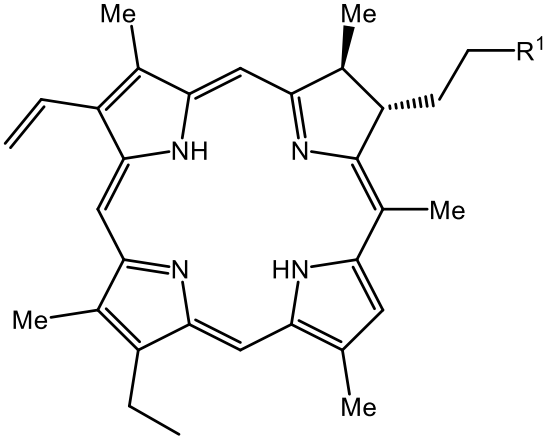
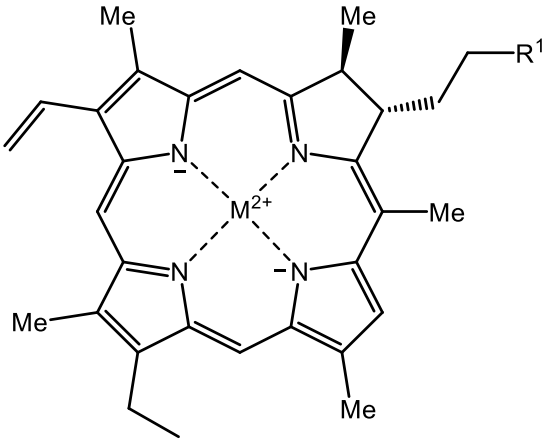
Claims

1. A compound of formula (I) or a complex of formula (II):



(I)



(II)

wherein

-R^1 is selected from -C(O)-OR^3, -C(O)-SR^3, -C(O)-$N(R^3)_2$, -C(S)-OR^3, -C(S)-SR^3 or -C(S)-$N(R^3)_2$;

-R^3, each independently, is selected from -H, -R^α-H, -R^β, -R^α-R^β, -R^α-OH, -R^α-OR^β, -R^α-SH, -R^α-SR^β, -R^α-S(O)R^β, -R^α-$S(O)_2R^\beta$, -R^α-NH_2, -R^α-$NH(R^\beta)$, -R^α-$N(R^\beta)_2$, -R^α-X, -R^α-$[N(R^5)_3]$Y, -R^α-$[P(R^5)_3]$Y or -R^α-$[R^6]$Y;

-R^α-, each independently, is selected from a C_1-C_{12} alkylene group, wherein the alkylene group may optionally be substituted with one or more C_1-C_4 alkyl, C_1-C_4 haloalkyl or halo groups, and wherein one or more carbon atoms in the backbone of the alkylene group may optionally be replaced by one or more heteroatoms O or S;

-R^β, each independently, is a saturated or unsaturated hydrocarbyl group, wherein the hydrocarbyl group may be straight-chained or branched, or be or include cyclic groups, wherein the hydrocarbyl group may optionally be substituted, and wherein the hydrocarbyl group may optionally include one or more heteroatoms N, O, S, P or Se in its carbon skeleton;

-R^5, each independently, is selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, halo, -$(CH_2CH_2O)_n$-H, -$(CH_2CH_2O)_n$-CH_3, phenyl or C_5-C_6 heteroaryl, wherein the phenyl or C_5-C_6 heteroaryl may optionally be substituted with one or more C_1-C_4 alkyl, C_1-C_4 haloalkyl, -O(C_1-C_4 alkyl), -O(C_1-C_4 haloalkyl), halo, -O-$(CH_2CH_2O)_n$-H or -O-$(CH_2CH_2O)_n$-CH_3 groups;

-R^6 is -[NC_5H_5] optionally substituted with one or more C_1-C_4 alkyl, C_1-C_4 haloalkyl, -O(C_1-C_4 alkyl), -O(C_1-C_4 haloalkyl), halo, -O-$(CH_2CH_2O)_n$-H or -O-$(CH_2CH_2O)_n$-CH_3 groups;

n is 1, 2, 3 or 4;

Y is a counter ion;

X is a halo group;

M^{2+} is a metal ion;

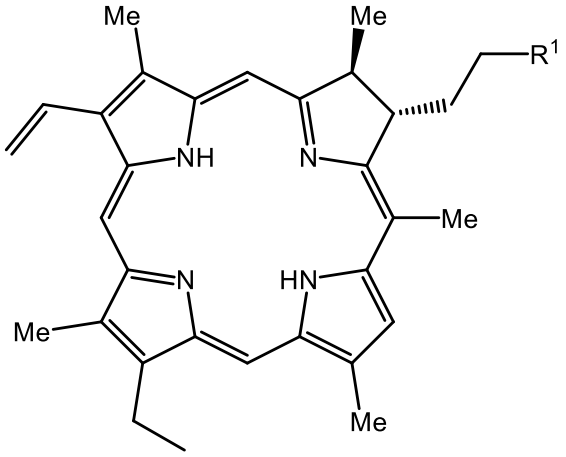
or a pharmaceutically acceptable salt thereof;

provided that the compound is not:

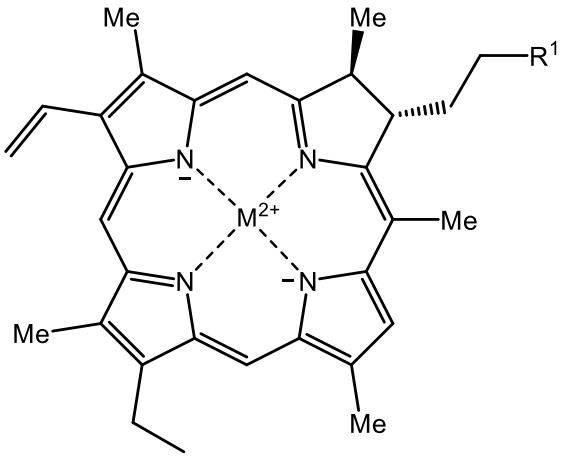
(1) phyllochlorin free acid; or

(2) phyllochlorin methyl ester.

2. A compound of formula (I) or a complex of formula (II):



(I)



(II)

wherein

-R^1 is selected from -C(O)-OR^3, -C(O)-SR^3, -C(O)-$N(R^3)_2$, -C(S)-OR^3, -C(S)-SR^3 or -C(S)-$N(R^3)_2$;

-R^3, each independently, is selected from -H, -R^α-H, -R^β, -R^α-R^β, -R^α-OH, -R^α-OR^β, -R^α-SH, -R^α-SR^β, -R^α-S(O)R^β, -R^α-$S(O)_2R^\beta$, -R^α-NH_2, -R^α-$NH(R^\beta)$, -R^α-$N(R^\beta)_2$, -R^α-X, -R^α-[$N(R^5)_3$]Y, -R^α-[$P(R^5)_3$]Y or -R^α-[R^6]Y;

-R^α-, each independently, is selected from a C_1-C_{12} alkylene group, wherein the alkylene group may optionally be substituted with one or more C_1-C_4 alkyl, C_1-C_4 haloalkyl or halo groups, and wherein one or more carbon atoms in the backbone of the alkylene group may optionally be replaced by one or more heteroatoms O or S;

-R^β, each independently, is a saturated or unsaturated hydrocarbyl group, wherein the hydrocarbyl group may be straight-chained or branched, or be or include

cyclic groups, wherein the hydrocarbyl group may optionally be substituted, and wherein the hydrocarbyl group may optionally include one or more heteroatoms N, O, S, P or Se in its carbon skeleton;

-R^5, each independently, is selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, halo, -$(CH_2CH_2O)_n$-H, -$(CH_2CH_2O)_n$-CH_3, phenyl or C_5-C_6 heteroaryl, wherein the phenyl or C_5-C_6 heteroaryl may optionally be substituted with one or more C_1-C_4 alkyl, C_1-C_4 haloalkyl, -O(C_1-C_4 alkyl), -O(C_1-C_4 haloalkyl), halo, -O-$(CH_2CH_2O)_n$-H or -O-$(CH_2CH_2O)_n$-CH_3 groups;

-R^6 is -[NC_5H_5] optionally substituted with one or more C_1-C_4 alkyl, C_1-C_4 haloalkyl, -O(C_1-C_4 alkyl), -O(C_1-C_4 haloalkyl), halo, -O-$(CH_2CH_2O)_n$-H or -O-$(CH_2CH_2O)_n$-CH_3 groups;

n is 1, 2, 3 or 4;

Y is a counter ion;

X is a halo group;

M^{2+} is a metal ion;

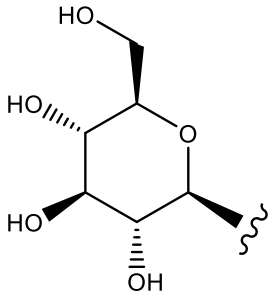
or a pharmaceutically acceptable salt thereof;

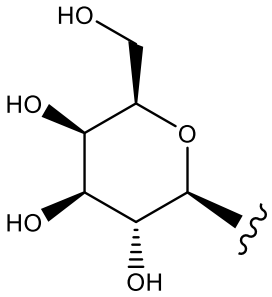
for use in medicine.

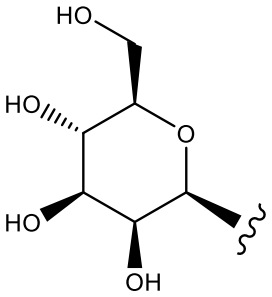
3. The compound or complex according to claim 1 or 2, wherein each -R^{α}- is independently selected from C_1-C_6 alkylene.

4. The compound or complex according to any preceding claim, wherein at least one -R^3 is selected from -R^{α}-OR^{β}, -R^{α}-SR^{β}, -R^{α}-S(O)R^{β} or -R^{α}-$S(O)_2R^{\beta}$, and -R^{β} is a saccharidyl group.

5. The compound or complex according to claim 4, wherein -R^{β} is a saccharidyl group selected from:

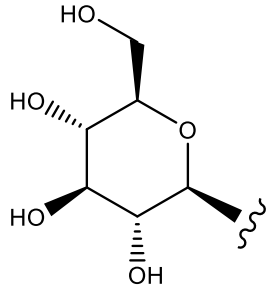






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6. The compound or complex according to claim 5, wherein the saccharidyl group is:

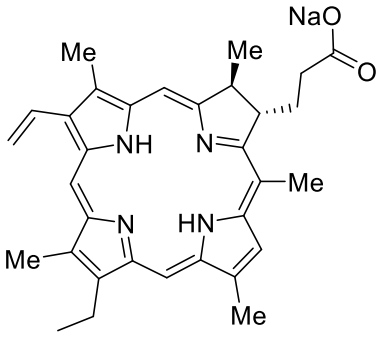


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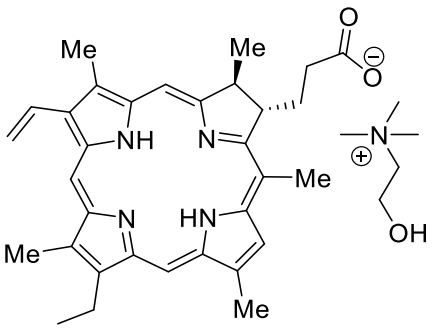
7. The compound or complex according to any preceding claim, wherein $-R^1$ is $-C(O)-N(R^3)_2$.

8. The compound or complex according to claim 7, wherein $-R^1$ is $-C(O)-N(R^3)(R^{3'})$, wherein $-R^3$ is selected from $-R^{\alpha}-OR^{\beta}$, $-R^{\alpha}-SR^{\beta}$, $-R^{\alpha}-S(O)R^{\beta}$ or $-R^{\alpha}-S(O)_2R^{\beta}$, and $-R^{\beta}$ is a saccharidyl group, and $-R^{3'}$ is H or C_1-C_4 alkyl.

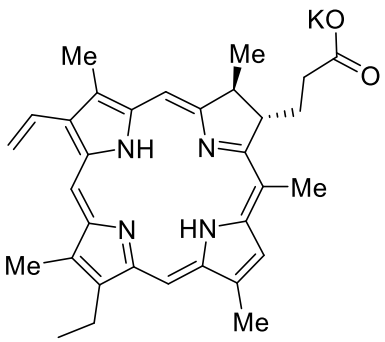
9. The compound or complex according to claim 1 or 2, wherein the compound or complex is:



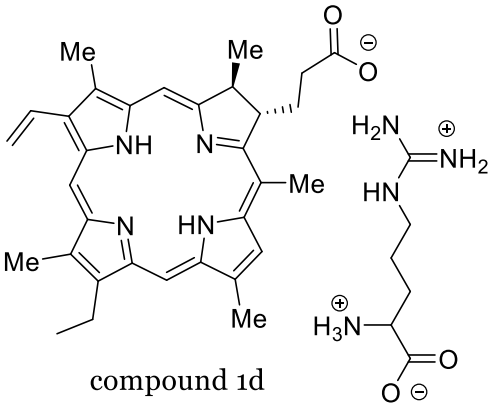
compound 1



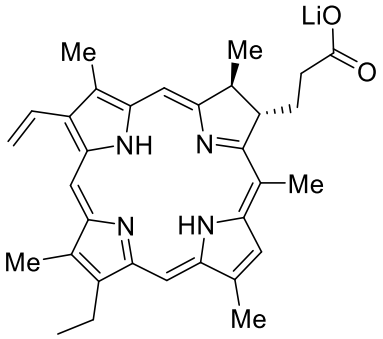
compound 1c



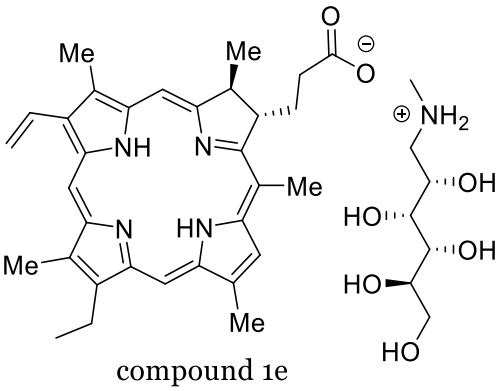
compound 1a



compound 1d

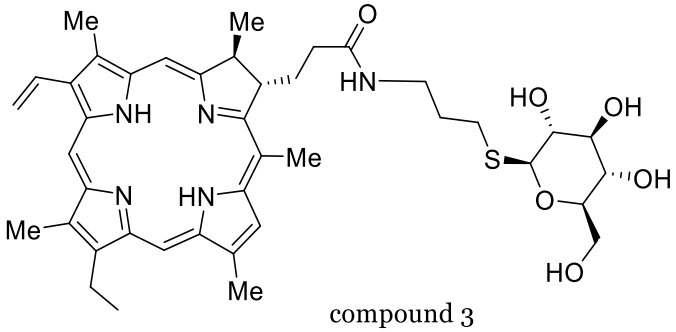


compound 1b

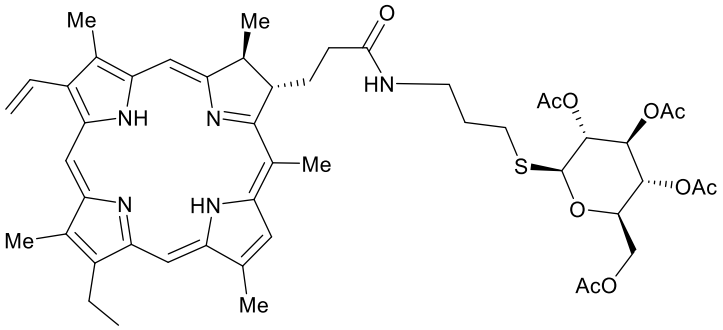


compound 1e

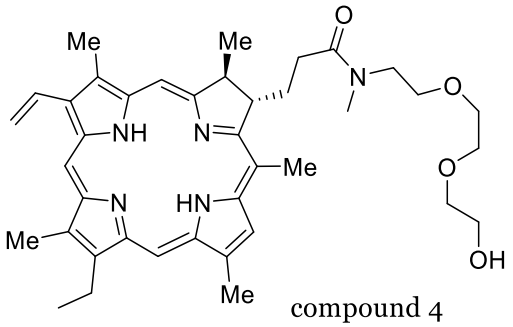
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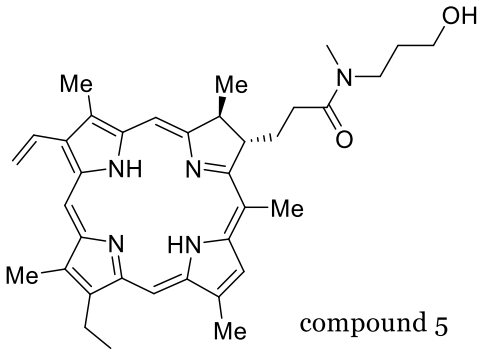
compound 3



tetra-acetylated compound 3

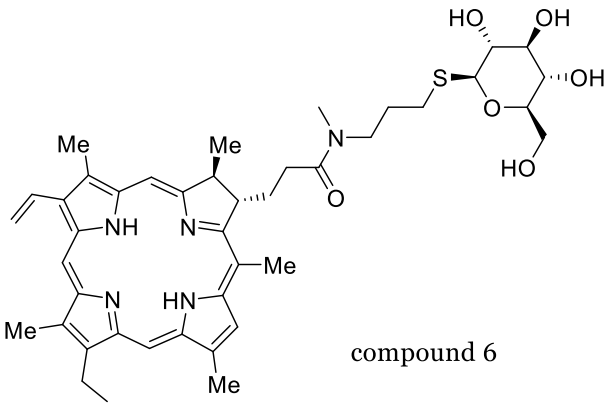


compound 4

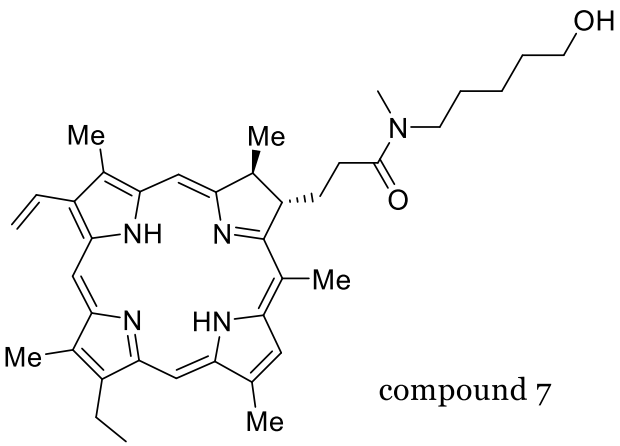


compound 5

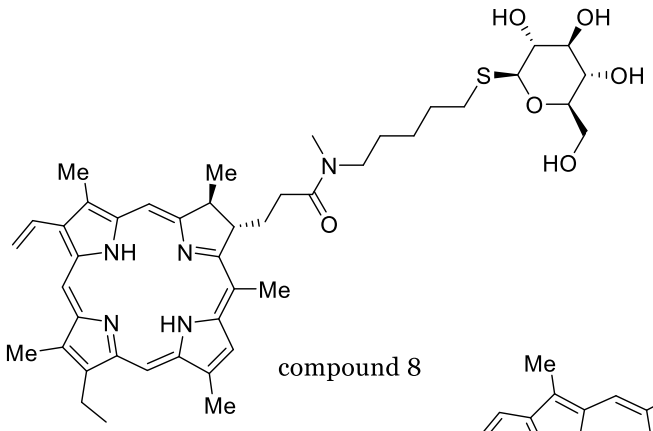
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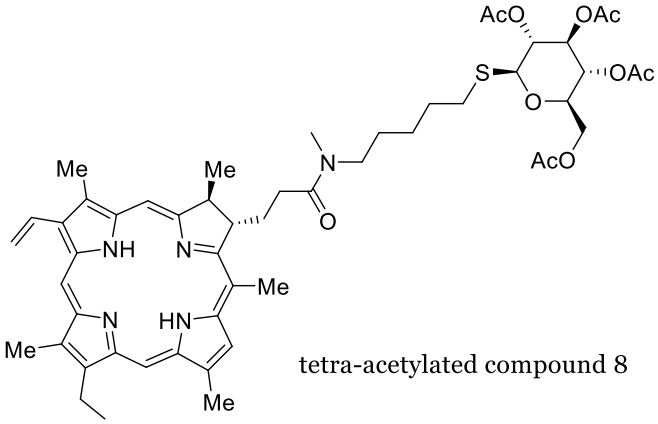
compound 6



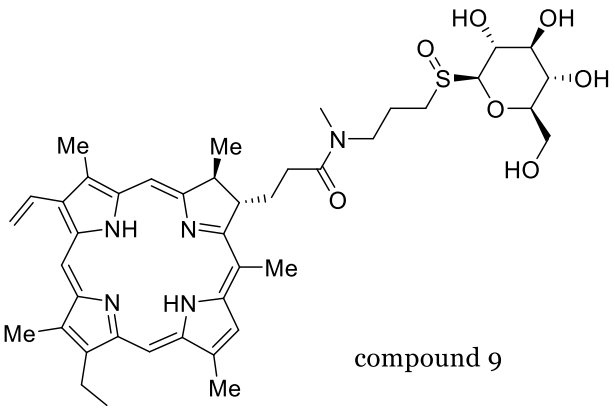
compound 7



compound 8

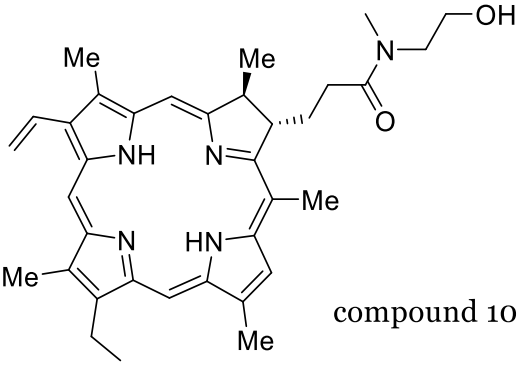


tetra-acetylated compound 8

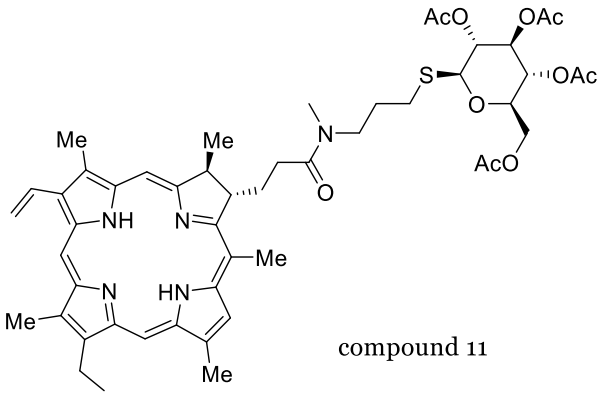


compound 9

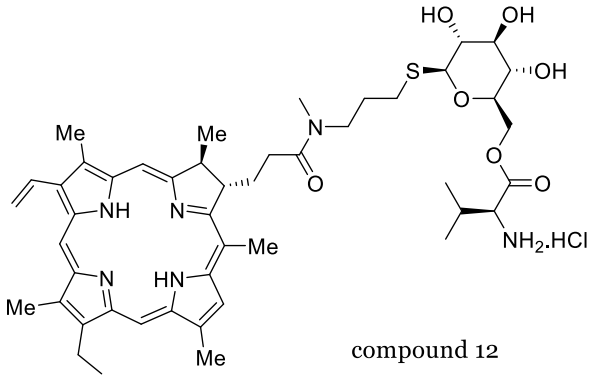
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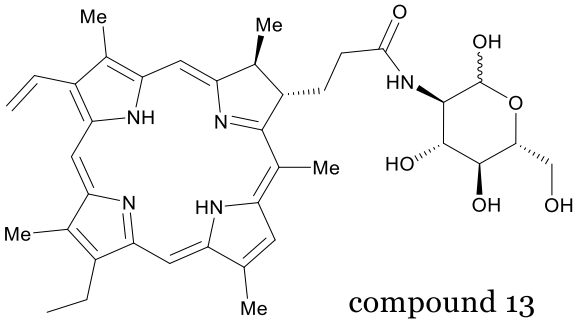
compound 10



compound 11

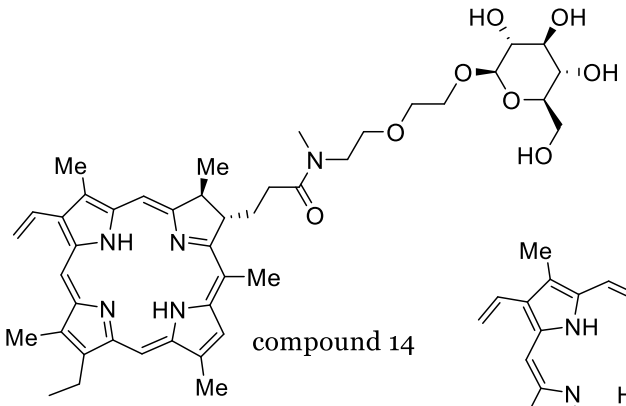


compound 12

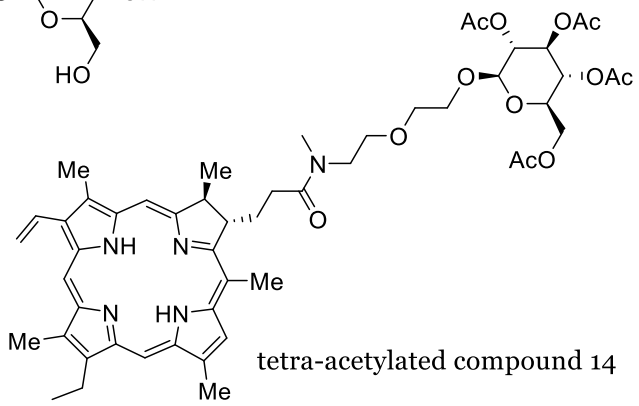


compound 13

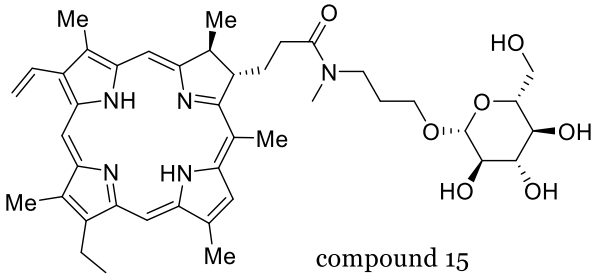
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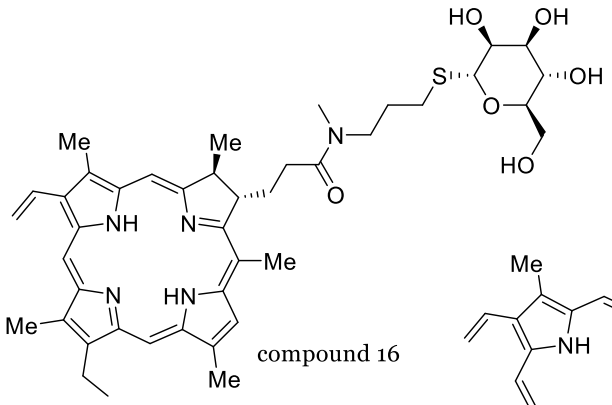
compound 14



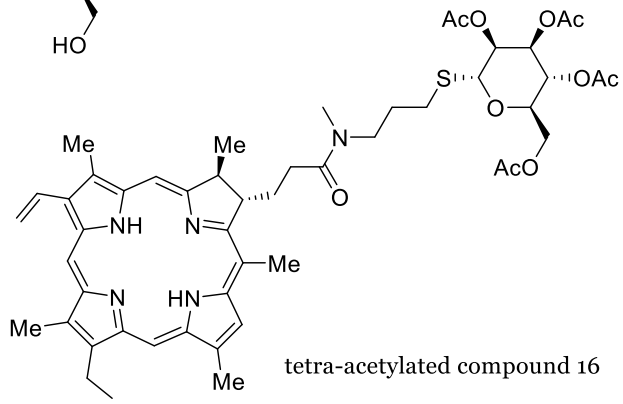
tetra-acetylated compound 14



compound 15

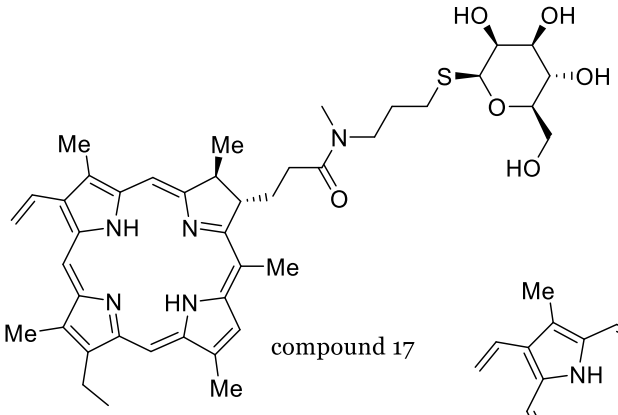


compound 16

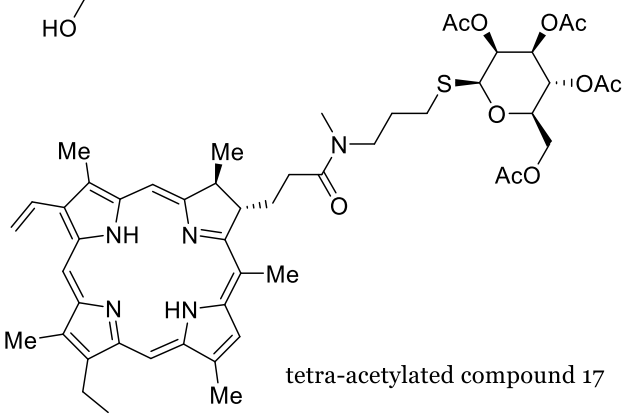


tetra-acetylated compound 16

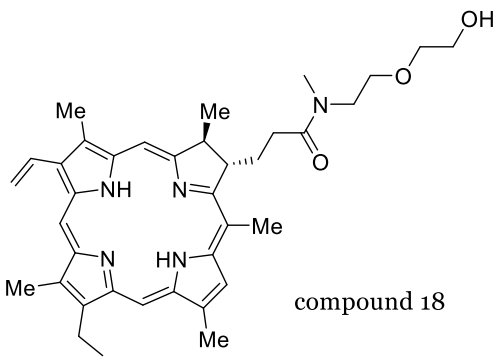
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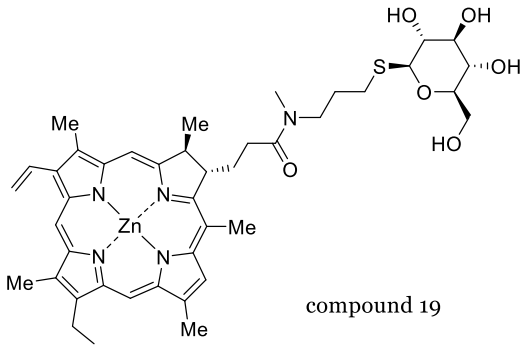
compound 17



tetra-acetylated compound 17

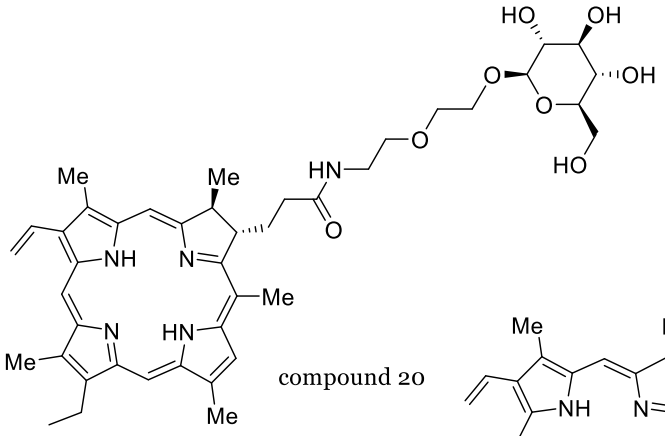


compound 18

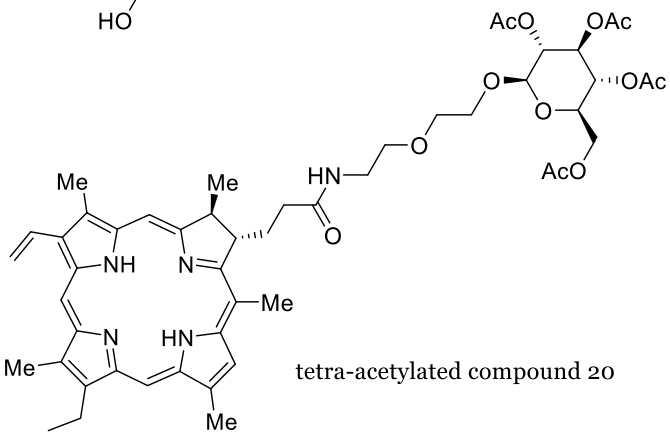


compound 19

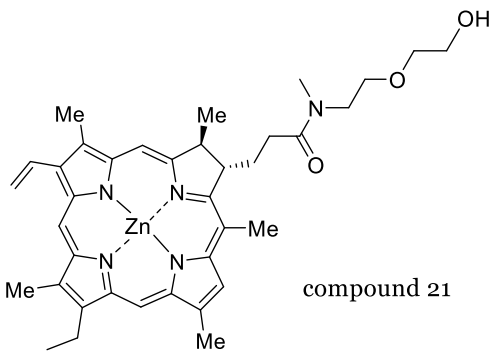
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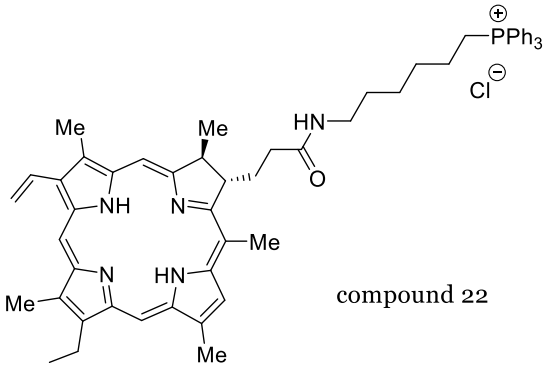
compound 20



tetra-acetylated compound 20

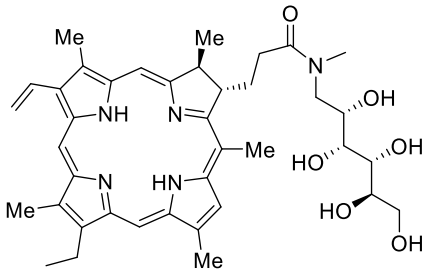


compound 21

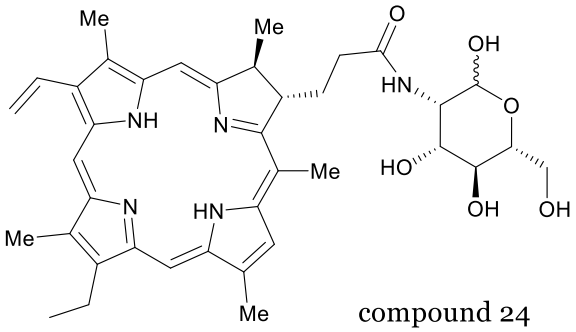


compound 22

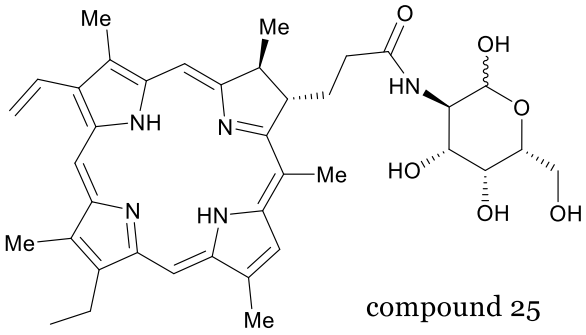
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compound 23

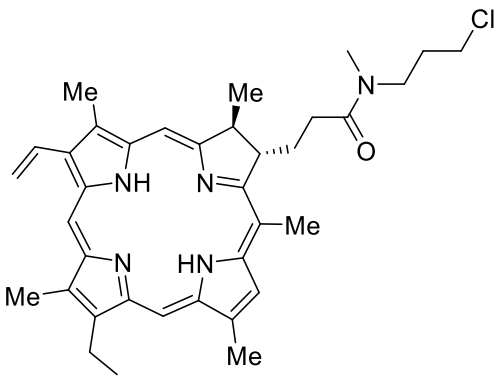


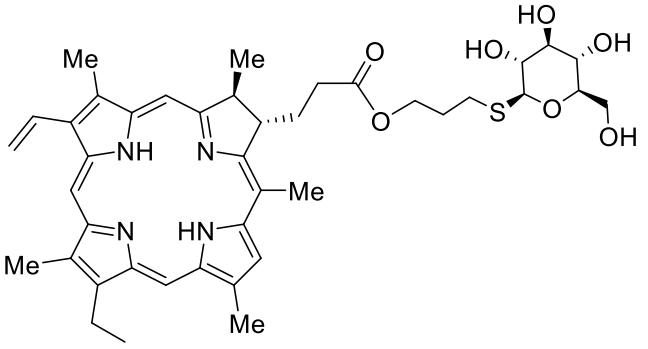
compound 24

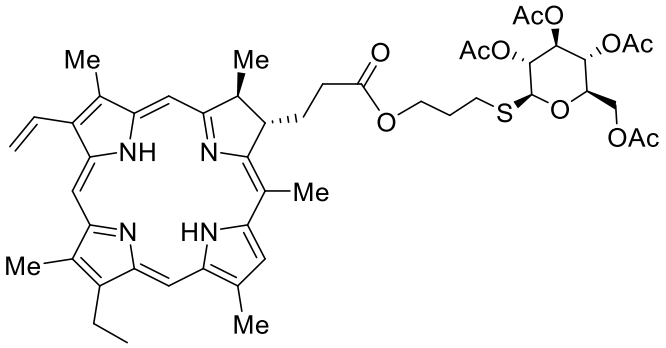


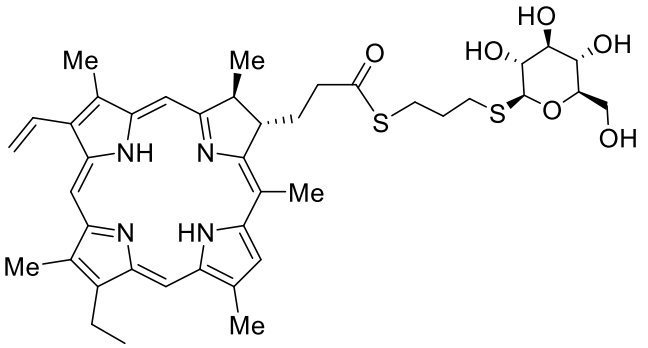
compound 25

5

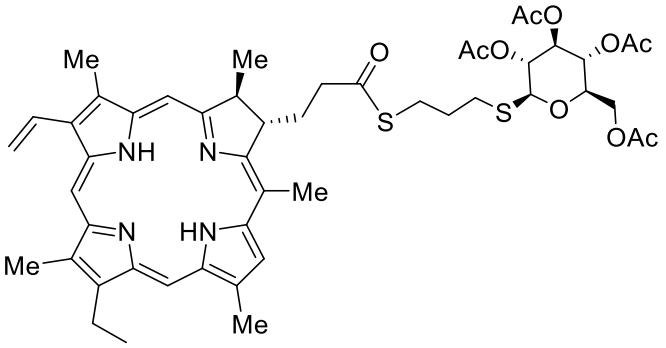








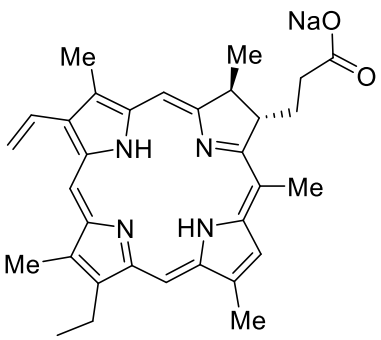
5



or ;

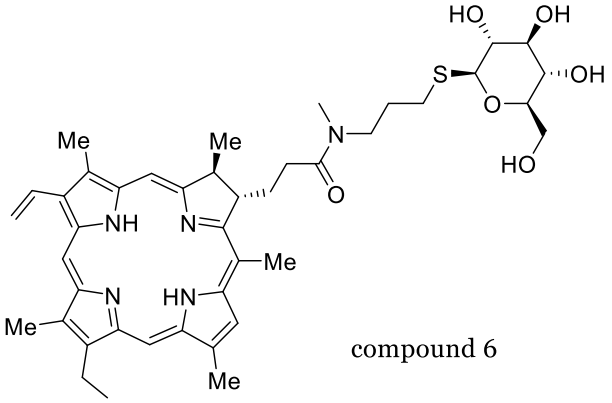
or a complex or a pharmaceutically acceptable salt thereof.

10. The compound or complex according to claim 1 or 2, wherein the compound or complex is:



compound 1

or



compound 6

.

11. The compound or complex according to claim 1 or 2, wherein the compound is phyllochlorin in the form of a pharmaceutically acceptable salt.

12. The compound or complex according to claim 11, wherein the compound is phyllochlorin sodium, potassium, lithium, choline, arginine or meglumine.

13. The compound or complex according to claim 2, wherein the compound is:

(1) phyllochlorin free acid; or

(2) phyllochlorin methyl ester.

14. The compound or complex according to any preceding claim:

(a) for use in photodynamic therapy or cytoluminescent therapy; or

(b) for the treatment of atherosclerosis; multiple sclerosis; diabetes; diabetic retinopathy; arthritis; rheumatoid arthritis; a fungal, viral, chlamydial, bacterial, nanobacterial or parasitic infectious disease; HIV; Aids; infection with sars virus (preferably severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)), Asian (chicken) flu virus, herpes simplex or herpes zoster; hepatitis; viral hepatitis; a cardiovascular disease; coronary artery stenosis; carotid artery stenosis; intermittent claudication; a dermatological condition; acne; psoriasis; a disease characterised by benign or malignant cellular hyperproliferation or by areas of neovascularisation; a benign or malignant tumour; early cancer; cervical dysplasia; soft tissue sarcoma; a germ cell tumour; retinoblastoma; age-related macular degeneration; lymphoma; Hodgkin's lymphoma; head and neck cancer; oral or mouth cancer; or cancer of the blood, prostate, cervix, uterus,

vaginal or other female adnexa, breast, naso-pharynx, trachea, larynx, bronchi, bronchioles, lung, hollow organs, esophagus, stomach, bile duct, intestine, colon, colorectum, rectum, bladder, ureter, kidney, liver, gall bladder, spleen, brain, lymphatic system, bones, skin or pancreas; or

(c) for the treatment of a disease characterised by benign or malignant cellular hyperproliferation or by areas of neovascularisation; or

(d) for the treatment of a benign or malignant tumour; or

(e) for the treatment of early cancer; cervical dysplasia; soft tissue sarcoma; a germ cell tumour; retinoblastoma; age-related macular degeneration; lymphoma; Hodgkin's lymphoma; head and neck cancer; oral or mouth cancer; or cancer of the blood, prostate, cervix, uterus, vaginal or other female adnexa, breast, naso-pharynx, trachea, larynx, bronchi, bronchioles, lung, hollow organs, esophagus, stomach, bile duct, intestine, colon, colorectum, rectum, bladder, ureter, kidney, liver, gall bladder, spleen, brain, lymphatic system, bones, skin or pancreas; or

(f) for use in photodynamic diagnosis; or

(g) wherein the compound is adapted for administration prior to administration of irradiation; or

(h) wherein the compound is adapted for administration prior to administration of irradiation, wherein the irradiation is electromagnetic radiation with a wavelength in the range of from 500nm to 1000nm; or

(i) wherein the compound is in a form suitable for oral, parenteral (including intravenous, subcutaneous, intramuscular, intradermal, intratracheal, intraperitoneal, intratumoral, intraarticular, intraabdominal, intracranial and epidural), transdermal, airway (aerosol), rectal, vaginal or topical (including buccal, mucosal and sublingual) administration; or

(j) wherein the compound is in a form suitable for oral or parenteral administration; or

(k) wherein the compound is in a form suitable for sublingual administration.

15. A pharmaceutical composition comprising a compound or complex according to any preceding claim and a pharmaceutically acceptable carrier or diluent.

16. The pharmaceutical composition according to claim 15, further comprising:

(a) polyvinylpyrrolidone; or

(b) an immune checkpoint inhibitor; or

(c) an immune checkpoint inhibitor, wherein the immune checkpoint inhibitor is selected from Pembrolizumab, Nivolumab, Cemiplimab, Atezolizumab, Avelumab, Durvalumab or Ipilimumab.

17. The pharmaceutical composition according to claim 15 or 16:

(a) for use in photodynamic therapy or cytoluminescent therapy; or

(b) for the treatment of atherosclerosis; multiple sclerosis; diabetes; diabetic retinopathy; arthritis; rheumatoid arthritis; a fungal, viral, chlamydial, bacterial, nanobacterial or parasitic infectious disease; HIV; Aids; infection with sars virus (preferably severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)), Asian (chicken) flu virus, herpes simplex or herpes zoster; hepatitis; viral hepatitis; a cardiovascular disease; coronary artery stenosis; carotid artery stenosis; intermittent claudication; a dermatological condition; acne; psoriasis; a disease characterised by benign or malignant cellular hyperproliferation or by areas of neovascularisation; a benign or malignant tumour; early cancer; cervical dysplasia; soft tissue sarcoma; a germ cell tumour; retinoblastoma; age-related macular degeneration; lymphoma; Hodgkin's lymphoma; head and neck cancer; oral or mouth cancer; or cancer of the blood, prostate, cervix, uterus, vaginal or other female adnexa, breast, naso-pharynx, trachea, larynx, bronchi, bronchioles, lung, hollow organs, esophagus, stomach, bile duct, intestine, colon, colorectum, rectum, bladder, ureter, kidney, liver, gall bladder, spleen, brain, lymphatic system, bones, skin or pancreas; or

(c) for the treatment of a disease characterised by benign or malignant cellular hyperproliferation or by areas of neovascularisation; or

(d) for the treatment of a benign or malignant tumour; or

(e) for the treatment of early cancer; cervical dysplasia; soft tissue sarcoma; a germ cell tumour; retinoblastoma; age-related macular degeneration; lymphoma; Hodgkin's lymphoma; head and neck cancer; oral or mouth cancer; or cancer of the blood, prostate, cervix, uterus, vaginal or other female adnexa, breast, naso-pharynx, trachea, larynx, bronchi, bronchioles, lung, hollow organs, esophagus, stomach, bile duct, intestine, colon, colorectum, rectum, bladder, ureter, kidney, liver, gall bladder, spleen, brain, lymphatic system, bones, skin or pancreas; or

(f) for use in photodynamic diagnosis; or

(g) wherein the pharmaceutical composition is adapted for administration prior to administration of irradiation; or

(h) wherein the pharmaceutical composition is adapted for administration prior to administration of irradiation, wherein the irradiation is electromagnetic radiation with a wavelength in the range of from 500nm to 1000nm; or

(i) wherein the pharmaceutical composition is in a form suitable for oral, parenteral (including intravenous, subcutaneous, intramuscular, intradermal, intratracheal, intraperitoneal, intratumoral, intraarticular, intraabdominal, intracranial and epidural), transdermal, airway (aerosol), rectal, vaginal or topical (including buccal, mucosal and sublingual) administration; or

(j) wherein the pharmaceutical composition is in a form suitable for oral or parenteral administration; or

(k) wherein the pharmaceutical composition is in a form suitable for sublingual administration.

18. Use of a compound or complex according to any one of claims 1-14, in the manufacture of a medicament for the treatment of atherosclerosis; multiple sclerosis; diabetes; diabetic retinopathy; arthritis; rheumatoid arthritis; a fungal, viral, chlamydial, bacterial, nanobacterial or parasitic infectious disease; HIV; Aids; infection with sars virus (preferably severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)), Asian (chicken) flu virus, herpes simplex or herpes zoster; hepatitis; viral hepatitis; a cardiovascular disease; coronary artery stenosis; carotid artery stenosis; intermittent claudication; a dermatological condition; acne; psoriasis; a disease characterised by benign or malignant cellular hyperproliferation or by areas of neovascularisation; a benign or malignant tumour; early cancer; cervical dysplasia; soft tissue sarcoma; a germ cell tumour; retinoblastoma; age-related macular degeneration; lymphoma; Hodgkin's lymphoma; head and neck cancer; oral or mouth cancer; or cancer of the blood, prostate, cervix, uterus, vaginal or other female adnexa, breast, naso-pharynx, trachea, larynx, bronchi, bronchioles, lung, hollow organs, esophagus, stomach, bile duct, intestine, colon, colorectum, rectum, bladder, ureter, kidney, liver, gall bladder, spleen, brain, lymphatic system, bones, skin or pancreas.

19. Use of a compound or complex according to any one of claims 1-14, in the manufacture of a phototherapeutic agent for use in photodynamic therapy or cytoluminescent therapy.

20. The use according to claim 19, wherein the phototherapeutic agent is for the treatment of atherosclerosis; multiple sclerosis; diabetes; diabetic retinopathy;

arthritis; rheumatoid arthritis; a fungal, viral, chlamydial, bacterial, nanobacterial or parasitic infectious disease; HIV; Aids; infection with sars virus (preferably severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)), Asian (chicken) flu virus, herpes simplex or herpes zoster; hepatitis; viral hepatitis; a cardiovascular disease; coronary artery stenosis; carotid artery stenosis; intermittent claudication; a dermatological condition; acne; psoriasis; a disease characterised by benign or malignant cellular hyperproliferation or by areas of neovascularisation; a benign or malignant tumour; early cancer; cervical dysplasia; soft tissue sarcoma; a germ cell tumour; retinoblastoma; age-related macular degeneration; lymphoma; Hodgkin's lymphoma; head and neck cancer; oral or mouth cancer; or cancer of the blood, prostate, cervix, uterus, vaginal or other female adnexa, breast, naso-pharynx, trachea, larynx, bronchi, bronchioles, lung, hollow organs, esophagus, stomach, bile duct, intestine, colon, colorectum, rectum, bladder, ureter, kidney, liver, gall bladder, spleen, brain, lymphatic system, bones, skin or pancreas.

21. The use according to any one of claims 18-20, wherein the medicament or the phototherapeutic agent is for the treatment of:

(a) a disease characterised by benign or malignant cellular hyperproliferation or by areas of neovascularisation; or

(b) a benign or malignant tumour; or

(c) early cancer; cervical dysplasia; soft tissue sarcoma; a germ cell tumour; retinoblastoma; age-related macular degeneration; lymphoma; Hodgkin's lymphoma; head and neck cancer; oral or mouth cancer; or cancer of the blood, prostate, cervix, uterus, vaginal or other female adnexa, breast, naso-pharynx, trachea, larynx, bronchi, bronchioles, lung, hollow organs, esophagus, stomach, bile duct, intestine, colon, colorectum, rectum, bladder, ureter, kidney, liver, gall bladder, spleen, brain, lymphatic system, bones, skin or pancreas.

22. Use of a compound or complex according to any one of claims 1-14, in the manufacture of a photodiagnostic agent for use in photodynamic diagnosis.

23. The use according to any one of claims 18-22, wherein the medicament, the phototherapeutic agent or the photodiagnostic agent is:

(a) adapted for administration prior to administration of irradiation; or

(b) adapted for administration prior to administration of irradiation, wherein the irradiation is electromagnetic radiation with a wavelength in the range of from 500nm to 1000nm; or

(c) in a form suitable for oral, parenteral (including intravenous, subcutaneous, intramuscular, intradermal, intratracheal, intraperitoneal, intratumoral, intraarticular, intraabdominal, intracranial and epidural), transdermal, airway (aerosol), rectal, vaginal or topical (including buccal, mucosal and sublingual) administration; or

(d) in a form suitable for oral or parenteral administration; or

(e) in a form suitable for sublingual administration.

24. A pharmaceutical combination comprising:

(a) a compound or complex according to any one of claims 1-14; and

(b) an immune checkpoint inhibitor.

25. The pharmaceutical combination according to claim 24, wherein the immune checkpoint inhibitor is selected from Pembrolizumab, Nivolumab, Cemiplimab, Atezolizumab, Avelumab, Durvalumab or Ipilimumab.