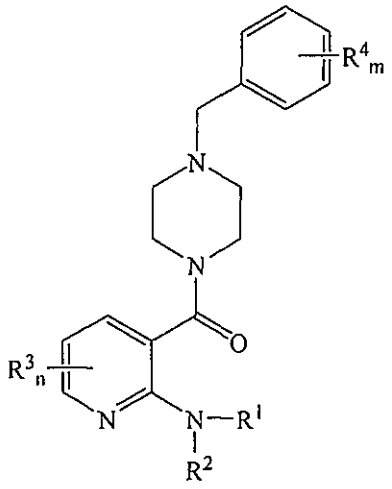
Claims

1. A method to synthesize a compound of the formula:



(1)

wherein

R^1 is alkyl;

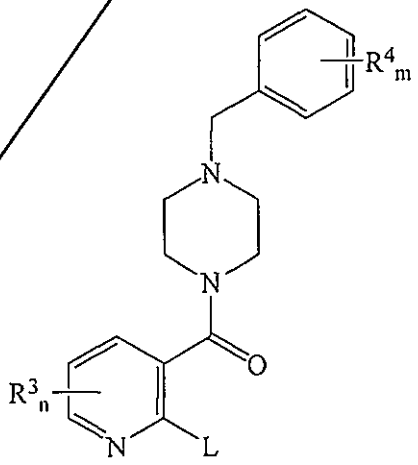
R^2 is H or alkyl;

each R^3 and R^4 is independently alkyl, alkenyl, halo, aryl, heteroaryl, arylalkyl, heteroarylalkyl, NR_2, SR, or OR where R is alkyl or aryl;

n is 0, 1 or 2;

m is 0, 1, 2 or 3;

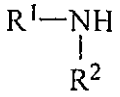
which method comprises reacting a compound of the formula



(2)

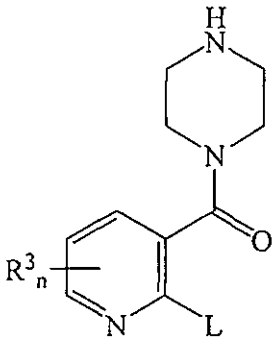
where R^3, R^4, m and n are as defined in formula (1) and L is a leaving group,

with a compound of the formula



wherein R^1 and R^2 are as defined in formula (1).

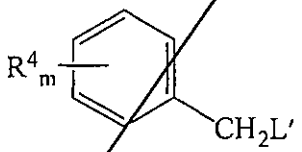
2. The method of claim 1 wherein the compound of formula (2) is prepared by reacting a compound of formula



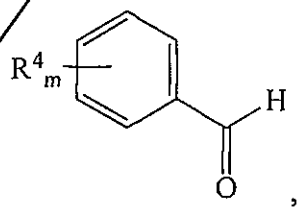
(3)

wherein R^3 and n are as defined in formula (1) and L is a leaving group,

with a compound of the formula



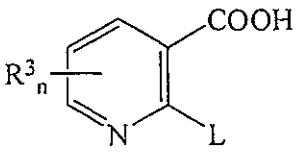
wherein R^4 and m are as defined in formula (1), and L′ is a leaving group, or with a compound of the formula



,

to form an imine followed by reducing said imine.

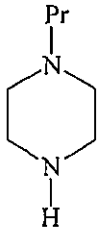
3. The method of claim 2 wherein the compound of formula (3) is obtained by reacting a compound of the formula



(4)

wherein R^3 and n are as defined in formula (1) and L is a leaving group,

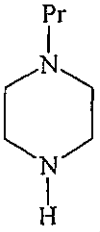
with a compound of the formula



wherein Pr is a protecting group, in the presence of a peptide coupling agent, followed by removing the protecting group; or

by selectively coupling the compound of formula (4) with unprotected piperazine; or

by converting the compound of formula (4) to the benzoyl chloride and coupling the chloride to the compound of the formula



followed by removing the protecting group.

4. The method of any of claims 1-3, wherein m and n are 0.

5. The method of any of claims 1-3, wherein R^3 and/or R^4 is alkyl.

6. The method of any of claims 1-3, wherein L and L′ are independently halo, OTs or OTf.

7. The method of any of claims 1-3, wherein Pr is Boc or Fmoc.

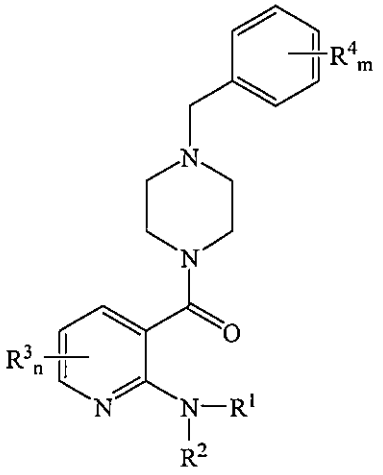
8. The method of any of claims 1-3, wherein L and L′ are independently halo.

9. The method of claim 1 which further includes converting the compound of formula (1) to a pharmaceutically acceptable salt.

10. The method of claim 9 wherein the salt is the phosphate salt.

Claims

1. A method to synthesize a compound of the formula:



(1)

wherein

R^1 is alkyl;

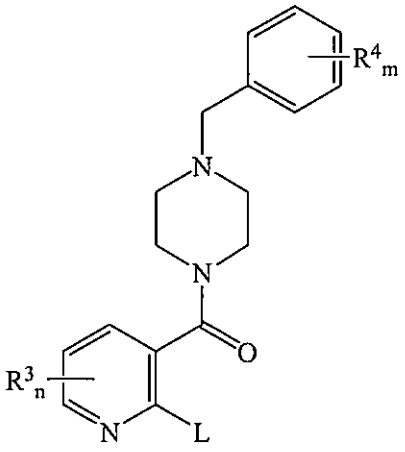
R^2 is H or alkyl;

each R^3 and R^4 is independently alkyl, alkenyl, halo, aryl, heteroaryl, arylalkyl, heteroarylalkyl, NR_2, SR, or OR where R is alkyl or aryl;

n is 0 or 1;

m is 0 or 1;

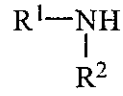
which method comprises reacting a compound of the formula



(2)

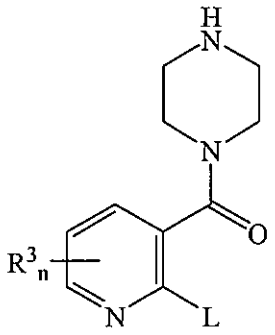
where R^3, R^4, m and n are as defined in formula (1) and L is a leaving group,

with a compound of the formula



wherein R^1 and R^2 are as defined in formula (1), and

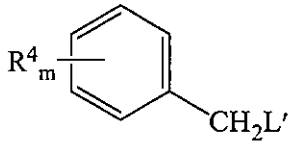
wherein the compound of formula (2) is prepared by reacting a compound of formula



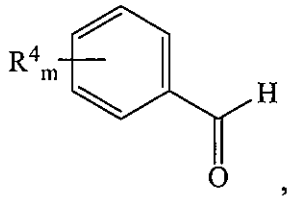
(3)

wherein R^3 and n are as defined in formula (1) and L is a leaving group,

with a compound of the formula



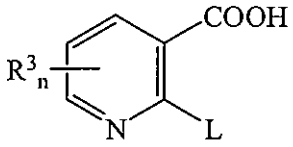
wherein R^4 and m are as defined in formula (1), and L′ is a leaving group, or with a compound of the formula



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to form an imine followed by reducing said imine.

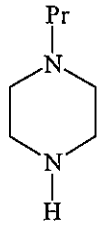
2. The method of claim 1 wherein the compound of formula (3) is obtained by reacting a compound of the formula



(4)

wherein R^3 and n are as defined in formula (1) and L is a leaving group,

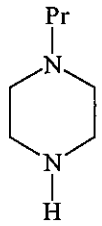
with a compound of the formula



wherein Pr is a protecting group, in the presence of a peptide coupling agent, followed by removing the protecting group; or

by selectively coupling the compound of formula (4) with unprotected piperazine; or

by converting the compound of formula (4) to the benzoyl chloride and coupling the chloride to the compound of the formula



followed by removing the protecting group.

3. The method of claim 1 or 2, wherein m and n are 0.

4. The method of any of claims 1-3, wherein R^1 is alkyl and R^2 is H.

5. The method of claim 4 wherein R^1 is isoamyl.

6. The method of any of claims 1-5, wherein L and L′ are independently halo, OTs or OTf.

7. The method of claim 6, wherein L and L′ are independently halo.

8. The method of any of claims 2-5, wherein Pr is Boc or Fmoc.

9. The method of any of claims 1-8 which further includes converting the compound of formula (1) to a pharmaceutically acceptable salt.

10. The method of claim 9 wherein the salt is the phosphate salt.