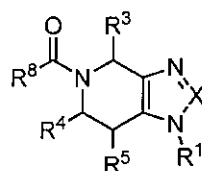


(b) at least one pharmaceutically acceptable excipient.

37. A pharmaceutical composition comprising a therapeutically effective amount of at least one compound of claim 34 and at least one pharmaceutically acceptable excipient.

38. A method of treating a subject suffering from or diagnosed with a disease, disorder, or medical condition mediated by P2X7 receptor activity, comprising administering to a subject in need of such treatment an effective amount of at least one compound selected from compounds of Formula (I):

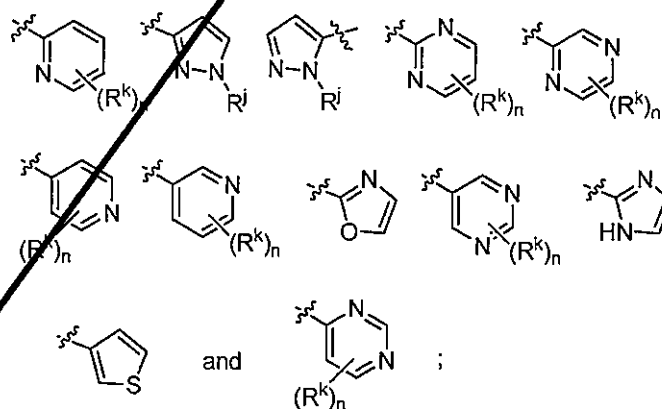


Formula (I)

wherein

~~R¹ is (a) phenyl, optionally substituted with zero to four groups independently selected from the group consisting of halo, C₁-C₄alkyl, alkoxy, perhaloalkyl and perhaloalkoxy; or~~

(b) heteroaryl, independently selected from the group consisting of:



wherein R^k is independently selected from the group consisting of H, halo, C₁-C₃alkyl, hydroxyl, perhaloalkyl and alkoxy;

R^j is independently selected from H or C_1 - C_3 alkyl wherein C_1 - C_3 alkyl is optionally substituted with from one to three halo substituents, one OH substituent or one alkoxy substituent; and
 n is an integer from 0-3;

X is N or CR^2 ;

R^2 is H, perhaloalkyl or C_1 - C_3 lower alkyl;

R^3 is H, perhaloalkyl, C_1 - C_4 alkyl, alkalkoxy, CH_2R^i , $-C(O)R^e$ or phenyl wherein said phenyl is optionally substituted with zero to two groups independently selected from the group consisting of halo, C_1 - C_3 alkyl, alkoxy, perhaloalkyl and perhaloalkoxy;

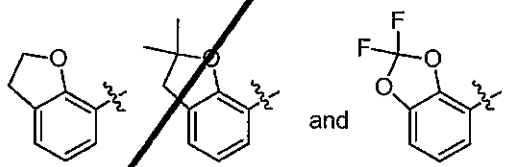
R^i is OH, NC_3H_6 , $N(C_1-C_3alkyl)_2$ or halo;

R^e is OH, OC_1-C_3 alkyl, $N(C_1-C_3alkyl)_2$ or NC_3H_6 ;

R^4 and R^5 are independently H or C_1 - C_3 alkyl;

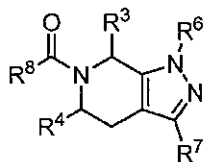
R^8 is phenyl or pyridyl, optionally substituted with zero to four R^m substituents wherein R^m is independently selected from the group consisting of halo, C_1 - C_3 alkyl, hydroxy, alkoxy, perhaloalkyl and perhaloalkoxy; or

R^8 is independently selected from the group consisting of:

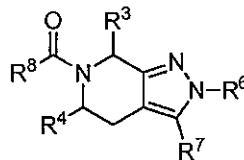


and pharmaceutically acceptable salts of compounds of Formula (I).

39. A method of treating a subject suffering from or diagnosed with a disease, disorder, or medical condition mediated by P2X7 receptor activity, comprising administering to a subject in need of such treatment an effective amount of at least one compound selected from compounds of Formula (IIa and IIb):



Formula (IIa)

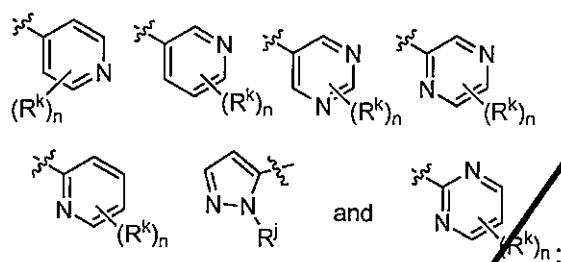


Formula (IIb)

R^3 , R^4 and R^6 are independently H or C_1 - C_3 alkyl;

R^8 is phenyl or pyridyl, optionally substituted with zero to three R^m substituents
wherein R^m is independently selected from the group consisting of: halo,
 C_1 - C_3 alkyl and perhaloalkyl;

R^7 is (a) phenyl, optionally substituted with zero to two groups independently
selected from the group consisting of halo and C_1 - C_3 alkyl; or
(b) heteroaryl, independently selected from the group consisting of:



wherein R^k is halo or C_1 - C_3 alkyl;

R^l is H or C_1 - C_3 alkyl; wherein C_1 - C_3 alkyl is optionally substituted with
one halo substituent or one alkoxy substituent; and

n is an integer from 0-3; and

pharmaceutically acceptable salts of compounds of Formula (IIa and IIb).

40. A method according to claim 38, wherein the disease, disorder, or medical
condition is selected from the group consisting of:

rheumatoid arthritis, osteoarthritis, psoriasis, septic shock, allergic
dermatitis, asthma, allergic asthma, mild to severe asthma, steroid resistant
asthma, idiopathic pulmonary fibrosis, allergic rhinitis, chronic obstructive
pulmonary disease; airway hyper-responsiveness, diseases of the nervous and
neuro-immune system, acute and chronic pain states of neuropathic pain,
inflammatory pain, spontaneous pain, opioid induced pain, diabetic neuropathy,
postherpetic neuralgia, low back pain, chemotherapy-induced neuropathic pain,
fibromyalgia, diseases involved with and without neuroinflammation of the central
nervous system, mood disorders, major depression, major depressive disorder,
treatment resistant depression, bipolar disorder, anxious depression, anxiety,
cognition, sleep disorders, multiple sclerosis, epileptic seizures, Parkinson's
disease, schizophrenia, Alzheimer's disease, Huntington's disease, autism, spinal
cord injury and cerebral ischemia/traumatic brain injury, stress-related disorders,

diseases of the cardiovascular, metabolic, gastrointestinal and urogenital systems such as diabetes, diabetes mellitus, thrombosis, irritable bowel syndrome, irritable bowel disease, Crohn's disease, ischemic heart disease, ischaemia, hypertension, cardiovascular disease, myocardial infarction, and lower urinary tract dysfunction such as incontinence, lower urinary tract syndrome, Polycystic Kidney Disease, Glomerulonephritis, skeletal disorders, osteoporosis, osteopetrosis, and glaucoma, interstitial cystitis, cough, ureteric obstruction, sepsis, Amyotrophic Lateral Sclerosis, Chaga's Disease, chlamydia, neuroblastoma, Tuberculosis, and migraine.

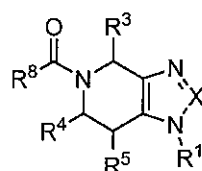
41. A method according to claim 39, wherein the disease, disorder, or medical condition is selected from the group consisting of:

rheumatoid arthritis, osteoarthritis, psoriasis, septic shock, allergic dermatitis, asthma, allergic asthma, mild to severe asthma, steroid resistant asthma, idiopathic pulmonary fibrosis, allergic rhinitis, chronic obstructive pulmonary disease; airway hyper-responsiveness, diseases of the nervous and neuro-immune system, acute and chronic pain states of neuropathic pain, inflammatory pain, spontaneous pain, opioid induced pain, diabetic neuropathy, postherpetic neuralgia, low back pain, chemotherapy-induced neuropathic pain, fibromyalgia, diseases involved with and without neuroinflammation of the central nervous system, mood disorders, major depression, major depressive disorder, treatment resistant depression, bipolar disorder, anxious depression, anxiety, cognition, sleep disorders, multiple sclerosis, epileptic seizures, Parkinson's disease, schizophrenia, Alzheimer's disease, Huntington's disease, autism, spinal cord injury and cerebral ischemia/traumatic brain injury, stress-related disorders, diseases of the cardiovascular, metabolic, gastrointestinal and urogenital systems such as diabetes, diabetes mellitus, thrombosis, irritable bowel syndrome, irritable bowel disease, Crohn's disease, ischemic heart disease, ischaemia, hypertension, cardiovascular disease, myocardial infarction, and lower urinary tract dysfunction such as incontinence, lower urinary tract syndrome, Polycystic Kidney Disease, Glomerulonephritis, skeletal disorders, osteoporosis, osteopetrosis, and glaucoma, interstitial cystitis, cough, ureteric obstruction, sepsis, Amyotrophic Lateral Sclerosis, Chaga's Disease, chlamydia, neuroblastoma, Tuberculosis, and migraine.

42. The method of claim 38 wherein the disease, disorder or medical condition is treatment resistant depression.

43. The method of claim 39, wherein the disease, disorder or medical condition is treatment resistant depression.

44. A process for the preparation of a compound of Formula (I)

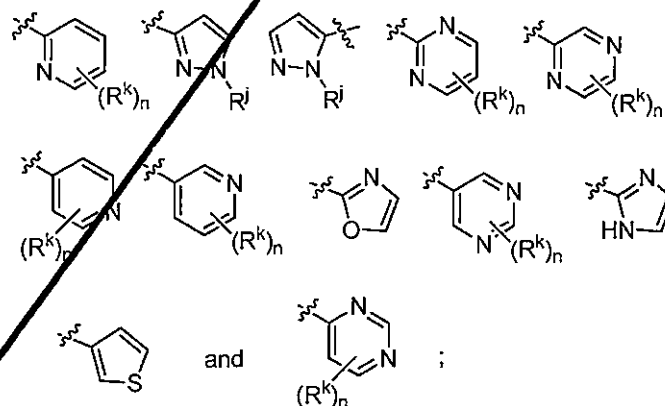


Formula (I)

wherein

R^1 is (a) phenyl, optionally substituted with zero to four groups independently selected from the group consisting of halo, C_1 - C_4 alkyl, alkoxy, perhaloalkyl and perhaloalkoxy; or

(b) heteroaryl, independently selected from the group consisting of:



wherein R^k is independently selected from the group consisting of H, halo, C_1 - C_3 alkyl, hydroxyl, perhaloalkyl and alkoxy;

R^j is independently selected from H or C_1 - C_3 alkyl wherein C_1 - C_3 alkyl is optionally substituted with from one to three halo substituents, one OH substituent or one alkoxy substituent; and

n is an integer from 0-3;

X is N or CR²;

R² is H, perhaloalkyl or C₁-C₃ lower alkyl;

R³ is H, perhaloalkyl, C₁-C₄ alkyl, alkalkoxy, CH₂Rⁱ, -C(O)R^e or phenyl, wherein said phenyl is optionally substituted with zero to two groups independently selected from the group consisting of halo, C₁-C₃alkyl, alkoxy, perhaloalkyl and perhaloalkoxy;

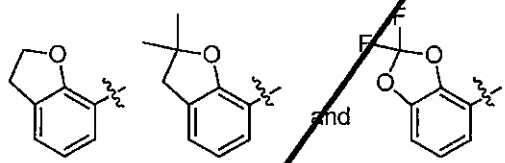
Rⁱ is OH, NC₃H₆, N(C₁-C₃alkyl)₂ or halo;

R^e is OH, OC₁-C₃ alkyl, N(C₁-C₃alkyl)₂, or NC₃H₆;

R⁴ and R⁵ are independently H or C₁-C₃ alkyl;

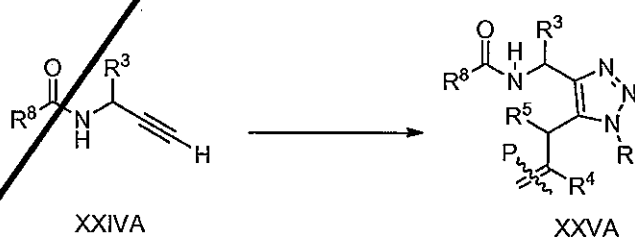
R⁸ is phenyl or pyridyl, optionally substituted with zero to four R^m substituents wherein R^m is independently selected from the group consisting of halo, C₁-C₃alkyl, hydroxy, alkoxy, perhaloalkyl and perhaloalkoxy; or

R⁸ is independently selected from the group consisting of:

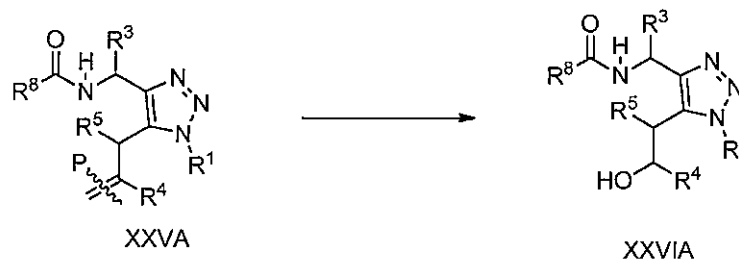


and pharmaceutically acceptable salts of compounds of Formula (I) comprising the steps:

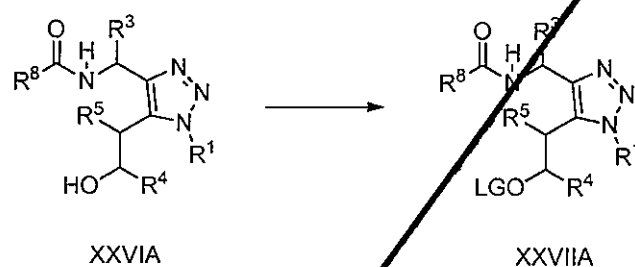
- (a) reacting compound XXIVA with an azide source, an alkylating agent, a first base and a copper (I) salt in a first organic solvent at a temperature of about -78 °C, to form compound XXVA;



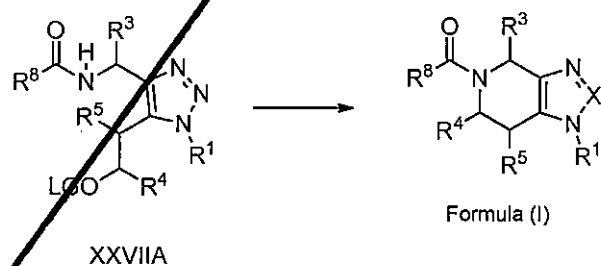
- (b) reacting compound XXVA with ozone in a second organic solvent chosen from the group consisting of: methanol, dichloromethane and tetrahydrofuran, at a temperature of about -78 °C, and subsequently treating the reaction mixture with NaBH₄ to form compound XXVIA;



- (c) reacting compound XXVIA with a sulfonyl chloride in a third organic solvent, a second base, and an acylation catalyst, to form compound XXVIIA; and



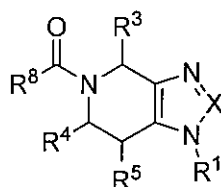
- (d) reacting compound XXVIIA in a fourth solvent, with a third base at a temperature of about 60 °C for approximately 3 hours to form a compound of Formula (I).



(b) at least one pharmaceutically acceptable excipient.

37. A pharmaceutical composition comprising a therapeutically effective amount of at least one compound of claim 34 and at least one pharmaceutically acceptable excipient.

38. The use of an effective amount of at least one compound selected from compounds of Formula (I):



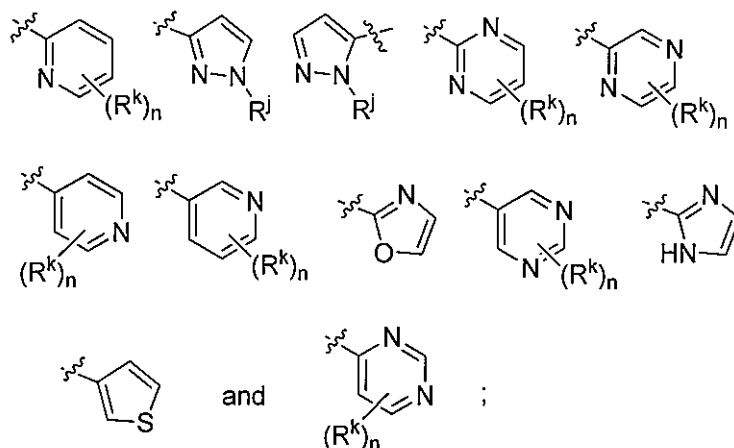
Formula (I)

in the manufacture of a medicament for the treatment of a disease, disorder, or medical condition mediated by P2X7 receptor activity,

wherein

R^1 is (a) phenyl, optionally substituted with zero to four groups independently selected from the group consisting of halo, C_1 - C_4 alkyl, alkoxy, perhaloalkyl and perhaloalkoxy; or

(b) heteroaryl, independently selected from the group consisting of:



wherein R^k is independently selected from the group consisting of H, halo, C_1 - C_3 alkyl, hydroxyl, perhaloalkyl and alkoxy;

R^1 is independently selected from H or C_1 - C_3 alkyl wherein C_1 - C_3 alkyl is optionally substituted with from one to three halo substituents, one OH substituent or one alkoxy substituent; and

n is an integer from 0-3;

X is N or CR^2 ;

R^2 is H, perhaloalkyl or C_1 - C_3 lower alkyl;

R^3 is H, perhaloalkyl, C_1 - C_4 alkyl, alkalkoxy, CH_2R^1 , $-C(O)R^e$ or phenyl, wherein said phenyl is optionally substituted with zero to two groups independently selected from the group consisting of halo, C_1 - C_3 alkyl, alkoxy, perhaloalkyl and perhaloalkoxy;

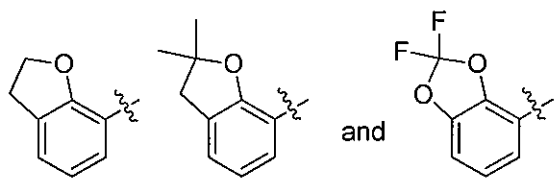
R^1 is OH, NC_3H_6 , $N(C_1-C_3alkyl)_2$ or halo;

R^e is OH, OC_1-C_3 alkyl, $N(C_1-C_3alkyl)_2$, or NC_3H_6 ;

R^4 and R^5 are independently H or C_1 - C_3 alkyl;

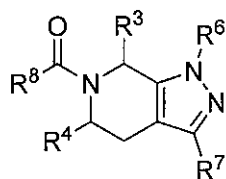
R^8 is phenyl or pyridyl, optionally substituted with zero to four R^m substituents wherein R^m is independently selected from the group consisting of halo, C_1 - C_3 alkyl, hydroxy, alkoxy, perhaloalkyl and perhaloalkoxy; or

R^8 is independently selected from the group consisting of:

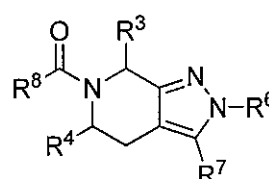


and pharmaceutically acceptable salts of compounds of Formula (I).

39. The use of an effective amount of at least one compound selected from compounds of Formula (IIa and IIb):



Formula (IIa)



Formula (IIb)

in the manufacture of a medicament for the treatment of a disease, disorder, or medical condition mediated by P2X7 receptor activity,

wherein

cord injury and cerebral ischemia/traumatic brain injury, stress-related disorders, diseases of the cardiovascular, metabolic, gastrointestinal and urogenital systems such as diabetes, diabetes mellitus, thrombosis, irritable bowel syndrome, irritable bowel disease, Crohn's disease, ischemic heart disease, ischaemia, hypertension, cardiovascular disease, myocardial infarction, and lower urinary tract dysfunction such as incontinence, lower urinary tract syndrome, Polycystic Kidney Disease, Glomerulonephritis, skeletal disorders, osteoporosis, osteopetrosis, and glaucoma, interstitial cystitis, cough, ureteric obstruction, sepsis, Amyotrophic Lateral Sclerosis, Chaga's Disease, chlamydia, neuroblastoma, Tuberculosis, and migraine.

41. The use according to claim 39, wherein the disease, disorder, or medical condition is selected from the group consisting of:

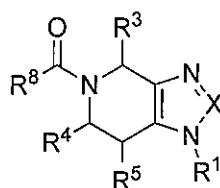
rheumatoid arthritis, osteoarthritis, psoriasis, septic shock, allergic dermatitis, asthma, allergic asthma, mild to severe asthma, steroid resistant asthma, idiopathic pulmonary fibrosis, allergic rhinitis, chronic obstructive pulmonary disease; airway hyper-responsiveness, diseases of the nervous and neuro-immune system, acute and chronic pain states of neuropathic pain, inflammatory pain, spontaneous pain, opioid induced pain, diabetic neuropathy, postherpetic neuralgia, low back pain, chemotherapy-induced neuropathic pain, fibromyalgia, diseases involved with and without neuroinflammation of the central nervous system, mood disorders, major depression, major depressive disorder, treatment resistant depression, bipolar disorder, anxious depression, anxiety, cognition, sleep disorders, multiple sclerosis, epileptic seizures, Parkinson's disease, schizophrenia, Alzheimer's disease, Huntington's disease, autism, spinal cord injury and cerebral ischemia/traumatic brain injury, stress-related disorders, diseases of the cardiovascular, metabolic, gastrointestinal and urogenital systems such as diabetes, diabetes mellitus, thrombosis, irritable bowel syndrome, irritable bowel disease, Crohn's disease, ischemic heart disease, ischaemia, hypertension, cardiovascular disease, myocardial infarction, and lower urinary tract dysfunction such as incontinence, lower urinary tract syndrome, Polycystic Kidney Disease, Glomerulonephritis, skeletal disorders, osteoporosis, osteopetrosis, and glaucoma, interstitial cystitis, cough, ureteric obstruction, sepsis, Amyotrophic Lateral

Sclerosis, Chaga's Disease, chlamydia, neuroblastoma, Tuberculosis, and migraine.

42. The use of claim 38 wherein the disease, disorder or medical condition is treatment resistant depression.

43. The use of claim 39, wherein the disease, disorder or medical condition is treatment resistant depression.

44. A process for the preparation of a compound of Formula (I)

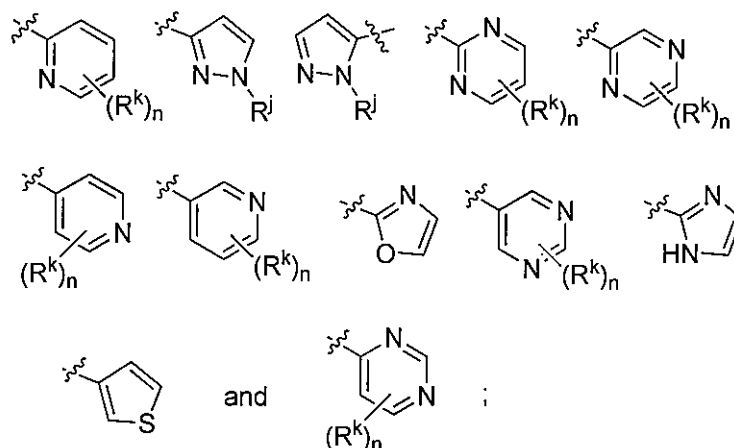


Formula (I)

wherein

R¹ is (a) phenyl, optionally substituted with zero to four groups independently selected from the group consisting of halo, C₁-C₄alkyl, alkoxy, perhaloalkyl and perhaloalkoxy; or

(b) heteroaryl, independently selected from the group consisting of:



wherein R^k is independently selected from the group consisting of H, halo, C₁-C₃alkyl, hydroxyl, perhaloalkyl and alkoxy;

R^j is independently selected from H or C_1 - C_3 alkyl wherein C_1 - C_3 alkyl is optionally substituted with from one to three halo substituents, one OH substituent or one alkoxy substituent; and

n is an integer from 0-3;

X is N or CR^2 ;

R^2 is H, perhaloalkyl or C_1 - C_3 lower alkyl;

R^3 is H, perhaloalkyl, C_1 - C_4 alkyl, alkalkoxy, CH_2R^i , $-C(O)R^e$ or phenyl, wherein said phenyl is optionally substituted with zero to two groups independently selected from the group consisting of halo, C_1 - C_3 alkyl, alkoxy, perhaloalkyl and perhaloalkoxy;

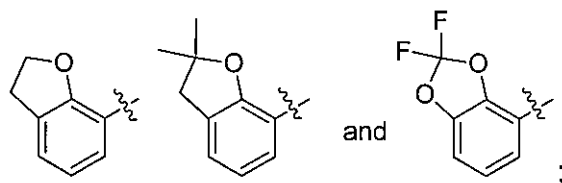
R^i is OH, NC_3H_6 , $N(C_1-C_3alkyl)_2$ or halo;

R^e is OH, OC_1-C_3 alkyl, $N(C_1-C_3alkyl)_2$, or NC_3H_6 ;

R^4 and R^5 are independently H or C_1 - C_3 alkyl;

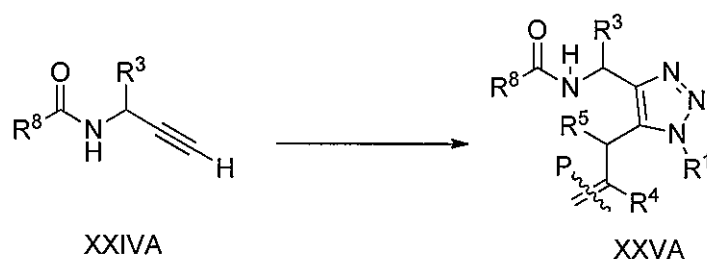
R^8 is phenyl or pyridyl, optionally substituted with zero to four R^m substituents wherein R^m is independently selected from the group consisting of halo, C_1 - C_3 alkyl, hydroxy, alkoxy, perhaloalkyl and perhaloalkoxy; or

R^8 is independently selected from the group consisting of:

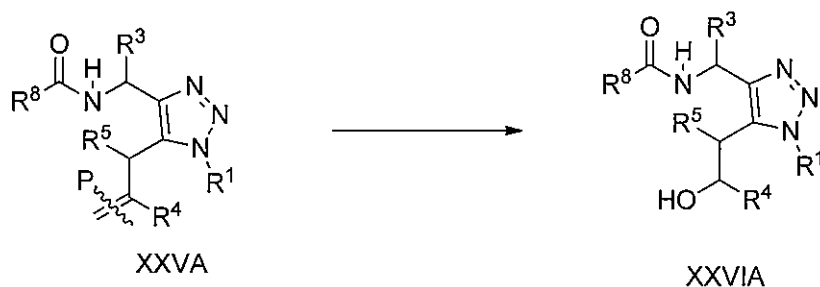


and pharmaceutically acceptable salts of compounds of Formula (I) comprising the steps:

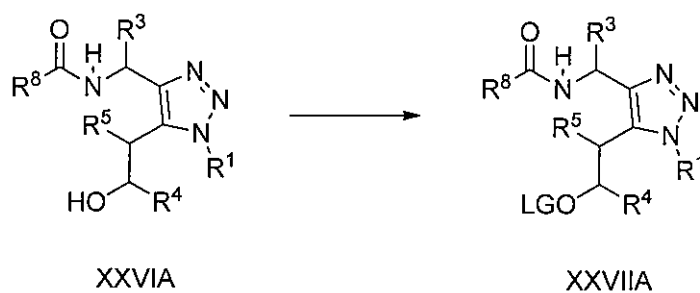
- (a) reacting compound XXIVA with an azide source, an alkylating agent, a first base and a copper (I) salt in a first organic solvent at a temperature of about $-78^\circ C$, to form compound XXVA;



- (b) reacting compound XXVA with ozone in a second organic solvent chosen from the group consisting of: methanol, dichloromethane and tetrahydrofuran, at a temperature of about -78°C , and subsequently treating the reaction mixture with NaBH_4 to form compound XXVIA;



- (c) reacting compound XXVIA with a sulfonyl chloride in a third organic solvent, a second base, and an acylation catalyst, to form compound XXVIIA; and



- (d) reacting compound XXVIIA in a fourth solvent, with a third base at a temperature of about 60°C for approximately 3 hours to form a compound of Formula (I).

