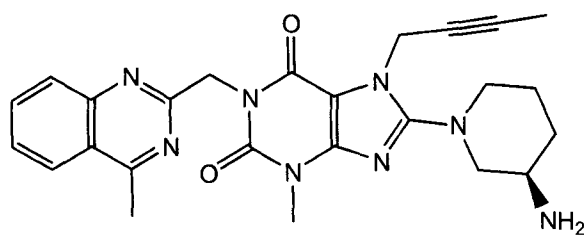


We Claim:

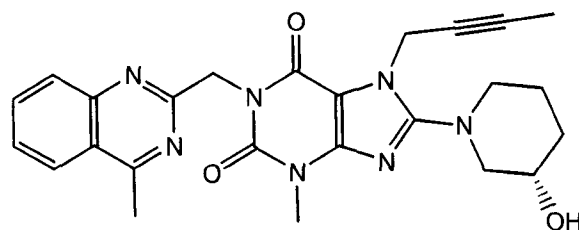
1. Process for the preparation of linagliptin (**A**; (*R*)-8-(3-amino-piperidin-1-yl)-7-but-2-ynyl-3-methyl-1-(4-methyl-quinazolin-2-ylmethyl)-3,7-dihydro-purine-2,6-dione)



(A)

comprising the steps of:

- a) preparing a compound of formula **J** (1-[(4-methylquinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*S*)-3-hydroxypiperidinyl)xanthine),



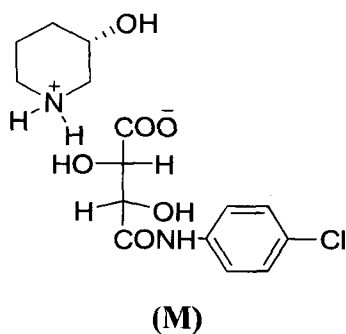
(J)

by combining 1-[(4-methylquinazolinyl-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-bromoxanthine (compound of formula **B**)



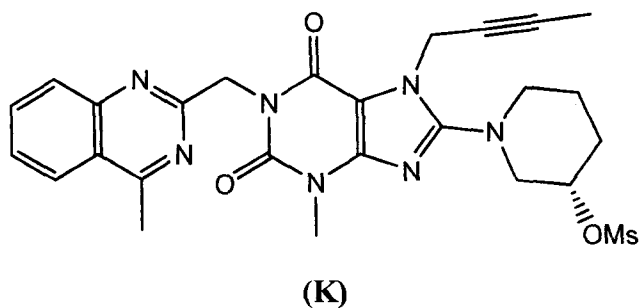
(B)

and the salt (*S*)-3-hydroxypiperidine (-)-4-chlorotartrate (M)

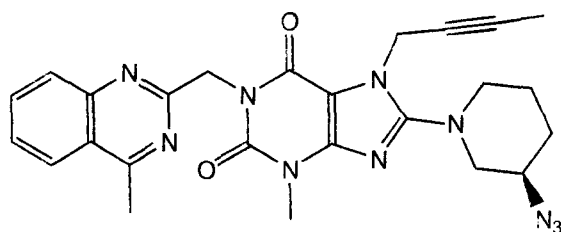


in a suitable solvent in presence of a base;

- b) mesylating the compound **J** using methane sulfonyl chloride to obtain 1-[(4-methylquinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*S*)-3-O-methanesulfonyl piperidinyl)xanthine (**K**);



- c) converting the compound **K** into the azido compound of formula L (1-[(4-methylquinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*S*)-3-azidopiperidinyl)xanthine) with an azide reagent in a suitable solvent with complete inversion in configuration at the chiral center;



(L)

d) reducing the azido group in compound **L** to obtain linagliptin (**A**) and optionally converting it to a pharmaceutically acceptable salt, hydrated or anhydrous.

2. According to claim 1(a), the suitable solvent is selected from the group of dipolar aprotic solvents N, N-dimethylformamide, dimethylacetamide, N-methylpyrrolidone, acetonitrile and dimethyl sulfoxide, preferably N, N-dimethylformamide, in the presence of an inorganic base such as sodium carbonate, lithium carbonate or potassium carbonate, preferably potassium carbonate.

3. According to claim 1(c), the azide reagent is selected from the group tosyl azide, diphenylphosphoryl azide and sodium azide, preferably sodium azide.

4. A process for preparation of 1-[(4-methylquinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((S)-3-hydroxypiperidinyl)xanthine (compound of formula **J**) by combining 1-[(4-methylquinazolinyl-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-bromoxanthine (compound of formula **B**) and the salt (S)-3-hydroxypiperidine (-)-4-chlorotartrate (**M**) in a suitable solvent selected from the group of dipolar aprotic solvents N,N-dimethylformamide, dimethylacetamide, N-methylpyrrolidone, acetonitrile and dimethyl sulfoxide, preferably N,N-dimethylformamide, in the presence of an inorganic base such as sodium carbonate, lithium carbonate or potassium carbonate, preferably potassium carbonate.

5. The compound 1-[(4-methylquinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((S)-3-O-methanesulfonyl piperidinyl)xanthine (**K**).

6. A process for the preparation of 1-[(4-methylquinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((S)-3-O-methanesulfonyl piperidinyl)xanthine (**K**) as per claim 5, comprising mesylating the compound **J** in dichloromethane using methane sulfonyl chloride, without inversion at the chiral center at position 3 in compound **J**.

7. The compound 1-[(4-methylquinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((S)-3-azidopiperidinyl)xanthine (**L**).

8. A process for preparation of 1-[(4-methylquinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((S)-3-azidopiperidinyl)xanthine (**L**) as per claim 7 comprising azidinating compound **K** with sodium azide in a suitable solvent, preferably dimethylacetamide with complete inversion in configuration at the chiral center.

9. A process for the preparation of linagliptin (**A**; (*R*)-8-(3-amino-piperidin-1-yl)-7-but-2-ynyl-3-methyl-1-(4-methyl-quinazolin-2-ylmethyl)-3,7-dihydro-purine-2,6-dione) comprising the steps of:

- a) preparing a compound of formula **J** (1-[(4-methylquinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*S*)-3-hydroxypiperidinyl)xanthine), by combining 1-[(4-methylquinazoliny-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-bromoxanthine (compound of formula **B**) and the salt (*S*)-3-hydroxypiperidine (-)-4-chlorotartranilate (**M**) in a suitable solvent, preferably *N,N*-dimethylacetamide and in presence of a base, preferably potassium carbonate

b) mesylating the compound **J** in a solvent, preferably dichloromethane using methane sulfonyl chloride to obtain 1-[(4-methylquinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*S*)-3-O-methanesulfonyl piperidinyl)xanthine (**K**) without inversion of configuration at the chiral center;

c) converting the compound **K** into the azido compound of formula L (1-[(4-methylquinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*S*)-3-azidopiperidinyl)xanthine) with an azide reagent, preferably sodium azide in a solvent, preferably dimethylacetamide with complete inversion in configuration at the chiral center;

d) reducing the azido group in compound **L** with triphenylphosphine-water in tetrahydrofuran to obtain linagliptin (**A**) and optionally converting it to a pharmaceutically acceptable salt, hydrated or anhydrous.

Dated 15th May 2013


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