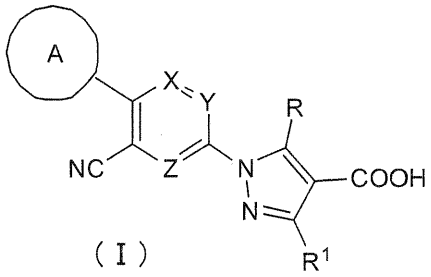
Solution to Problem

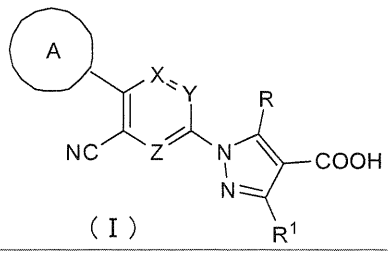
As a result of earnest studies on compounds having xanthine oxidase inhibitory activity, the inventors have completed the present invention based on the findings: that a compound represented by the following formula (I)



(I)

i.e., a pyrazole derivative which has a tricyclic triaryl structure and has as the central ring a pyridine ring possessing one nitrogen atom and substituted with a cyano group, has xanthine oxidase inhibitory activity; further that it has novel xanthine oxidase inhibitory activity accompanied by an excellent uric acid lowering effects; and further that it has sustained xanthine oxidase inhibitory activity that enables particularly excellent uric acid lowering effect over a long period of time. In addition, the inventors have completed the present invention based on the finding that the pyrazole derivative can be a good therapeutic or prophylactic agent for gout, hyperuricemia, tumor lysis syndrome, urinary calculus, hypertension, dyslipidemia, diabetes, cardiovascular diseases such as arteriosclerosis or heart failure, renal diseases such as diabetic nephropathy, respiratory diseases such as chronic obstructive pulmonary disease, inflammatory bowel diseases, autoimmune diseases, or the like.

In one aspect, there is provided a compound or a pharmaceutically acceptable salt thereof represented by the following formula (I)



(I)

wherein:

A represents a phenyl group which may be unsubstituted or substituted with 1 to 3 groups Q which are the same or different from one another and selected from the group consisting of a halogen atom, a C_{1-6} alkyl group, a C_{3-7} cycloalkyl group, a C_{1-6} halogenalkyl group, a phenyl group, -O- R^2 and -O- C_{1-6} halogenalkyl;

X, and Z represent CH and Y represents a nitrogen atom;

R represents a hydrogen atom;

R^1 represents a hydrogen atom; and

R^2 represents a hydrogen atom or a C_{1-6} alkyl group.

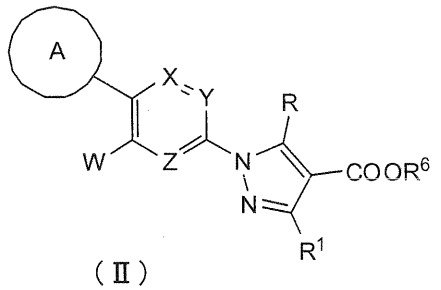
~~The present invention is~~In another embodiment, there is provided a compound represented by the following formula (I):

thereof, and a pharmaceutically acceptable carrier.

The present invention is also a xanthine oxidase inhibitor comprising a compound represented by the above formula (I), or a pharmaceutically acceptable salt thereof, as an active ingredient.

The present invention is also a therapeutic or prophylactic agent for diseases associated with xanthine oxidase, such as gout, hyperuricemia, tumor lysis syndrome, urinary calculus, hypertension, dyslipidemia, diabetes, cardiovascular diseases such as arteriosclerosis or heart failure, renal diseases such as diabetic nephropathy, respiratory diseases such as chronic obstructive pulmonary disease, inflammatory bowel diseases, or autoimmune diseases, comprising a compound represented by the above formula (I), or a pharmaceutically acceptable salt thereof, as an active ingredient.

In another aspect, there is provided a compound represented by formula (II):



(Ⅱ)

wherein:

A represents a phenyl group which, wherein the aryl group or heteroaryl group may be unsubstituted or substituted with 1 to 3 groups Q which are the same or different from one another and selected from the group consisting of a halogen atom, a C_{1-16} atom, a C_{1-6} alkyl group, a C_{3-7} cycloalkyl group, a C_{1-6} halogenalkyl group, a phenyl group, -O-R^2, and –O- C_{1-6} halogenalkyl;

X, and Z represent C H and Y represents a nitrogen atom;

R represents a hydrogen atom;

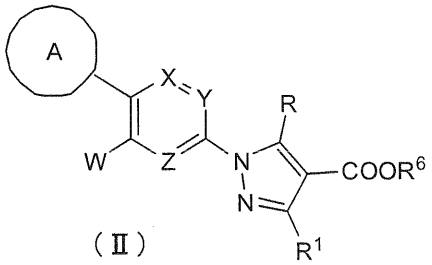
R^1 represents a hydrogen atom;

R^2 represents a hydrogen atom or a C_{1-6} alkyl group;

R^6 represents a protective group of a carboxyl group; and

W represents a halogen atom, a methanesulfonyloxy group, a p-toluenesulfonyloxy group, a trifluoromethanesulfonyloxy group, or a cyano group.

~~Furthermore, the present invention is~~In another embodiment, there is provided a compound represented by the following formula (II) which can be used as an intermediate in the manufacture of the compound represented by the above formula (I):



(Ⅱ)

wherein:

A represents a C_{6-10} aryl group or a heteroaryl group, wherein the aryl group or heteroaryl group may be unsubstituted or substituted with 1 to 3 groups Q which are the same or different from one another and selected from the group consisting of a halogen atom, -CN, $-NO_2$, a C_{1-6} alkyl group, a C_{3-7} cycloalkyl group, a C_{1-6} halogenoalkyl group, a phenyl group, $-CH_2-O-R^2$, $-O-R^2$, $-O-C_{1-6}$ halogenoalkyl, -O-benzyl, -O-

phenyl, -O-CO-R^2, -NR^3R^4, -NH-CO-R^2, -CO_2-R^2, -CO-R^2, -CO-NR^3R^4, -NH-SO_2-R^2, -CO-aryl, -S-R^2, -SO_2-C_{1-6} alkyl, and -SO_2-phenyl;

X, Y, and Z represent CR^5 or a nitrogen atom, wherein one of X, Y, and Z represents a nitrogen atom and the remaining two represent CR^5;

R represents a hydrogen atom or a C_{1-6} alkyl group;

R^1 represents a hydrogen atom, an amino group, or a C_{1-6} alkyl group;

R^2 represents a hydrogen atom or a C_{1-6} alkyl group;

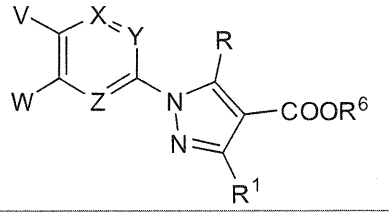
R^3 and R^4 are the same or different from each other and are a hydrogen atom or a C_{1-6} alkyl group, where R^3 and R^4 may be taken together to form with the nitrogen atom to which they are attached a nitrogen-containing saturated monocyclic heterocycle; and

R^5 represents a hydrogen atom, a halogen atom, or a C_{1-6} alkyl group;

R^6 represents a protective group of a carboxyl group; and

W represents a halogen atom, a methanesulfonyloxy group, a p-toluenesulfonyloxy group, a trifluoromethanesulfonyloxy group, or a cyano group.

In another aspect, there is provided a compound represented by formula (III):



(Ⅲ)

wherein,

X, and Z represent CH and Y represents a nitrogen atom;

R represents a hydrogen atom;

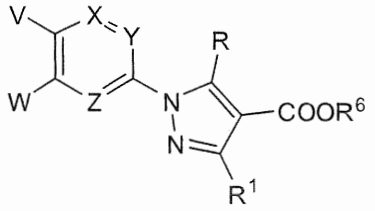
R^1 represents a hydrogen atom;

R^6 represents a protective group of a carboxyl group;

V represents a halogen atom, a methanesulfonyloxy group, a p-toluenesulfonyloxy group, a trifluoromethanesulfonyloxy group, a hydroxyl group, or a benzyloxy group; and

W represents a halogen atom, a methanesulfonyloxy group, a p-toluenesulfonyloxy group, a trifluoromethanesulfonyloxy group, or a cyano group.

~~Furthermore, the present invention is~~In another aspect, there is provided a compound represented by the following formula (III) which can be used as an intermediate in the manufacture of the compound represented by the above formula (I):



(Ⅲ)

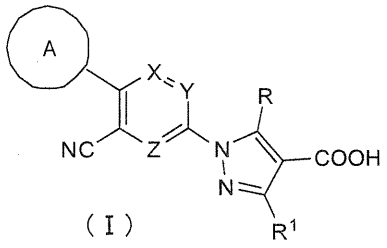
Wherein,

X, Y, and Z represent CR^5 or a nitrogen atom, wherein one of X, Y, and Z represents a nitrogen atom and the remaining two represent CR^5;

R represents a hydrogen atom or a C_{1-6} alkyl group;

CLAIMS

1. A compound or a pharmaceutically acceptable salt thereof represented by the following formula (I)



(I)

wherein:

A represents a phenyl ~~C_{6-10} aryl~~ group ~~or a heteroaryl group, wherein the aryl group or heteroaryl group~~ which may be unsubstituted or substituted with 1 to 3 groups Q which are the same or different from one another and selected from the group consisting of a halogen atom, a C_{1-6} alkyl group, a C_{3-7} cycloalkyl group, a C_{1-6} halogenalkyl group, a phenyl group, -O- R^2 and -O- C_{1-6} halogenalkyl~~a halogen atom, CN, NO_2, a C_{1-6} alkyl group, a C_{3-7} cycloalkyl group, a C_{1-6} halogenoalkyl group, a phenyl group, CH_2-O-R^2, -O-R^2, -O-C_{1-6} halogenoalkyl, O-benzyl, O-phenyl, -O-CO-R^2, NR^3R^4, -NH-CO-R^2, $-CO_2-R^2$, -CO-R^2, -CO-NR^3R^4, -NH-SO_2-R^2, -CO-aryl, -S-R^2, $-SO_2-C_{1-6}$ alkyl, and $-SO_2$-phenyl~~;

X, ~~Y,~~ and Z represent ~~CR^5~~ CH and Y represents ~~or~~ a nitrogen atom~~, wherein one of X, Y, and Z represents a nitrogen atom and the remaining two represent CR^5~~;

R represents a hydrogen atom~~ or a C_{1-6} alkyl group~~;

R^1 represents a hydrogen atom~~, an amino group, or a C_{1-6} alkyl group~~; and

R^2 represents a hydrogen atom or a C_{1-6} alkyl group~~.~~;

~~R^3 and R^4 are the same or different from each other and are a hydrogen atom or a C_{1-6} alkyl group, where R^3 and R^4 may be taken together to form with the nitrogen atom to which they are attached a nitrogen-containing saturated monocyclic heterocycle; and~~

R^5 represents a hydrogen atom, a halogen atom, or a C_{1-6} alkyl group.

2. The compound or a pharmaceutically acceptable salt thereof according to Claim 1, wherein X and Z represent CR^5, and Y represents a nitrogen atom.

3. The compound or a pharmaceutically acceptable salt thereof according to Claim 1, wherein Y and Z represent CR^5, and X represents a nitrogen atom.

4. The compound or a pharmaceutically acceptable salt thereof according to Claim 1, wherein X and Y represent CR^5, and Z represents a nitrogen atom.

5. The compound or a pharmaceutically acceptable salt thereof according to any of Claims 1 to 4, wherein R^5 represents a hydrogen atom.

6. The compound or a pharmaceutically acceptable salt thereof according to any of Claims 1 to 5, wherein R and R^1 represent hydrogen atom.

7. The compound or a pharmaceutically acceptable salt thereof according to any of Claims 1 to 6, wherein A represents a C_{6-10} aryl group which may be unsubstituted or substituted with 1 to 2 groups Q which are the same or different from one another and selected from the group consisting of a halogen atom, -CN, $-NO_2$, a C_{1-6} alkyl group, a C_{3-7} cycloalkyl group, a C_{1-6} halogenoalkyl group, a phenyl group, $-CH_2-O-R^2$, $-O-R^2$, $-O-C_{1-6}$ halogenoalkyl, -O-benzyl, -O-phenyl, $-O-CO-R^2$, $-NR^3R^4$, $-NH-CO-R^2$, $-CO_2-R^2$, $-CO-R^2$, $-CO-NR^3R^4$, $-NH-SO_2-R^2$, -CO-aryl, $-S-R^2$, $-SO_2-C_{1-6}$ alkyl, and $-SO_2$-phenyl.

8. The compound or a pharmaceutically acceptable salt thereof according to Claim 7, wherein A represents a phenyl group which may be unsubstituted or substituted with 1 to 2 groups Q which are the same or different from one another and selected from the group consisting of a halogen atom, -CN, $-NO_2$, a C_{1-6} alkyl group, a C_{3-7} cycloalkyl group, a C_{1-6} halogenoalkyl group, a phenyl group, $-CH_2-O-R^2$, $-O-R^2$, $-O-C_{1-6}$ halogenoalkyl, -O-benzyl, -O-phenyl, $-O-CO-R^2$, $-NR^3R^4$, $-NH-CO-R^2$, $-CO_2-R^2$, $-CO-R^2$, $-CO-NR^3R^4$, $-NH-SO_2-R^2$, -CO-aryl, $-S-R^2$, $-SO_2-C_{1-6}$ alkyl, and $-SO_2$-phenyl.

9. The compound or a pharmaceutically acceptable salt thereof according to any of Claims 1 to 6, wherein A represents a heteroaryl group which may be unsubstituted or substituted with 1 to 2 groups Q which are the same or different from one another and selected from the group consisting of a halogen atom, -CN, $-NO_2$, a C_{1-6} alkyl group, a C_{3-7} cycloalkyl group, a C_{1-6} halogenoalkyl group, a phenyl group, $-CH_2-O-R^2$, $-O-R^2$, $-O-C_{1-6}$ halogenoalkyl, -O-benzyl, -O-phenyl, $-O-CO-R^2$, $-NR^3R^4$, $-NH-CO-R^2$, $-CO_2-R^2$, $-CO-R^2$, $-CO-NR^3R^4$, $-NH-SO_2-R^2$, -CO-aryl, $-S-R^2$, $-SO_2-C_{1-6}$ alkyl, and $-SO_2$-phenyl.

10. The compound or a pharmaceutically acceptable salt thereof according to Claim 9, wherein A represents a thienyl group which may be unsubstituted or substituted with 1 to 2 groups Q which are the same or different from one another and selected from the group consisting of a halogen atom, -CN, $-NO_2$, a C_{1-6} alkyl group, a C_{3-7} cycloalkyl group, a C_{1-6} halogenoalkyl group, a phenyl group, $-CH_2-O-R^2$, $-O-R^2$, $-O-C_{1-6}$ halogenoalkyl, -O-benzyl, -O-phenyl, $-O-CO-R^2$, $-NR^3R^4$, $-NH-CO-R^2$, $-CO_2-R^2$, $-CO-R^2$, $-CO-NR^3R^4$, $-NH-SO_2-R^2$, -CO-aryl, $-S-R^2$, $-SO_2-C_{1-6}$ alkyl, and $-SO_2$-phenyl.

2~~11~~. The compound or a pharmaceutically acceptable salt thereof accoding to claim 1~~any of Claims 1 to 10~~, wherein A is unsubstituted.

~~12. The compound or a pharmaceutically acceptable salt thereof according to any of Claims 1 to 10, wherein Q is selected from the group consisting of a halogen atom, a C_{1-6} alkyl group, a C_{3-7} cycloalkyl group, a C_{1-6} halogenoalkyl group, a phenyl group, $-O-R^2$, and $-O-C_{1-6}$ halogenoalkyl.~~

3~~13~~. The compound or a pharmaceutically acceptable salt thereof according to claims 1 or 2~~12~~, wherein A is substituted with 1 to 3 groups Q which are the same or different from one another and~~Q~~ is selected from the group consisting of a halogen atom, a methyl group, and a methoxy group.

4~~14~~. A compound selected from the following (1) to (46~~107~~):

(1) 1-(4-cyano-5-phenylpyridin-2-yl)-1H-pyrazole-4-carboxylic acid;

(2) 1-[4-cyano-5-(4-methoxyphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(3) 1-[4-cyano-5-(2-ethoxyphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(4) 1-[4-cyano-5-(2-methylphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(5) 1-[4-cyano-5-(2-fluorophenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(6) 1-[4-cyano-5-(2-chlorophenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(7) 1-[4-cyano-5-(2-methoxyphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(8) 1-{4-cyano-5-[2-(trifluoromethyl)phenyl]pyridin-2-yl}-1H-pyrazole-4-carboxylic acid;

(9) 1-{4-cyano-5-[2-(trifluoromethoxy)phenyl]pyridin-2-yl}-1H-pyrazole-4-carboxylic acid;

(10) 1-[4-cyano-5-(3-methylphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(11) 1-[4-cyano-5-(3-fluorophenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(12) 1-[4-cyano-5-(3-chlorophenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(13) 1-[4-cyano-5-(3-methoxyphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(14) 1-[4-cyano-5-(4-methylphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(15) 1-[4-cyano-5-(4-chlorophenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(16) 1-[4-cyano-5-(4-hydroxyphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(17) 1-[4-cyano-5-(2-ethoxy-6-fluorophenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(18) 1-[4-cyano-5-(2-fluoro-6-methoxyphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(19) 1-[4-cyano-5-(2-fluoro-3-methoxyphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(20) 1-[4-cyano-5-(2,3-difluorophenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

~~(21) 1-[4-cyano-5-(thiophen-3-yl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;~~

~~(22) 1-[4-cyano-5-(3-methylthiophen-2-yl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;~~

~~(23) 1-[4-cyano-5-(furan-3-yl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;~~

~~(24) 1-[4-cyano-5-(3-methoxypyridin-4-yl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;~~

~~(25) 1-[4-cyano-5-(pyridin-3-yl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;~~

~~(26) 1-(4-cyano-5-phenylpyridin-2-yl)-3-methyl-1H-pyrazole-4-carboxylic acid;~~

~~(27) 1-(4-cyano-5-phenylpyridin-2-yl)-3-(propan-2-yl)-1H-pyrazole-4-carboxylic acid;~~

~~(28) 1-(4-cyano-5-phenylpyridin-2-yl)-3,5-dimethyl-1H-pyrazole-4-carboxylic acid;~~

(21~~29~~) 1-[4-cyano-5-(4-fluorophenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(22~~30~~) 1-[4-cyano-5-(3-ethoxyphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(2331) 1-[4-cyano-5-(3-propoxyphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(2432) 1-[4-cyano-5-(2,4-difluorophenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(2533) 1-[4-cyano-5-(2-fluoro-4-methylphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(2634) 1-[4-cyano-5-(2-fluoro-5-methylphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(2735) 1-[4-cyano-5-(2,5-difluorophenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(2836) 1-[4-cyano-5-(2-fluoro-3-methylphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(3937) 1-[4-cyano-5-(4-fluoro-3-methylphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(3038) 1-[4-cyano-5-(2,3-dimethylphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(3139) 1-[4-cyano-5-(3-fluoro-4-methylphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(3240) 1-[4-cyano-5-(3-chloro-4-fluorophenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

~~(41) 1-[4-cyano-5-(3-chloro-2-fluorophenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;~~

~~(42) 1-[5-(4-carboxyphenyl)-4-cyanopyridin-2-yl]-1H-pyrazole-4-carboxylic acid;~~

(3343) 1-{4-cyano-5-[4-(trifluoromethyl)phenyl]pyridin-2-yl}-1H-pyrazole-4-carboxylic acid;

(3444) 1-{4-cyano-5-[4-(trifluoromethoxy)phenyl]pyridin-2-yl}-1H-pyrazole-4-carboxylic acid;

(3545) 1-{4-cyano-5-[3-(trifluoromethyl)phenyl]pyridin-2-yl}-1H-pyrazole-4-carboxylic

acid;

(3646) 1-{4-cyano-5-[3-(difluoromethoxy)phenyl]pyridin-2-yl}-1H-pyrazole-4-carboxylic acid;

(3747) 1-{4-cyano-5-[4-(propane-2-yl)phenyl]pyridin-2-yl}-1H-pyrazole-4-carboxylic acid;

(3848) 1-{4-cyano-5-[3-(propane-2-yl)phenyl]pyridin-2-yl}-1H-pyrazole-4-carboxylic acid;

(3949) 1-[4-cyano-5-(4-fluoro-2-methylphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(4050) 1-[4-cyano-5-(4-fluoro-2-methoxyphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(4151) 1-[4-cyano-5-(4-chloro-3-methylphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(4252) 1-{ 4-cyano-5-[(4-propan-2-yloxy)phenyl]pyridin-2-yl}-1H-pyrazole-4-carboxylic acid;

(4353) 1-[5-(4-tert-butylphenyl)-4-cyanopyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(4454) 1-[4-cyano-5-(4-phenoxyphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(4555) 1-{4-cyano-5-[4-(methoxymethyl)phenyl]pyridin-2-yl}-1H-pyrazole-4-carboxylic acid;

(4656) 1-{4-cyano-5-[3-(2-methylpropoxy)phenyl]pyridin-2-yl}-1H-pyrazole-4-carboxylic acid;

~~(57) 1-[4-cyano-5-(naphthalen-2-yl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;~~

~~(58) 1-[4-cyano-5-(4-methoxypyridin-3-yl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;~~

~~(59) 1-{4-cyano-5-[6-(dimethylamino)pyridin-3-yl]pyridin-2-yl}-1H-pyrazole-4-~~

carboxylic acid;

(60) 1-[4-cyano-5-(5-fluoropyridin-3-yl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(61) 1-[5-(1-benzothiophen-3-yl)-4-cyanopyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(62) 1-[4-cyano-5-(pyridin-4-yl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(63) 1-{4-cyano-5-[4-(methylsulfanyl)phenyl]pyridin-2-yl}-1H-pyrazole-4-carboxylic acid;

(64) 1-{4-cyano-5-[4-(morpholin-4-yl)phenyl]pyridin-2-yl}-1H-pyrazole-4-carboxylic acid;

(65) 1-[4-cyano-5-(4-phenylphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxyic acid;

(66) 1-{5-[4-(benzyloxy)phenyl]-4-cyanopyridin-2-yl}-1H-pyrazole-4-carboxylic acid;

(67) 1-{4-cyano-5-[3-(dimethylamino)phenyl]pyridin-2-yl}-1H-pyrazole-4-carboxylic acid;

(68) 1-[5-(4-aminophenyl)-4-cyanopyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

_(69) 1-[4-cyano-5-(4-methanesulfonamidophenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(70) 1-(4-cyano-5-{4-[(morpholin-4-yl)carbonyl]phenyl}pyridin-2-yl)-1H-pyrazole-4-carboxylic acid;

(71) 1-[5-(4-acetophenyl)-4-cyanopyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(72) 1-[4-cyano-5-(3-nitrophenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(73) 1-[5-(4-benzoylphenyl)-4-cyanopyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(74) 1-[4-cyano-5-(4-methanesulfonylphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(75) 1-(5-cyano-6-phenylpyridin-3-yl)-1H-pyrazole-4-carboxylic acid;

(76) 1-[5-cyano-6-(2-fluorophenyl)pyridin-3-yl]-1H-pyrazole-4-carboxylic acid;

(77) 1-[5-cyano-6-(2,4-difluorophenyl)pyridin-3-yl]-1H-pyrazole-4-carboxylic acid;

(78) 1-[5-cyano-6-(2-fluoro-4-methylphenyl)pyridin-3-yl]-1H-pyrazole-4-carboxylic acid;

(79) 1-[5-cyano-6-(2-fluoro-5-methylphenyl)pyridin-3-yl]-1H-pyrazole-4-carboxylic acid;

(80) 1-[5-cyano-6-(2,5-difluorophenyl)pyridin-3-yl]-1H-pyrazole-4-carboxylic acid;

(81) 1-[5-cyano-6-(2,3-difluorophenyl)pyridin-3-yl]-1H-pyrazole-4-carboxylic acid;

(82) 1-[5-cyano-6-(4-fluoro-3-methylphenyl)pyridin-3-yl]-1H-pyrazole-4-carboxyic acid;

(83) 1-[5-cyano-6-(3-fluoro-4-methylphenyl)pyridin-3-yl]-1H-pyrazole-4-carboxylic acid;

(84) 1-[5-cyano-6-(2-fluoro-5-methoxyphenyl)pyridin-3-yl]-1H-pyrazole-4-carboxylic acid;

(85) 1-(6-cyano-5-phenylpyridin-2-yl)-1H-pyrazole-4-carboxylic acid;

(86) 1-[6-cyano-5-(2-fluorophenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(87) 1-[6-cyano-5-(2-fluoro-4-methylphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(88) 1-[6-cyano-5-(2-fluoro-5-methylphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(89) 1-[6-cyano-5-(4-fluorophenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(90) 1-[6-cyano-5-(2,4-difluorophenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(91) 1-[6-cyano-5-(2-fluoro-5-methoxyphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(92) 1-[6-cyano-5-(3-methylphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(93) 1-[6-cyano-5-(3-ethoxyphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(94) 1-[6-cyano-5-(4-fluoro-3-methylphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(95) 1-[6-cyano-5-(2,6-difluorophenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(96) 1-[6-cyano-5-(2-fluoro-6-methoxyphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(97) 3-amino-1-(4-cyano-5-phenylpyridin-2-yl)-1H-pyrazole-4-carboxylic acid;

(98) 3-amino-1-[4-cyano-5-(2-fluorophenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(99) 3-amino-1-[4-cyano-5-(4-fluorophenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(100) 3-amino-1-[4-cyano-5-(4-chlorophenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(101) 3-amino-1-[4-cyano-5-(3-methylphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(102) 3-amino-1-[4-cyano-5-(3-methoxyphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(103) 3-amino-1-[4-cyano-5-(2-fluoro-4-methylphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(104) 3-amino-1-[4-cyano-5-(2-fluoro-5-methylphenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(105) 3-amino-1-[4-cyano-5-(2,4-difluorophenyl)pyridin-2-yl]-1H-pyrazole-4-carboxylic acid;

(106) 3-amino-1-[4-cyano-5-(4-fluoro-3-methylphenyl)pyridin-2-yl]-1H-pyrazole-4-

~~carboxylic acid; and~~

~~(107) 3-amino-1-[4-cyano-5-(2-fluoro-5-methoxyphenyl)pyridine-2-yl]-1H-pyrazole-4-carboxylic acid;~~

or a pharmaceutically acceptable salt thereof.

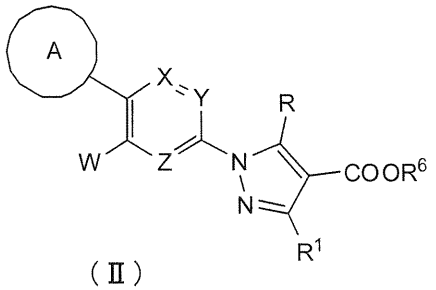
~~5~~15. A pharmaceutical composition comprising the compound according to any of claims 1 to ~~4~~14, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

~~6~~16. A xanthine oxidase inhibitor comprising the compound according to any of claims 1 to ~~4~~14, or a pharmaceutically acceptable salt thereof, as an active ingredient.

~~7~~17. A therapeutic or prophylactic agent for gout, hyperuricemia, tumor lysis syndrome, urinary calculus, hypertension, dyslipidemia, diabetes, cardiovascular diseases such as arteriosclerosis or heart failure, renal diseases such as diabetic nephropathy, respiratory diseases such as chronic obstructive pulmonary disease, inflammatory bowel diseases, or autoimmune diseases, comprising the compound according to any of claims 1 to 14, or a pharmaceutically acceptable salt thereof, as an active ingredient.

~~8~~18. A therapeutic or prophylactic agent for gout or hyperuricemia, comprising the compound according to any of claims 1 to 14, or a pharmaceutically acceptable salt thereof, as an active ingredient.

~~9~~19. A compound represented by formula (II):



(Ⅱ)

wherein:

A represents a ~~C6-10 aryl group or a heteroaryl~~phenyl group which, wherein the aryl group or heteroaryl group may be unsubstituted or substituted with 1 to 3 groups Q which are the same or different from one another and selected from the group consisting of a halogen atom, a C_{1-16} atom, a C_{1-6} alkyl group, a C_{3-7} cycloalkyl group, a C_{1-6} halogenalkyl group, a phenyl group, -O-R^2, and –O-C_{1-6} halogenalkyl ~~a halogen atom, –CN, –NO2, a C1-6 alkyl group, a C3-7 cycloalkyl group, a C1-6 halogenoalkyl group, a phenyl group, –CH2–O–R2, –O–R2, –O–C1-6 halogenoalkyl, –O-benzyl, –O-phenyl, –O–CO–R2, –NR3R4, –NH–CO–R2, –CO2–R2, –CO–R2, –CO–NR3R4, –NH–SO2–R2, –CO-aryl, –S–R2, –SO2–C1-6 alkyl, and –SO2-phenyl~~;

X, ~~Y,~~ and Z represent C~~R~~5 H and ~~or~~ Y represents a nitrogen atom~~, wherein one of X, Y, and Z represents a nitrogen atom and the remaining two represent CR5~~;

R represents a hydrogen atom ~~or a C1-6 alkyl group~~;

R^1 represents a hydrogen atom~~, an amino group, or a C1-6 alkyl group~~;

R^2 represents a hydrogen atom or a C_{1-6} alkyl group;

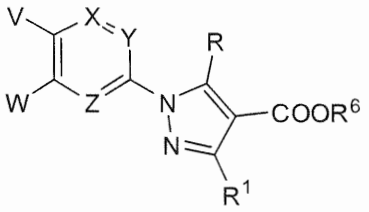
~~R3 and R4 are the same or different from each other and are a hydrogen atom or a C1-6 alkyl group, where R3 and R4 may be taken together to form with the nitrogen atom to which they are attached a nitrogen-containing saturated monocyclic heterocycle; and~~

~~R5 represents a hydrogen atom, a halogen atom, or a C1-6 alkyl group;~~

R^6 represents a protective group of a carboxyl group; and

W represents a halogen atom, a methanesulfonyloxy group, a p-toluenesulfonyloxy group, a trifluoromethanesulfonyloxy group, or a cyano group.

1020. A compound represented by formula (III):



(Ⅲ)

wherein,

X, ~~Y,~~ and Z represent C~~R~~^{5} H and Y represents ~~or~~ a nitrogen atom~~, wherein one of X, Y, and Z represents a nitrogen atom and the remaining two represent CR^5~~;

R represents a hydrogen atom~~ or a C_{1-6} alkyl group~~;

R^1 represents a hydrogen atom~~, an amino group, or a C_{1-6} alkyl group~~;

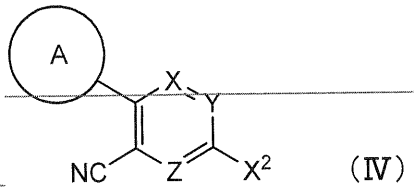
~~R^5 represents a hydrogen atom, a halogen atom, or a C_{1-6} alkyl group;~~

R^6 represents a protective group of a carboxyl group;

V represents a halogen atom, a methanesulfonyloxy group, a p-toluenesulfonyloxy group, a trifluoromethanesulfonyloxy group, a hydroxyl group, or a benzyloxy group; and

W represents a halogen atom, a methanesulfonyloxy group, a p-toluenesulfonyloxy group, a trifluoromethanesulfonyloxy group, or a cyano group.

~~21. A compound represented by formula (IV):~~



(IV)

wherein:

A represents a C_{6-10} aryl group or a heteroaryl group, wherein the aryl group or heteroaryl group may be unsubstituted or substituted with 1 to 3 groups Q which are the same or different from one another and selected from the group consisting of a halogen atom, -CN, $-NO_2$, a C_{1-6} alkyl group, a C_{3-7} cycloalkyl group, a C_{1-6} halogenoalkyl group, a phenyl group, $-CH_2-O-R^2$, $-O-R^2$, $-O-C_{1-6}$ halogenoalkyl, -O-benzyl, -O-phenyl, $-O-CO-R^2$, $-NR^3R^4$, $-NH-CO-R^2$, $-CO_2-R^2$, $-CO-R^2$, $-CO-NR^3R^4$, $-NH-SO_2-R^2$, -CO-aryl, $-S-R^2$, $-SO_2-C_{1-6}$ alkyl, and $-SO_2$-phenyl;

X, Y, and Z represent CR^5 or a nitrogen atom, wherein one of X, Y, and Z represents a nitrogen atom and the remaining two represent CR^5;

R^2 represents a hydrogen atom or a C_{1-6} alkyl group;

R^3 and R^4 are the same or different from each other and are a hydrogen atom or a C_{1-6} alkyl group, where R^3 and R^4 may be taken together to form with the nitrogen atom to which they are attached a nitrogen-containing saturated monocyclic heterocycle; R^5 represents a hydrogen atom, a halogen atom, or a C_{1-6} alkyl group; and

X^2 represents a halogen atom, a methanesulfonyloxy group, a p-toluenesulfonyloxy group or a trifluoromethanesulfonyloxy group.