogen, alkyl and cycloalkyl;

- R^5 , R^6 and R^7 are independently selected from H, alkyl and cycloalkyl;

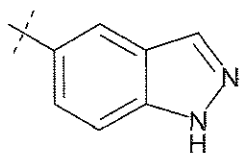
- R^8 , R^9 and R^{10} are independently selected from H, alkyl, hydroxyalkyl, haloalkyl, hydroxyhaloalkyl, cycloalkyl, cycloalkylalkyl, cycloalkylalkoxy, cycloalkoxy, cycloalkoxyalkyl, cycloalkylalkoxyalkyl, alkoxy, alkoxyalkyl, haloalkoxy, alkoxyhaloalkyl, alkoxyalkoxy, alkoxyalkoxyalkyl, phenyl, substituted phenyl, pyridinyl, substituted pyridinyl, pyrrolyl, substituted pyrrolyl, pyrrolydinyl, substituted pyrrolydinyl, tetrahydrofuranyl, substituted tetrahydrofuranyl, halogen, hydroxy, cyano, alkylsulfanyl, haloalkylsulfanyl, cycloalkylsulfanyl, alkylsulfinyl, haloalkylsulfinyl, cycloalkylsulfinyl, alkylcarbonyl, haloalkylcarbonyl, cycloalkylcarbonyl, alkylsulfonyl, haloalkylsulfonyl, 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 H, alkyl, cycloalkyl, cycloalkylalkyl, hydroxyalkyl, alkoxyalkyl, alkylcarbonyl and cycloalkylcarbonyl, and wherein substituted phenyl, substituted pyrrolyl, substituted pyrrolydinyl, substituted tetrahydrofuranyl, and substituted pyridinyl are

substituted with one to three substituents independently selected from alkyl, halogen, haloalkyl, alkoxy and haloalkoxy;

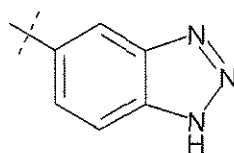
m, n, p and q are independently selected from 1 or 2;



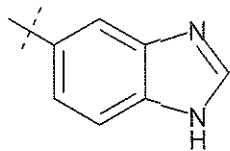
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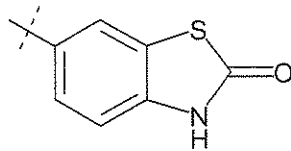
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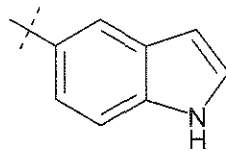
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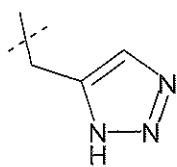
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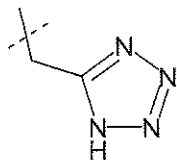
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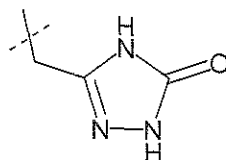
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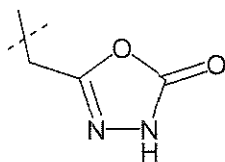
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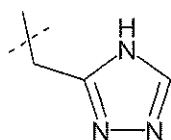
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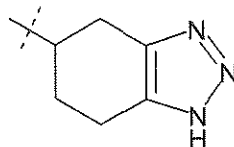
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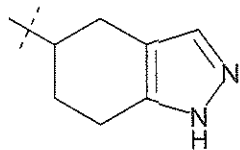
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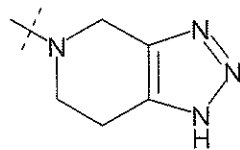
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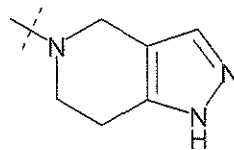
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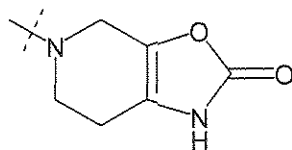
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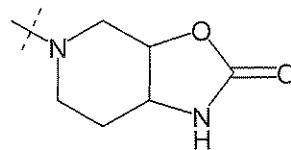
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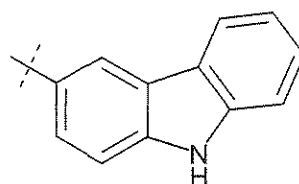
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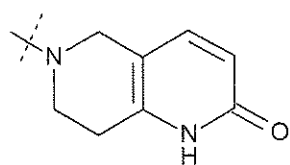
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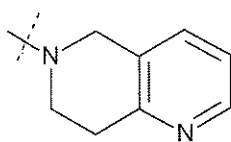
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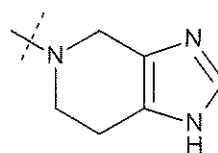
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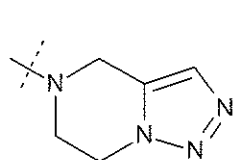
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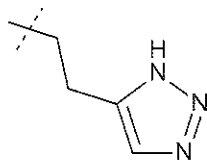
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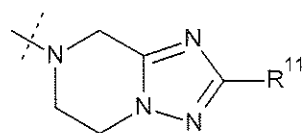
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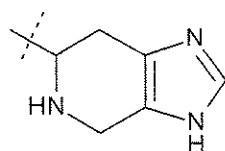
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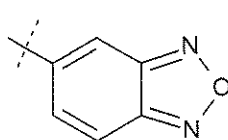
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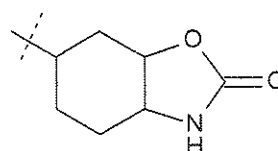
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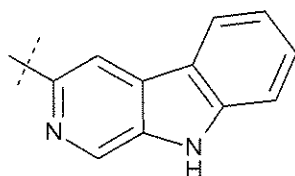
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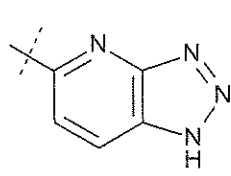
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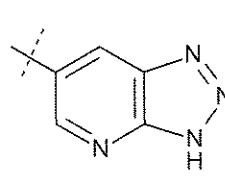
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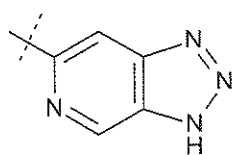
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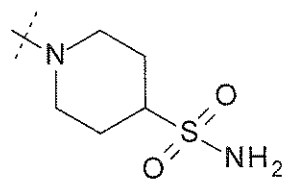
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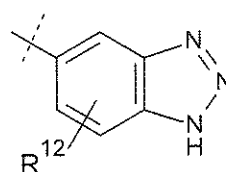
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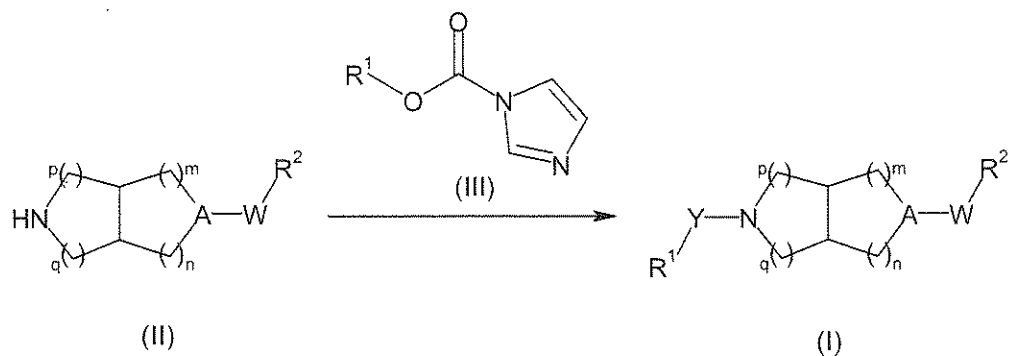
AJ

R^{11} is H, alkyl, haloalkyl or cycloalkyl;

R^{12} is alkyl, halogen, haloalkyl and alkoxy; R^2 is selected from the ring systems B, C, D, E, F, G, H, I, J, K, L, M, N, O, P, Q, R, S, T, U, V, X, Z, AA, AB, AC, AD, AE, AF, AG, AH, AI and AJ;

5 and pharmaceutically acceptable salts.

In a second aspect, there is provided a process to prepare a compound as defined herein comprising the reaction of a compound of formula (II) in the presence of a compound of formula (III), wherein R^1 , R^2 , A, W, m, n, p and q are as defined above, Y is $-\text{OC}(\text{O})-$.



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

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

10 In a fifth aspect, there is provided a compound as defined herein 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.

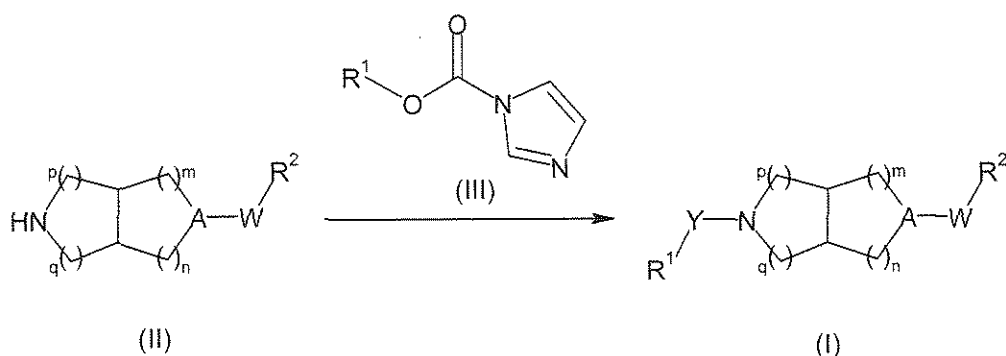
15 In a sixth aspect, there is provided use of a compound as defined herein for the preparation of a medicament for the treatment or prophylaxis of renal conditions, liver conditions, inflammatory conditions, conditions of the nervous system, fibrotic diseases and acute and chronic organ transplant rejection.

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

The term “alkenyl” denotes a monovalent linear or branched hydrocarbon group of 2 to 7 carbon atoms with at least one double bond. In particular embodiments, alkenyl has 2 to 4 carbon atoms with at least one double bond. Examples of alkenyl include ethenyl, propenyl, prop-2-enyl, isopropenyl, n-butenyl and iso-butenyl. Particular alkenyl group is ethenyl.

The term “alkoxy” denotes a group of the formula $-\text{O}-\text{R}'$, wherein R' is an alkyl group. Examples of alkoxy group include methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, isobutoxy and tert-butoxy. Particular alkoxy group include methoxy.

The term “alkoxyalkoxy” denotes an alkoxy group wherein at least one of the hydrogen atoms of the alkoxy group has been replaced by another alkoxy group. Examples of alkoxyalkoxy group include methoxymethoxy, ethoxymethoxy, methoxyethoxy, ethoxyethoxy,



50. A compound according to any one of claims 1 to 48 for use as therapeutically active substance.

5 51. A pharmaceutical composition comprising a compound according to any one of claims 1 to 48 and a therapeutically inert carrier.

~~52. The use of a compound according to any one of claims 1 to 48 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.~~

10 ~~53~~52. A compound according to any one of claims 1 to 48 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.

~~54~~53. The use of a compound according to any one of claims 1 to 48 for the preparation of a medicament for the treatment or prophylaxis of renal conditions, liver conditions,
15 inflammatory conditions, conditions of the nervous system, fibrotic diseases and acute and chronic organ transplant rejection.

~~55. 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
20 method comprises administering an effective amount of a compound according to any one of claims 1 to 48.~~

~~56~~54. A compound according to any one of claims 1 to 48, when manufactured according to a process of claim 49.