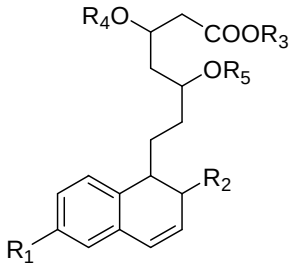
Claims

1. A compound of Formula (I), or a stereoisomer, tautomer, racemate, metabolite, prodrug, pharmaceutically acceptable salt or solvate thereof:



Formula (I)

R_1 is selected from C_1-C_6 alkyl, halo C_1-C_6 alkyl, $(CH_2)_{1-6}OH$, C_3-C_7 cycloalkyl, halo C_3-C_7 cycloalkyl, C_1-C_6 alkoxy, halo C_1-C_6 alkoxy, C_1-C_6 alkylthio, halo C_1-C_6 alkylthio, halogen, nitro, amino and cyano;

R_2 is selected from H, C_1-C_6 alkyl, halo C_1-C_6 alkyl, $(CH_2)_{1-6}OR_6$, C_3-C_7 cycloalkyl, halo C_3-C_7 cycloalkyl, C_1-C_6 alkoxy, halo C_1-C_6 alkoxy, C_1-C_6 alkylthio, halo C_1-C_6 alkylthio, halogen, nitro, amino and cyano;

R_3 is selected from H, C_1-C_6 alkyl;

R_4 and R_5 each are independently selected from: H, $-COR_7$, $-SO_2R_8$, and $-SiR_9R_{10}R_{11}$;

wherein, R_7 is selected from C_1-C_6 alkyl and halo C_1-C_6 alkyl; R_8 is selected from C_1-C_6 alkyl, optionally substituted C_1-C_6 alkyl, C_6-C_{10} aryl, and optionally substituted C_6-C_{10} aryl; R_9, R_{10} and R_{11} are independently selected from C_1-C_6 alkyl;

wherein, R_6 has the same definition as R_4 and R_5;

wherein, the compound of Formula (I) wherein R_1 is $(CH_2)OH$, R_2 is methyl, and R_3, R_4 and R_5 are H, is excluded.

2. The compound according to claim 1, wherein,

R_1 is selected from C_1-C_3 alkyl, halo C_1-C_3 alkyl, $(CH_2)_{1-3}OH$, C_3-C_6 cycloalkyl, halo C_3-C_6 cycloalkyl, C_1-C_3 alkoxy, halo C_1-C_3 alkoxy, C_1-C_3 alkylthio, halo C_1-C_3 alkylthio, halogen, nitro, amino and cyano.

3. The compound according to claim 1, wherein,

R_1 is selected from C_1-C_3 alkyl, halo C_1-C_3 alkyl, $(CH_2)_{1-3}OH$, halogen, nitro, amino and cyano.

4. The compound according to claim 1, wherein

R_1 is selected from C_1-C_3 alkyl, and $(CH_2)_{1-3}OH$.

5. The compound according to any one of claims 1-4, wherein

R_2 is selected from H, C_1-C_3 alkyl, halo C_1-C_3 alkyl, $(CH_2)_{1-3}OR_6$, C_3-C_6 cycloalkyl, halo C_3-C_6 cycloalkyl, C_1-C_3 alkoxy, halo C_1-C_3 alkoxy, C_1-C_3 alkylthio, halo C_1-C_3 alkylthio, halogen, nitro, amino and cyano;

wherein, R_6 is selected from H, $-COR_7$, $-SO_2R_8$, and $-SiR_9R_{10}R_{11}$;

wherein, R_7 is selected from C_1-C_6 alkyl, and halo C_1-C_6 alkyl; R_8 is selected from C_1-C_6 alkyl, optionally substituted C_1-C_6 alkyl, C_6-C_{10} aryl, and optionally substituted C_6-C_{10} aryl; R_9, R_{10} and R_{11} are independently selected from C_1-C_6 alkyl.

6. The compound according to any one of claims 1-4, wherein

R_2 is selected from H, C_1-C_3 alkyl, halo C_1-C_3 alkyl, $(CH_2)_{1-3}OR_6$, C_3-C_6 cycloalkyl, halo C_3-C_6 cycloalkyl, C_1-C_3 alkoxy, halo C_1-C_3 alkoxy, C_1-C_3 alkylthio, halo C_1-C_3 alkylthio, halogen, nitro, amino and cyano;

wherein, R_6 is selected from: H, $-COR_7$, $-SO_2R_8$, and $-SiR_9R_{10}R_{11}$;

wherein, R_7 is selected from C_1-C_3 alkyl, and halo C_1-C_3 alkyl; R_8 is selected from C_1-C_3 alkyl, optionally substituted C_1-C_3 alkyl, C_6-C_{10} aryl, and optionally substituted C_6-C_{10} aryl; R_9, R_{10} and R_{11} are independently selected from C_1-C_6 alkyl.

7. The compound according to any one of claims 1-4, wherein

R_2 is selected from H, C_1-C_3 alkyl, halo C_1-C_3 alkyl, $(CH_2)_{1-3}OR_6$, C_3-C_6 cycloalkyl, halo C_3-C_6 cycloalkyl, C_1-C_3 alkoxy, halo C_1-C_3 alkoxy, C_1-C_3 alkylthio, halo C_1-C_3 alkylthio, halogen, nitro, amino and cyano;

wherein, R_6 is selected from: H, $-COR_7$, $-SO_2R_8$, and $-SiR_9R_{10}R_{11}$;

wherein, R_7 is selected from $-CH_3$; R_8 is selected from $-CF_3$ and p-methylphenyl; R_9, R_{10} and R_{11} are independently selected from methyl and tert-butyl.

8. The compound according to any one of claims 1-4, wherein

R_2 is selected from H, C_1-C_3 alkyl, halo C_1-C_3 alkyl, $(CH_2)_{1-3}OR_6$, halogen, nitro, amino and cyano;

wherein, R_6 is selected from H, $-COR_7$, $-SO_2R_8$, and $-SiR_9R_{10}R_{11}$;

wherein, R_7 is selected from C_1-C_6 alkyl, and halo C_1-C_6 alkyl; R_8 is selected from C_1-C_6 alkyl, optionally substituted C_1-C_6 alkyl, C_6-C_{10} aryl, and optionally substituted C_6-C_{10} aryl; R_9, R_{10} and R_{11} are independently selected from C_1-C_6 alkyl.

9. The compound according to any one of claims 1-4, wherein

R_2 is selected from H, C_1-C_3 alkyl, halo C_1-C_3 alkyl, $(CH_2)_{1-3}OR_6$, halogen, nitro, amino and cyano;

wherein, R_6 is selected from: H, -COR_7, -SO_2R_8, and -$SiR_9R_{10}R_{11}$;

wherein, R_7 is selected from C_1-C_3 alkyl and halo C_1-C_3 alkyl; R_8 is selected from C_1-C_3 alkyl, optionally substituted C_1-C_3 alkyl, C_6-C_{10} aryl, and optionally substituted C_6-C_{10} aryl; R_9, R_{10} and R_{11} are independently selected from C_1-C_6 alkyl.

10. The compound according to any one of claims 1-4, wherein

R_2 is selected from H, C_1-C_3 alkyl, halo C_1-C_3 alkyl, $(CH_2)_{1\text{-}3}OR_6$, halogen, nitro, amino and cyano;

wherein, R_6 is selected from: H, -COR_7, -SO_2R_8 and -$SiR_9R_{10}R_{11}$;

wherein, R_7 is selected from -CH_3; R_8 is selected from -CF_3 and p-methyl phenyl; R_9, R_{10} and R_{11} are independently selected from methyl and tert-butyl.

11. The compound according to any one of claims 1-4, wherein

R_2 is selected from H, C_1-C_3 alkyl and $(CH_2)_{1\text{-}3}OR_6$;

wherein, R_6 is selected from H, -COR_7, -SO_2R_8 and -$SiR_9R_{10}R_{11}$;

wherein, R_7 is selected from C_1-C_6 alkyl and halo C_1-C_6 alkyl; R_8 is selected from C_1-C_6 alkyl, optionally substituted C_1-C_6 alkyl, C_6-C_{10} aryl, and optionally substituted C_6-C_{10} aryl; R_9, R_{10} and R_{11} are independently selected from C_1-C_6 alkyl.

12. The compound according to any one of claims 1-4, wherein

R_2 is selected from H, C_1-C_3 alkyl, and $(CH_2)_{1\text{-}3}OR_6$;

wherein, R_6 is selected from H, -COR_7, -SO_2R_8, and -$SiR_9R_{10}R_{11}$;

wherein, R_7 is selected from C_1-C_3 alkyl and halo C_1-C_3 alkyl; R_8 is selected from C_1-C_3 alkyl, optionally substituted C_1-C_3 alkyl, C_6-C_{10} aryl, and optionally substituted C_6-C_{10} aryl; R_9, R_{10} and R_{11} are independently selected from C_1-C_6 alkyl.

13. The compound according to any one of claims 1-4, wherein

R_2 is selected from H, C_1-C_3 alkyl, and $(CH_2)_{1\text{-}3}OR_6$;

wherein, R_6 is selected from H, -COR_7, -SO_2R_8, and -$SiR_9R_{10}R_{11}$;

wherein, R_7 is selected from -CH_3; R_8 is selected from -CF_3 and p-methyl phenyl; R_9, R_{10} and R_{11} are independently selected from methyl and tert-butyl.

14. The compound according to any one of claims 1-13, wherein

R_3 is selected from H and C_1-C_3 alkyl.

15. The compound according to any one of claims 1-13, wherein

R_3 is C_1-C_3 alkyl.

16. The compound according to any one of claims 1-15, wherein

R_4 and R_5 each are independently selected from: H, $-COR_7$, $-SO_2R_8$, and $-SiR_9R_{10}R_{11}$;

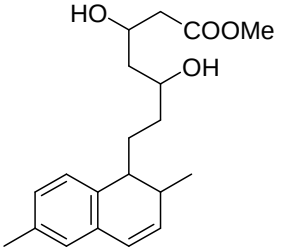
wherein, R_7 is selected from C_1-C_3 alkyl, and halo C_1-C_3 alkyl; R_8 is selected from C_1-C_3 alkyl, optionally substituted C_1-C_3 alkyl, C_6-C_{10} aryl, and optionally substituted C_6-C_{10} aryl; R_9, R_{10} and R_{11} are independently selected from C_1-C_6 alkyl.

17. The compound according to any one of claims 1-15, wherein

R_4 and R_5 each are independently selected from: H, $-COR_7$, $-SO_2R_8$, and $-SiR_9R_{10}R_{11}$;

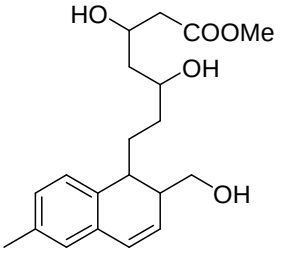
wherein, R_7 is selected from $-CH_3$; R_8 is selected from $-CF_3$, and p-methyl phenyl; R_9, R_{10} and R_{11} are independently selected from methyl, and tert-butyl.

18. The following compound, selected from:



Compound 5

and diacetate, bis(4-methylbenzenesulfonate), bis(trifluoromethanesulfonate), and bis(tert-butyldimethylsilyl ether) of Compound 5;



Compound 5a

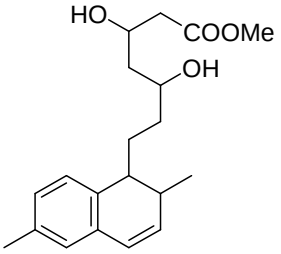
and triacetate, tri(4-methylbenzenesulfonate), tri(trifluoromethanesulfonate), and tri(tert-butyldimethylsilyl ether) of Compound 5a.

19. A pharmaceutical composition, comprising the compound according to any one of claims 1-18 and optionally, a pharmaceutically acceptable excipient.

20. Use of the compound according to any one of claims 1-18 in the manufacture of a medicament, wherein the medicament is useful for inhibiting HMG-CoA reductase activity.

21. Use of the compound according to any one of claims 1-18 in the manufacture of a medicament, wherein the medicament is useful for inhibiting cholesterol synthesis.

22. A method for extracting Compound 5 from *Monascus*-fermented rice or extract thereof, comprising the following steps of:



Compound 5

1) extracting *Monascus*-fermented rice or extract thereof with ethyl acetate (or dichloromethane or methanol or ethanol, or methanol/ethanol aqueous solution) as a solvent;

2) separating the ethyl acetate (or dichloromethane or methanol or ethanol, or methanol/ethanol aqueous solution) extract obtained in Step 1) by silica gel column chromatography, and carrying out gradient elution with petroleum ether, ethyl acetate and methanol, to obtain the ethyl acetate eluting fraction;

3) separating the ethyl acetate eluting fraction obtained in Step 2) by silica gel column chromatography, carrying out elution with dichloromethane-ethyl acetate-methanol, detecting and combining the fractions, to obtain the fractions in Step 3);

4) separating the second fraction obtained in Step 3) by C18 column chromatography, and carrying out gradient elution with acetonitrile-methanol-water, to obtain 82% (acetonitrile-methanol 1: 1) aqueous solution eluting fraction;

5) further separating the 82% (acetonitrile-methanol 1: 1) aqueous solution eluting fraction obtained in Step 4) by sephadex LH-20 column chromatography using dichloromethane-methanol as a mobile phase, analyzing and combining the fractions, to obtain the fractions in Step 5); and

6) purifying the third fraction obtained in Step 5) by chromatographic method, to obtain Compound 5.

23. The method according to claim 22, wherein,

1) extracting *Monascus*-fermented rice or extract thereof with 2-6-fold volume of ethyl acetate (or dichloromethane or methanol or ethanol, or methanol/ethanol aqueous solution) as a solvent for three times, 20-40 min for each time, combining the extracting solution, and concentrating it under reduced pressure to recover the solvent, and to obtain the ethyl acetate extract;

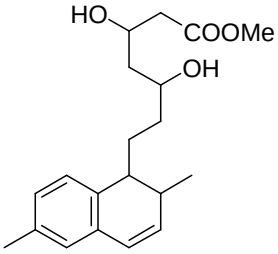
2) separating the ethyl acetate (or dichloromethane or methanol or ethanol, or methanol/ethanol aqueous solution) extract obtained in Step 1) by silica gel column chromatography, and carrying out gradient elution with petroleum ether, ethyl acetate and methanol or ethanol, or methanol/ethanol aqueous solution, to obtain the ethyl acetate eluting fraction;

3) separating the ethyl acetate eluting fraction obtained in Step 2) by silica gel column chromatography, carrying out elution with dichloromethane-ethyl acetate-methanol (30: 30: 1), and combining the fractions, to obtain 5 fractions;

4) separating the second fraction obtained in Step 3) by C18 column chromatography, and carrying out gradient elution with 82% (acetonitrile-methanol 1: 1) aqueous solution ~ 100% (acetonitrile-methanol 1: 1), to obtain 82% (acetonitrile-methanol 1: 1) aqueous solution eluting fraction;

5) further separating the 82% (acetonitrile-methanol 1: 1) aqueous solution eluting fraction obtained in Step 4) by sephadex LH-20 column chromatography using dichloromethane-methanol (2: 1) as a mobile phase, and combining the fractions, to obtain 6 fractions in Step 5); and

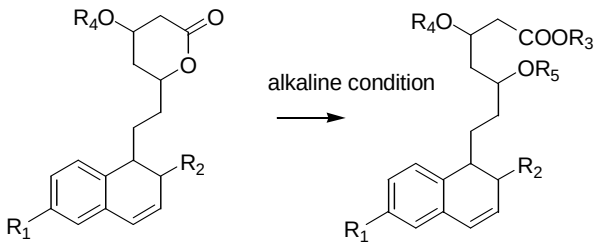
6) purifying the third fraction obtained in Step 5) by chromatography using acetonitrile-methanol-water as a mobile phase and using C18 chromatographic column as a stationary phase, to obtain Compound 5



Compound 5 .

24. A method for synthesizing the compound of Formula (I) according to any one of claims 1-17, and Compound 5 and Compound 5a according to claim 18:

reacting a compound of Formula (II) under alkaline condition, or adding an esterification reagent under alkaline condition, to prepare the compound of Formula (I),

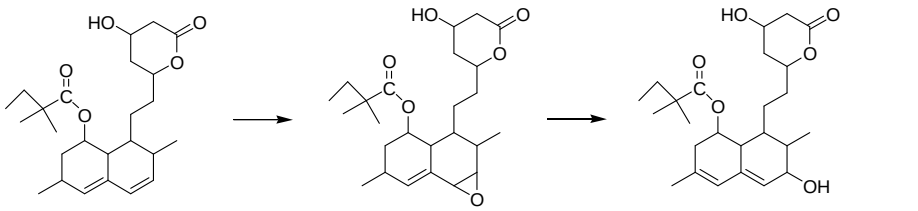


II I

wherein, in Formula (II), R_1, R_2 and R_4 have the same meanings as defined in Formula (I) according to any one of claims 1-17,

the pH range of the alkaline condition is 7.5-14, and optionally, an alkaline reagent such as sodium hydroxide, potassium hydroxide, ammonia water and sodium carbonate, or a solvent may be added; the esterification reagent may be selected from lower alcohol such as methanol and ethanol; anhydride (acetic anhydride, sulfonic anhydride, trifluormethanesulfonic anhydride, etc.), acyl chloride (toluenesulfonyl chloride), and chlorosilane (tert-butyldimethylchlorosilane).

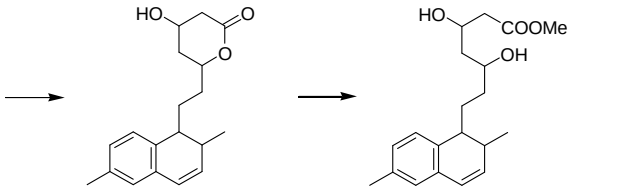
25. A method for synthesizing compound 5:



Chemical formula: $C_{25}H_{38}O_5$
Exact molecular weight: 418.27
1

Chemical formula: $C_{25}H_{38}O_6$
Exact molecular weight: 434.27
2

Chemical formula: $C_{25}H_{38}O_6$
Exact molecular weight: 434.27
3



Chemical formula: $C_{19}H_{24}O_3$
Exact molecular weight: 300.17
4

Chemical formula: $C_{20}H_{28}O_4$
Exact molecular weight: 332.20
5

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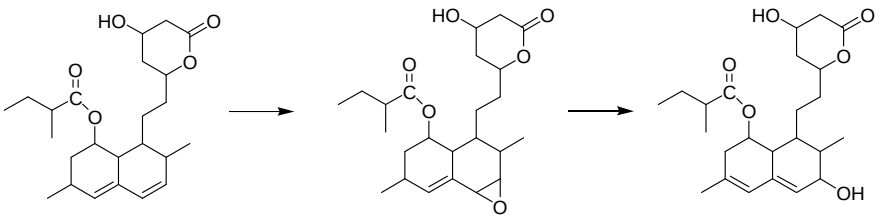
26. A method for synthesizing Compound 5:



Chemical formula: $C_{24}H_{36}O_5$
Exact molecular weight: 404.26

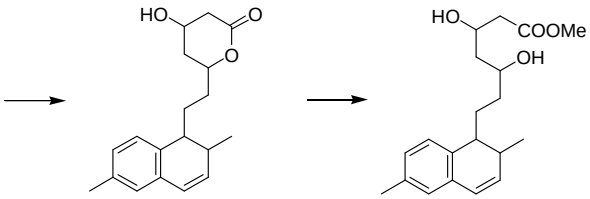
1b

Chemical formula: $C_{24}H_{36}O_6$
Exact molecular weight: 420.25

2b

Chemical formula: $C_{24}H_{36}O_6$
Exact molecular weight: 420.25

3b



Chemical formula: $C_{19}H_{24}O_3$
Exact molecular weight: 300.17

4

Chemical formula: $C_{20}H_{28}O_4$
Exact molecular weight: 332.20

5