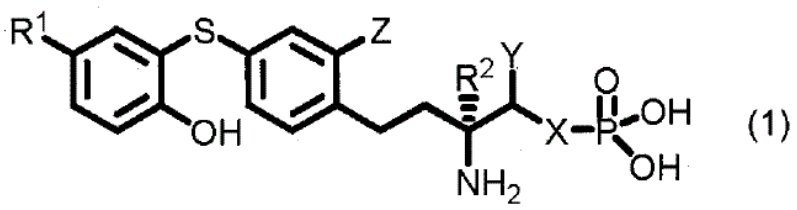
CLAIMS

1. A diphenyl sulfide ~~derivative~~ compound, or a pharmaceutically acceptable salt or hydrate thereof, represented by ~~the general~~ formula (1),

~~[Formula 1]~~

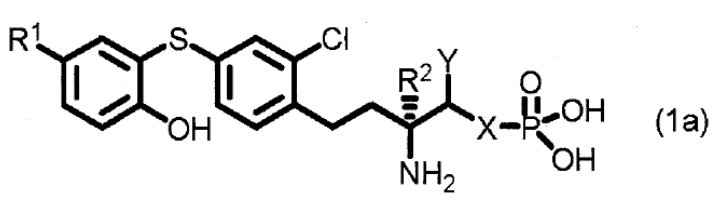


(1)

~~(In the formula (1),~~ wherein R^1 represents a hydrogen atom, a halogen atom, a trifluoromethyl group, an optionally substituted alkyl group having 1 to 6 carbon atoms, an optionally substituted cycloalkyl group having 3 to 6 carbon atoms, an optionally substituted aryl group having 6 to 10 carbon atoms, an optionally substituted alkoxy group having 1 to 4 carbon atoms, an optionally substituted benzyloxy group, an optionally substituted acyl group having 1 to 4 carbon atoms, a cyano group, or a carboxyl group; R^2 represents an optionally substituted alkyl group having 1 to 6 carbon atoms or an optionally substituted alkenyl group having 2 to 6 carbon atoms; X represents a methylene group which may be substituted with 1 or 2 fluorine atoms or represents an oxygen atom; Y represents a hydrogen atom or an optionally substituted alkyl group having 1 to 6 carbon atoms; and Z represents a halogen atom~~)~~.

2. The diphenyl sulfide ~~derivative~~ compound according to claim 1, or a pharmaceutically acceptable salt or hydrate thereof, wherein the compound ~~represented by the general formula (1)~~ is represented by ~~the general~~ formula (1a),

~~[Formula 2]~~



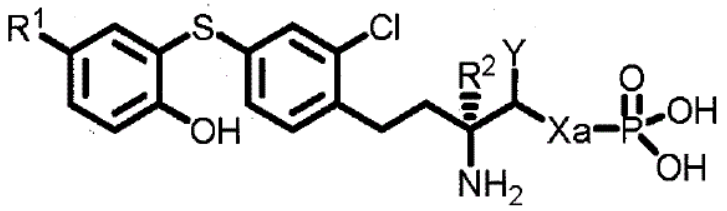
(1a)

.

~~(In the formula (1a), R1, R2, X, and Y are as defined above).~~

3. The diphenyl sulfide ~~derivative~~ compound according to claim 1, or a pharmaceutically acceptable salt or hydrate thereof, wherein the compound ~~represented by the general formula (1)~~ is represented by ~~the general~~ formula (1b),

~~[Formula 3]~~

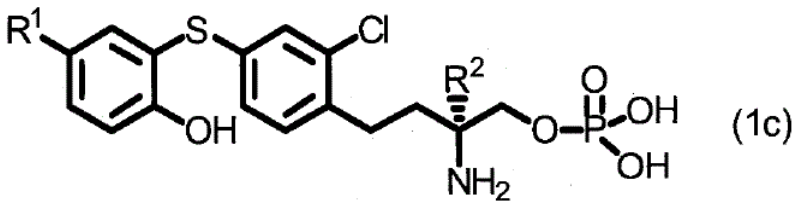


(1b)

~~(In the formula (1b),~~ wherein Xa represents an oxygen atom or $-CH_2-$~~,~~ ~~and R1, R2, and Y are as defined above)~~.

4. The diphenyl sulfide ~~derivative~~ compound according to claim 1, or a pharmaceutically acceptable salt or hydrate thereof, wherein the compound ~~represented by the general formula (1)~~ is represented by ~~the general~~ formula (1c),

~~[Formula 4]~~



(1c)

.

~~(In the formula (1c), R^1 and R^2 are as defined above).~~

5. The diphenyl sulfide ~~derivative~~ compound according to claim 4, or a pharmaceutically acceptable salt or hydrate thereof, wherein R^1 represents a trifluoromethyl group, an alkyl group having 1 to 6 carbon atoms, a cycloalkyl group having 3 to 6 carbon atoms, an aryl group having 6 to 10 carbon atoms, or a benzyloxy group.

6. The diphenyl sulfide ~~derivative~~ compound according to claim 1, or a pharmaceutically acceptable salt or hydrate thereof, wherein the compound represented by ~~the general~~ formula (1) is (*S*)-2-amino-4-[2-chloro-4-(2-hydroxy-5-trifluoromethylphenylthio)phenyl]-2-propylbutylphosphoric acid monoester, (*R*)-2-allyl-2-amino-4-[2-chloro-4-(2-hydroxy-5-trifluoromethyl

phenylthio)phenyl]butylphosphoric acid monoester,

(*S*)-2-amino-4-[2-chloro-4-(2-hydroxy-5-trifluoromethylphenylthio)phenyl]-2-methylbutylphosphoric acid monoester,

(*S*)-2-amino-4-[2-chloro-4-(2-hydroxy-5-isopropylphenylthio)phenyl]-2-methylbutylphosphoric acid monoester,

(*S*)-2-amino-4-[2-chloro-4-(5-cyclopropyl-2-hydroxyphenylthio)phenyl]-2-methylbutylphosphoric acid monoester,

(*S*)-2-amino-4-[4-(5-benzyloxy-2-hydroxyphenylthio)-2-chlorophenyl]-2-methylbutylphosphoric acid monoester,

(*S*)-2-amino-4-[2-chloro-4-(2-hydroxy-5-propylphenylthio)phenyl]-2-propylbutylphosphoric acid monoester,

(*S*)-2-amino-4-[2-chloro-4-(2-hydroxy-5-isopropylphenylthio)phenyl]-2-propylbutylphosphoric acid monoester,

(*S*)-2-amino-4-[2-chloro-4-(5-cyclopropyl-2-hydroxyphenylthio)phenyl]-2-propylbutylphosphoric acid monoester,

(*S*)-2-amino-4-[4-(5-t-butyl-2-hydroxyphenylthio)-2-chlorophenyl]-2-propylbutylphosphoric acid monoester,

(*S*)-2-amino-4-[2-chloro-4-(2-hydroxy-5-biphenylthio)phenyl]-2-propylbutylphosphoric acid monoester, or

(*S*)-2-amino-4-[4-(5-benzyloxy-2-hydroxyphenylthio)-2-chlorophenyl]-2-propylbutylphosphoric acid monoester.

7. The diphenyl sulfide ~~derivative~~ compound according to claim 1, or a pharmaceutically acceptable salt or hydrate thereof, wherein the compound represented by ~~the general~~ formula (1) is

(-)-2-amino-4-[2-chloro-4-(2-hydroxy-5-trifluoromethylphenylthio)phenyl]-2-propylbutylphosphoric acid monoester,

(-)-2-allyl-2-amino-4-[2-chloro-4-(2-hydroxy-5-trifluoromethylphenylthio)phenyl]butylphosphoric acid monoester,

(-)-2-amino-4-[2-chloro-4-(2-hydroxy-5-trifluoromethylphenylthio)phenyl]-2-methylbutylphosphoric acid monoester,

(-)-2-amino-4-[2-chloro-4-(2-hydroxy-5-isopropylphenylthio)phenyl]-2-methylbutylphosphoric acid monoester,

(-)-2-amino-4-[2-chloro-4-(5-cyclopropyl-2-hydroxyphenylthio)phenyl]-2-methylbutylphosphoric acid monoester,

(-)-2-amino-4-[4-(5-benzyloxy-2-hydroxyphenylthio)-2-chlorophenyl]-2-methylbutylphosphoric acid monoester,

(-)-2-amino-4-[2-chloro-4-(2-hydroxy-5-propylphenylthio)phenyl]-2-propylbutylphosphoric acid monoester,

(-)-2-amino-4-[2-chloro-4-(2-hydroxy-5-isopropylphenylthio)phenyl]-2-propylbutylphosphoric acid monoester,

(-)-2-amino-4-[2-chloro-4-(5-cyclopropyl-2-hydroxyphenylthio)phenyl]-2-propylbutylphosphoric acid monoester,

(-)-2-amino-4-[4-(5-t-butyl-2-hydroxyphenylthio)-2-chlorophenyl]-2-propylbutylphosphoric acid monoester,

(-)-2-amino-4-[2-chloro-4-(2-hydroxy-5-biphenylthio)phenyl]-2-propylbutylphosphoric acid monoester, or

(-)-2-amino-4-[4-(5-benzyloxy-2-hydroxyphenylthio)-2-chlorophenyl]-2-propylbutylphosphoric acid monoester.

~~8. A medicine that is based on a sphingosine-1-phosphate 3 (S1P3) receptor-antagonistic action, the medicine comprising as an active ingredient the diphenyl sulfide derivative according to any one of claims 1 to 7, or a pharmaceutically acceptable salt or hydrate thereof.~~

~~9. The medicine according to claim 8, wherein the medicine is a therapeutic or preventive medicine for respiratory tract contraction, bronchial asthma, chronic obstructive pulmonary disease (COPD), pulmonary emphysema, tracheal stenosis, diffuse panbronchiolitis, bronchitis resulting from infection, connective tissue disease, or transplantation, diffuse pulmonary hamartoangiomyomatosis, adult respiratory distress syndrome (ARDS), interstitial pneumonitis, lung cancer, pneumonia hypersensitivity, idiopathic interstitial pneumonia, fibrosis of the lung, sepsis, or cytokine storm caused by an influenza virus or RS virus infection.~~

~~10. The medicine according to claim 8, wherein the medicine is a therapeutic medicine for arterial sclerosis, blood vessel intimal hypertrophy, solid tumors, diabetic retinopathy, rheumatoid arthritis, cardiac arrest, ischemia reperfusion disorders, cerebral blood vessel spasms after subarachnoid bleeding, angina pectoris or myocardial infarction caused by coronary vessel spasms, glomerulonephritis, thrombosis, lung disease caused by pulmonary edema, cardiac arrhythmia, eye disease, eye hypertension, glaucoma,~~

~~glaucomatous retinopathy, optic neuropathy, or macula-lutea degeneration.~~

~~11. The medicine according to claim 8, wherein the medicine is a therapeutic or preventive medicine for sepsis.~~

8~~12~~. A pharmaceutical composition comprising the diphenyl sulfide ~~derivative~~ compound according to ~~any one of~~ claim~~s~~ 1 ~~to 7~~, or a pharmaceutically acceptable salt or hydrate thereof, and a pharmaceutically acceptable carrier.

9. The use of the pharmaceutical composition according to claim 8 in the manufacture of a medicament for inducing a sphingosine-1-phosphate 3 (S1P3) receptor-antagonistic action.

10. The use of the pharmaceutical composition according to claim 8 in the manufacture of a medicament for the treatment of sepsis.