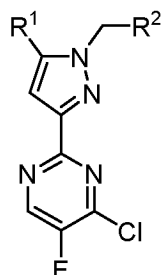


CLAIMS

1. A process for preparing a compound of **Formula II**:



Formula II

wherein:

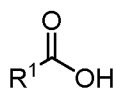
R^1 is unsubstituted phenyl or 5 to 6-membered heteroaryl ring containing up to three ring heteroatoms independently selected from N, O or S;

R^2 is phenyl or a 6-membered heteroaryl, both optionally substituted with up to three instances of R^5 ; wherein said 6-membered heteroaryl ring contains up to 2 nitrogen ring atoms; and

each R^5 is independently selected from C_{1-6} alkyl, C_{1-6} alkoxy or halogen;

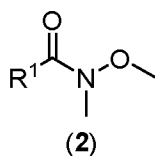
said process comprising the steps of:

i) amidating starting material **(1)**



(1)

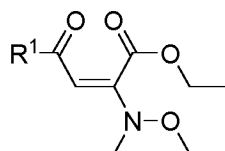
by reacting it with an appropriate amount of oxalyl chloride or an equivalent reagent, in a suitable mixture of water and an aprotic organic solvent, at a suitable temperature, in the presence of an appropriate amount of a suitable catalyst; followed by an appropriate amount of N,O-dimethylhydroxylamine hydrochloride, in the presence of an appropriate excess of a suitable base, at a suitable temperature, in a suitable mixture of water and an aprotic organic solvent to afford amide **(2)**;



(2)

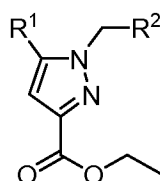
wherein R^1 is unsubstituted phenyl or 5 to 6-membered heteroaryl ring containing up to three ring heteroatoms independently selected from N, O or S;

ii) alkylating intermediate amide **(2)** with an appropriate amount of ethyl propiolate, in a suitable aprotic organic solvent, at a suitable temperature, in the presence of an appropriate amount of a suitable base, to afford β -enaminoketoester **(3)**;



(3) ;

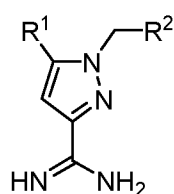
iii) condensing β -enaminoketoester **(3)** with an appropriate amount of a hydrazine of formula $R^2\text{-CH}_2\text{-NH-NH}_2$ or its HCl salt, optionally in the presence of an appropriate amount of a suitable base, in a suitable protic solvent, at a suitable temperature, affording pyrazole ester intermediate **(4)**



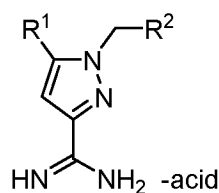
(4) ,

wherein R^2 is phenyl or a 6-membered heteroaryl, both optionally substituted with up to three instances of R^5 ; wherein the 6-membered heteroaryl ring contains up to 2 nitrogen ring atoms;

iv) aminating pyrazole ester intermediate **(4)** with an appropriate amount of ammonium chloride, in the presence of an appropriate amount of trimethylaluminum, in a suitable aprotic organic solvent, at a suitable temperature, affording amidine **(5A)** or, after treatment with a suitable aqueous mineral acid, amidine salt **(5B)**:

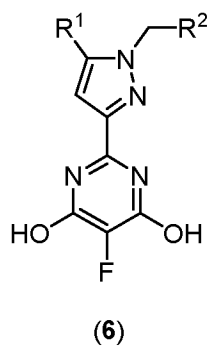


(5A)

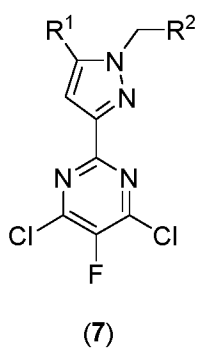


(5B) ;

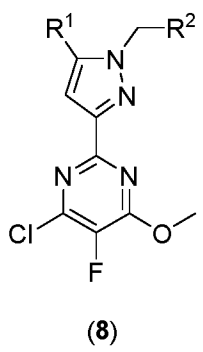
v) condensing amidine (**5A**) or amidine salt (**5B**) and an appropriate amount of fluoromalonate, optionally in the presence of an appropriate amount of a suitable base, in a suitable protic solvent, at a suitable temperature to afford, after treatment with an appropriate amount of a suitable mineral acid, diol (**6**)



vi) chlorinating diol (**6**) with an appropriate amount of phosphoryl chloride, at a suitable temperature, in a suitable aprotic organic solvent, optionally in the presence of an appropriate amount of a suitable base, to afford dichloropyrimidine (**7**)

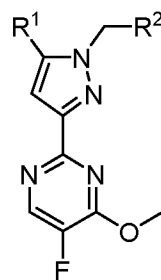


vii) mono-methoxylating dichloropyrimidine (**7**) with an appropriate amount of sodium methoxide, at a suitable temperature, in an appropriate protic solvent, to afford methoxypyrimidine (**8**)



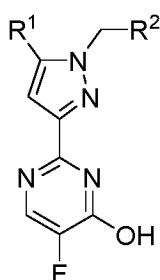
viii) de-chlorinating methoxypyrimidine (**8**) with hydrogen gas or a transfer hydrogenation reagent and, optionally, an appropriate amount of a suitable metal catalyst, in

the presence of an appropriate amount of a suitable base, at a suitable temperature, in an appropriate organic solvent, to provide fluoromethoxypyrimidine **(9)**



(9) ;

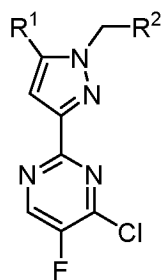
ix) de-methylating fluoromethoxypyrimidine **(9)** by reacting it with an appropriate amount of an aqueous acid in an appropriate protic solvent, at a suitable temperature, to afford alcohol **(10)**



(10) ; and

x) chlorinating alcohol **(10)** with an appropriate amount of phosphoryl chloride and optionally an appropriate amount of a suitable base, at a suitable temperature, in a suitable aprotic organic solvent.

2. A process for preparing a compound of Formula II:



Formula II

wherein:

R¹ is unsubstituted phenyl or 5 to 6-membered heteroaryl ring containing up to three

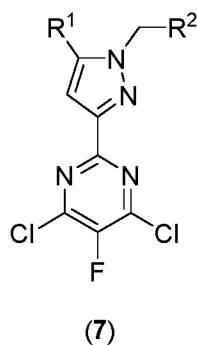
ring heteroatoms independently selected from N, O or S;

R^2 is phenyl or a 6-membered heteroaryl, both optionally substituted with up to three instances of R^5 ; wherein said 6-membered heteroaryl ring contains up to 2 nitrogen ring atoms; and

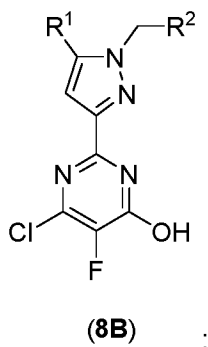
each R^5 is independently selected from C_{1-6} alkyl, C_{1-6} alkoxy or halogen;

said process comprising the steps of:

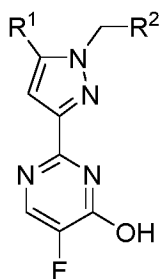
1) mono-hydroxylating a dichloropyrimidine (**7**)



with an appropriate amount of sodium hydroxide, at a suitable temperature, in a suitable mixture of an aprotic and a protic solvent, in the presence of an appropriate amount of a suitable phase transfer catalyst, to afford hydroxypyrimidine (**8B**);



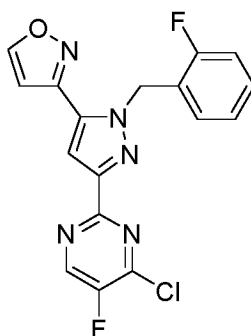
2) de-chlorinating hydroxypyrimidine (**8B**) with hydrogen gas or a transfer hydrogenation reagent and, optionally, an appropriate amount of a suitable metal catalyst, in the presence of an appropriate amount of a suitable base, at a suitable temperature, in a suitable organic solvent, to provide fluorohydroxypyrimidine (**10**);



(10) ; and

3) chlorinating the alcohol of fluorohydroxypyrimidine **(10)** with an appropriate amount of phosphoryl chloride and optionally an appropriate amount of a suitable base, at a suitable temperature, in a suitable aprotic organic solvent.

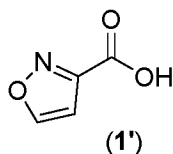
3. The process of claim 1 for preparing a compound of **Formula IV**



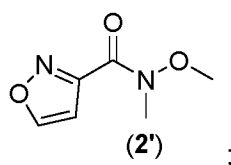
Formula IV

wherein said process comprises the steps of:

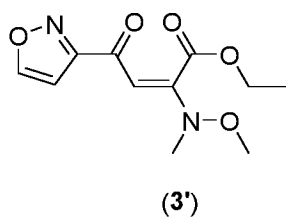
i) amidating starting material **(1')**



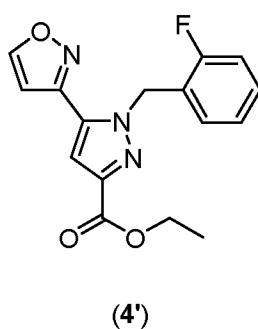
by reacting it with an appropriate amount of oxalyl chloride or an equivalent reagent, in a suitable aprotic organic solvent, at a suitable temperature, in the presence of an appropriate amount of a suitable catalyst; followed by an appropriate amount of N,O-dimethylhydroxylamine hydrochloride, in the presence of an appropriate excess of a suitable base, at a suitable temperature, in a suitable mixture of water and an aprotic organic solvent to afford amide **(2')**



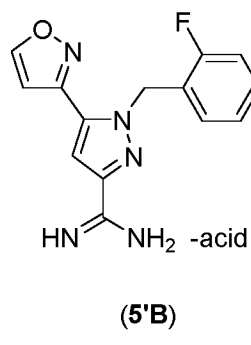
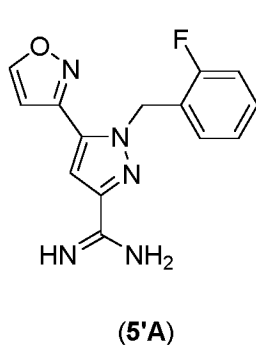
ii) alkylating intermediate amide **(2')** with an appropriate amount of ethyl propiolate, in a suitable aprotic organic solvent, at a suitable temperature, in the presence of an appropriate amount of a suitable base, to afford β -enaminoketoester **(3')**



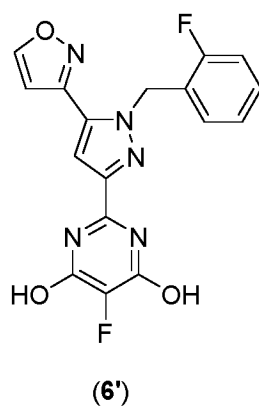
iii) condensing β -enaminoketoester **(3')** with an appropriate amount of a hydrazine of formula $\text{NH}_2\text{NH}-\text{CH}_2-(2\text{-fluorophenyl})$ or its HCl salt, optionally in the presence of an appropriate amount of a suitable base, in a suitable protic solvent, at a suitable temperature, affording a pyrazole ester intermediate **(4')**



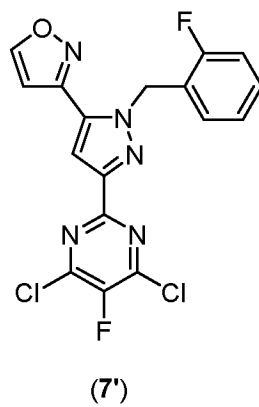
iv) aminating pyrazole ester intermediate **(4')** with an appropriate amount of ammonium chloride, in the presence of an appropriate amount of trimethylaluminum, in a suitable aprotic organic solvent, at a suitable temperature, affording amidine **(5'A)** or, after treatment with a suitable aqueous mineral acid, amidine salt **(5'B)**;



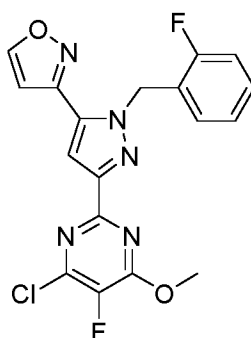
v) condensing amidine (**5'A**) or amidine salt (**5'B**) and an appropriate amount of fluoromalonate, optionally in the presence of an appropriate amount of a suitable base, in a suitable protic solvent, at a suitable temperature to afford, after treatment with an appropriate amount of a suitable mineral acid, diol (**6'**);



vi) chlorinating diol (**6'**) with an appropriate amount of phosphoryl chloride, at a suitable temperature, in a suitable aprotic organic solvent, optionally in the presence of an appropriate amount of a suitable base, to afford dichloropyrimidine (**7'**);

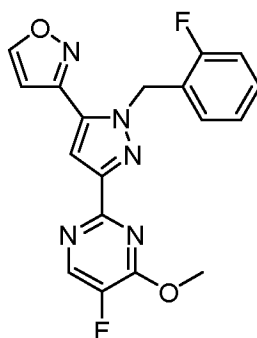


vii) mono-methoxylating dichloropyrimidine (**7'**) with an appropriate amount of sodium methoxide, at a suitable temperature, in an appropriate protic solvent, to afford methoxypyrimidine (**8'**);



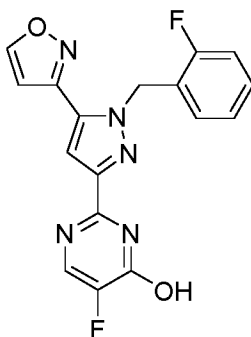
(8') ;

viii) dechlorinating methoxypyrimidine (8') with hydrogen gas or a transfer hydrogenation reagent and, optionally, an appropriate amount of a suitable metal catalyst, in the presence of an appropriate amount of a suitable base, at a suitable temperature, in an appropriate organic solvent, to provide fluoromethoxypyrimidine (9');



(9') ;

ix) de-methylating fluoromethoxypyrimidine (9') by reacting it with an appropriate amount of an aqueous acid, in an appropriate protic solvent, at a suitable temperature, to afford alcohol (10');

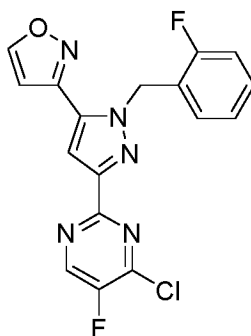


(10') ; and

x) chlorinating alcohol (10') with an appropriate amount of phosphoryl chloride and, optionally, an appropriate amount of a suitable base, at a suitable temperature, in a suitable

aprotic organic solvent.

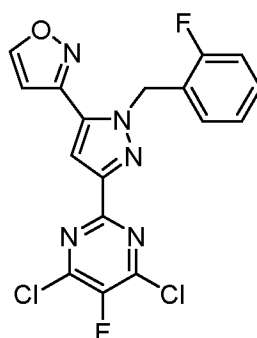
4. The process of claim 2, for preparing a compound of Formula IV



Formula IV

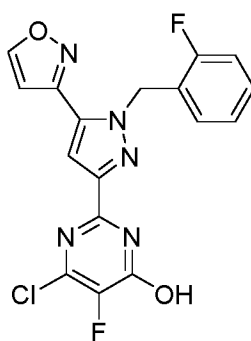
wherein said process comprises the steps of

- 1) mono-hydroxylating a dichloropyrimidine (**7'**)



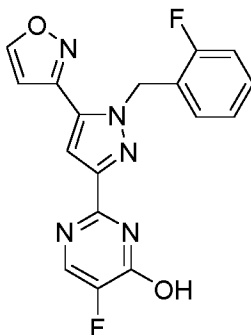
(**7'**)

with an appropriate amount of sodium hydroxide, at a suitable temperature, in a suitable mixture of an aprotic and a protic solvent, in the presence of an appropriate amount of a suitable phase transfer catalyst, to afford hydroxypyrimidine (**8'B**);



(**8'B**)

2) de-chlorinating hydroxypyrimidine (**8'B**) with hydrogen gas or a transfer hydrogenation reagent and, optionally, an appropriate amount of a suitable metal catalyst, in the presence of an appropriate amount of a suitable base, at a suitable temperature, in a suitable organic solvent, to provide fluorohydroxypyrimidine (**10'**);



(**10'**) ; and

3) chlorinating alcohol (**10'**) with an appropriate amount of phosphoryl chloride and optionally an appropriate amount of a suitable base, at a suitable temperature, in a suitable aprotic organic solvent.

5. The process according to claim 1 or 2, wherein R¹ is a 5-membered heteroaryl ring containing up to three heteroatoms independently selected from N, O or S.
6. The process according to claim 5, wherein R¹ is isoxazolyl.
7. The process according to claim 5, wherein R¹ is 3-isoxazolyl.
8. The process according to claim 1 or 2, wherein R² is phenyl optionally substituted with up to three instances of R⁵.
9. The process according to claim 8, wherein R² is phenyl substituted with one instance of R⁵, wherein R⁵ is halogen.
10. The process according to claim 9, wherein R⁵ is fluoro.
11. The process according to claim 8, wherein R² is phenyl substituted with two instances of R⁵; wherein each instance of R⁵ is independently selected from halogen.
12. The process according to claim 11, wherein each instance of R⁵ is fluoro.