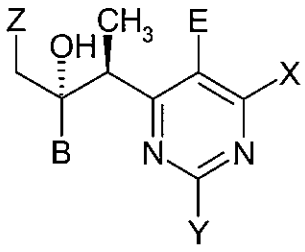
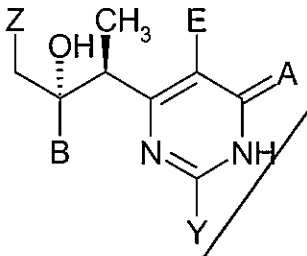
Claims

1. A process for preparing a compound of formula:



or



(XI) (XII)

wherein:

X is H, halo, $-NH_2$, $-NH(C_1-C_6$ alkyl), $-N(C_1-C_6$ alkyl)$(C_1-C_6$ alkyl), $-Si(R^3)_3$ [wherein R^3 is, independently in each case, C_1-C_6 alkyl, aryl or aryl$(C_1-C_6$ alkyl)], $-O(C_1-C_6$ alkyl), -O-aryl, $-S(C_1-C_6$ alkyl), $-OSO_2(C_1-C_6$ alkyl), $-NHSO_2(C_1-C_6$ alkyl) or -S-aryl;

Y is H, halo, $-NH_2$, $-NH(C_1-C_6$ alkyl), $-N(C_1-C_6$ alkyl)$(C_1-C_6$ alkyl), $-Si(R^3)_3$ [wherein R^3 is as defined above], $-O(C_1-C_6$ alkyl), -O-aryl, $-S(C_1-C_6$ alkyl), $-OSO_2(C_1-C_6$ alkyl), $-NHSO_2(C_1-C_6$ alkyl) or -S-aryl;

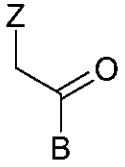
Z is optionally substituted heteroaryl, $-Si(R^3)_3$ (wherein R^3 is as defined above), -OH, a protected hydroxyl group, halo, nitro, cyano, -SH, a protected thio group, C_1-C_6 alkyl or C_1-C_6 alkoxy;

A is O, S or NH;

B is phenyl substituted by one or more halo atoms; and

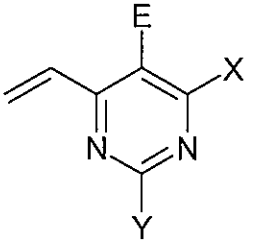
E is a halo atom;

by reacting a compound of formula:

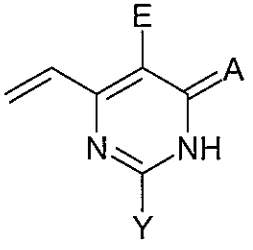


(XIII)

wherein Z and B are as defined above, with a compound of formula:



or



(XIV) (XV)

respectively, wherein X, Y, A and E are as defined above, in the presence of a transition metal catalyst, a ligand suitable for use with the catalyst and a reducing agent.

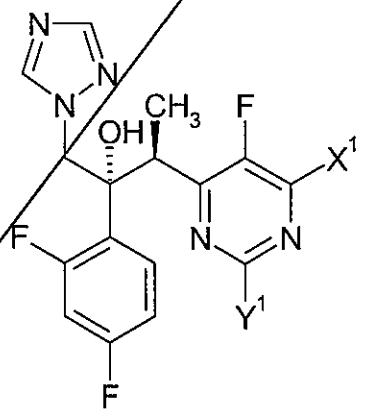
2. A process as claimed in claim 1 wherein Z is 1,2,4-triazol-1-yl.

3. A process as claimed in claim 1 or claim 2 wherein X is chloro and Y is H.

4. A process as claimed in any one of the preceding claims wherein B is 2,4-difluorophenyl.

5. A process as claimed in any one of the preceding claims wherein E is fluoro.

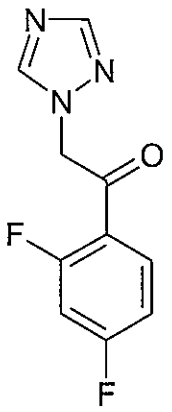
6. A process as claimed in claim 1 for preparing a compound of formula:



(XVI)

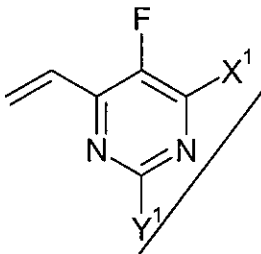
wherein X^1 and Y^1 are both H or one of X^1 and Y^1 is H and the other is chloro;

by reacting a compound of formula:



(XVII)

with a compound of formula:



(XVIII)

respectively, wherein X^1 and Y^1 are as defined above, in the presence of a copper catalyst, a chiral phosphine ligand and a reducing agent.

7. A process as claimed in claim 6 in which X^1 is chloro and Y^1 is H.

8. A process as claimed in any preceding claim wherein the catalyst is a copper(I) catalyst.

9. A process as claimed in claim 8 wherein the catalyst is $CuF(PPh_3)_3$.methanol solvate or $CuF(PPh_3)_3$.ethanol solvate.

10. A process as claimed in any preceding claim wherein the ligand is (*S*)-1-{(S_P)-2-[2-(diphenylphosphino)phenyl]ferrocenyl}ethylbis[3,5-bis-(trifluoromethyl)phenyl]phosphine.

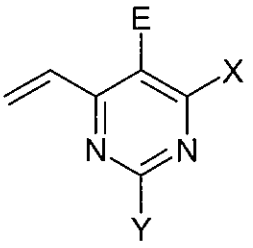
11. A process as claimed in any preceding claim wherein the reducing agent is phenysilane.

12. A process as claimed in any preceding claim wherein the temperature of the reaction is about -9°C.

13. A process as claimed in any preceding claim wherein the reaction is performed as a solution in 2-methyl-2-butanol.

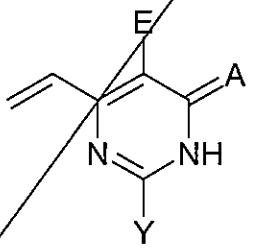
14. A process as claimed in any preceding claim wherein the product is voriconazole or the product is further transformed in one or more steps to provide voriconazole.

15. A compound of formula:



(XIV)

or



(XV)

wherein

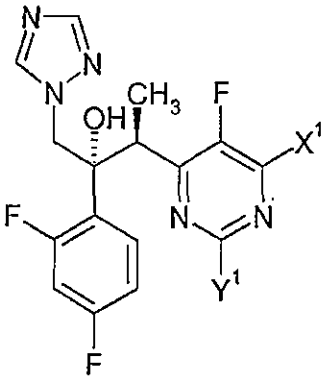
X is H, halo, $-NH_2$, $-NH(C_1-C_6$ alkyl), $-N(C_1-C_6$ alkyl)$(C_1-C_6$ alkyl), $-Si(R^3)_3$ [wherein R^3 is, independently in each case, C_1-C_6 alkyl, aryl or aryl$(C_1-C_6$ alkyl)], $-O(C_1-C_6$ alkyl), -O-aryl, $-S(C_1-C_6$ alkyl), $-OSO_2(C_1-C_6$ alkyl), $-NHSO_2(C_1-C_6$ alkyl) or -S-aryl;
Y is H, halo, $-NH_2$, $-NH(C_1-C_6$ alkyl), $-N(C_1-C_6$ alkyl)$(C_1-C_6$ alkyl), $-Si(R^3)_3$ [wherein R^3 is as defined above], $-O(C_1-C_6$ alkyl), -O-aryl, $-OSO_2(C_1-C_6$ alkyl), $-NHSO_2(C_1-C_6$ alkyl) or -S-aryl;
A is O, S or NH; and
E is a halo atom;

with the proviso that the compound of formula (XIV) is not 5-bromo-4-vinylpyrimidine.

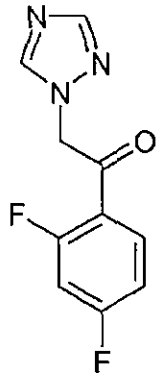
16. A compound as claimed in claim 15 which is:
4-chloro-5-fluoro-6-vinylpyrimidine;
5-fluoro-4-vinylpyrimidine; or
2-chloro-5-fluoro-4-vinylpyrimidine.

Claims

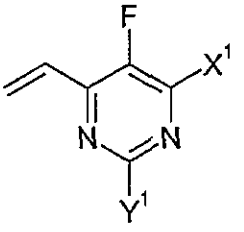
1. A process for preparing a compound of formula:



wherein X^1 and Y^1 are both H or one of X^1 and Y^1 is H and the other is chloro; by reacting a compound of formula:



with a compound of formula:



wherein X^1 and Y^1 are as defined above, in the presence of a copper catalyst, a chiral phosphine ligand and a reducing agent; wherein the reaction is performed in the presence of an organic solvent which is an alcohol.

2. A process as claimed in claim 1 wherein the organic solvent is a tertiary alcohol.

3. A process as claimed in claim 2 in which the organic solvent is 2-methyl-2-butanol.

4. A process as claimed in any preceding claim in which X^1 is chloro and Y^1 is H.

5. A process as claimed in any preceding claim wherein the catalyst is a copper(I) catalyst.

6. A process as claimed in claim 5 wherein the catalyst is $CuF(PPh_3)_3$.methanol solvate or $CuF(PPh_3)_3$.ethanol solvate.

7. A process as claimed in any preceding claim wherein the ligand is (S)-1-{(S_P)-2-[2-(diphenylphosphino)phenyl]ferrocenyl}ethylbis[3,5-bis-(trifluoromethyl)phenyl]phosphine.

8. A process as claimed in any preceding claim wherein the reducing agent is phenysilane.

9. A process as claimed in any preceding claim wherein the temperature of the reaction is about -9°C.

10. A process as claimed in any preceding claim wherein the product is voriconazole or the product is further transformed in one or more steps to provide voriconazole.

11. A compound which is:

4-chloro-5-fluoro-6-vinylpyrimidine;
5-fluoro-4-vinylpyrimidine; or
2-chloro-5-fluoro-4-vinylpyrimidine.