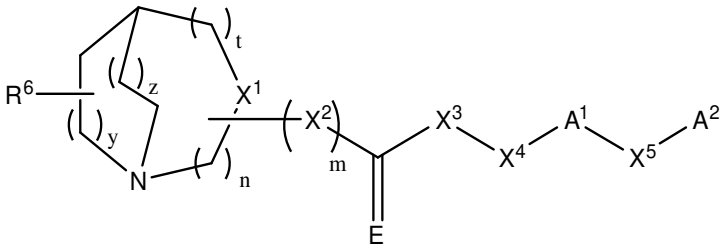
CLAIMS

1. A method of preparing a compound of the formula,



I

wherein:

n is 1, 2 or 3;

m is 1;

t is 0, 1 or 2;

y is 1 or 2;

z is 0, 1 or 2;

E is O;

$X^1$is CR^1;

X^2 is O;

X^3 is -NH;

X^4 is CR^4R^5, CH_2 CR^4R^5 or CH_2 –(C_1-C_6) alkyl-CR^4R^5;

X^5 is a direct bond~~, O, S, SO_2, CR^4R^5; (C_1-C_6)alkyl, (C_1-C_6)alkyloxy, (C_1-C_6)alkenyl, (C_1-C_6)alkenyloxy~~;

R^1 is H~~, CN, (C_1-C_6)alkylcarbonyl, or (C_1-C_6)alkyl~~;

R^4 ~~is independently (C_1-C_6)alkyl;~~and

R^5 ~~is~~ are independently selected from H or (C_1-C_6)alkyl; or

R^4 and R^5 may be taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring;

R^6 is -H~~, halogen, -CN, (C_6-C_{12})aryl, (C_6-C_{12})aryloxy, (C_1-C_6)alkyloxy; (C_1-C_6)alkyl optionally substituted by one to four halo or (C_1-C_6)alkyl~~;

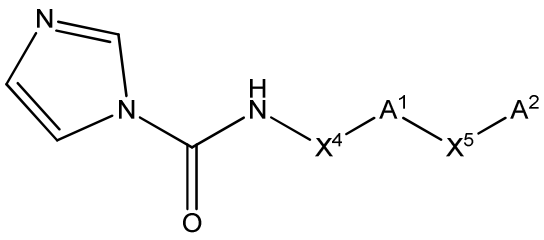
A^1 is ~~(C_2-C_6)alkynyl; (C_3-C_{10})cycloalkyl, (C_6-C_{12})aryl,~~ (C_2-C_9)heteroaryl, ~~(C_2-C_9)heterocycloalkyl or benzo(C_2-C_9)heterocycloalkyl~~ optionally substituted with one or

more substituents selected from the group consisting of halo**,** (C_1-C_6)alkyl optionally substituted by one to three halo; (C_1-C_6)alkenyl, amino, (C_1-C_6)alkylamino, (C_1-C_6)dialkylamino, (C_1-C_6)alkoxy, nitro, CN, -OH, (C_1-C_6)alkyloxy optionally substituted by one to three halo; (C_1-C_6)alkoxycarbonyl, and (C_1-C_6) alkylcarbonyl;

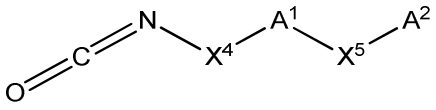
A^2 is ~~H, (C_3-C_{10})cycloalkyl,~~ (C_6-C_{12})aryl, ~~(C_2-C_9)heteroaryl, (C_2-C_9)heterocycloalkyl or benzo(C_2-C_9)heterocycloalkyl~~ optionally substituted with one or more substituents selected from the group consisting of halo**,** (C_1-C_6)alkyl optionally substituted by one to three halo; (C_1-C_6)alkylenyl, amino, (C_1-C_6) alkylamino, (C_1-C_6)dialkylamino, (C_1-C_6)alkoxy, O(C3-C6 cycloalkyl), (C_3-C_6) cycloalkoxy, nitro, CN, OH, (C_1-C_6)alkyloxy optionally substituted by one to three halo; (C_3-C_6) cycloalkyl, (C_1-C_6) alkoxycarbonyl, (C_1-C_6) alkylcarbonyl, (C_1-C_6) haloalkyl;

with the proviso that the sum of n + t + y + z is not greater than 6;

comprising reacting the compounds of Formula II and Formula IV

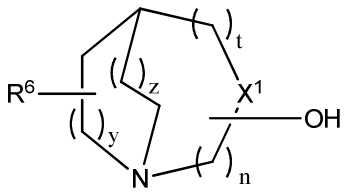


II



IV

with a compound of Formula III



III

wherein n, t, y, z, X^4, A^1, X^5 and A^2 are as defined above.

2. A method according to claim 1, wherein n is 1; t is 0; y is 1 and z is 1.

3. A method according to claim 2, wherein X^4 is CR^4R^5.

4. A method according to claim 3, wherein R^4 and R^5 are each methyl.

~~5. A method according to claim 4, wherein A^1 is (C_2-C_9)heteroaryl.~~

~~6~~5. A method according to claim ~~5~~4, wherein A^1 is thiophene, thiazole, isothiazole, furane, oxazole, isoxazole, pyrrole, imidazole, pyrazole, triazole, pyridine, pymiridine, pyridazine, indole, benzothiazole, benzoisoxazole, benzopyrazole, benzoimidazole, benzofuran or benzooxazole.

~~7~~6. A method according to claim ~~6~~5, wherein A^1 is thiazole.

~~8. A method according to claim 7, wherein R^6 is H.~~

~~9. A method according to claim 8, wherein X^5 is a direct bond.~~

~~10. A method according to claim 9, wherein A^2 is (C_6-C_{12})aryl.~~

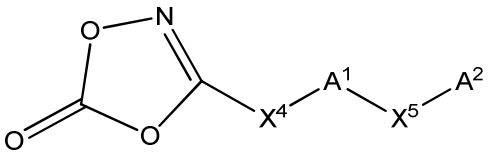
~~11~~7. A method according to claim ~~10~~6, wherein A^2 is phenyl.

~~12~~8. A method according to claim ~~11~~7, wherein the phenyl group is substituted by halo.

~~13~~9. A method according to claim ~~12~~8, wherein the halo group is fluoro.

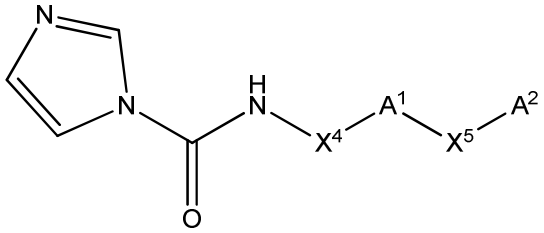
~~14. A method according to claim 13, wherein R^1 is hydrogen.~~

~~15~~10. A method according to claim 1, further including reacting, while heating to reflux, the compound of Formula V

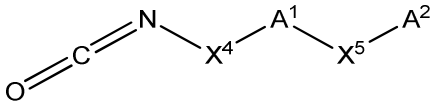


V

with imidazole to form the compounds of Formula II and Formula IV



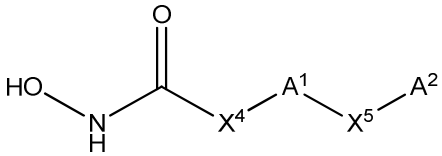
II



IV

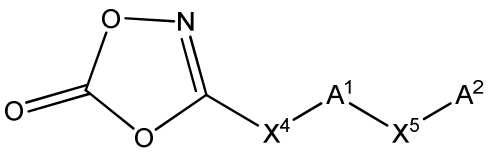
wherein X^4, A^1, X^5 and A^2 are as defined above.

~~16~~11. A method according to claim ~~15~~10, further including reacting the compound of Formula VI



VI

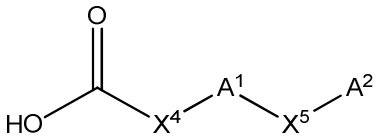
with N, N'- carbonyldiimidazole to form the compound of Formula V



V

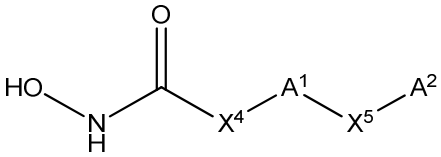
wherein X^4, A^1, X^5 and A^2 are as defined above.

~~17~~12. A method according to claim ~~16~~11, further including reacting the compound of Formula VII



VII

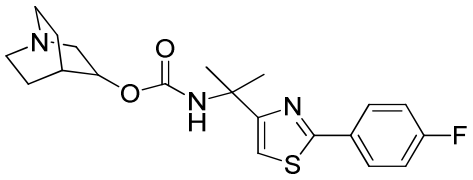
with N, N'- carbonyldiimidazole and hydroxylamine to form the compound of Formula VI



VI

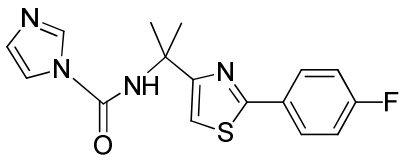
wherein X^4, A^1, X^5 and A^2 are as defined above.

~~18~~13. A method of preparing the compound of Formula VIII

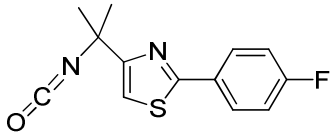


VIII

comprising reacting ~~a~~ compounds of Formula IX and Formula X



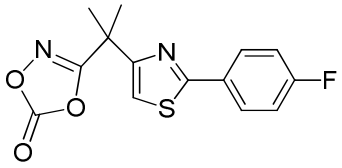
IX;



X

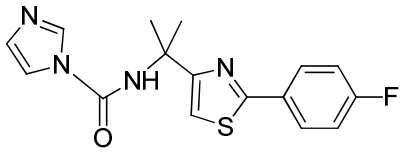
with quinuclidinol.

~~19~~14. A method according to claim ~~18~~13, further including reacting, while heating to reflux, the compound of Formula XI

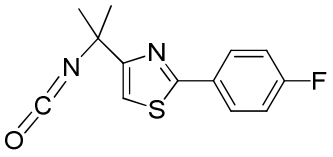


XI

with imidazole to form the compounds of Formula IX and Formula X

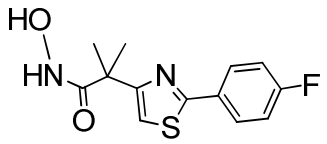


IX;



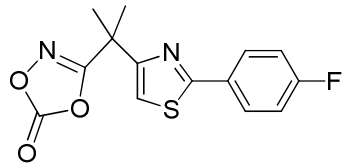
X.

~~20~~15. A method according to claim ~~19~~14, further including reacting the compound of Formula XII



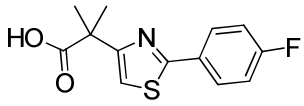
XII

with N, N'- carbonyldiimidazole to form the compound of Formula XI



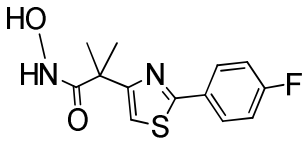
XI.

~~21~~16. A method according to claim ~~20~~15, further including reacting the compound of Formula XIII



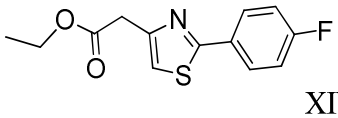
XIII

with N, N'- carbonyldiimidazole and hydroxylamine to form the compound of Formula XII



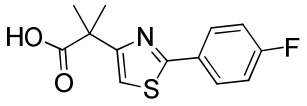
XII.

~~22~~17. A method according to claim ~~21~~16, further including reacting the compound of Formula XIV



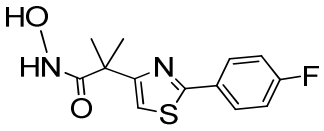
XIV

with potassium tert-butoxide and methyl iodine followed by reacting the ethyl ester so formed with lithium hydroxide to form the compound of Formula XIII



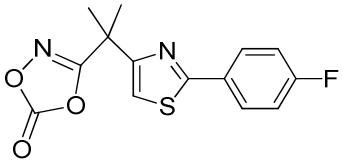
XIII.

~~23~~18. A compound of Formula XII



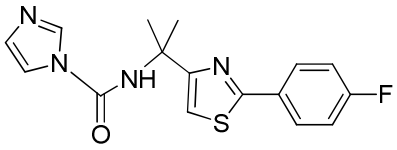
XII .

~~24~~19. A compound of Formula XI



XI .

~~25~~20. A compound of Formula IX



IX .