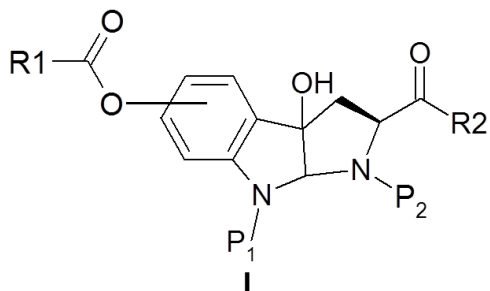


CLAIMS

1. A hydroxy-substituted derivative of 2-carboxy-3a-hydroxy-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole according to Formula I



wherein R1 is selected from alkyl, aryl, heteroaryl, substituted alkyl, substituted aryl, and substituted heteroaryl;

P₁ is hydrogen or a protecting group;

P₂ is hydrogen or a protecting group, ~~particularly a protecting group~~; and

R2 is selected from OH, OR1, and a polypeptide chain consisting of 1-7 amino acid residues.

2. The hydroxy-substituted derivative of 2-carboxy-3a-hydroxy-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole of claim 1, wherein the protecting group, when present, is independently selected from Boc, PhCH₂OCO-, CH₂=CHCH₂O-CO-, and trityl.
3. The hydroxy-substituted derivative of 2-carboxy-3a-hydroxy-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole of claim 1 or 2, wherein the substituent R1-C(=O)-O- is attached to position 5 in Formula I.
4. The hydroxy-substituted derivative of 2-carboxy-3a-hydroxy-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole of claim 1 or 2, wherein the substituent R1-C(=O)-O- is attached to position 6 in Formula I.

5. A method for the synthesis of a linear precursor comprising eight amino acid residues of an amanitin derivative comprising a hydroxylated tryptophan moiety, comprising the step of using a hydroxy-substituted derivative of 2-carboxy-3a-hydroxy-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole of any one of claims 1 to 5 in the peptide synthesis of said precursor.
6. A method for the synthesis of an amanitin derivative comprising a hydroxylated tryptophan moiety, comprising the steps of.
 - (i) causing or allowing the formation of a bond between the cysteine residue and the tryptophan moiety of the linear precursor of claim 5; and
 - (ii) causing or allowing the formation of said amanitin derivative by reacting the N-terminus of the linear precursor of claim 5 with the C-terminus of said precursor.
7. The method of claim 6, further comprising the oxidation of the sulfur atom of the cysteine moiety to form a sulfoxide or a sulfone, ~~particularly a sulfoxide.~~
8. The method of claim 7, comprising the oxidation of the sulfur atom of the cysteine moiety to form a sulfoxide.
89. An amanitin derivative comprising a hydroxylated tryptophan moiety, which is selected from (i) S-desoxy-4'-hydroxy-amanin, 4'-hydroxy-amanin, S-desoxy-5'-hydroxy-amanin, 5'-hydroxy-amanin, S-desoxy-7'-hydroxy-amanin, 7'-hydroxy-amanin, (ii) S-desoxy-4'-hydroxy-amaninamide, 4'-hydroxy-amaninamide, S-desoxy-5'-hydroxy-amaninamide, 5'-hydroxy-amaninamide, S-desoxy-7'-hydroxy-amaninamide, and 7'-hydroxy-amaninamide, (iii) a derivative of the amanitin according to (i), wherein the free carboxylic acid moiety of amino acid 1 is converted to an carboxylic ester $-C(=O)OR_1$ or to a moiety $-C(=O)NH-OR_1$, wherein R1 is selected from alkyl, aryl, heteroaryl, substituted alkyl, substituted aryl, and substituted heteroaryl.

- ~~9~~10. The amanitin derivative of claim ~~89~~9, which is selected from S-desoxy-5'-hydroxy-amanin, 5'-hydroxy-amanin, S-desoxy-5'-hydroxy-amaninamide, and 5'-hydroxy-amaninamide.
- ~~10~~11. A conjugate comprising (a) amanitin derivative comprising a hydroxylated tryptophan moiety of claim ~~89~~9 or ~~910~~10; (b) a target-binding moiety; and (c) optionally a linker linking said amanitin derivative and said target-binding moiety.
- ~~11~~12. A pharmaceutical composition comprising the amanitin derivative of claim ~~89~~9 or ~~910~~10 or the conjugate of claim ~~10~~11.
- ~~12~~13. The amanitin derivative of claim ~~89~~9 or ~~910~~10, or the conjugate of claim 10, or the pharmaceutical composition of claim 11 for use in the treatment of cancer in a patient, particularly wherein the cancer is selected from the group consisting of breast cancer, pancreatic cancer, cholangiocarcinoma, colorectal cancer, lung cancer, prostate cancer, ovarian cancer, prostate cancer, stomach cancer, kidney cancer, malignant melanoma, leukemia, and malignant lymphoma.
14. The amanitin derivative of claim 9 or 10, or the conjugate of claim 11 for use in the treatment of cancer in a patient, wherein the cancer is selected from the group consisting of breast cancer, pancreatic cancer, cholangiocarcinoma, colorectal cancer, lung cancer, ovarian cancer, prostate cancer, stomach cancer, kidney cancer, malignant melanoma, leukemia, and malignant lymphoma.
15. The pharmaceutical composition of claim 12 for use in the treatment of cancer in a patient.
16. The pharmaceutical composition of claim 12 for use in the treatment of cancer in a patient, wherein the cancer is selected from the group consisting of breast cancer, pancreatic cancer, cholangiocarcinoma, colorectal cancer, lung cancer, ovarian cancer, prostate cancer, stomach cancer, kidney cancer, malignant melanoma, leukemia, and malignant lymphoma.

~~13~~17. A construct comprising (a) an amanitin derivative of claim ~~89~~ or ~~910~~; and (b) a linker moiety carrying a reactive group Y for linking said amanitin derivative to a target-binding moiety.