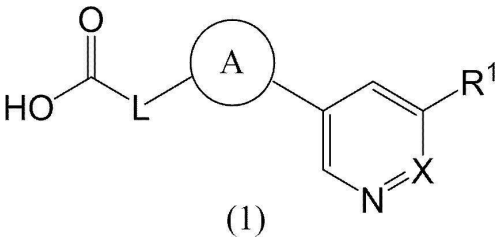
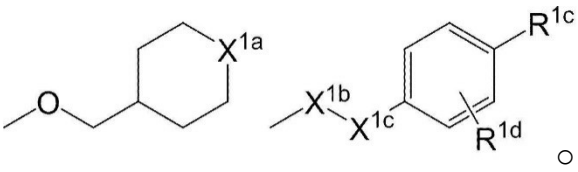
CLAIMS

1. A carboxylic acid compound represented by the following formula (1) or a pharmacologically acceptable salt thereof

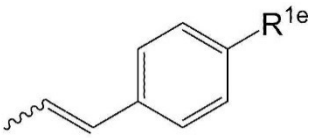


(1)

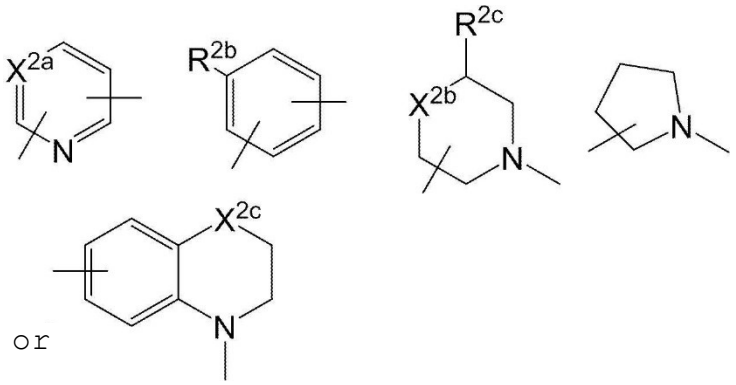
wherein, $R^1$ is



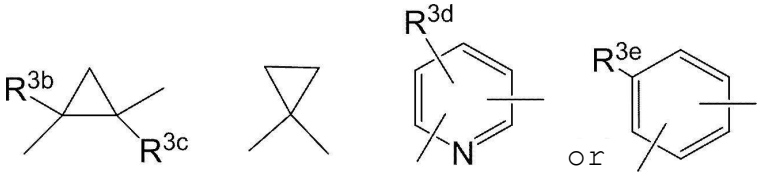
or



wherein $X^{1a}$ is $-C(R^{1a})_2-$ wherein plural symbols $R^{1a}$ are the same or different and each is a hydrogen atom, a halogen atom, $C_1$-$C_2$ perfluoroalkyl, $C_1$-$C_2$ perfluoroalkoxy or $C_1$-$C_6$ alkyl, or plural symbols $R^{1a}$ are bonded to form 1,1-$C_3$-$C_6$ cycloalkylene or $-NR^{1b}-$
wherein $R^{1b}$ is a hydrogen atom or $C_1$-$C_2$ perfluoroalkyl,
$X^{1b}$ and $X^{1c}$ are the same or different and each is -O- or $-CH_2-$
provided $X^{1b}$ and $X^{1c}$ are not simultaneously -O-,
$R^{1c}$ is a hydrogen atom, a halogen atom, $C_1$-$C_2$ perfluoroalkyl, $C_1$-$C_2$ perfluoroalkoxy, $C_1$-$C_6$ alkyl or $C_1$-$C_2$ perfluoroalkylthio,
$R^{1d}$ is a hydrogen atom, a halogen atom or $C_1$-$C_6$ alkyl, and
$R^{1e}$ is a hydrogen atom, $C_1$-$C_2$ perfluoroalkyl or $C_1$-$C_2$ perfluoroalkoxy,
X is -N= or -CH=,
ring A is

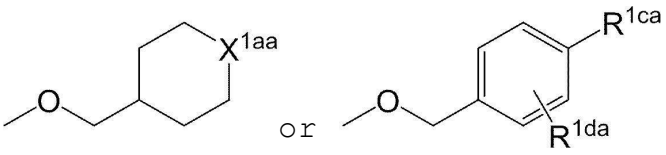



wherein $X^{2a}$ is -N= or $-CR^{2a}$= wherein $R^{2a}$ is a hydrogen atom, a halogen atom, $C_1$-$C_6$ alkyl or $C_1$-$C_6$ alkoxy,
$R^{2b}$ is a hydrogen atom, a halogen atom, $C_1$-$C_6$ alkyl or $C_1$-$C_6$ alkoxy,
$R^{2c}$ is a hydrogen atom or $C_1$-$C_6$ alkyl,
$X^{2b}$ is -O-, $-NR^{2d}$- wherein $R^{2d}$ is a hydrogen atom or $C_1$-$C_2$ perfluoroalkyl or $-CHR^{2e}$- wherein $R^{2e}$ is a hydrogen atom or $C_1$-$C_6$ alkyl,
$X^{2c}$ is $-(CH_2)_{n'}$- wherein n' is 0 or 1 or -O-,
L is $-(CHR^{3a})_n$- wherein n is 0, 1, 2 or 3, plural symbols $R^{3a}$ are the same or different and each is a hydrogen atom or a $C_1$-$C_6$ alkyl, $-(CH_2)_m$-O-$(CH_2)_{m'}$- wherein m and m' are the same or different and each is 0, 1 or 2, $C_2$-$C_3$ alkenylene,



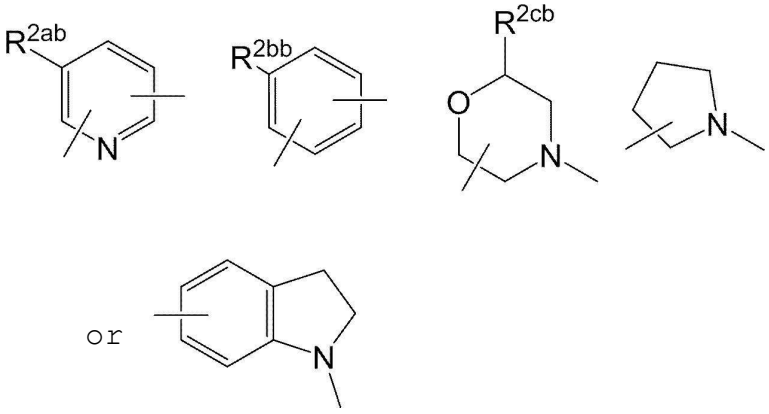

wherein $R^{3b}$ and $R^{3c}$ are the same or different and each is a hydrogen atom or $C_1$-$C_6$ alkyl, $R^{3d}$ is a hydrogen atom, $C_1$-$C_6$ alkoxy, $C_1$-$C_6$ alkyl or $C_1$-$C_2$ perfluoroalkyl, $R^{3e}$ is a hydrogen atom, $C_1$-$C_6$ alkoxy, $C_1$-$C_6$ alkyl or $C_1$-$C_2$ perfluoroalkyl.

2. The carboxylic acid compound according to claim 1 wherein $R^1$ is



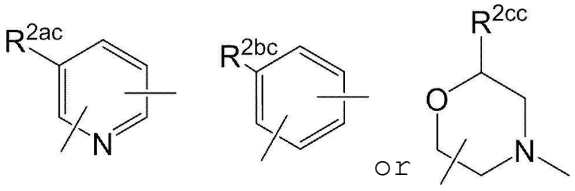

wherein $X^{1aa}$ is $-C(R^{1aa})_2-$ wherein plural symbols $R^{1aa}$ are the same or different and each is a hydrogen atom, $C_1$-$C_2$ perfluoroalkyl or $C_1$-$C_6$ alkyl, or plural symbols $R^{1aa}$ are bonded to form 1,1-$C_3$-$C_6$ cycloalkylene, or $-NR^{1ba}-$ wherein $R^{1ba}$ is a hydrogen atom or $C_1$-$C_2$ perfluoroalkyl, $R^{1ca}$ is $C_1$-$C_2$ perfluoroalkyl, $C_1$-$C_2$ perfluoroalkoxy or $C_1$-$C_2$ perfluoroalkylthio, and $R^{1da}$ is a halogen atom or $C_1$-$C_6$ alkyl, or a pharmacologically acceptable salt thereof.

3. The carboxylic acid compound according to claim 1 or 2 wherein ring A is



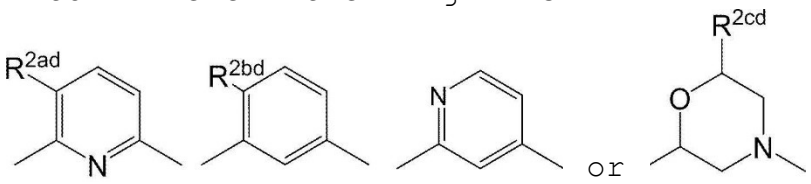

wherein $R^{2ab}$ is a hydrogen atom, $C_1$-$C_6$ alkoxy or $C_1$-$C_6$ alkyl, $R^{2bb}$ is a hydrogen atom, $C_1$-$C_6$ alkoxy or $C_1$-$C_6$ alkyl, and $R^{2cb}$ is a hydrogen atom or $C_1$-$C_6$ alkyl, or a pharmacologically acceptable salt thereof.

4. The carboxylic acid compound according to any one of claims 1 to 3 wherein the ring A is



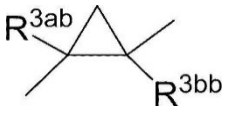

wherein $R^{2ac}$ is a hydrogen atom, $C_1$-$C_6$ alkoxy or $C_1$-$C_6$ alkyl, $R^{2bc}$ is a hydrogen atom, $C_1$-$C_6$ alkoxy or $C_1$-$C_6$ alkyl, and $R^{2cc}$ is a hydrogen atom or $C_1$-$C_6$ alkyl, or a pharmacologically acceptable salt thereof.

5. The carboxylic acid compound according to any one of claims 1 to 4 wherein the ring A is




wherein $R^{2ad}$ is a hydrogen atom, $C_1$-$C_6$ alkoxy or $C_1$-$C_6$ alkyl, $R^{2bd}$ is a hydrogen atom, $C_1$-$C_6$ alkoxy or $C_1$-$C_6$ alkyl, and $R^{2cd}$ is a hydrogen atom or $C_1$-$C_6$ alkyl, or a pharmacologically acceptable salt thereof.

6. The carboxylic acid compound according to any one of claims 1 to 5, wherein L is $-(CH_2)_n-$ wherein n is 1 or 2 or




wherein $R^{3ab}$ and $R^{3bb}$ are the same or different and each is a hydrogen atom or $C_1$-$C_6$ alkyl, or a pharmacologically acceptable salt thereof.

7. The carboxylic acid compound according to any one of claims 1 to 6, wherein X is -N=, or a pharmacologically acceptable salt thereof.

8. The carboxylic acid compound according to claim 1, wherein the compound represented by the formula (1) is any of the following, or a pharmacologically acceptable salt thereof:
trans-2-[2-methoxy-5-(5-{[4-(trifluoromethoxy)benzyl]oxy}pyridin-3-yl)phenyl]cyclopropanecarboxylic acid,
trans-2-[2-methoxy-5-(6-{[4-(trifluoromethoxy)benzyl]oxy}pyridazin-4-yl)phenyl]cyclopropanecarboxylic acid,
(1S,2S)-2-[2-methoxy-5-(6-{[trans-4-(trifluoromethyl)cyclohexyl]methoxy}pyridazin-4-yl)phenyl]cyclopropanecarboxylic acid,
(1R,2R)-2-[2-methoxy-5-(6-{[trans-4-(trifluoromethyl)cyclohexyl]methoxy}pyridazin-4-yl)phenyl]cyclopropanecarboxylic acid,
(1S,2S)-2-(5-methoxy-5'-{[4-(trifluoromethoxy)benzyl]oxy}-2,3'-bipyridin-6-yl)cyclopropanecarboxylic acid,
(1S,2S)-2-[3-methoxy-6-(6-{[4-(trifluoromethoxy)benzyl]oxy}pyridazin-4-yl)pyridin-2-yl]cyclopropanecarboxylic acid,
(1S,2S)-2-[3-methoxy-6-(6-{[trans-4-(trifluoromethyl)cyclohexyl]methoxy}pyridazin-4-yl)pyridin-2-yl]cyclopropanecarboxylic acid,
(1S,2S)-2-(5-{[4-(trifluoromethoxy)benzyl]oxy}-3,4'-bipyridin-2'-yl)cyclopropanecarboxylic acid,
(1R,2R)-2-(5-{[4-(trifluoromethoxy)benzyl]oxy}-3,4'-bipyridin-2'-yl)cyclopropanecarboxylic acid,
(1S,2S)-2-(5-{[trans-4-(trifluoromethyl)cyclohexyl]methoxy}-3,4'-bipyridin-2'-yl)cyclopropanecarboxylic acid,
(1R,2R)-2-(5-{[trans-4-(trifluoromethyl)cyclohexyl]methoxy}-3,4'-bipyridin-2'-yl)cyclopropanecarboxylic acid,
(1S,2S)-2-[4-(6-{[trans-4-(trifluoromethyl)cyclohexyl]methoxy}pyridazin-4-yl)pyridin-2-yl]cyclopropanecarboxylic acid,
(1R,2R)-2-[4-(6-{[trans-4-(trifluoromethyl)cyclohexyl]methoxy}pyridazin-4-yl)pyridin-2-

yl]cyclopropanecarboxylic acid,
(1S,2S)-2-(5′-{[trans-4-(trifluoromethyl)cyclohexyl]methoxy}-2,3′-bipyridin-6-yl)cyclopropanecarboxylic acid,
(1R,2R)-2-(5′-{[trans-4-(trifluoromethyl)cyclohexyl]methoxy}-2,3′-bipyridin-6-yl)cyclopropanecarboxylic acid,
(1S,2S)-2-[3-methoxy-6-(6-{[trans-4-(trifluoromethyl)cyclohexyl]methoxy}pyridazin-4-yl)pyridin-2-yl]-1-methylcyclopropanecarboxylic acid,
(1R,2R)-2-[3-methoxy-6-(6-{[trans-4-(trifluoromethyl)cyclohexyl]methoxy}pyridazin-4-yl)pyridin-2-yl]-1-methylcyclopropanecarboxylic acid,
(1S,2S)-2-[2-ethoxy-5-(6-{[1-(2,2,2-trifluoroethyl)piperidin-4-yl]methoxy}pyridazin-4-yl)phenyl]cyclopropanecarboxylic acid,
3-[(2S)-4-(5-{[4-(trifluoromethoxy)benzyl]oxy}pyridin-3-yl)morpholin-2-yl]propanoic acid,
3-[(2S)-4-(5-{[trans-4-(trifluoromethyl)cyclohexyl]methoxy}pyridin-3-yl)morpholin-2-yl]propanoic acid,
3-[(2S)-4-(5-{[3-fluoro-4-(trifluoromethoxy)benzyl]oxy}pyridin-3-yl)morpholin-2-yl]propanoic acid,
3-[(2S)-4-(5-{[2-fluoro-4-(trifluoromethoxy)benzyl]oxy}pyridin-3-yl)morpholin-2-yl]propanoic acid,
3-[(2S)-4-(5-{[2-methyl-4-(trifluoromethoxy)benzyl]oxy}pyridin-3-yl)morpholin-2-yl]propanoic acid,
3-[(2S)-4-(5-{[3-chloro-4-(trifluoromethoxy)benzyl]oxy}pyridin-3-yl)morpholin-2-yl]propanoic acid,
3-[(2S,6R)-6-methyl-4-(5-{[4-(trifluoromethoxy)benzyl]oxy}pyridin-3-yl)morpholin-2-yl]propanoic acid,
(1S,2S)-2-[(2S)-4-(5-{[trans-4-(trifluoromethyl)cyclohexyl]methoxy}pyridin-3-yl)morpholin-2-yl]cyclopropanecarboxylic acid,
(1R,2R)-2-[(2S)-4-(5-{[trans-4-(trifluoromethyl)cyclohexyl]methoxy}pyridin-3-yl)morpholin-2-yl]cyclopropanecarboxylic acid,
(1R,2R)-2-[(2R)-4-(5-{[trans-4-

(trifluoromethyl)cyclohexyl]methoxy}pyridin-3-yl)morpholin-2-yl]cyclopropanecarboxylic acid, or
(1S,2S)-2-[(2R)-4-(5-{[trans-4-(trifluoromethyl)cyclohexyl]methoxy}pyridin-3-yl)morpholin-2-yl]cyclopropanecarboxylic acid.

9. A pharmaceutical composition comprising the carboxylic acid compound according to any one of claims 1 to 8, or a pharmacologically acceptable salt thereof, and a pharmaceutically acceptable carrier.

10. Use of the carboxylic acid compound according to any one of claims 1 to 8 in manufacture of an agent for the treatment or prophylaxis of cancer or tumor, a fibrotic disease, an inflammatory disease, an ophthalmic disease, a urological disease, type II diabetes-related obesity or an acute coronary syndrome.

11. The use according to claim 10, wherein the cancer or tumor is malignant melanoma, brain tumor, neuroblastoma, glioblastoma multiforme, EBV positive Hodgkin lymphoma, glioblastoma, non-small cell lung cancer, lung tumor, breast tumor, ovary tumor, pancreas tumor, prostate intraepithelial tumor, prostate tumor, thyroid gland tumor, follicular lymphoma, liver tumor or renal cell carcinoma.

12. The use according to claim 10, wherein the fibrotic disease is lung fibrosis, scleroderma, hepatic fibrosis, renal fibrosis, diabetic nephropathy or atherosclerosis.

13. The use according to claim 10, wherein the fibrotic disease is lung fibrosis, scleroderma, hepatic fibrosis or renal fibrosis.

14. The use according to claim 10, wherein the inflammatory disease is asthma, COPD, rheumatoid arthritis, arthritis

deformans, NASH, NAFLD, inflammatory bowel disease, Crohn’s disease, ulcerative colitis, neuropathic pain or pruritus.

15. The use according to claim 14, wherein the inflammatory disease is asthma or COPD.

16. The use according to claim 14, wherein the inflammatory disease is rheumatoid arthritis or arthritis deformans.

17. The use according to claim 14, wherein the inflammatory disease is NASH or NAFLD.

18. The use according to claim 14, wherein the inflammatory disease is an inflammatory bowel disease, a Crohn’s disease or ulcerative colitis.

19. The use according to claim 14, wherein the inflammatory disease is neuropathic pain or pruritus.

20. The use according to claim 10, wherein the acute coronary syndrome is angina pectoris or myocardial infarction.

21. The use according to claim 10, wherein the ophthalmic disease is glaucoma.

22. The use according to claim 10, wherein the urological disease is prostatomegaly.