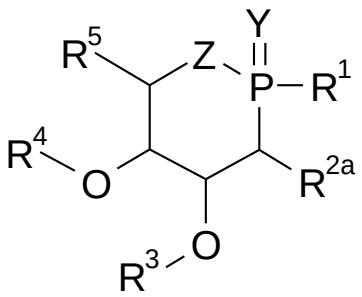
CLAIMS

1. Use of a compound of formula (1) in the manufacture of a medicament for the treatment of fibrotic diseases, wherein the compound has the following formula (1):



(1)

wherein Y represents an oxygen, a sulfur or a selenium atom, preferably an oxygen atom,
Z represents O, S, Se, NH or a NR_6 group, wherein R_6 is an aryl or an optionally substituted alkyl group, preferably an oxygen atom,
R_1 represents a hydrogen atom, an optionally substituted alkyl group or an aryl group,
R^{2a} represents a hydrogen atom, halogen, azide (N_3), a carbonate or dithiocarbonate group, a 1H-[1,2,3]triazolyl group or a group —X—R2, wherein
X represents an oxygen, a sulfur, a selenium atom, a NH or NR_7 group, R_7 being an optionally substituted aryl or alkyl group; X preferably represents O or NH, and;
R_2 represents an aryl group, an optionally substituted alkyl group, a hydrogen atom, a trichloroacetimidate group (-C(=NH)CCl_3), an acyl, formyl, sulfonyl, sulfinyl, tert-butyldiphenylsilyl, allyl group, a saccharyl, ester, amide, thioamide, sulfonamide group, or X-R_2 represents a P(O)R_2R_6 group, in which R_2 and R_6 represent independently from each other an aryl group, an optionally substituted alkyl group, OH, an alkoxy or an aryloxy group,
R_3 and R_4 represent independently from each other an aryl, an optionally substituted alkyl group, an hydrogen atom, a trichloroacetimidate group, an acyl, formyl, sulfonyl, sulfinyl, tert-butyldiphenylsilyl group, an allyl, ester, amide, thioamide, sulfonamide group, or R_3 and R_4 taken together form a divalent radical of formula -R_3-R_4-, wherein -R_3-R_4- preferably represents an isopropylidene, benzylidene, diphenyl methylidene, cyclohexyl methylidene group, and their substituted analogues, for example a 4-methoxybenzylidene group, or a linear alkylene group such as an ethylene group,
R_5 represents a hydrogen atom or a hydrocarbon group comprising one or more heteroatoms, preferably selected from oxygen, sulfur or nitrogen, more preferably oxygen.

2. The use according to claim 1, wherein the fibrotic disease is a lung, heart, liver, kidney, muscle, skin, soft tissue, bone marrow, intestinal, aortic or joint fibrosis.

3. The use according to claim 1, wherein the fibrotic disease is a skin disease, kidney disease, pulmonary fibrosis, idiopathic pulmonary fibrosis, cystic fibrosis, endomyocardial fibrosis, mediastinal fibrosis, myelofibrosis, retroperitoneal fibrosis, progressive massive fibrosis, nephrogenic systemic fibrosis, Crohn's Disease, keloid, old myocardial infarction, scleroderma, systemic sclerosis, arthrofibrosis or an adhesive capsulitis.

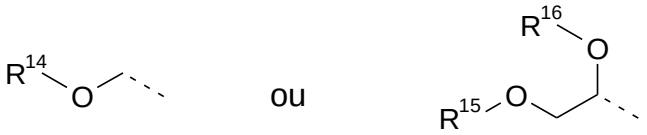
4. The use according to claim 1, wherein the fibrotic disease is a liver or kidney fibrosis.

5. The use according to claim 1, wherein the fibrotic disease is an aortic fibrosis.

6. The use according to claim 1, wherein the fibrotic disease is a skin fibrosis, including keloids or scleroderma.

7. The use according to any one of claims 1-6, wherein the compound is of formula (1) with Y = Z = O.

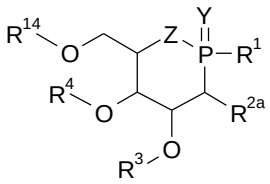
8. The use according to any one of claims 1-7, wherein R_5 is selected from the following groups:



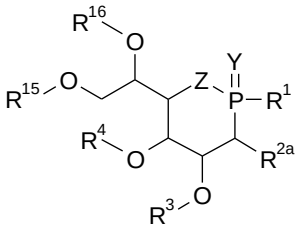
wherein R^{14}, R^{15} and R^{16} represent, independantly from each other, a hydrogen atom, an aryl group, an optionally substituted alkyl group, a trichloroacetimidate group, an acyl, formyl, sulfonyl, sulfinyl, *tert*-butyldiphenylsilyl, allyl, ester, amide or a sulfonamide group, or R^{15} and R^{16}, taken together, form a divalent radical of formula $-R^{15}-R^{16}-$, wherein $-R^{15}-R^{16}-$ preferably represents an isopropylidene, benzylidene, diphenyl methylidene, or a cyclohexyl methylidene group, and their substituted analogues, for example a 4-methoxybenzylidene group, or a linear alkylene group, such as an ethylene group.

9. The use according to any one of claims 1-8, wherein R1 is a phenyl group and/or X-R2 is OH and/or R3 and R4 represent a benzyl group.

10. The use according to any one of claims 1-9, wherein the compound has the following formula (2) or (3):



(2)

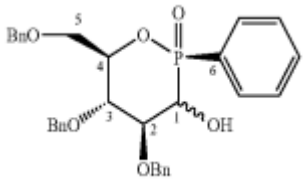


(3)

wherein R1, R2a, R3, R4, Y and Z are as defined in any one of claims 1, 8, 9 and 10, and R14, R15 and R16 represent, independently from each other, a hydrogen atom, an aryl, an optionally substituted alkyl group, a trichloroacetimidate group, an acyl, formyl, sulfonyl, sulfinyl, tert-butyldiphenylsilyl group, an allyl, ester, amide, thioamide, sulfonamide group, or R15 and R16, taken together, form a divalent radical of formula -R^{15}-R^{16}-, wherein -R^{15}-R^{16}- preferably represents an isopropylidene, benzylidene, diphenyl methylidene, cyclohexyl methylidene group, and their substituted analogues, for example a 4-methoxybenzylidene group, or a linear alkylene group such as an ethylene group, preferably R14 represents a benzyl group.

11. The use according to any one of claims 1-10, wherein the compound of formula (1) is 3-Hydroxy-4,5-bis-benzyloxy-6-benzyloxymethyl-2-phenyl-2-oxo-2λ5-[1,2]oxaphosphinane.

12. The use according to any one of the preceding claims, wherein the compound has the following Formula (I):



(I)

13. The use according to any one of claims 1-12, wherein the treatment of fibrosis is by inhibition of the production of collagen fibers, more specifically collagen of types 1, 3 and/or 4, and/or by inhibition of mechanisms implicated in cell matrix and/or cell/cell interactions, including inhibition of fibroblast migration.

14. Use of a kit comprising a compound of formula (1) as defined in anyone of claims 1 and 8-13, and instructions for use, in the manufacture of a medicament for the treatment of fibrosis diseases.