Other diseases with an important role for dysfunctional B cells are B cell malignancies. Indeed anti-CD20 therapy is used effectively in the clinic for the treatment of follicular lymphoma, diffuse large B-cell lymphoma and chronic lymphocytic leukemia [Lim et al, Haematologica, **95** (2010) pp135-143]. The reported role for Btk in the regulation of proliferation and apoptosis of B cells indicates there is potential for Btk inhibitors in the treatment of B cell lymphomas as well. Inhibition of Btk seems to be relevant in particular for B cell lymphomas due to chronic active BCR signaling [Davis et al, Nature, **463** (2010) pp88-94].

Some classes of 6-5 membered fused pyridine ring compounds have been described as kinase inhibitors e.g. Imidazo[1,5-f][1,2,4]triazine compounds have been described in WO2005097800 and WO2007064993;. Imidazo[1,5-a]pyrazine compounds have been described in WO2005037836 and WO2001019828 as IGF-1R enzyme inhibitors.

Some of the Btk inhibitors reported are not selective over Src-family kinases. With dramatic adverse effects reported for knockouts of Src-family kinases, especially for double and triple knockouts, this is seen as prohibitive for the development of Btk inhibitors that are not selective over the Src-family kinases. Both Lyn-deficient and Fyn-deficient mice exhibit autoimmunity mimicking the phenotype of human lupus nephritis. In addition, Fyn-deficient mice also show pronounced neurological defects. Lyn knockout mice also show an allergic-like phenotype, indicating Lyn as a broad negative regulator of the IgE-mediated allergic response by controlling mast cell responsiveness and allergy-associated traits [Odom et al, J. Exp. Med., **199** (2004) pp1491-1502]. Furthermore, aged Lyn knock-out mice develop severe splenomegaly (myeloid expansion) and disseminated monocyte/macrophage tumors [Harder et al, Immunity, **15** (2001) pp603-615]. These observations are in line with hyperresponsive B cells, mast cells and myeloid cells, and increased Ig levels observed in Lyn-deficient mice.

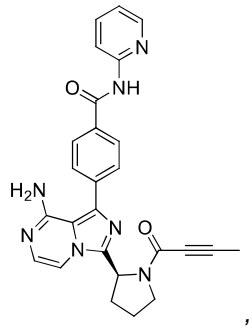
Female Src knockout mice are infertile due to reduced follicle development and ovulation [Roby et al, Endocrine, **26** (2005) pp169-176].

The double knockouts $Src^{-/-}Fyn^{-/-}$ and $Src^{-/-}Yes^{-/-}$ show a severe phenotype with effects on movement and breathing. The triple knockouts $Src^{-/-}Fyn^{-/-}Yes^{-/-}$ die at day 9.5 [Klinghoffer et al, EMBO J., **18** (1999) pp2459-2471]. For the double knockout $Src^{-/-}Hck^{-/-}$, two thirds of the mice die at birth, with surviving mice developing osteopetrosis, extramedullary hematopoiseis, anemia, leukopenia [Lowell et al, Blood, **87** (1996) pp1780-1792].

Hence, an inhibitor that inhibits multiple or all kinases of the Src-family kinases simultaneously may cause serious adverse effects.

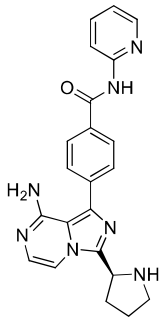
Summary

In one aspect, the present disclosure refers to a process of preparing compound (1):



,

or a pharmaceutically acceptable salt thereof, wherein the process comprises reacting compound (2):

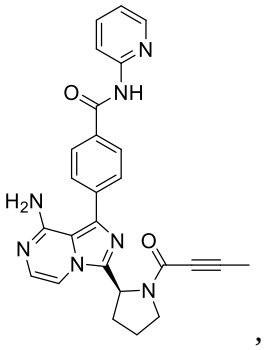


with 2-butynoic acid to provide compound (1).

Detailed description of the invention

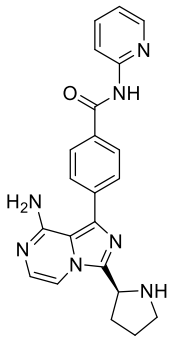
Claims

1. A process of preparing compound (1):



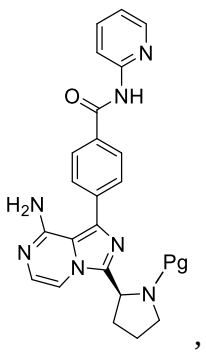
,

or a pharmaceutically acceptable salt thereof, wherein the process comprises reacting compound (2):



with 2-butynoic acid to provide compound (1).

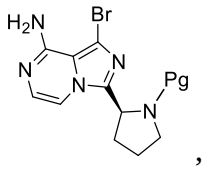
2. The process according to claim 1, wherein compound (2) is prepared by deprotecting compound (3):



,

wherein Pg is a protecting group, to provide compound (2).

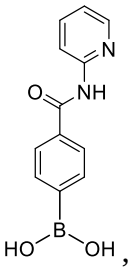
3. The process according to claim 2, wherein compound (3) is prepared by reacting compound (4):



,

wherein Pg is a protecting group,

with compound (5):



,

to provide compound (3).

4. The process according to any one of claims 1 to 3, wherein compound (2) is reacted with 2-butynoic acid in the presence of a base.

5. The process according to claim 4, wherein the base comprises triethylamine.

6. The process according to any one of claims 1 to 5, wherein compound (2) is reacted with 2-butynoic acid in the presence of a coupling agent.

7. The process according to claim 6, wherein the coupling agent comprises O-(7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyluroniumhexafluoro phosphate.

8. The process according to claim 2, wherein the deprotecting step is carried out with an acid.

9. The process according to claim 2 or 3, wherein the protecting group is benzyloxycarbonyl.

10. The process according to claim 3, wherein compound (4) is contacted with compound (5) in the presence of a base.

11. The process according to claim 10, wherein the base is a carbonate.

12. The process according to claim 10, wherein the base is potassium carbonate.

13. The process according to claim 3, wherein compound (4) is contacted with compound (5) in the presence of a catalyst.

14. The process according to claim 13, wherein the catalyst comprises a palladium catalyst.

15. The process according to claim 13, wherein the catalyst comprises 1, 1'-bis(diphenylphosphino)ferrocene palladium (II) chloride or tetrakis(triphenylphosphine) palladium(0).