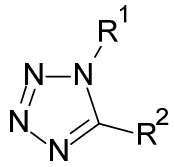
Claims

1. A process for the preparation of a compound of formula (I)



(I)

wherein

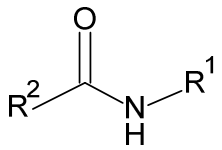
R^1 is alkyl, cycloalkyl, aryl, arylalkyl, alkyloxy, alkenyl, alkynyl, heterocyclyl or heteroaryl, all optionally substituted with one to three substituents independently selected from halogen, hydroxyl, alkyl, haloakyl, hydroxyalkyl, cycloalkyl, halocycloalkyl, hydroxycycloalkyl, alkoxy and cyano;

R^2 is $-CH_2-X$ or aryl optionally substituted with one to three substituents independently selected from halogen, hydroxyl, alkyl, haloakyl, hydroxyalkyl, cycloalkyl, halocycloalkyl, hydroxycycloalkyl, alkoxy and cyano;

or R^1 and R^2 together form alkylene; and

X is halogen, aryloxy, alkyoxycarbonyl, haloalkyl, hydroxyl, mesyl, tosyl, alkoxy, alkylamino or dialkylamino, wherein aryloxy is optionally substituted with one to three substituents independently selected from halogen, hydroxyl, alkyl, haloakyl, hydroxyalkyl, cycloalkyl, halocycloalkyl, hydroxycycloalkyl, alkoxy and cyano;

comprising the flow chemistry, three components reaction of a compound of formula (II)



(II)

wherein R^1 and R^2 are as defined above;

with trimethylsilyl azide ($TMSN_3$) and a chlorinating agent in acetonitrile.

2. A process according to claim 1, wherein the compound of formula (II) is injected in the flow chemistry reactor at a concentration between around 0.5 M and around 9M, in particular at around 6 M.

3. A process according to claim 1 or 2, wherein the chlorinating agent is injected in the flow chemistry reactor at a concentration between around 1 M and neat, in particular around 6 M.

4. A process according to any one of claims 1 to 3, wherein $TMSN_3$ is injected in the flow chemistry reactor at a concentration between around 1M and neat, in particular neat.

5. A process according to any one of claims 1 to 4, wherein between around 0.9 equivalent and around 2.0 equivalent of $TMSN_3$, in particular around 1.5 equivalent of $TMSN_3$, is present at the start of the three component reaction.

6. A process according to any one of claims 1 to 5, wherein the compound of formula (II), the chlorinating agent and/or $TMSN_3$ are introduced in the flow chemistry reactor as acetonitrile solutions.

7. A process according to any one of claims 1 to 6, wherein the reaction is performed at a temperature between around 40 °C and around 160 °C, in particular between around 60 °C and around 150 °C, in particular between around 100 °C and around 140 °C.

8. A process according to any one of claims 1 to 7, wherein the residence time of the reactant in the reaction chamber wherein the flow chemistry, three component reaction takes place is between around 1 minute and around 60 minutes, in particular between around 5 minutes and around 15 or 20 minutes.

9. A process according to any one of claims 1 to 8, wherein the reaction flow is cooled to a temperature of between around 0 and around 30 °C, in particular between around 10 and around 25 °C before the reaction is quenched.

10. A process according to any one of claims 1 to 9, wherein the reaction is quenched with a base, in particular sodium hydroxide.

11. A process according to any one of claims 1 to 10, wherein the reaction completion is continuously monitored through NMR, HPLC, IR, MS, UPLC, LC-MS, GC, UV-visible and/or fluorescence spectroscopy.

12. A process according to any one of claims 1 to 11, wherein R^1 is, alkyl, cycloalkyl or arylalkyl.

13. A process according to any one of claims 1 to 12, wherein R^1 is alkyl, in particular methyl.

14. A process according to any one of claims 1 to 13, wherein R^2 is $-CH_2-X$.

15. A process according to any one of claims 1 to 14, wherein X is halogen, aryloxy, alkoxycarbonyl or haloalkyl.

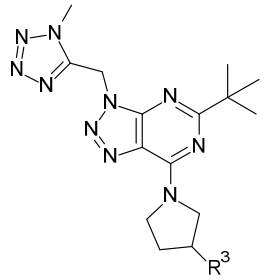
16. A process according to any one of claims 1 to 15, wherein X is halogen, in particular chlorine, bromine or iodine, more particularly chloride.

17. A process according to any one of claims 1 to 16, wherein the chlorinating agent is $POCl_3$, $SOCl_2$, SO_2Cl_2 or cyanuric chloride, in particular $POCl_3$.

18. A process according to any one of claims 1 to 17, wherein the compound of formula (I) is 5-(chloromethyl)-1-methyl-1H-tetrazole, the compound of formula (II) is 2-chloro-N-methyl-acetamide and the chlorinating agent is $POCl_3$.

19. A process according to any one of claims 1 to 18, further comprising the reaction of 5-(chloromethyl)-1-methyl-1H-tetrazole with trifluoro-acetic acid (S)-1-(5-tert-butyl-3H-[1,2,3]triazolo[4,5-d]pyrimidin-7-yl)-pyrrolidin-3-yl-ester in the presence of a base to arrive at (S)-1-[5-tert-butyl-3-(1-methyl-1H-tetrazol-5-ylmethyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-7-yl]-pyrrolidin-3-ol.

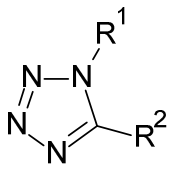
20. A process according to any of the claims 1 to 19, further comprising the preparation of compound of formula (IV),



(IV)

wherein R^3 is halogen, aryloxy, alkyoxycarbonyl, haloalkyl, hydroxyl, mesyl, tosyl, alkoxy, alkylamino or dialkylamino, wherein aryloxy is optionally substituted with one to three substituents independently selected from halogen, hydroxyl, alkyl, haloakyl, hydroxyalkyl, cycloalkyl, halocycloalkyl, hydroxycycloalkyl, alkoxy and cyano, particularly hydroxyl, mesyl, and tosyl, more particularly hydroxyl;

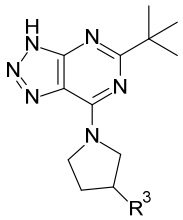
comprising the reaction of compound of formula (I),



(I)

wherein R^1 and R^2 are as defined in claim 1 or any of the claims 12 to 16,

with the compound of formula (III),



(III)

wherein R^3 is as described above.

21. A process acoording to any of the claims 1 to 20 wherein R^3 is hydroxyl.

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