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ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

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(54) Title: PHTHALOCYANINE DYE COMPOUNDS, CONJUGATES AND METHODS OF USE THEREOF

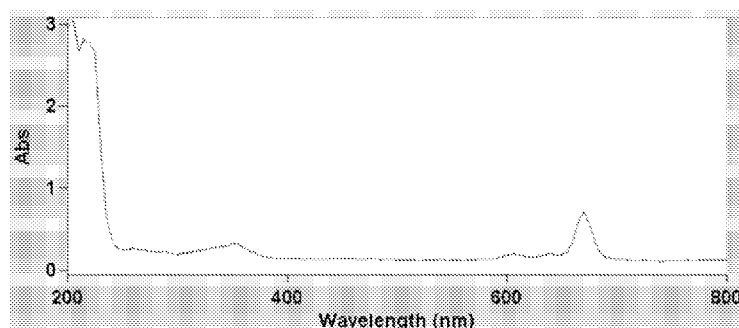


FIG. 1

(57) Abstract: Disclosed herein are phthalocyanine dyes, and conjugates thereof, useful as fluorescent reporters for bioassays, for optical imaging and as therapeutic conjugates as the photosensitizing agents in light-based therapies including photoimmuno therapy (PIT). Certain phthalocyanine dyes disclosed herein are water soluble, and possess photophysical and photochemical profiles useful for use in imaging or therapy.

PHTHALOCYANINE DYE COMPOUNDS, CONJUGATES AND METHODS OF USE THEREOF

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Patent Application No. 63/008,476, filed on April 10, 2020, and U.S. Provisional Patent Application No. 63/008,502, filed on April 10, 2020, both of which are herein incorporated by reference in their entirety.

FIELD OF THE INVENTION

[0002] Provided herein are phthalocyanine dye compounds and conjugates with phthalocyanine dye compounds that find use in therapeutics and diagnostic applications such as reporters for bioassays, for optical imaging and as photosensitizing agents in light-based therapies including photoimmunotherapy. Also provided herein are methods for preparing the phthalocyanine dye compounds and compositions and kits comprising the phthalocyanine dye compounds provided herein. Also provided herein are methods for preparing phthalocyanine dye conjugates and methods of treatment using the phthalocyanine dye conjugates.

BACKGROUND OF THE INVENTION

[0003] Phthalocyanine (Pc) dye compounds are currently used as fluorescent reporter groups in bioassays, as fluorescent markers for optical imaging and as photosensitizers in light based therapies such as photodynamic therapy (PDT), photothermal therapy (PTT) and photoimmunotherapy (PIT). Pcs are particularly attractive in light based therapies given the stability and high extinction coefficients in the near infrared radiation of certain phthalocyanine dyes. Improved phthalocyanine dyes are needed to improve the effectiveness, cost and availability of biological assays, optical imaging and therapies dependent on these dyes. Provided herein are such compounds, compositions and methods that meet such needs.

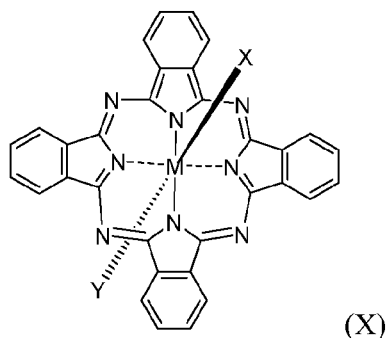
SUMMARY OF THE INVENTION

[0004] In one aspect, provided herein are phthalocyanine dye compounds that may be used as an unconjugated fluorescent dye, or when conjugated to a molecule may be used in biological assays, diagnostics and light-based therapies. In another aspect, provided herein are phthalocyanine dye compounds and conjugates thereof for use in biological assays, diagnostics and light-based therapies. In one embodiment, provided herein are phthalocyanine dye compounds of Formula (0) comprising an unsubstituted phthalocyanine scaffold containing a core metal or metalloid atom, which are coordinated to two axial ligands, the first ligand comprising at least one water soluble group and the second ligand comprising at least one reactive group. The phthalocyanine dye compounds provided herein do not exist as

regioisomers. Because the core phthalocyanine structure is unsubstituted, synthesis of the compounds herein does not create regioisomers, and the manufacturing of the present compounds is thus efficient, cost effective and improves the effectiveness of isolation and/or separation procedures.

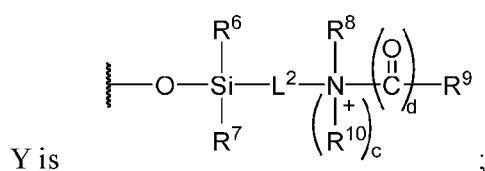
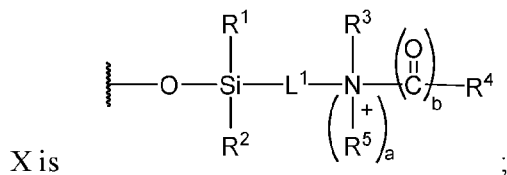
[0005] In one aspect, provided herein are conjugates comprising a phthalocyanine dye covalently linked to a targeting molecule, wherein the phthalocyanine dye comprises Formula (0) for use in the conjugates, pharmaceutical compositions and methods herein, and where the Formula (0) compound comprises a metal or metalloid atom, such as a silicon atom, coordinated by (a) an unsubstituted phthalocyanine, (b) a first axial silicon-containing ligand having a conjugatable group; and (c) a second axial silicon-containing ligand having a water-solubilizing group that is not a conjugatable group. In some embodiments of Formula (0) the axial silicon-containing ligand having a conjugatable group further comprises a water-solubilizing group. In some embodiments, the chemical structures of the first and second axial ligands are different from one another.

[0006] In one aspect, provided herein are phthalocyanine dye compounds having the Formula (X):



or a salt, stereoisomer, or tautomer thereof, wherein:

M is a metal or metalloid;



R¹ and R² are each independently optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted heterocyclyl,

optionally substituted heterocyclylalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, or optionally substituted heteroaralkyl;

R^3 , R^4 or R^5 are selected from substituent group (a) or substituent group (b) wherein,

(a) R^3 is hydrogen, $-L^3-H$, $-L^3-A$, or $-L^3-Z$;

R^4 is $-L^4-H$, $-(NH)_m-L^4-A$, $-(NH)_m-L^4-Z$, $-(O)_m-L^4-A$ or $-(O)_m-L^4-Z$;

R^5 is $-L^5-H$ or $-L^5-A$; and

(b) R^3 is $-L^3-H$, or $-L^3-A$;

R^4 is $-L^4-H$, $-(NH)_m-L^4-A$, or $-(O)_m-L^4-A$; wherein R^3 and R^4 are connected with a bond to form a heterocyclyl substituted with $-L^4-A$; and

R^5 is $-L^5-H$ or $-L^5-A$;

provided at least one of R^3 , R^4 and R^5 is a group containing A;

A is a reactive group capable of forming a covalent bond with a thiol, hydroxyl, carboxyl or amino group of a second moiety, or a protected form thereof or a reacted form thereof;

R^6 and R^7 are each independently optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl or optionally substituted heteroaralkyl;

R^8 , R^9 or R^{10} are selected from substituent group (a) or substituent group (b) wherein,

(a) R^8 is hydrogen, $-L^8-H$ or $-L^8-Z$;

R^9 is $-L^9-H$, $-(NH)_n-L^9-Z$ or $-(O)_n-L^9-Z$;

R^{10} is $-L^{10}-Z$; and

(b) R^8 and R^9 are connected with a bond to form a heterocyclyl substituted with $-L^9-Z$ and R^{10} is $-L^{10}-H$ or $-L^{10}-Z$;

provided at least one of R^8 , R^9 and R^{10} is a group containing Z;

Z is a water soluble group optionally substituted with A or $L'-A$;

L^1 and L^2 are each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkyl, or optionally substituted heterocyclyl;

L^3 , L^4 , L^5 , L^8 , L^9 and L^{10} are each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkylene, optionally substituted heterocyclene, optionally substituted arylene, optionally substituted aralkylene, optionally substituted heteroaralkylene, or optionally substituted heteroarylene, where the carbon atom of the alkylene, heteroalkylene, alkenylene, heteroalkenylene, cycloalkylene, heterocyclene,

arylene, aralkylene, heteroaralkylene, or optionally substituted heteroarylene is further optionally substituted with Z and each nitrogen atom of the heteroalkylene or heteroalkenylene is optionally substituted with one or two L'-Z;

L' is each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkylene, optionally substituted heterocyclene, optionally substituted arylene, optionally substituted aralkylene, optionally substituted heteroaralkylene, or optionally substituted heteroarylene;

a is 0 or 1;

b is 0 or 1;

c is 0 or 1;

d is 0 or 1;

m is 0 or 1;

n is 0 or 1;

provided that if b is 1, then a is 0;

if d is 1, then c is 0;

if m is 1, b is 1; and

if n is 1, c is 1.

[0007] In yet another aspect, provided herein is a compound of Formula (0) comprising a silicon atom coordinated by (a) an unsubstituted phthalocyanine, (b) an axial silicon-containing ligand having a conjugatable group; and (c) an axial silicon-containing ligand having a water-solubilizing group that is not a conjugatable group.

[0008] The conjugates provided herein include one or more targeting molecule(s), such as where wherein the targeting molecule(s) is a polypeptide or other molecule that binds to the surface of a cell. In some embodiments, the one or more targeting molecule(s) of the conjugate is an antibody or an antigen-binding antibody fragment. In some embodiments, the one or more targeting molecule(s) is an antigen-binding antibody fragment such as a Fab, single VH domain, multiple VH domain, a single chain variable fragment (scFv), a multivalent scFv, a bispecific scFv, and/or an scFv-CH3 dimer. In some embodiments, the one or more targeting molecule(s) is an antibody or an antigen-binding antibody fragment that binds to at least one of CD25, CEA, CTLA-4, EGFR/HER1, FAP, HER2, MUC-1, PD-1, PD-L1, and/or PSMA. In some embodiments, the targeting molecule is an antibody or an antigen-binding antibody fragment that binds to CD25, such as an antibody or antigen-binding fragment that binds CD25 but does not block interleukin-2 (IL-2) signaling of the IL-2

receptor. In some embodiments, the targeting molecule is an antibody or an antigen-binding antibody fragment that binds to CEA. In some embodiments, the targeting molecule is an antibody or an antigen-binding antibody fragment that binds to CTLA-4. In some embodiments, the targeting molecule is an antibody or an antigen-binding antibody fragment that binds to EGFR/HER1. In some embodiments, the targeting molecule is an antibody or an antigen-binding antibody fragment that binds to HER2. In some embodiments, the targeting molecule is an antibody or an antigen-binding antibody fragment that binds to MUC-1. In some embodiments, the targeting molecule is an antibody or an antigen-binding antibody fragment that binds to PD-1. In some embodiments, the targeting molecule is an antibody or an antigen-binding antibody fragment that binds to PD-L1. In some embodiments, the targeting molecule is an antibody or an antigen-binding antibody fragment that binds to PSMA.

[0009] In some embodiments, the conjugates provided herein include a targeting molecule that is an antibody or an antigen-binding antibody fragment of 3F8, 8H9, AB122, ab75705, Abagovomab, Abciximab, Abituzumab, Abrezekimab, Abrilumab, Actoxumab, Adalimumab, Adecatumumab, ADG116, ADU-1604, Aducanumab, Afasevikumab, Afelimomab, Afutuzumab, AGEN1181, AGEN1884, AGX-115, AK104, AK105, Alacizumab pegol, Alemtuzumab, Alirocumab, Altumomab pentetate, Amatuximab, AMG 404, AMP-224, AMP-514, Anatumomab mafenatox, Andecaliximab, Anetumab ravtansine, Anifrolumab, Anrukinzumab, anti-CD133, Apolizumab, Aprutumab ixadotin, Arcitumomab, arcitumomab Fab fragment, Ascrinvacumab, Aselizumab, Atezolizumab, Atidortoxumab, Atinumab, Atlizumab (Tocilizumab), ATOR-1015, Atorolimomab, Avelumab, Azintuxizumab vedotin, B72.3, Bapineuzumab, Basiliximab, Bavituximab, BCD-100, BCD-135, BCD-145, BCD-217, Bectumomab, Begelomab, Belantamab mafodotin, Belimumab, Bemarituzumab, Benralizumab, Berlimatoxumab, Bermekimab, Bersanlimab, Bertilimumab, Besilesomab, Bevacizumab, Bezlotoxumab, BGB-A333, BI 754091, Biciromab, Bimagrumab, Bimekizumab, Birtamimab, Bivatuzumab, Bivatuzumab mertansine, BL-8040, Bleselumab, Blinatumomab, Blontuvetmab, Blosozumab, BMS-936559, BMS-986218, Bococizumab, Brazikumab, Brentuximab vedotin, Briakinumab, Brodalumab, Brolucizumab, Brontictuzumab, Burosumab, Cabiralizumab, Camidanlumab tesirine, Camrelizumab, Canakinumab, Cantuzumab mertansine, Cantuzumab ravtansine, Caplacizumab, Capromab, Capromab pendetide, Carlumab, Carotuximab, Catumaxomab, cBR96-doxorubicin immunoconjugate, CBT-502, CC-90002, CDC-022, Cedelizumab, Cemiplimab, Cergutuzumab amunaleukin, Certolizumab pegol, Cetrelimab, Cetuximab, Cibisatamab,

Cirmtuzumab, Citatuzumab bogatox, Cixutumumab, Clazakizumab, Clenoliximab, Clivatuzumab tetraxetan, CMAB302, Codrituzumab, Cofetuzumab pelidotin, Coltuximab ravtansine, Conatumumab, Concizumab, Cosfroviximab, Cosibelimab, CP-870,893, CR6261, Crenezumab, Crizanlizumab, Crotedumab, CS1001, CS1003, Cusatuzumab, CX-188, Dacetuzumab, Daclizumab, Dalotuzumab, Dapirolizumab pegol, Daratumumab, Dectrekumab, Demcizumab, Denintuzumab mafodotin, Denosumab, Depatuxizumab mafodotin, Derlotuximab biotin, Detumomab, Dezamizumab, Dinutuximab, Diridavumab, Domagrozumab, Dorlimomab aritox, Dostarlimab, Drozitumab, DS-8201, Duligotumab, Duligotuzumab, Dupilumab, Durvalumab, Dusigitumab, Duvortuxizumab, Echromeximab, Eculizumab, Edobacomab, Edrecolomab, Efalizumab, Eftilagimod alpha, Efungumab, Eldelumab, Elezanumab, Elgemitumab, Elotuzumab, Elsilimomab, Emactuzumab, Emapalumab, Emibetuzumab, Emicizumab, Enapotamab vedotin, Enavatuzumab, Enfortumab vedotin, Enlimomab pegol, Enoblituzumab, Enokizumab, Enoticumab, Ensituximab, Epitumomab cituxetan, Epratuzumab, Eptinezumab, Erenumab, Erlizumab, Ertumaxomab, Etaracizumab, Etigilimab, Etrolizumab, Evinacumab, Evolocumab, Exbivirumab, F3, F520, Fanolesomab, Faralimomab, Faricimab, Farletuzumab, Fasinumab, FAZ053, FBTA05, Felvizumab, Fezakinumab, Fibatuzumab, Ficlatuzumab, Figitumumab, Firivumab, Flanvotumab, Fletikumab, Flotetuzumab, Fontolizumab, Foralumab, Foravirumab, Fremanezumab, Fresolimumab, Frovocimab, Frunevetmab, Fulranumab, Futuximab, Galcanezumab, Galiximab, Gancotamab, Ganitumab, Gantenerumab, Gatipotuzumab, Gavilimomab, GB221, Gedivumab, Gemtuzumab ozogamicin, genolimzumab, Gevokizumab, Gilvetmab, Gimsilumab, Girentuximab, Glembatumumab vedotin, GLS-010, Golimumab, Gomiliximab, Gosuranemab, Guselkumab, HD201, Hervycta, HLX02, HLX10, HLX20, HLX22, HX008, HX009, Ianalumab, Ibalizumab, IBI308, Ibiritumomab tiuxetan, Icrucumab, Idarucizumab, Ieramilimab, Ifabotuzumab, Igovomab, Iladatuzumab vedotin, IMAB362, Imalumab, Imaprelimab, Imciromab, Imgatuzumab, INBRX-105, Inclacumab, Indatuximab ravtansine, Indusatumab vedotin, Inebilizumab, Infliximab, Inolimomab, Inotuzumab ozogamicin, Intetumumab, Iomab-B, IPH2101, Ipilimumab, Iratumumab, Isatuximab, Iscalimab, Istiratumab, Itolizumab, Ixekizumab, JTX-4014, Keliximab, KN035, KN046, Labetuzumab, Lacnotuzumab, Ladiratuzumab vedotin, Lambrolizumab (Pembrolizumab), Lampalizumab, Lanadelumab, Landogrozumab, Laprituximab emtansine, Larcaviximab, LDP, Lebrikizumab, Lemalesomab, Lendalizumab, Lenvervimab, Lenzilumab, Lerdelimumab, Leronlimab, Lesofavumab, Letolizumab, Lexatumumab, Libivirumab, Lifestuzumab vedotin, Ligelizumab, Lilotomab

satetraxetan, Lintuzumab, Lirilumab, Lodelcizumab, Lokivetmab, Loncastuximab tesirine, Lorvotuzumab mertansine, Losatuxizumab vedotin, Lucatumumab, Lulizumab pegol, Lumiliximab, Lumretuzumab, Lupartumab, Lupartumab amadotin, Lutikizumab, LY3300054, LY3415244, LZM009, mAb114, Mapatumumab, Margetuximab, Marstacimab, Maslimomab, Matuzumab, Mavrilimumab, MCLA-145, MED16469, MEDI6383, Mepolizumab, Metelimumab, MGA012, MGD013, MGD019, Milatuzumab, Minretumomab, Mirikizumab, Mirvetuximab soravtansine, Mitumomab, MK-1308, MK-4166, MNRP1685A, Modotuximab, Mogamulizumab, Monalizumab, Morolimumab, Mosunetuzumab, Motavizumab, Moxetumomab pasudotox, MOXR0916, MSB2311, Muromonab-CD3, Nacolomab tafenatox, Namilumab, Naptumomab estafenatox, Naratuximab emtansine, Narnatumab, Natalizumab, Navicixizumab, Navivumab, Naxitamab, Nebacumab, Necitumumab, Nemolizumab, NEOD001, Nerelimomab, Nesvacumab, Netakimab, Nimotuzumab, Nirsevimab, Nivolumab, NM-01, Nofetumomab merpentan, Obiltoxaximab, Obinutuzumab, OC125 monoclonal antibody, Ocaratuzumab, Ocrelizumab, Odulimumab, Ofatumumab, Olaratumab, Oleclumab, Olendalizumab, Olokizumab, Omalizumab, Omburtamab, OMS721, Onartuzumab, Ontuxizumab, Onvatilimab, Opicinumab, Oportuzumab monatox, Oregovomab, Orticumab, Otelixizumab, Otilimab, Otlertuzumab, Oxelumab, Ozanezumab, Ozoralizumab, Pagibaximab, Palivizumab, Pamrevlumab, Panitumumab, Pankomab, Panobacumab, Parsatuzumab, Pascolizumab, Pasotuxizumab, Pateclizumab, Patritumab, PDR001, Pembrolizumab, Pentumomab, Perakizumab, Pertuzumab, Pexelizumab, PF-05280014, PF-06801591, Pidilizumab, Pinatuzumab vedotin, Pintumomab, Placulumab, Plozalizumab, Pogalizumab, Polatuzumab vedotin, Ponezumab, Porgaviximab, Prasinezumab, Prezalizumab, Prezalumab, Priliximab, Pritoxaximab, Pritumumab, PRO 140, Quilizumab, Racotumomab, Radretumab, Rafivirumab, Ralpancizumab, Ramucirumab, Ranevetmab, Ranibizumab, Ravagalimab, Ravulizumab, Raxibacumab, Refanezumab, Regavirumab, REGN2810, REGN3504, REGN4659, REGN-EB3, Relatlimab, Remtolumab, Reslizumab, rHlgM12B7, Rilotumumab, Rinucumab, Risankizumab, Rituximab, Rituximab, Rivabazumab pegol, Rmab, RO7121661, Robatumumab, Roledumab, Romilkimab, Romosozumab, Rontalizumab, Rosmantuzumab, Rovalpituzumab tesirine, Rovelizumab, Rozanolixizumab, Ruplizumab, SA237, Sacituzumab, Sacituzumab govitecan, Samalizumab, Samrotamab vedotin, Sarilumab, Satralizumab, Satumomab pendetide, SB3, SCT-I10A, SEA-CD40, Secukinumab, Selicrelumab, Seribantumab, Setoxaximab, Setrusumab, Sevirumab, SG001, SGN-CD19A, SHP647, SHR-1316, SIBP-01, Sibrotuzumab, Sifalimumab, Siltuximab, Simtuzumab,

Sintilimab, Siplizumab, Sirtratumab vedotin, Sirukumab, Sofituzumab vedotin, Solanezumab, Solitomab, Sonepcizumab, Sontuzumab, Spartalizumab, Stamulumab, STI-3031, Sulesomab, Suptavumab, Sutimlimab, Suvizumab, Suvratroxumab, Sym021, Tabalumab, Tacatuzumab tetraxetan, Tadocizumab, Talacotuzumab, Talizumab, Tamtuvatmab, Tanezumab, Taplitumomab paptox, Tarextumab, Tavolimab, Tefibazumab, Telimomab aritox, Telisotuzumab, Telisotuzumab vedotin, Tenatumomab, Teneliximab, Teplizumab, Tepoditamab, Teprotumumab, Tesidolumab, Tetulomab, Tezepelumab, TG-1501, TGN1412, Tibulizumab, Ticilimumab, Tigatuzumab, Tildrakizumab, Timigutuzumab, Timolumab, Tiragolumab, Tiragotumab, Tislelizumab, Tisotumab vedotin, TNX-650, Tocilizumab, Tocilizumab, Tomuzotuximab, Toralizumab, Toripalimab, Tosatoxumab, Tositumomab, Tositumomab, Tovetumab, Tralokinumab, Trastuzumab, Trastuzumab deruxtecan, Trastuzumab-anns, trastuzumab-dkst, Trastuzumab emtansine, TRBS07, Tregalizumab, Tremelimumab, Trevogrumab, TRX385, TRX518, TSR-042, Tucotuzumab celmoleukin, Tuvirumab, TX05, Ublituximab, Ulocuplumab, Urelumab, Urtoxazumab, Ustekinumab, Utomilumab, Vadastuximab talirine, Vanalizumab, Vandortuzumab vedotin, Vantictumab, Vanucizumab, Vapaliximab, Varisacumab, Varlilumab, Vatelizumab, Vedolizumab, Veltuzumab, Vepalimomab, Vesencumab, Visilizumab, Vobarilizumab, Volociximab, Vonlerolizumab, Vopratelimab, Vorsetuzumab mafodotin, Votumumab, Vunakizumab, Xentuzumab, XmAb20717, XmAb22841, XMAB-5574, Zalutumumab, Zanolimumab, Zatuximab, Zenocutuzumab, Ziralimumab, ZKAB001, Zolbetuximab, Zolimomab aritox, or an antigen-binding fragment thereof.

[00010] In some embodiments, the conjugates provided herein include a targeting molecule that is Alacizumab pegol, Cetuximab, Depatuxizumab mafodotin, Futuximab, Icrucumab, Imgatuzumab, Laprituximab emtansine, Matuzumab, Modotuximab, Necitumumab, Nimotuzumab, Panitumumab, Ramucirumab, Tomuzotuximab, Zalutumumab, or an antigen-binding fragment thereof.

[00011] In some embodiments, the conjugates provided herein include a targeting molecule that is an anti-CD25 antibody such as Basiliximab (SIMULECT), Camidanlumab tesirine, daclizumab (Zinbryta; Zenapax), Inolimomab, RA8, STI-003, Xenopax or an antigen-binding fragment thereof.

[00012] In some embodiments, the conjugates provided herein include a targeting molecule that is an anti-PD-L1 antibody such as atezolizumab (MPDL3280A, Tecentriq), avelumab (Bavencio), durvalumab (MEDI4736, Imfinzi), LDP, NM-01, STI-3031, KN035, LY3300054, M7824 (MSB0011359C), BMS-936559, MSB2311, BCD-135, BGB-A333,

CBT-502, cosibelimab (CK-301), CS1001, FAZ053, MDX-1105, SHR-1316, TG-1501, ZKAB001, INBRX-105, MCLA-145, KN046, LY3415244, REGN3504, HLX20, and antigen-binding fragments of any thereof.

[00013] In some embodiments, the conjugates provided herein include a targeting molecule that is an anti-PD-1 antibody selected from the group consisting of pembrolizumab (MK-3475, Keytruda), nivolumab (Opdivo), cemiplimab (Libtayo), toripalimab (JS001), HX008, SG001, GLS-010, dostarlimab (TSR-042), tislelizumab (BGB-A317), cetrelimab (JNJ-63723283), pidilizumab (CT-011), genolimzumab (APL-501, GB226), BCD-100, cemiplimab (REGN2810), F520, sintilimab (IBI308), GLS-010, CS1003, LZM009, camrelizumab (SHR-1210), SCT-II0A, MGA012, AK105, PF-06801591, AMP-224, AB122, AMG 404, BI 754091, HLX10, JTX-4014, MEDI0680, Sym021, MGD019, MGD013, AK104, XmAb20717, RO7121661, CX-188, spartalizumab and, antigen-binding fragments of any thereof.

[00014] In some embodiments, the conjugates provided herein include a targeting molecule that is ipilimumab (Yervoy®), tremelimumab (ticilimumab), AGEN1181, AGEN1884, ADU-1064, BCD-145, BCD-217, or an antigen-binding fragment of any thereof.

[00015] In some embodiments, the conjugates provided herein include a targeting molecule that is CDC-022 (HERtiCAD), CMAB302 (Cipterbin), DS-8201, Gancotamab, GB221, HD201, Hervycta, HLX02, HLX22, Margetuximab, Pertuzumab (Perjeta), PF-05280014 (Trazimera), SB3, SIBP-01, Timigutuzumab, Trastuzumab (Herceptin), trastuzumab deruxtecan (ENHERTU), Trastuzumab emtansine (Kadcyla), trastuzumab-anns (Kanjinti), trastuzumab-dkst (Ogivri), TX05, or an antigen-binding fragment thereof.

[00016] In some embodiments, the conjugates provided herein include a targeting molecule that includes the antibody or an antigen-binding antibody fragment of cetuximab, basiliximab, daclizumab, F3, trastuzumab, panitumumab, or antigen-binding fragment thereof. In some embodiments, the conjugates provided herein include a targeting molecule that is a peptide or small molecule that binds to EGFR, HER2, CD25, PD-1, PD-L1, MUC1, PSMA, FAP, or CTLA-4. In some embodiments, the conjugates provided herein include a targeting molecule that binds to a viral particle or a viral capsid protein or a portion thereof.

[00017] In some aspects, the conjugates of a targeting molecule and a phthalocyanine dye of Formula (X), Formula (0), Formula (I) or Formula (II) have a dye to targeting molecule ratio of about 5:1, 4:1, 3:1, 2:1 or 1:1. In some embodiments, the conjugates have a dye to targeting

molecule ratio between about 1:1 to 5:1, 1.5:1 to 4:1, 1.5:1 to 3.5:1, 1.5:1 to 3:1 or about 2:1 to 3:1.

[00018] In some aspects, the phthalocyanine dye of the conjugates such as the compounds of Formula (X), Formula (0), Formula (I) or Formula (II) have a maximum absorption at a wavelength between about 600 nm to 800 nm, about 620 nm to 720 nm, about 640 to 700 nm, or about 640 to 680nm.

[00019] Among the conjugates provided herein are conjugates of a targeting molecule (also referred to interchangeably as a targeting moiety) and a phthalocyanine dye is selected from Compound 1, 5, 12, 13, 14, 16, 17, 18 or 19 of Table A.

[00020] Among the conjugates provided herein are conjugates of a targeting molecule (also referred to interchangeably as a targeting moiety) and a phthalocyanine dye is selected from Table A.

[00021] Also provided herein are pharmaceutical compositions of a conjugate and a pharmaceutically acceptable excipient. The conjugates provided herein and the pharmaceutical compositions find use in methods of treatment. In some embodiments, the methods include a method of treating a subject having a disease or condition by administering to a subject a conjugate or pharmaceutical composition of a conjugate described herein, after administering the conjugate, illuminating a target region of the subject at a wavelength of at or about 600 nm to at or about 850 nm at a dose of or of about 10 J/cm² to a dose of or of about 200 J/cm² or at a dose from at or about 10 J/cm fiber length to at or about 100 J/cm fiber length, thereby treating the disease or condition in the subject. In some embodiments of the method, the wavelength is at least about 600 nm, 610 nm, 620 nm, 630, nm, 640 nm, 650 nm, 660 nm, 670 nm, 680, nm, 690 nm or 700 nm. In some embodiments of the method, the wavelength is between 660 nm and 680 nm. In some embodiments of the method, the wavelength is at or about 670 ± 50 nm, or at or about 670 ± 40 nm or at or about 670 ± 20 nm, or at or about 670 ± 10 nm. In some embodiments of the method, the wavelength is less than 690 nm or less than 680 nm.

[00022] In certain aspects, the methods of treatment herein include treatment of where the target region is a tumor cell, a mass of tumor cells, a solid tumor, in the vicinity of a solid tumor, a metastasis, a metastasized tumor cell, in the vicinity of a metastasis or a pre-cancerous lesion.

[00023] In some embodiments of the methods, the illumination is performed at least 5 minutes after administration of the conjugate. In some embodiments of the methods, the illumination is performed at about 1 hour, 5 hours, 10 hours, 15 hours, 20 hours, 21 hours, 22 hours, 23 hours, 24 hours, 25 hours, 26 hours, 27 hours, 28 hours, 29 hours, 30 hours, 36 hours, 40 hours, 48 hours, 72 hours, or 96 hours after administration of the conjugate. In some embodiments of the methods, the illumination is performed 24 +/- 4 h after administration of the conjugate.

[00024] The methods provided herein include those where the disease or condition for treatment is a cancer. In some aspects, the cancer is selected from the group consisting of colon cancer, colorectal cancer, pancreatic cancer, breast cancer, skin cancer, lung cancer, non-small cell lung carcinoma, renal cell carcinoma, thyroid cancer, prostate cancer, head and neck cancer, gastrointestinal cancer, stomach cancer, cancer of the small intestine, spindle cell neoplasm, hepatic carcinoma, liver cancer, cholangiocarcinoma, cancer of peripheral nerve, brain cancer, cancer of skeletal muscle, cancer of smooth muscle, bone cancer, cancer of adipose tissue, cervical cancer, uterine cancer, cancer of genitals, lymphoma, and multiple myeloma. In some aspects of the methods of treatment herein, the steps of administering the conjugate and illuminating are repeated.

[00025] Also provided herein are methods of imaging a cell or tissue having a target molecule that include administering to a subject a conjugate or the pharmaceutical composition of a conjugate described herein, after administering the conjugate, illuminating a target region of the subject at a wavelength of at or about 600 nm to at or about 850 nm, thereby providing an image of the presence of the target molecule on the cell or tissue.

[00026] Also provided herein are systems for treating a subject having a disease or condition that include a conjugate or pharmaceutical composition of a conjugate described herein, a laser capable of emitting light at a wavelength of between 600 nm to about 800 nm, such as 670 ± 20 nm, an optic fiber operably connected to the laser for transmitting the light to a target region of the subject; and a light diffusing device comprising a non-circular core fiber. In some embodiments, the non-circular core fiber has a "top hat" core irradiance distribution. In some embodiments, the light diffusing device is a cylindrical diffuser or a frontal diffuser.

[00027] In yet certain embodiments, provided herein is a kit comprising a compound Formula (X), Formula (0), Formula (I) or Formula (II), and instructions for use. In yet certain embodiments, the kit further comprises additional reagents.

BRIEF DESCRIPTION OF THE DRAWINGS

- [00028] Figure 1 provides the UV-Vis spectra of Chemical Synthesis Example 1.
- [00029] Figure 2 provides the UV-Vis spectra of Chemical Synthesis Example 12.
- [00030] Figure 3 depicts the dose-dependent cytotoxicity of free dyes Compound 12 and Compound 13 following illumination.
- [00031] Figure 4 depicts the dose-dependent cytotoxicity of CTX-C12 and CTX-C13 conjugates following photoimmunotherapy (PIT).
- [00032] Figure 5A depicts the dose response curves of percent cell death following PIT for an antibody conjugate.
- [00033] Figure 5B depicts the dose response curves of percent cell death following PIT for a Fab conjugate.
- [00034] Figure 5C depicts the dose response curves of percent cell death following PIT for a VHH/nanobody conjugate.
- [00035] Figure 6 depicts the response to treatment of tumors over time for CTX- C13 and CTX-C13 with illumination (CTX-C13 + PIT) as described in Example 8.
- [00036] Figure 7 depicts the response to treatment of tumors over time for anti-EphA2-C13 conjugates and anti-EphA2-C13 conjugates with illumination as described in Example 9.

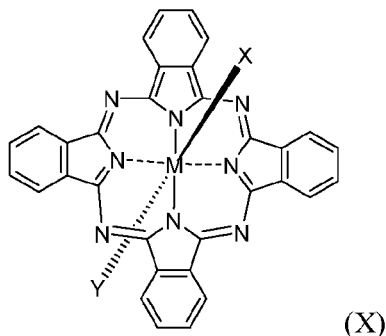
DETAILED DESCRIPTION OF THE INVENTION

A. PHTHALOCYANINE DYE COMPOUNDS

- [00037] Phthalocyanines are a group of photosensitizer compounds having the phthalocyanine ring system. Phthalocyanines are azaporphyrins that contain four benzoindole groups connected by nitrogen bridges in a 16-membered ring of alternating carbon and nitrogen atoms (i.e., $C_{32}H_{18}N_8$) which form stable chelates with a metal or metalloid cation. In these compounds, the ring center is occupied by a metal ion (either a diamagnetic or a paramagnetic ion) that may, depending on the ion, carry zero, one or two ligands. In addition, the ring periphery may be either unsubstituted or substituted.
- [00038] In some embodiments, phthalocyanines strongly absorb red or near IR radiation with absorption peaks falling between about 600 nm and 810 nm, which, in some cases, allow deep penetration of tissue by the light. Phthalocyanines are generally photostable. This photostability is typically advantageous in pigments and dyes and in many of the other applications of phthalocyanines.
- [00039] In some embodiments, the phthalocyanine dye is water soluble and contains a luminescent fluorophore moiety having at least one aqueous-solubilizing moiety. In some embodiments, the aqueous solubilizing moiety contains silicon. In some embodiments, the

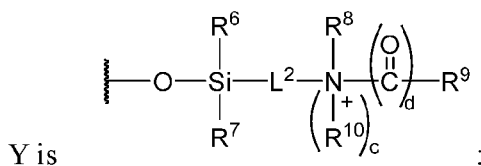
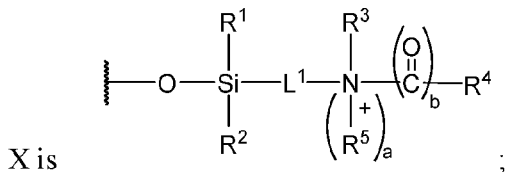
phthalocyanine dye has a core atom such as Si, Ge, Sn, Al, or Zn. In some embodiments, the phthalocyanine dye contains a linker that has a reactive group, which is able to form a bond between the linker and another molecule, i.e., to form a conjugate. In some embodiments, the phthalocyanine dye can be tailored to fluoresce at a particular wavelength.

[00040] In some embodiments, the phthalocyanine dye contains a linker, i.e., is a linker-phthalocyanine dye moiety (L-D). In some embodiments, the linker contains a reactive group. In one aspect, provided herein are phthalocyanine dye compounds having the Formula (X):



or a salt, stereoisomer, or tautomer thereof, wherein:

M is a metal or metalloid;



R¹ and R² are each independently optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, or optionally substituted heteroaralkyl;

R³, R⁴ or R⁵ are selected from substituent group (a) or substituent group (b) wherein,

(a) R³ is hydrogen, -L³-H, -L³-A, or -L³-Z;

R⁴ is -L⁴-H, -(NH)_m-L⁴-A, -(NH)_m-L⁴-Z, -(O)_m-L⁴-A or -(O)_m-L⁴-Z;

R⁵ is -L⁵-H or -L⁵-A; and

(b) R³ is -L³-H, or -L³-A;

R⁴ is -L⁴-H, -(NH)_m-L⁴-A, or -(O)_m-L⁴-A; wherein R³ and R⁴ are connected with a bond to form a heterocyclyl substituted with -L⁴-A; and

R^5 is $-L^5-H$ or $-L^5-A$;

provided at least one of R^3 , R^4 and R^5 is a group containing A;

A is a reactive group capable of forming a covalent bond with a thiol, hydroxyl, carboxyl or amino group of a second moiety, or a protected form thereof or a reacted form thereof;

R^6 and R^7 are each independently optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl or optionally substituted heteroaralkyl;

R^8 , R^9 or R^{10} are selected from substituent group (a) or substituent group (b) wherein,

(a) R^8 is hydrogen, $-L^8-H$ or $-L^8-Z$;

R^9 is $-L^9-H$, $-(NH)_n-L^9-Z$ or $-(O)_n-L^9-Z$;

R^{10} is $-L^{10}-Z$; and

(b) R^8 and R^9 are connected with a bond to form a heterocyclyl substituted with $-L^9-Z$ and R^{10} is $-L^{10}-H$ or $-L^{10}-Z$;

provided at least one of R^8 , R^9 and R^{10} is a group containing Z;

Z is a water soluble group optionally substituted with A or $L'-A$;

L^1 and L^2 are each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkyl, or optionally substituted heterocyclyl;

L^3 , L^4 , L^5 , L^8 , L^9 and L^{10} are each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkylene, optionally substituted heterocyclene, optionally substituted arylene, optionally substituted aralkylene, optionally substituted heteroaralkylene, or optionally substituted heteroarylene, where the carbon atom of the alkylene, heteroalkylene, alkenylene, heteroalkenylene, cycloalkylene, heterocyclene, arylene, aralkylene, heteroaralkylene, or optionally substituted heteroarylene is further optionally substituted with Z and each nitrogen atom of the heteroalkylene or heteroalkenylene is optionally substituted with one or two $L'-Z$;

L' is each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkylene, optionally substituted heterocyclene, optionally substituted arylene, optionally substituted aralkylene, optionally substituted heteroaralkylene, or optionally substituted heteroarylene;

a is 0 or 1;

b is 0 or 1;

c is 0 or 1;

d is 0 or 1;

m is 0 or 1;

n is 0 or 1;

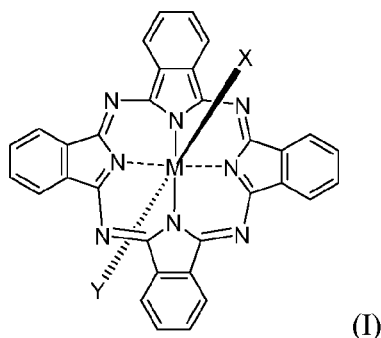
provided that if b is 1, then a is 0;

if d is 1, then c is 0;

if m is 1, b is 1; and

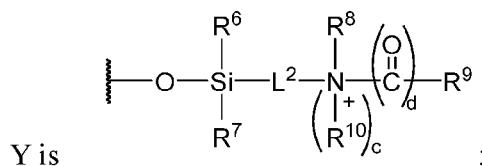
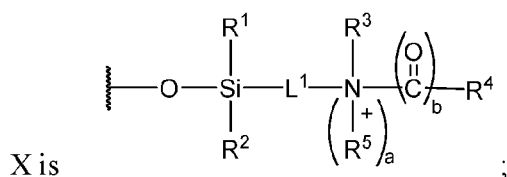
if n is 1, c is 1.

[00041] In some embodiments, the phthalocyanine dye contains a linker, i.e., is a linker-phthalocyanine dye moiety (L-D). In some embodiments, the linker contains a reactive group. In some embodiments the phthalocyanine dye is of Formula (I):



or a salt, stereoisomer, or tautomer thereof, wherein,

M is a metal or metalloid;



R¹ and R² are each independently optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, or optionally substituted heteroaralkyl;

R³, R⁴ or R⁵ are selected from substituent group (a) or substituent group (b) wherein,

(a) R^3 is hydrogen, $-L^3-H$, $-L^3-A$, or $-L^3-Z$;

R^4 is $-L^4-H$, $-(NH)_m-L^4-A$, $-(NH)_m-L^4-Z$, $-(O)_m-L^4-A$ or $-(O)_m-L^4-Z$;

R^5 is $-L^5-H$ or $-L^5-A$; and

(b) R^3 is $-L^3-H$, or $-L^3-A$;

R^4 is $-L^4-H$, $-(NH)_m-L^4-A$, or $-(O)_m-L^4-A$; wherein R^3 and R^4 are connected with a bond to form a heterocyclyl substituted with $-L^4-A$; and

R^5 is $-L^5-H$ or $-L^5-A$;

provided at least one of R^3 , R^4 and R^5 is a group containing A;

A is a reactive group capable of forming a covalent bond with a thiol, hydroxyl, carboxyl or amino group of a second moiety, or a protected form thereof or a reacted form thereof;

R^6 and R^7 are each independently optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl or optionally substituted heteroaralkyl;

R^8 , R^9 or R^{10} are selected from substituent group (a) or substituent group (b) wherein,

(a) R^8 is hydrogen, $-L^8-H$ or $-L^8-Z$;

R^9 is $-L^9-H$, $-(NH)_n-L^9-Z$ or $-(O)_n-L^9-Z$;

R^{10} is $-L^{10}-Z$; and

(b) R^8 and R^9 are connected with a bond to form a heterocyclyl substituted with $-L^9-Z$ and R^{10} is $-L^{10}-H$ or $-L^{10}-Z$;

provided at least one of R^8 , R^9 and R^{10} is a group containing Z;

Z is a water soluble group optionally substituted with A or $L'-A$;

L^1 and L^2 are each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkyl, or optionally substituted heterocyclyl;

L^3 , L^4 , L^5 , L^8 , L^9 and L^{10} are each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkylene, optionally substituted heterocyclene, optionally substituted arylene, optionally substituted aralkylene, optionally substituted heteroaralkylene, or optionally substituted heteroarylene, where the carbon atom of the alkylene, heteroalkylene, alkenylene, heteroalkenylene, cycloalkylene, heterocyclene, arylene, aralkylene, heteroaralkylene, or optionally substituted heteroarylene is further optionally substituted with Z and each nitrogen atom of the heteroalkylene or heteroalkenylene is optionally substituted with one or two $L'-Z$;

L' is each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkylene, optionally substituted heterocyclene, optionally substituted arylene, optionally substituted aralkylene, optionally substituted heteroaralkylene, or optionally substituted heteroarylene;

a is 0 or 1;

b is 0 or 1;

c is 0 or 1;

d is 0 or 1;

m is 0 or 1;

n is 0 or 1;

provided that if b is 1, then a is 0;

if d is 1, then c is 0;

if m is 1, b is 1; and

if n is 1, c is 1; and

provided that when R⁶ and R⁷ are both methyl, and L² is propylene, c is 1 and d is 0, then L⁸, L⁹ and L¹⁰ are each not propylene.

[00042] In certain embodiments, provided herein are compounds of Formula (I) with the proviso that when R⁶ and R⁷ are both methyl, and L² is propylene, c is 1 and d is 0; then L⁸, L⁹ and L¹⁰ are each not propylene.

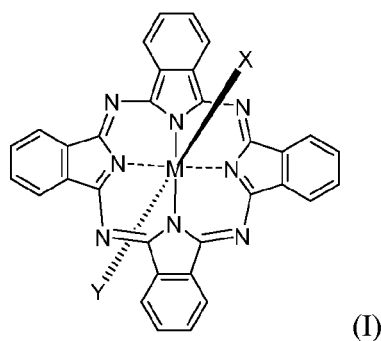
[00043] In certain embodiments, provided herein are compounds of Formula (I) with the proviso that when R⁶ and R⁷ are both methyl, and L² is propylene, then c is 0 and d is 1.

[00044] In certain embodiments, provided herein are compounds of Formula (I) with the proviso that when R⁶ and R⁷ are both methyl, L² is propylene, c is 1 and d is 0 and L⁸, L⁹ and L¹⁰ are each propylene, then Z is not -SO₃⁻.

[00045] In certain embodiments, the alkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl of R¹, R², R⁶ and R⁷ is optionally substituted with halo, haloalkyl, hydroxyl, alkoxy, haloalkoxy, amino or cyano.

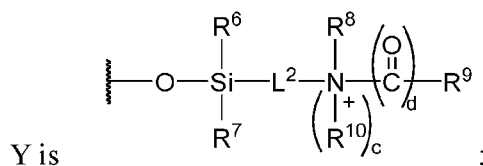
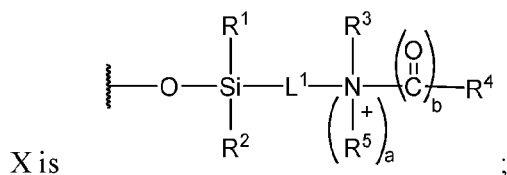
[00046] In certain embodiments, a carbon atom of the alkylene, heteroalkylene, alkenylene or heteroalkenylene of L¹ and L² is each independently and optionally substituted with halo, oxo, haloalkyl, hydroxyl, alkoxy, haloalkoxy, amino or cyano.

[00047] In certain embodiments, provided herein are compounds of Formula (I):



wherein,

M is a metal or metalloid;



R¹ and R² are each independently optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl or optionally substituted heteroaralkyl;

R³, R⁴ or R⁵ are selected from (a) and (b) wherein,

(a) R³ is hydrogen, -L³-H, -L³-A, or -L³-Z;

R⁴ is -L⁴-H, -(NH)_m-L⁴-A, -(NH)_m-L⁴-Z, -(O)_m-L⁴-A or -(O)_m-L⁴-Z;

R⁵ is -L⁵-H or -L⁵-A; and

(b) R³ and R⁴ are connected with a bond to form a heterocyclyl substituted with -L⁴-A and

R⁵ is -L⁵-H or -L⁵-A;

provided at least one of R³, R⁴ and R⁵ is a group containing A;

A is a reactive group capable of forming a covalent bond with a second moiety, or a protected form thereof or a reacted form thereof;

R⁶ and R⁷ are each methyl;

R⁸ is -L⁸-Z;

R⁹ is -L⁹-Z;

R¹⁰ is -L¹⁰-Z; and

Z is a water soluble group optionally substituted with A, or L'-A;

L^1 is selected from optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, or optionally substituted heteroalkenylene;

L^2 is propylene;

L^3 , L^4 , L^5 are each independently selected from optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkylene, optionally substituted heterocyclene, optionally substituted arylene, or optionally substituted heteroarylene where the carbon atom of the alkylene, heteroalkylene, alkenylene, heteroalkenylene, cycloalkylene, heterocyclene or arylene is optionally substituted with a Z, and each nitrogen atom of the heteroalkylene or heteroalkenylene is optionally substituted with one or two L' -Z;

L' is each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkylene, optionally substituted heterocyclene, optionally substituted arylene, or optionally substituted heteroarylene;

L^8 , L^9 and L^{10} are each propylene; a is 0 or 1; b is 0 or 1; c is 0 or 1; d is 0 or 1;

m is 0 or 1; n is 0 or 1;

provided that if b is 1, then a is 0;

if d is 1, then c is 0;

if m is 1, then b is 1; and

if n is 1, then c is 1.

[00048] In certain embodiments, a carbon atom of the alkylene, heteroalkylene, alkenylene, heteroalkenylene, cycloalkylene, heterocyclene or arylene of L^3 , L^4 , L^5 , L^8 , L^9 and L^{10} is optionally substituted with halo, oxo, haloalkyl, hydroxyl, alkoxy, haloalkoxy, amino, cyano or Z and a nitrogen atom of the heteroalkylene or heteroalkenylene is optionally substituted with one or two L' -Z; L' is each independently alkylene, heteroalkylene, alkenylene, heteroalkenylene, cycloalkylene, heterocyclene, arylene or heteroarylene where a carbon atom of the alkylene, heteroalkylene, alkenylene, heteroalkenylene, cycloalkylene, heterocyclene, arylene or heteroarylene is optionally substituted with halo, oxo, haloalkyl, hydroxyl, alkoxy, haloalkoxy, amino or cyano.

[00049] In certain embodiments, L^3 , L^4 , L^5 , L^8 , L^9 and L^{10} are each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene or optionally substituted heteroalkenylene, where each nitrogen atom of the heteroalkylene or heteroalkenylene is further optionally substituted with one or two L' -Z and L' is

independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene or optionally substituted heteroalkenylene.

[00050] In certain embodiments, L^1 and L^2 , are each independently optionally substituted C_{1-10} alkylene, optionally substituted hetero C_{1-10} alkylene, optionally substituted C_{2-10} alkenylene or hetero C_{2-10} alkenylene. In yet certain embodiments, L^1 and L^2 , are each independently C_{2-4} alkylene, hetero C_{2-4} alkylene, optionally substituted C_{2-4} alkenylene or optionally substituted hetero C_{2-4} alkenylene. In yet certain embodiments, L^1 and L^2 are each optionally substituted C_{2-4} alkylene.

[00051] In certain embodiments, the reactive group A is each independently $-C(O)OR^{11}$, $-NR^{12}R^{13}$, $-NHC(O)R^{14}$, $-C(O)R^{15}$, $-OR^{16}$, $-SR^{16}$, $-OS(O)_2R^{17}$, $-OP(OR^{18})(NR^{19}R^{20})$, $-N=C=O$; $-N=C=S$, $-S-C\equiv N$, $-SO_2-F$, $-SO_2-Cl$, $-SO_2-Br$, $-S-SR^{21}$ or 5- or 6- membered dioxo-substituted heterocyclyl;

each R^{11} is independently hydrogen, alkyl, haloalkyl, alkenyl, heterocyclyl, aryl or heteroaryl, where the heterocyclyl, aryl or heteroaryl is optionally substituted with one to five groups each independently selected from halo, $-SO_3^-$ and $-SO_2F$;

each R^{12} is independently hydrogen or alkyl or haloalkyl;

each R^{13} is independently aryl or heteroaryl where the aryl or heteroaryl is optionally substituted with one to five groups each independently selected from halo, $-SO_3^-$ and $-SO_2F$; or optionally, R^{12} and R^{13} , together with the nitrogen to which they are attached, form a cyclic imide;

each R^{14} is independently haloalkyl;

each R^{15} is independently aryl optionally substituted with one to five groups each independently halo, heterocyclyl, $-SO_3^-$ or $-SO_2F$;

each R^{16} is independently aryl optionally substituted with one to five groups each independently halo or heterocyclyl;

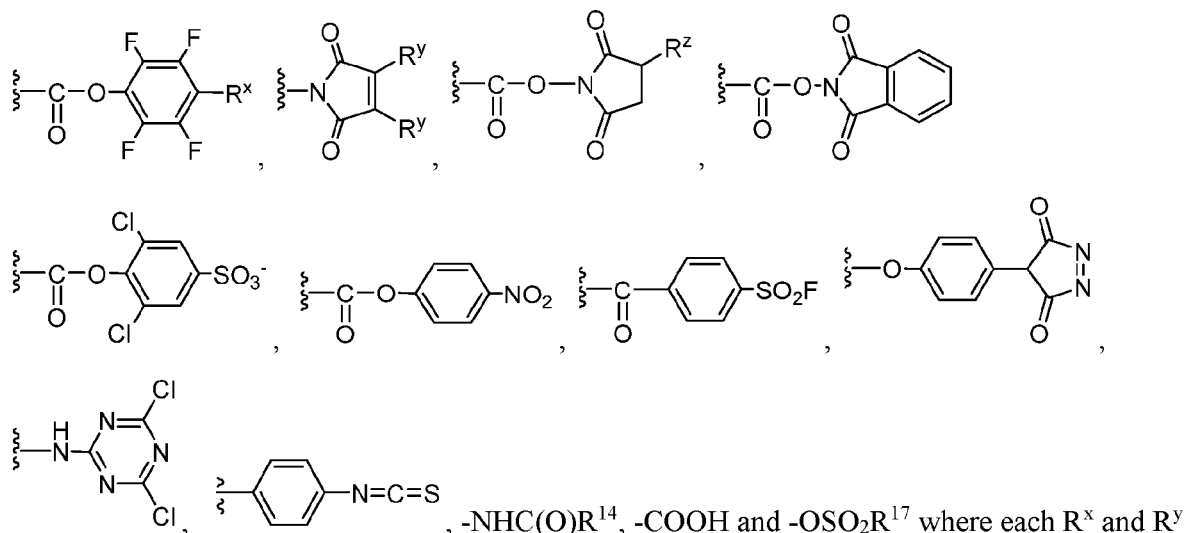
each R^{17} is independently optionally substituted alkyl, optionally substituted haloalkyl, optionally substituted alkenyl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, optionally substituted aryl or optionally substituted heteroaryl, wherein the heterocyclyl, aryl or heteroaryl is optionally substituted with one to five groups each independently selected from halo, $-SO_3^-$, $-SO_2F$ and $-C(O)OR^c$;

each R^c is independently optionally substituted alkyl, optionally substituted haloalkyl, optionally substituted cycloalkyl or optionally substituted aryl;

R^{18} , R^{19} and R^{20} are each independently optionally substituted alkyl or optionally substituted haloalkyl; and

R^{21} is a heteroaryl.

[00052] In certain embodiments, the reactive group A is selected from the group consisting of:



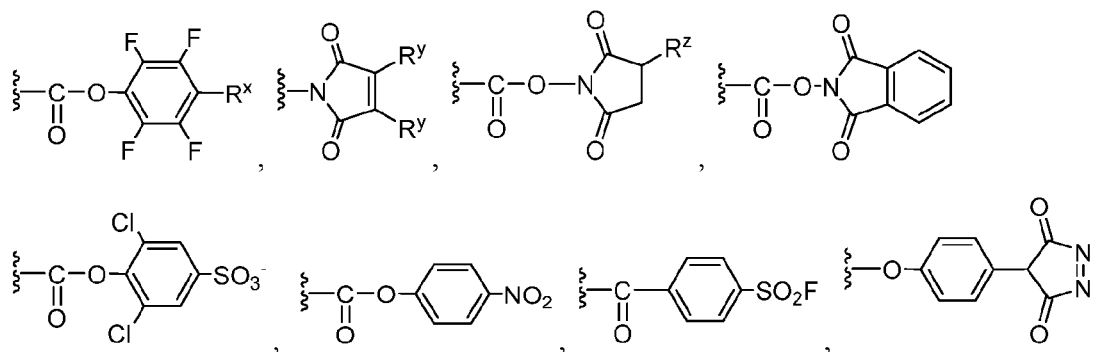
are independently hydrogen or halo, and R^Z is hydrogen or $-\text{SO}_3^-$;

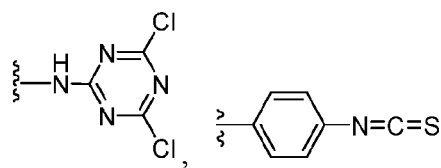
R^{14} is optionally substituted haloalkyl or optionally substituted aralkyl; and

R^{17} is each R^{17} is independently optionally substituted alkyl, optionally substituted haloalkyl, optionally substituted alkenyl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, optionally substituted aryl or optionally substituted heteroaryl, wherein the heterocyclyl, aryl or heteroaryl is optionally substituted with one to five groups each independently selected from halo, $-\text{SO}_3^-$, $-\text{SO}_2\text{F}$ and $-\text{C}(\text{O})\text{OR}^c$; and

each R^c is independently optionally substituted alkyl, optionally substituted haloalkyl, optionally substituted cycloalkyl or optionally substituted aryl.

[00053] In yet certain embodiments, the reactive group A or the conjugatable group A' is selected from the group consisting of:



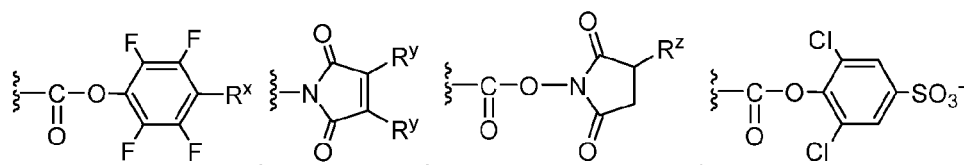
, -NHC(O)R¹⁴, and -OSO₂R¹⁷ where each R^x and R^y are independently hydrogen or halo, and R^z is hydrogen or -SO₃⁻;

each R¹⁴ is independently haloalkyl or alkyl substituted aralkyl; and

each R¹⁷ is independently optionally substituted alkyl, optionally substituted haloalkyl, optionally substituted alkenyl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, optionally substituted aryl or optionally substituted heteroaryl, wherein the heterocyclyl, aryl or heteroaryl is optionally substituted with one to five groups each independently selected from halo, -SO₃⁻, -SO₂F and -C(O)OR^c; and

each R^c is independently optionally substituted alkyl, optionally substituted haloalkyl, optionally substituted cycloalkyl or optionally substituted aryl.

[00054] In yet certain embodiments, the reactive group A is

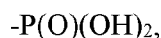
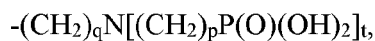
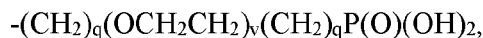
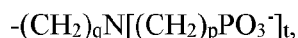
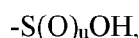
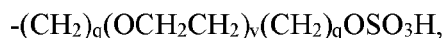
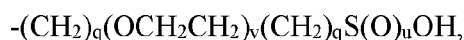
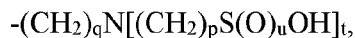
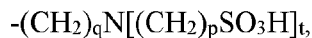
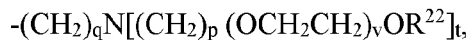
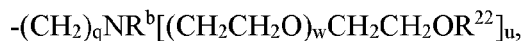
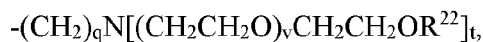
, or COOH where each R^x and R^y are independently hydrogen or halo, and R^z is hydrogen or -SO₃⁻.

[00055] In certain embodiments, reactive group is each independently -C(O)OR¹¹ or -NR¹²R¹³; R¹¹ is each independently hydrogen, alkyl, haloalkyl, alkenyl, heterocyclyl, aryl or heteroaryl, wherein the heterocyclyl, aryl or heteroaryl is optionally substituted;

R¹² is each independently hydrogen or alkyl and R¹³ is aryl or heteroaryl optionally substituted with one to five groups each independently selected from halo, -SO₃⁻ and -SO₂F; or R¹² and R¹³, together with the nitrogen to which they are attached, form heterocyclyl;

[00056] In certain embodiments, the water soluble group Z is

-C(O)OH,
 -(CH₂)_q(OCH₂CH₂)_v(CH₂)_qC(O)OH,
 -(CH₂CH₂O)_v(CH₂)_pC(O)OH,
 -(CH₂)_q(OCH₂CH₂)_vOR²²,
 -(CH₂CH₂O)_v(CH₂)_pOR²²,
 -(CH₂)_q(OCH₂CH₂)_vSR²²,
 -(CH₂CH₂O)_v(CH₂)_pSR²²,
 -O(CH₂)_vN[(CH₂CH₂O)_mCH₂CH₂OR²²]_t,
 -(CH₂)_q(OCH₂CH₂)_vN[(CH₂CH₂O)_wCH₂CH₂OR²²]_t,



glutamate, aspartate, histidine, 1,3-beta-glucan or 1,4-beta-glucan;

each R^{22} is independently alkyl, haloalkyl, cycloalkyl or aryl;

each R^b is independently hydrogen, alkyl optionally substituted with $-\text{CO}_2\text{H}$, heteroalkylene optionally substituted with $-\text{CO}_2\text{H}$, haloalkyl or cycloalkyl;

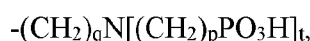
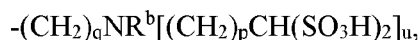
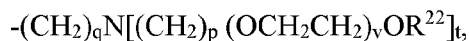
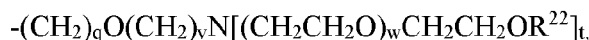
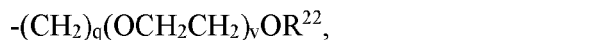
each v , w and p are independently an integer from 1 to 10;

each q is independently an integer from 0 to 10;

t is 2 or 3; and

u is 1 or 2.

[00057] In certain embodiments, the water soluble group Z is selected from



each R^{22} is independently alkyl, haloalkyl, cycloalkyl or aryl;

each R^b is independently hydrogen, alkyl, haloalkyl or cycloalkyl;

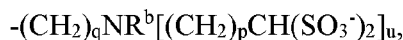
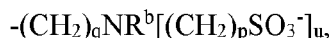
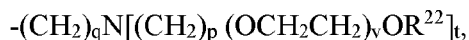
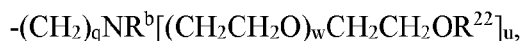
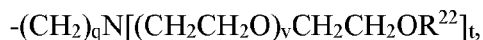
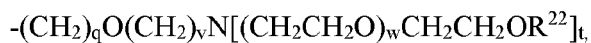
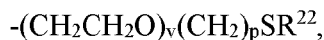
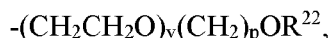
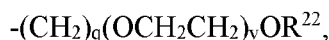
each v, w and p are independently an integer from 1 to 10;

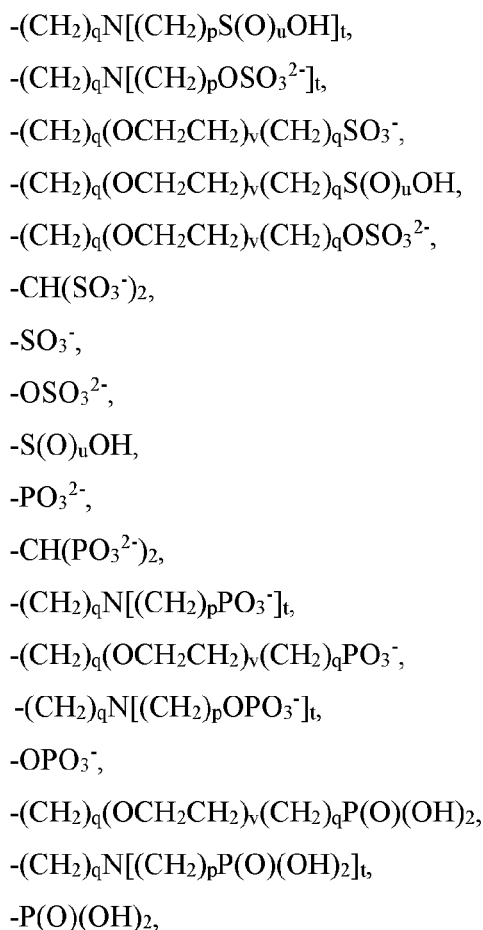
each q is independently an integer from 0 to 10;

t is 2 or 3; and

u is 1 or 2.

[00058] In certain embodiments, the water soluble group Z is





glutamate, aspartate, histidine, 1,3-beta-glucan or 1,4-beta-glucan;

each R^{22} is independently alkyl, haloalkyl, cycloalkyl or aryl;

each R^b is independently hydrogen, alkyl, haloalkyl or cycloalkyl;

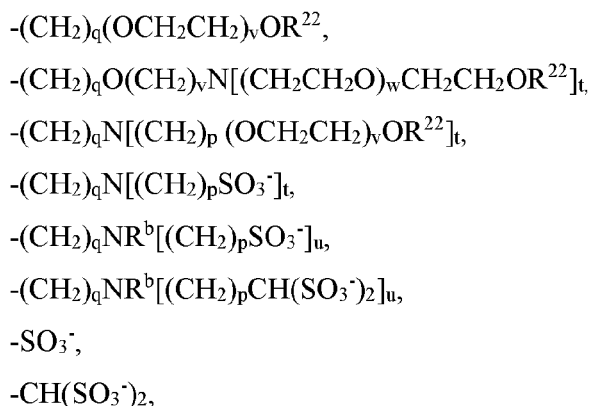
each v , w and p are independently an integer from 1 to 10;

each q is independently an integer from 0 to 10;

t is 2 or 3; and

u is 1 or 2.

[00059] In yet certain embodiments, the water soluble group Z is





each R^{22} is independently alkyl, haloalkyl, cycloalkyl or aryl;

each R^b is independently hydrogen, alkyl, haloalkyl or cycloalkyl;

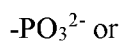
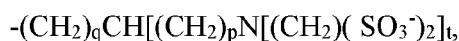
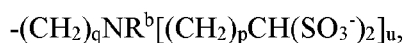
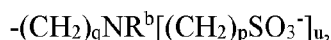
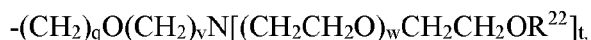
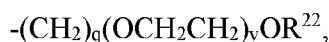
each v , w and p are independently an integer from 1 to 10;

each q is independently an integer from 0 to 10;

t is 2 or 3; and

u is 1 or 2.

[00060] In yet certain embodiments, the water soluble group Z is



each R^{22} is independently alkyl, haloalkyl, cycloalkyl or aryl;

each R^b is independently hydrogen, alkyl, haloalkyl or cycloalkyl;

each v , w and p are independently an integer from 1 to 10;

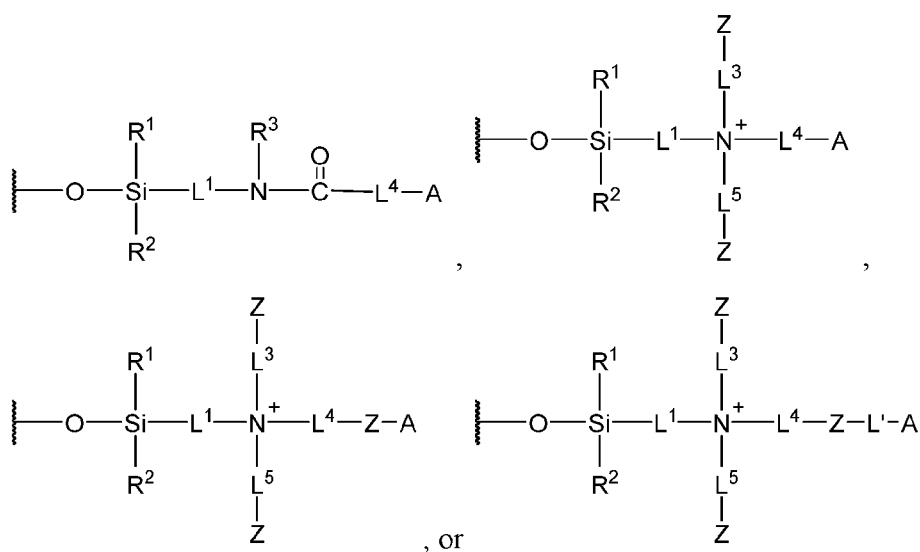
each q is independently an integer from 0 to 10;

t is 2 or 3; and

u is 1 or 2.

[00061] In certain embodiments, a and c are 0 and b and d are 1. In certain embodiments, a and c are 1 and b and d are 0. In yet certain embodiments, c is 0 and d is 1.

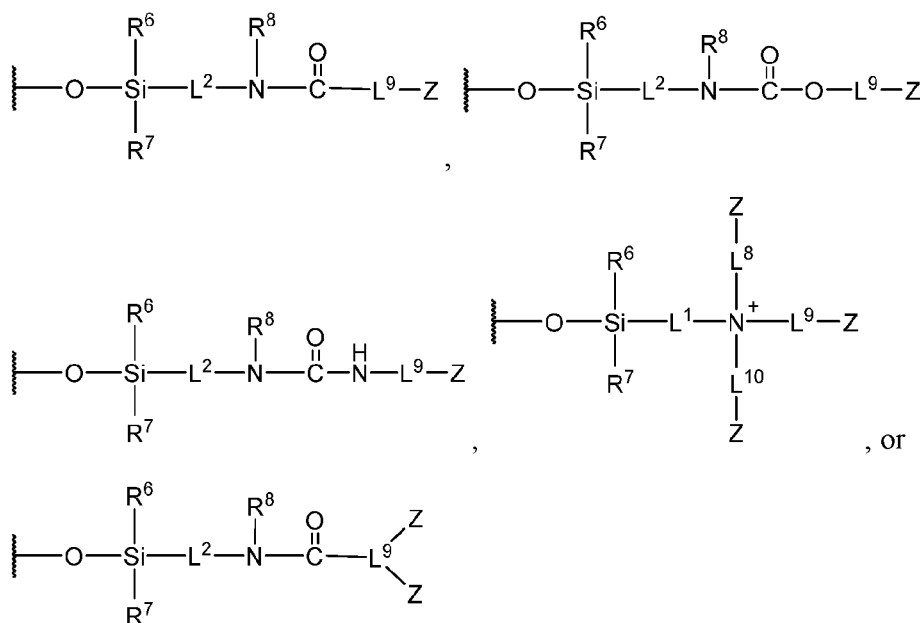
[00062] In certain embodiments, X is:



wherein R^1 , R^2 , R^3 , L^1 , L^3 , L^4 , L^5 , Z and A are as described for Formula (I).

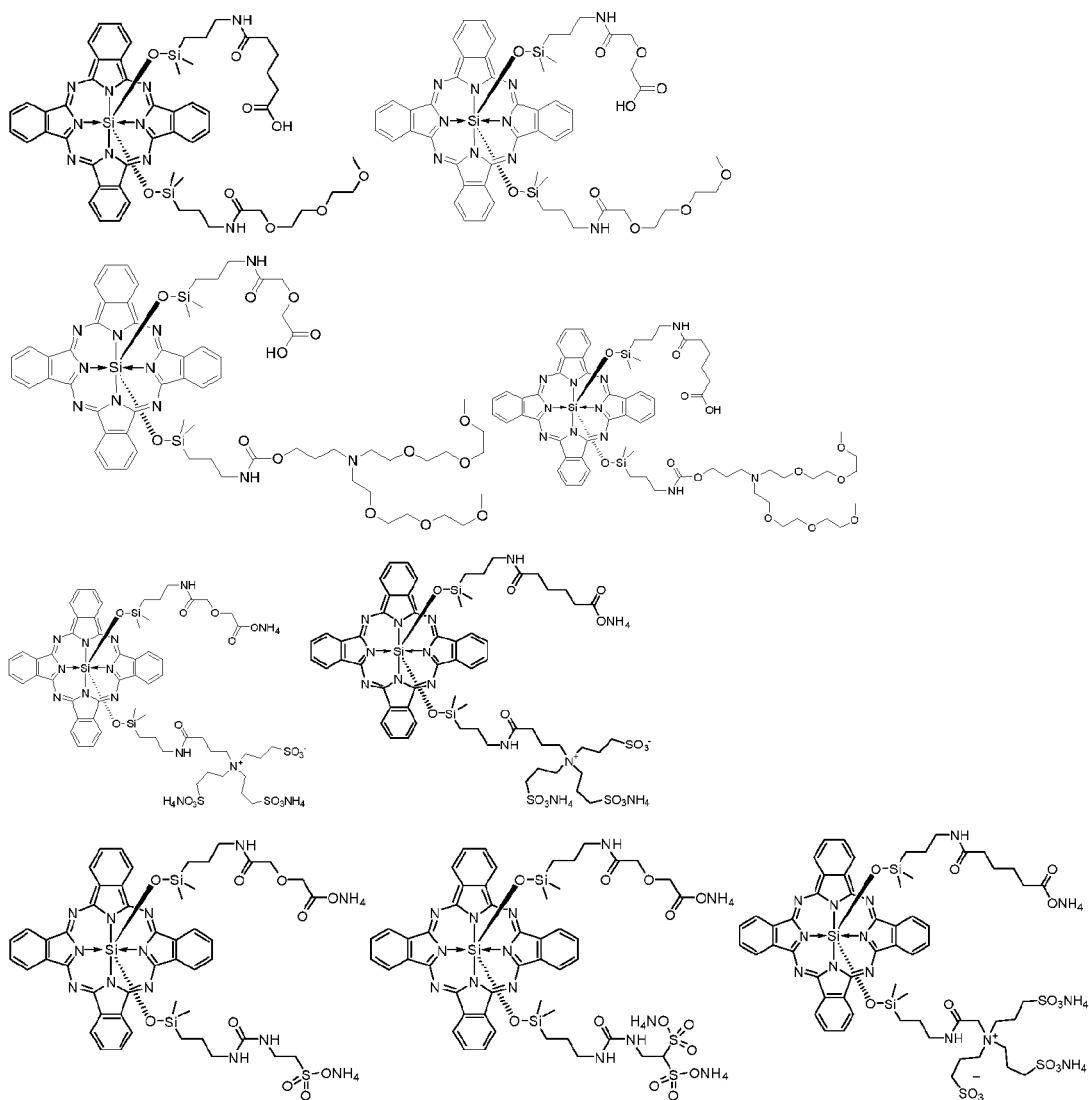
[00063] In certain embodiments, L^4 is optionally substituted alkylene or optionally substituted alkenylene. In certain embodiments, L^4 is optionally substituted alkylene.

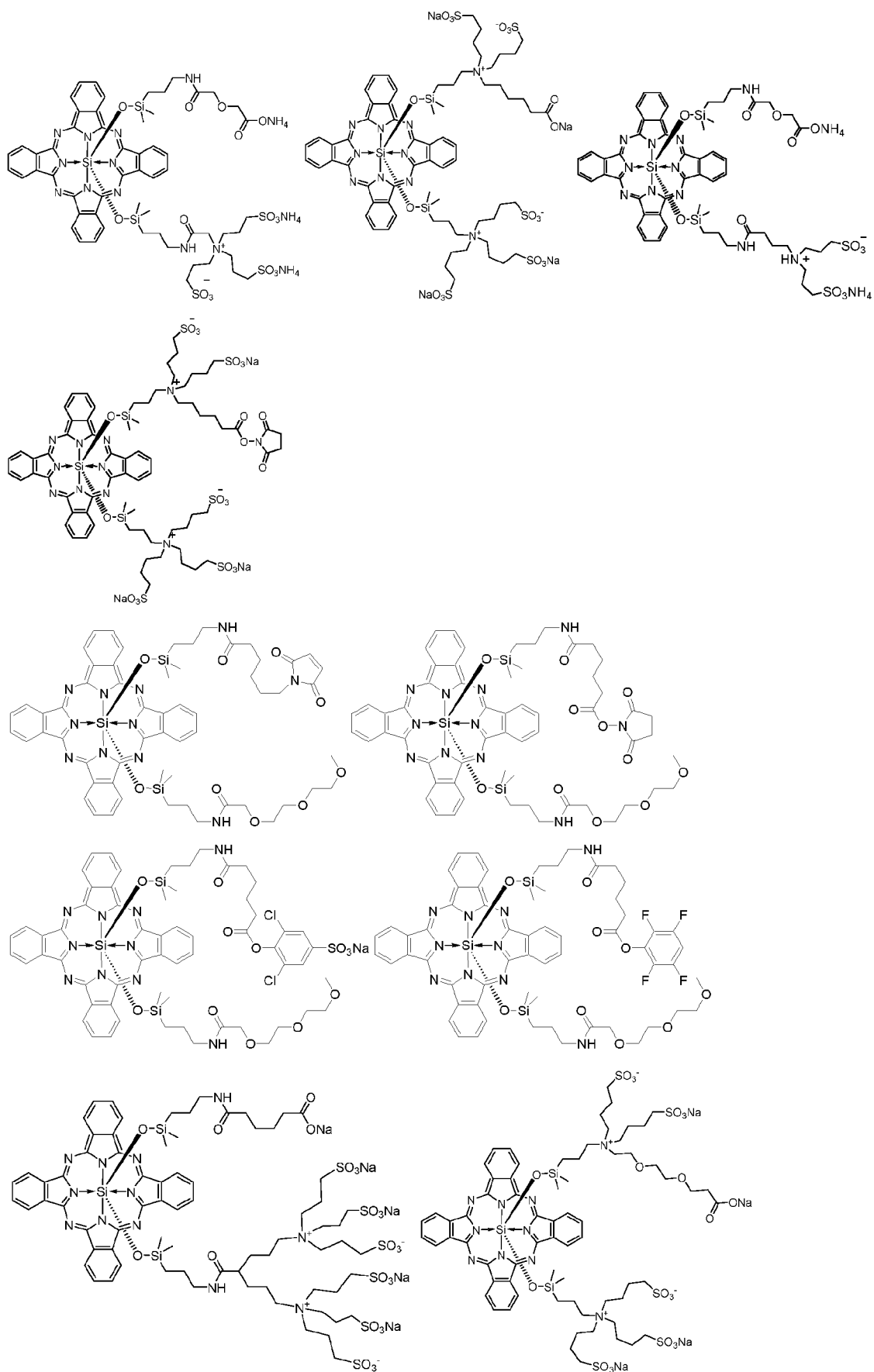
[00064] In certain embodiments, Y is:

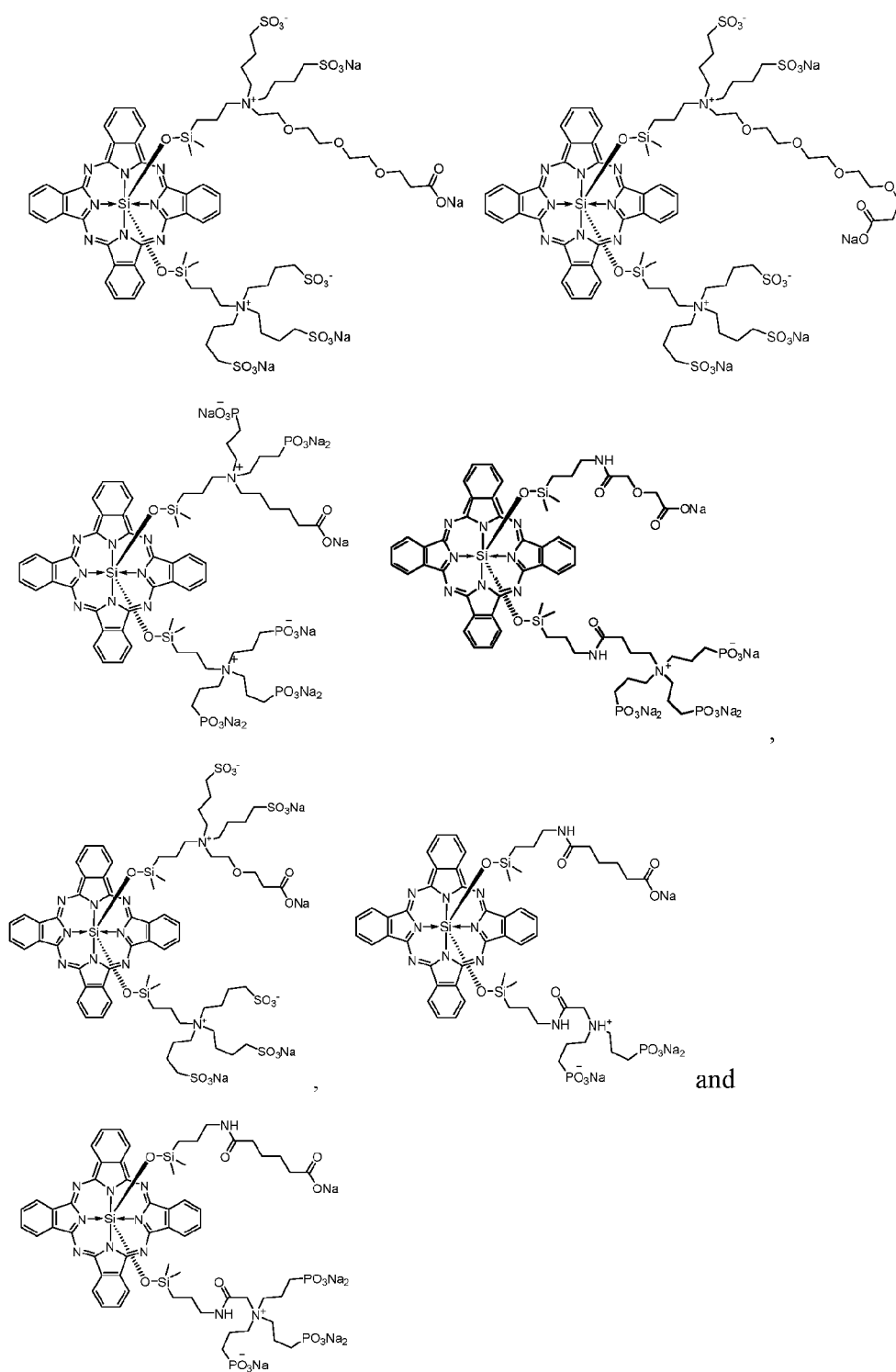


[00065] In certain embodiments, M is Si, Ge, Sn or Al. In yet certain embodiments, M is Si or Ge.

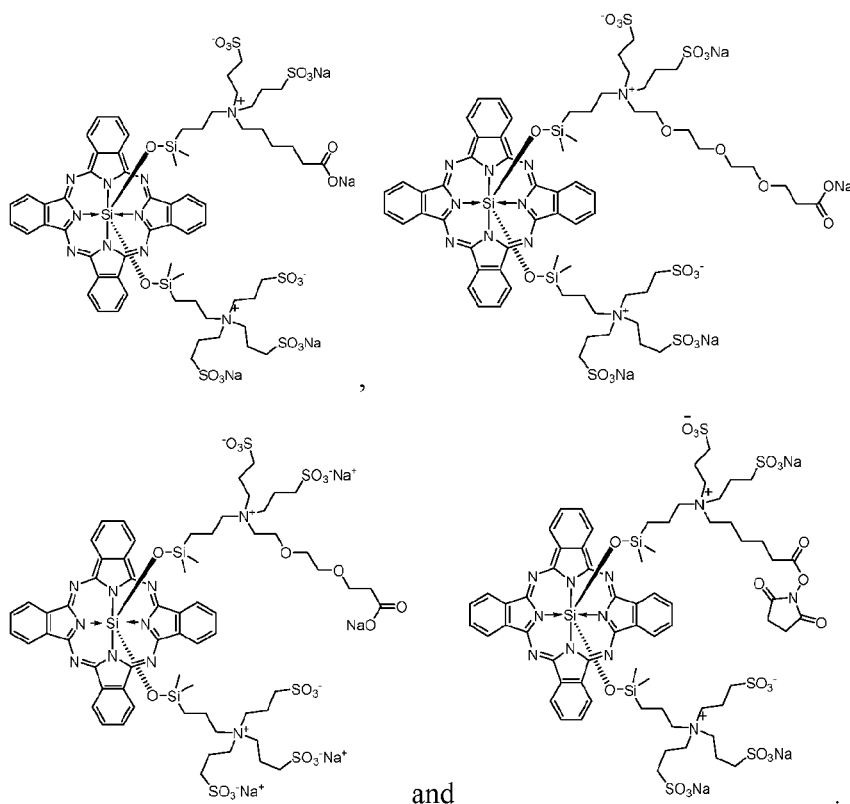
[00066] In certain embodiments, provided herein are compounds of Formula (X) or Formula (I) selected from the group consisting of:







[00067] In yet certain embodiments, the compound of Formula (X) or Formula (I) is selected from the group consisting of:

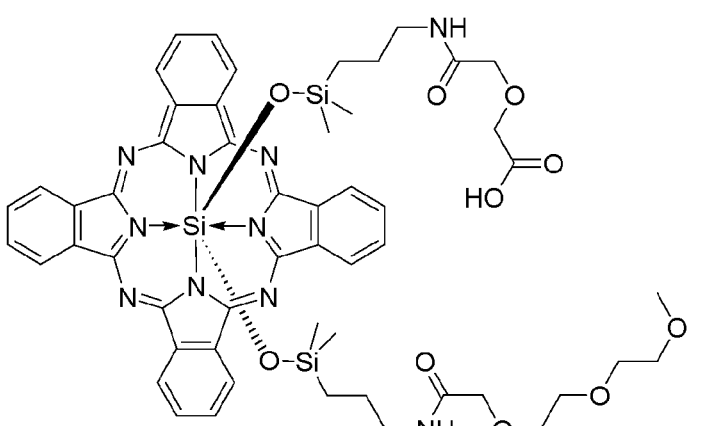
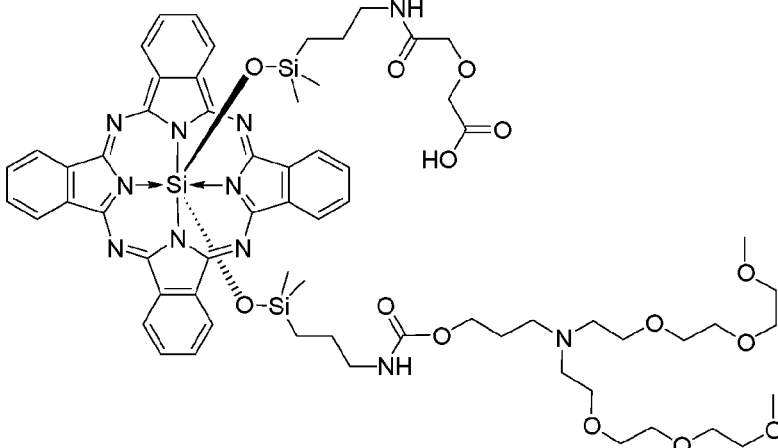


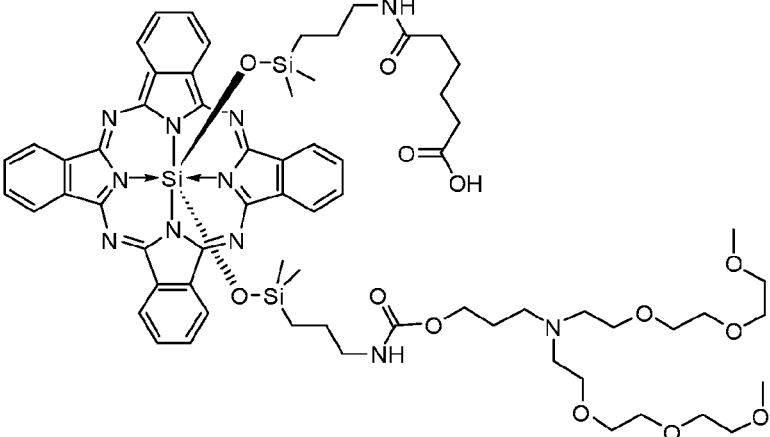
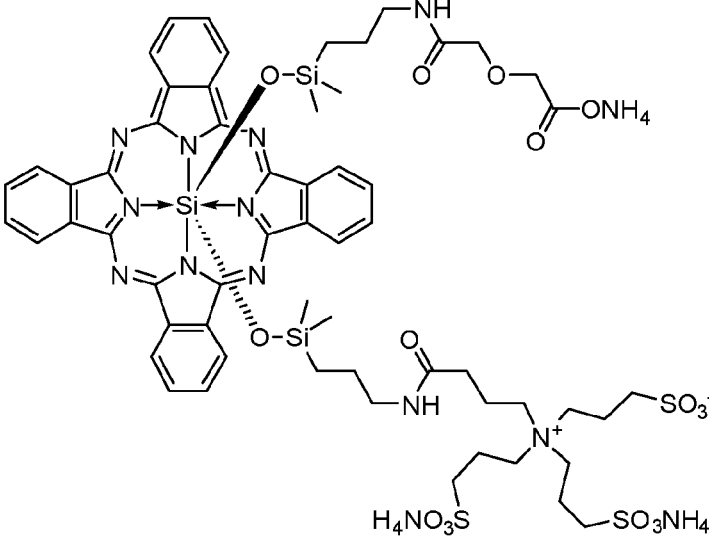
[00068] In certain embodiments, the reactive group is capable of forming a covalent bond

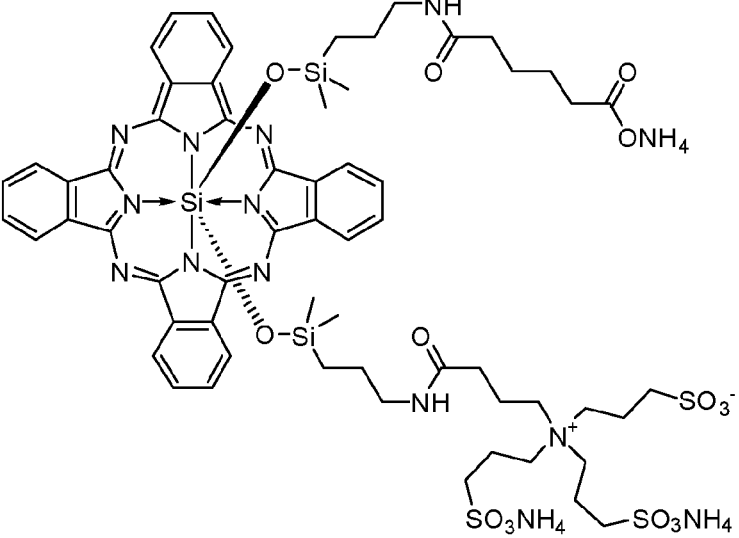
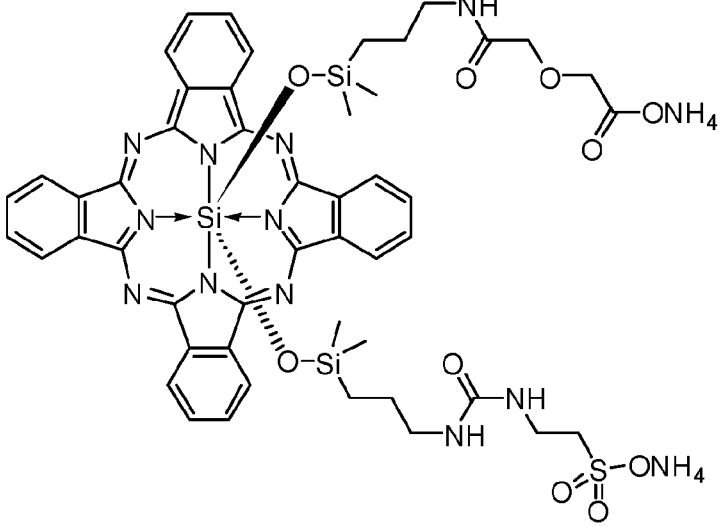
[00069] In certain embodiments, provided herein are compound selected from Table 1.

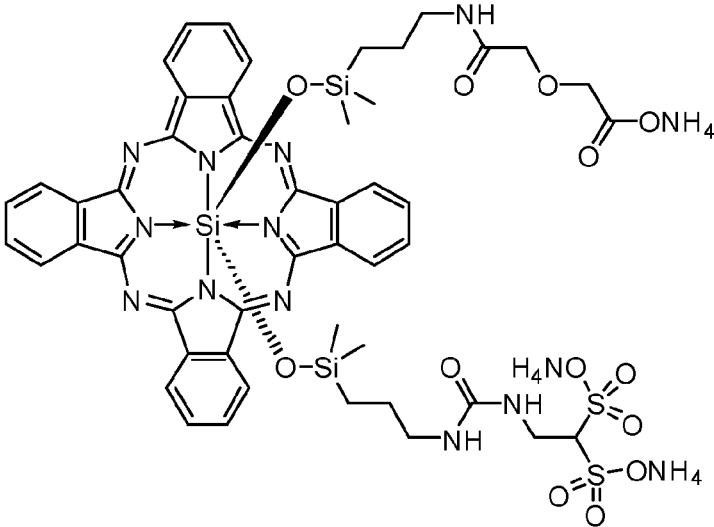
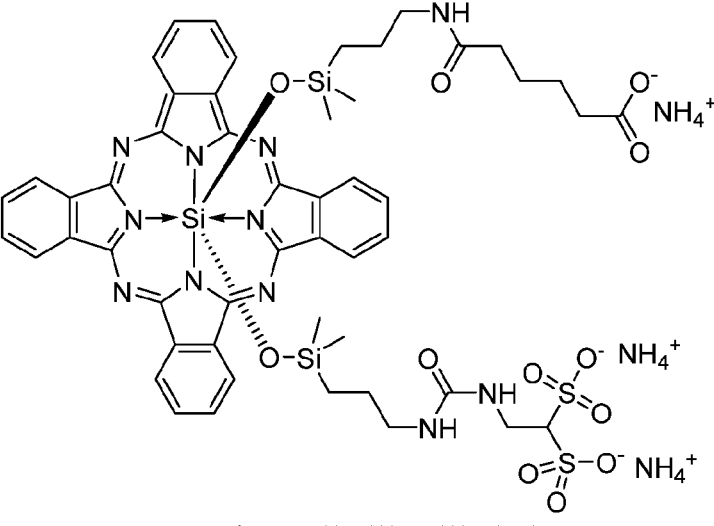
Table 1

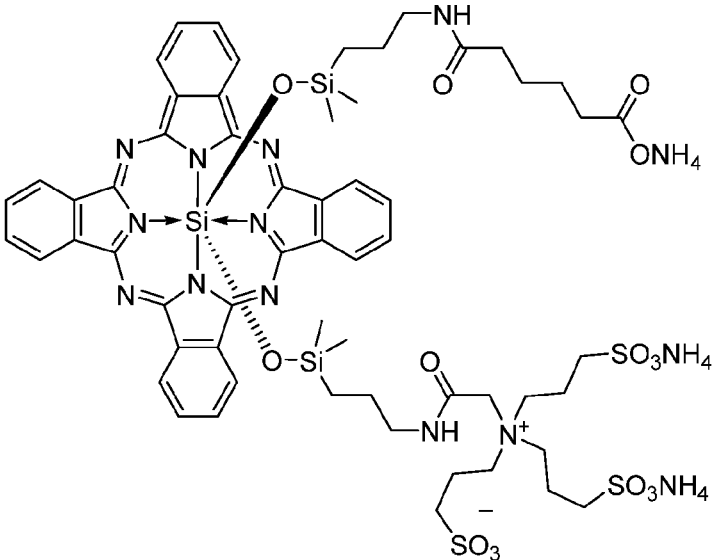
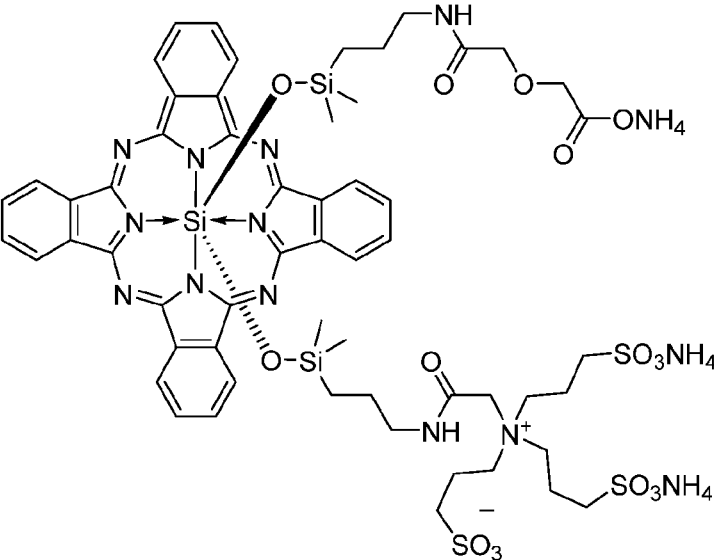
Ex. No.	Structure Name
1	6-((3-(dimethyl((19-((15-methyl-10-oxo-2,5,8-trioxa-11-aza-15-silahexadecan-15-yl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)silyl)propyl)amino)-6-oxohexanoic acid

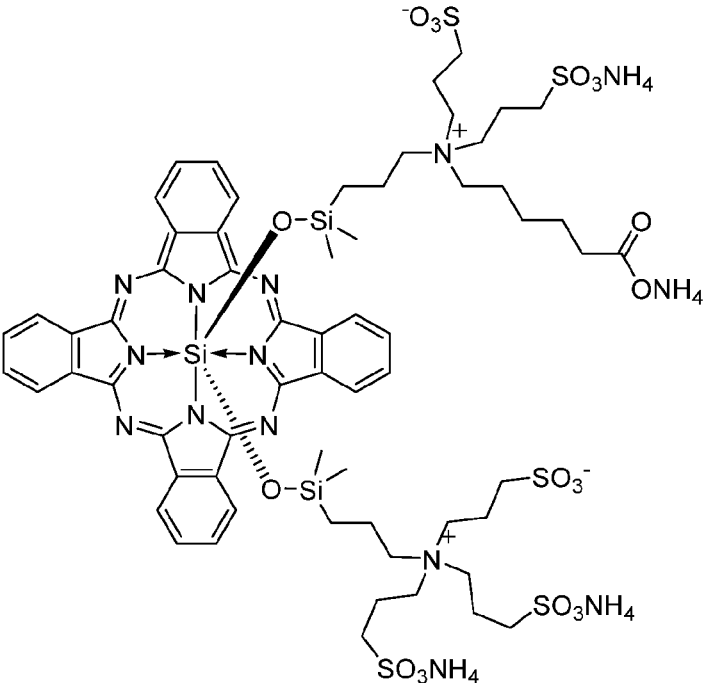
Ex. No.	Structure Name
2	 2-(2-((3-(dimethyl((19-((15-methyl-10-oxo-2,5,8-trioxa-11-aza-15-silahexadecan-15-yl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)silyl)propyl)amino)-2-oxoethoxy)acetic acid
3	 2-(2-((3-(((19-((11-(2-(2-(2-methoxyethoxy)ethoxy)ethyl)-21-methyl-16-oxo-2,5,8,15-tetraoxa-11,17-diaza-21-siladocosan-21-yl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-2-oxoethoxy)acetic acid

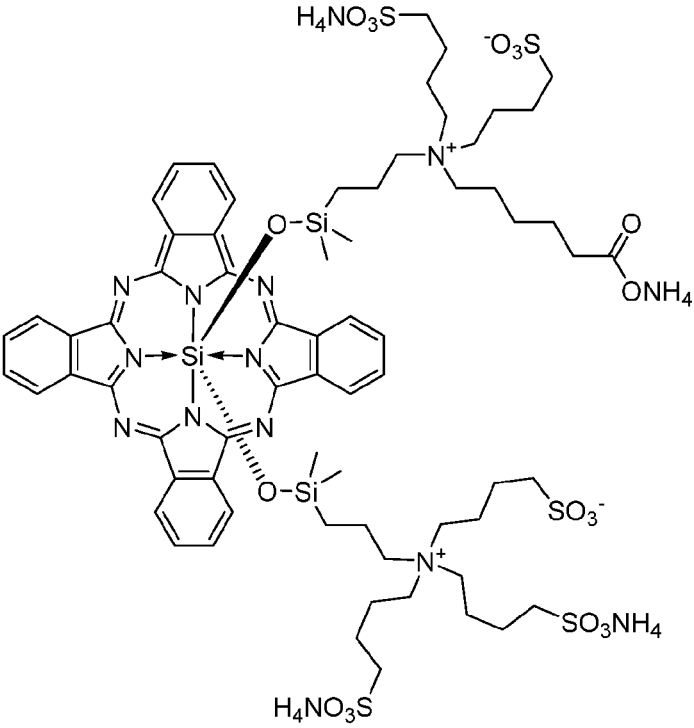
Ex. No.	Structure Name
4	 6-((3-(((19-((11-(2-(2-(2-methoxyethoxy)ethoxy)ethyl)-21-methyl-16-oxo-2,5,8,15-tetraoxa-11,17-diaza-21-siladocosan-21-yl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-6-oxohexanoic acid
5	 Ammonium 3-((4-((3-(((19-((3-(2-(carboxymethoxy)acetamido)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-4-oxobutyl)bis(3-sulfopropyl)ammonio)propane-1-sulfonate

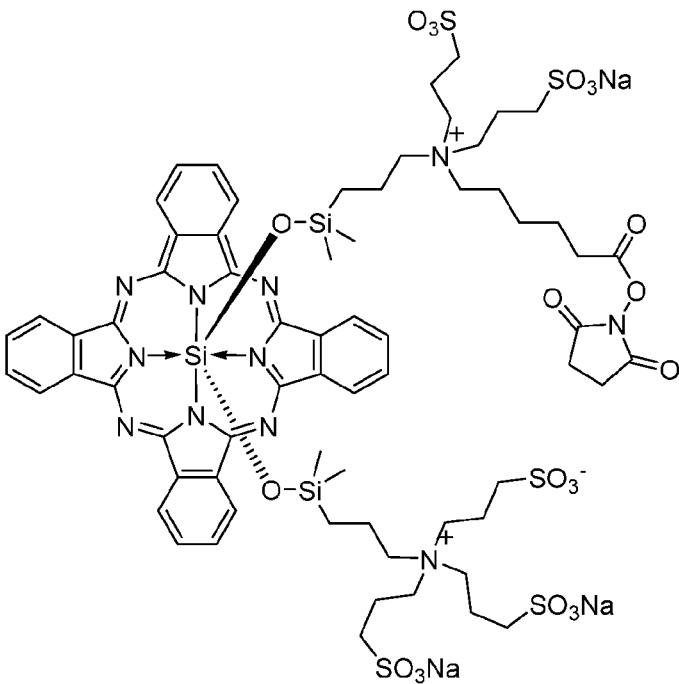
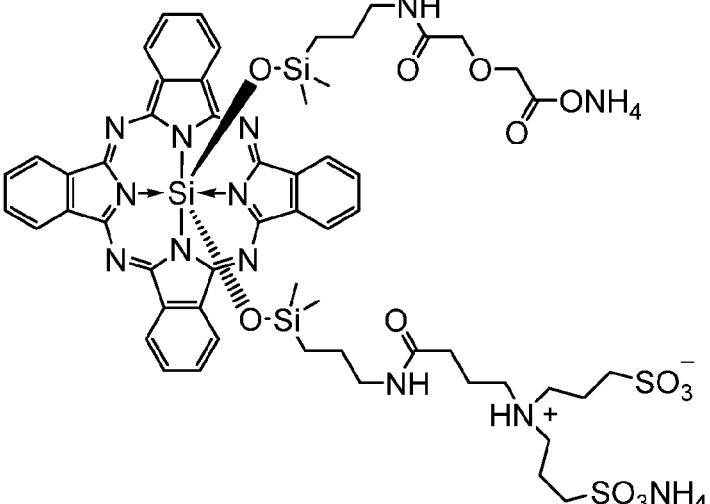
Ex. No.	Structure Name
6	 3-((4-((3-(((19-(((3-(6-((λ⁵-azaneyl)oxy)-6-oxohexanamido)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-4-oxobutyl)bis(3-(((λ⁵-azaneyl)oxy)sulfonyl)propyl)ammonio)propane-1-sulfonate
7	 Ammonium 2-(2-((3-(((19-((dimethyl(3-(3-(2-sulfonatoethyl)ureido)propyl)silyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-2-oxoethoxy)acetate

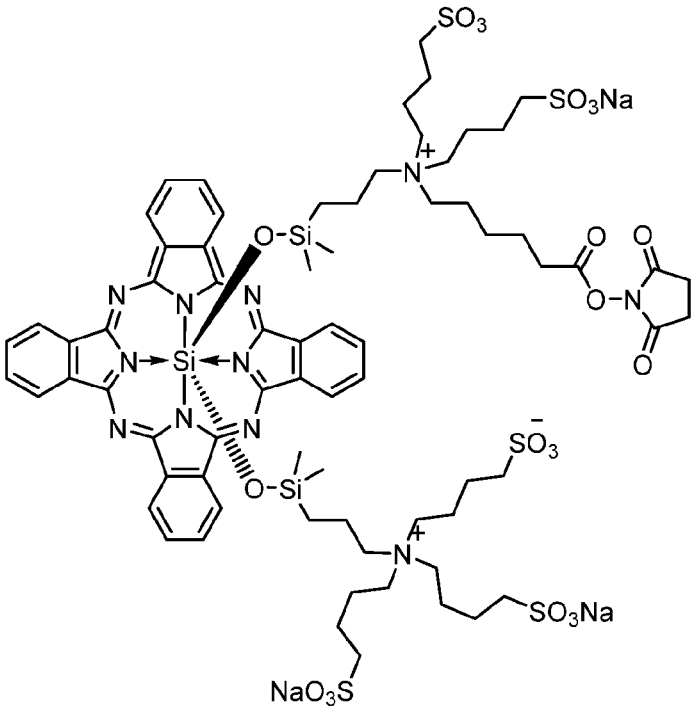
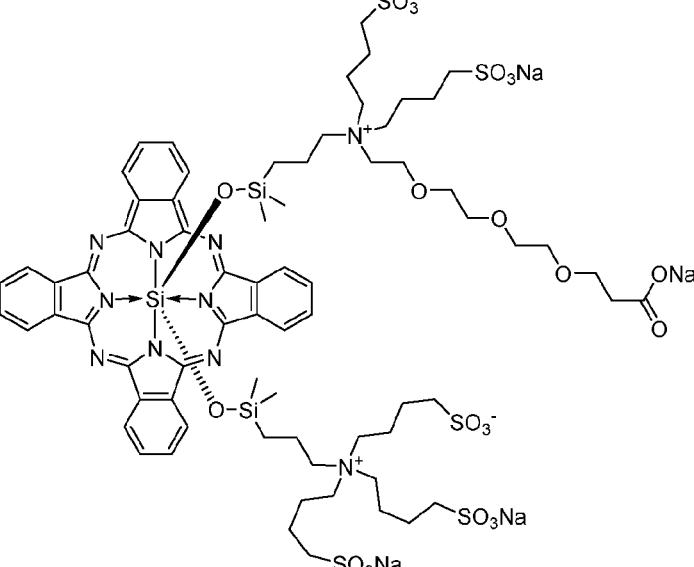
Ex. No.	Structure Name
8	 Ammonium 2-(2-(((3-(((19-(((3-(3-(2,2-disulfonatoethyl)ureido)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-2-oxoethoxy)acetate
9	 Ammonium 6-(((3-(((19-(((3-(3-(2,2-disulfonatoethyl)ureido)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-6-oxohexanoate

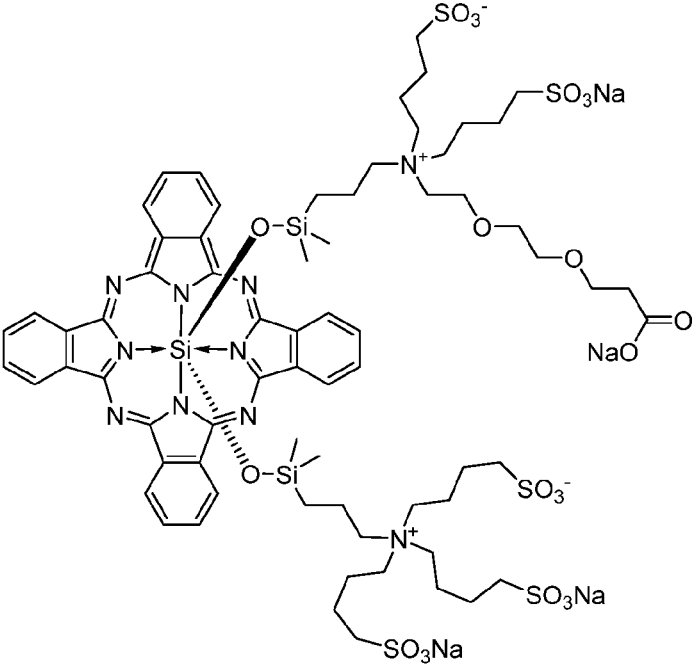
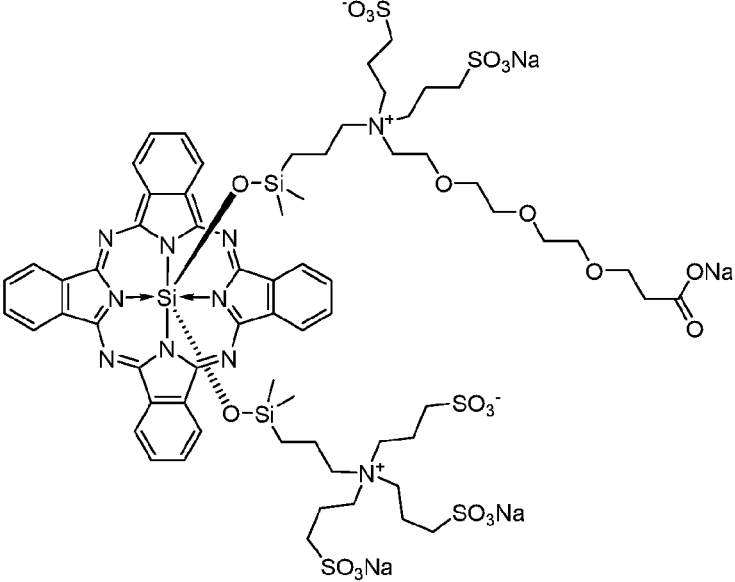
Ex. No.	Structure Name
10	 3-((2-((3-(((19-(((3-(6-((λ⁵-azaneyl)oxy)-6-oxohexanamido)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-2-oxoethyl)bis(3-(((λ⁵-azaneyl)oxy)sulfonyl)propyl)ammonio)propane-1-sulfonate
11	 3-((2-((3-(((19-(((3-(2-(2-((λ⁵-azaneyl)oxy)-2-oxoethoxy)acetamido)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-2-oxoethyl)bis(3-(((λ⁵-azaneyl)oxy)sulfonyl)propyl)ammonio)propane-1-sulfonate

Ex. No.	Structure Name
12	 3-((6-((λ5-azaneyl)oxy)-6-oxohexyl)(3-(((λ5-azaneyl)oxy)sulfonyl)propyl)(3-(((19-(((3-bis(3-(((λ5-azaneyl)oxy)sulfonyl)propyl)(3-sulfonatopropyl)ammonio)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)ammonio)propane-1-sulfonate

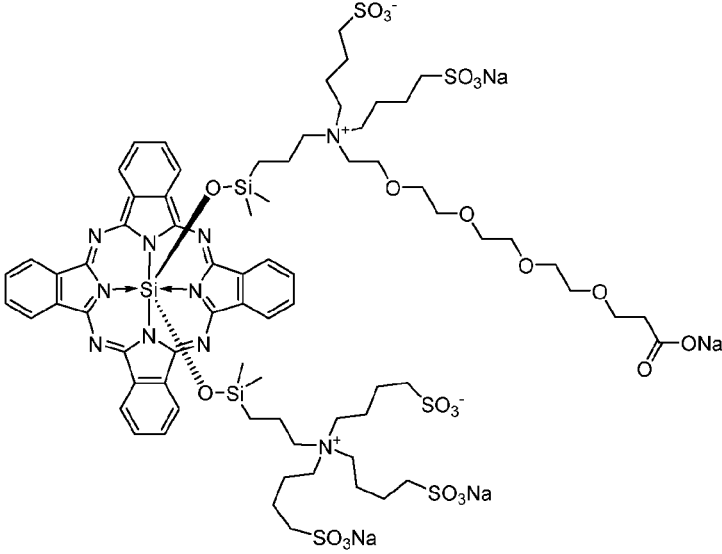
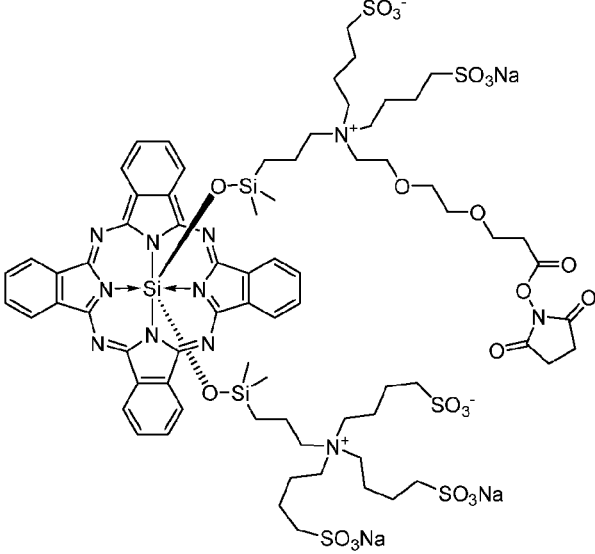
Ex. No.	Structure Name
13	 4-(((6-((λ5-azaneyl)oxy)-6-oxohexyl)(4-(((λ5-azaneyl)oxy)sulfonyl)butyl)(3-(((19-(((3-(bis(4-(((λ5-azaneyl)oxy)sulfonyl)butyl)(4-sulfonatobutyl)ammonio)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)ammonio)butane-1-sulfonate

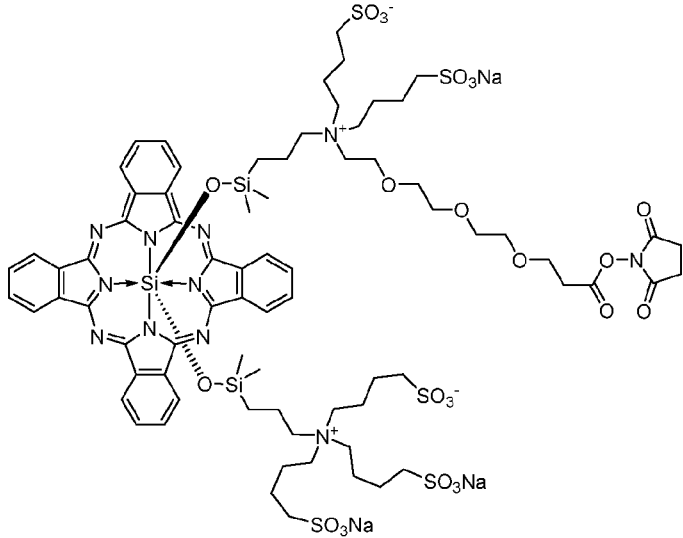
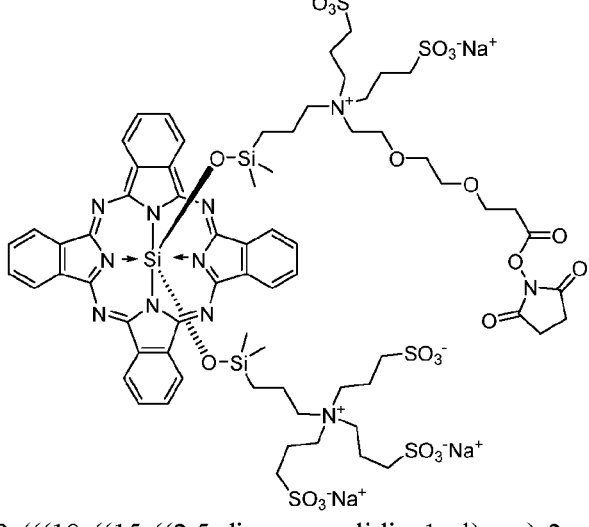
Ex. No.	Structure Name
14	 Sodium 3,3',3''-((3-(((19-(((3-((6-((2,5-dioxopyrrolidin-1-yl)oxy)-6-oxohexyl)bis(3-sulfonatopropyl)ammonio)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)ammonio)tris(propane-1-sulfonate))
15	 Ammonium 2-(2-((3-(((19-(((3-4-(bis(3-sulfonatopropyl)ammonio)butanamido)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-2-oxoethoxy)acetate

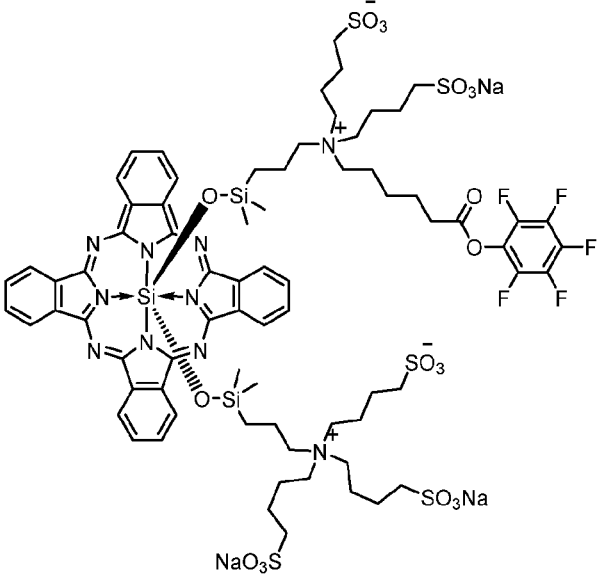
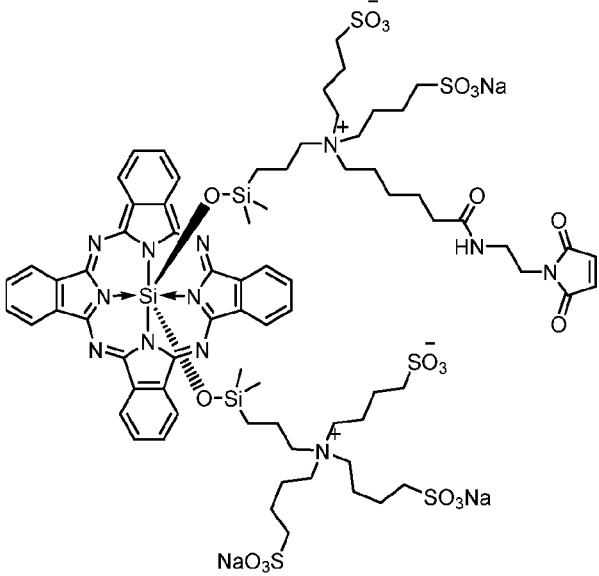
Ex. No.	Structure Name
16	 Sodium 4,4',4''-((3-(((19-(((3-((6-((2,5-dioxopyrrolidin-1-yl)oxy)-6-oxohexyl)bis(4-sulfonatobutyl)ammonio)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)ammonio)tris(butane-1-sulfonate)
17	 Sodium 2-((19-((dimethyl(3-(tris(4-sulfonatobutyl)ammonio)propyl)silyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)-2-methyl-6,6-bis(4-sulfonatobutyl)-9,12,15-trioxa-6-aza-2-silaoctadecan-6-ium-18-oate

Ex. No.	Structure Name
18	 Sodium 2-((19-((dimethyl(3-(tris(4-sulfonatobutyl)ammonio)propyl)silyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)-2-methyl-6,6-bis(4-sulfonatobutyl)-9,12-dioxa-6-aza-2-silapentadecan-6-ium-15-oate
19	 Sodium 2-((19-((dimethyl(3-(tris(3-sulfonatopropyl)ammonio)propyl)silyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)-2-methyl-6,6-bis(3-sulfonatopropyl)-9,12,15-trioxa-6-aza-2-silaoctadecan-6-ium-18-oate

Ex. No.	Structure Name
20	Sodium 6-((3-(((19-((dimethyl(3-(5-(tris(3-sulfonatopropyl)ammonio)-2-(3-(tris(3-sulfonatopropyl) ammonio)propyl)pentanamido)propyl)silyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-6-oxohexanoate)
21	Sodium 2-((19-((dimethyl(3-(tris(3-sulfonatopropyl)ammonio)propyl)silyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)-2-methyl-6,6-bis(3-sulfonatopropyl)-9,12-dioxa-6-aza-2-silapentadecan-6-ium-15-oate)

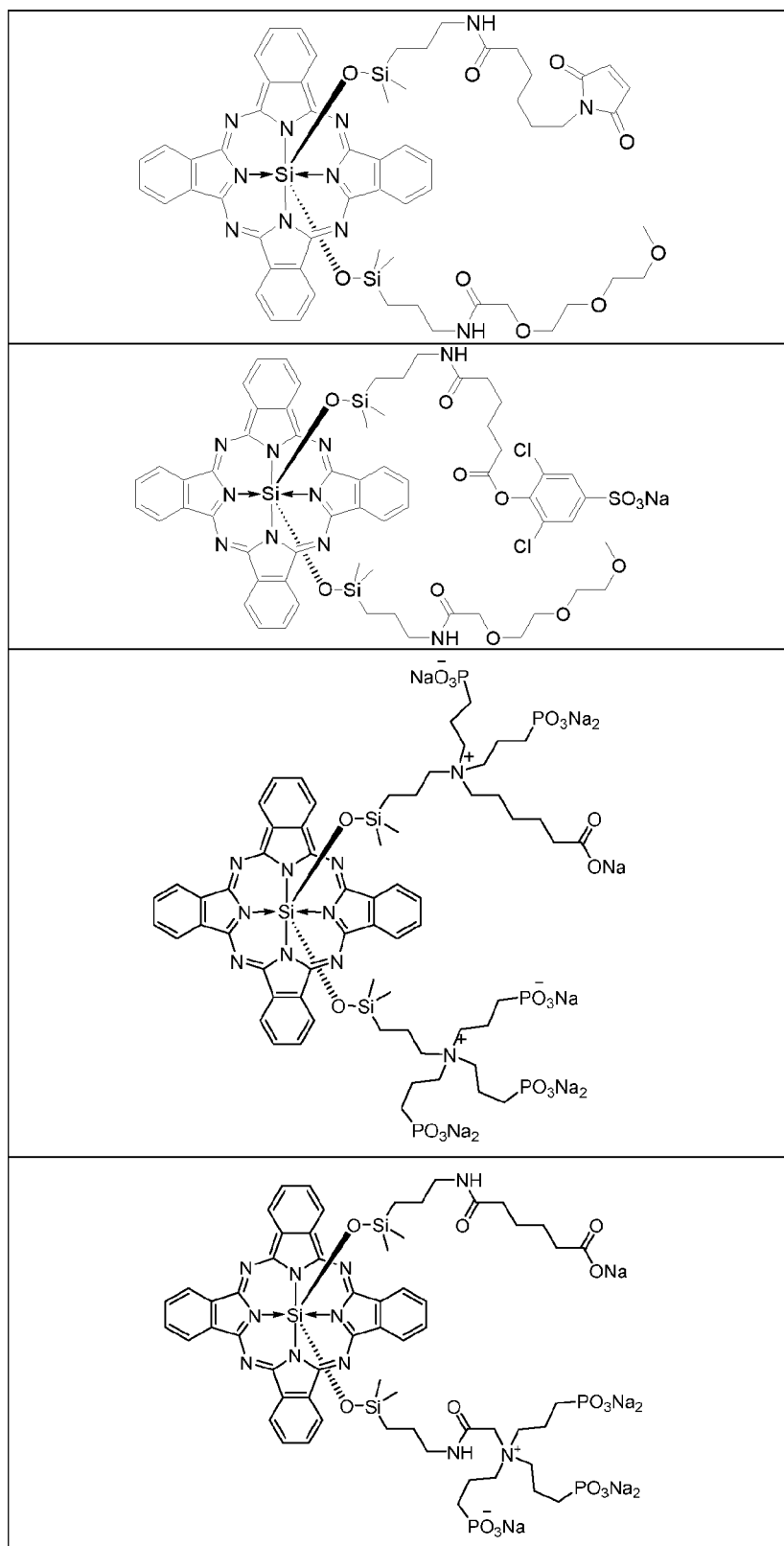
Ex. No.	Structure Name
22	 Sodium 2-((19-((dimethyl(3-(tris(4-sulfonatobutyl)ammonio)propyl)silyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)-2-methyl-6,6-bis(4-sulfonatobutyl)-9,12,15,18-tetraoxa-6-aza-2-silahenicosan-6-ium-21-oate
23	 Sodium 4,4',4''-((3-(((19-((15-((2,5-dioxopyrrolidin-1-yl)oxy)-2-methyl-15-oxo-6,6-bis(4-sulfonatobutyl)-9,12-dioxa-6-aza-2-silapentadecan-6-ium-2-yl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)ammonio)tris(butane-1-sulfonate)

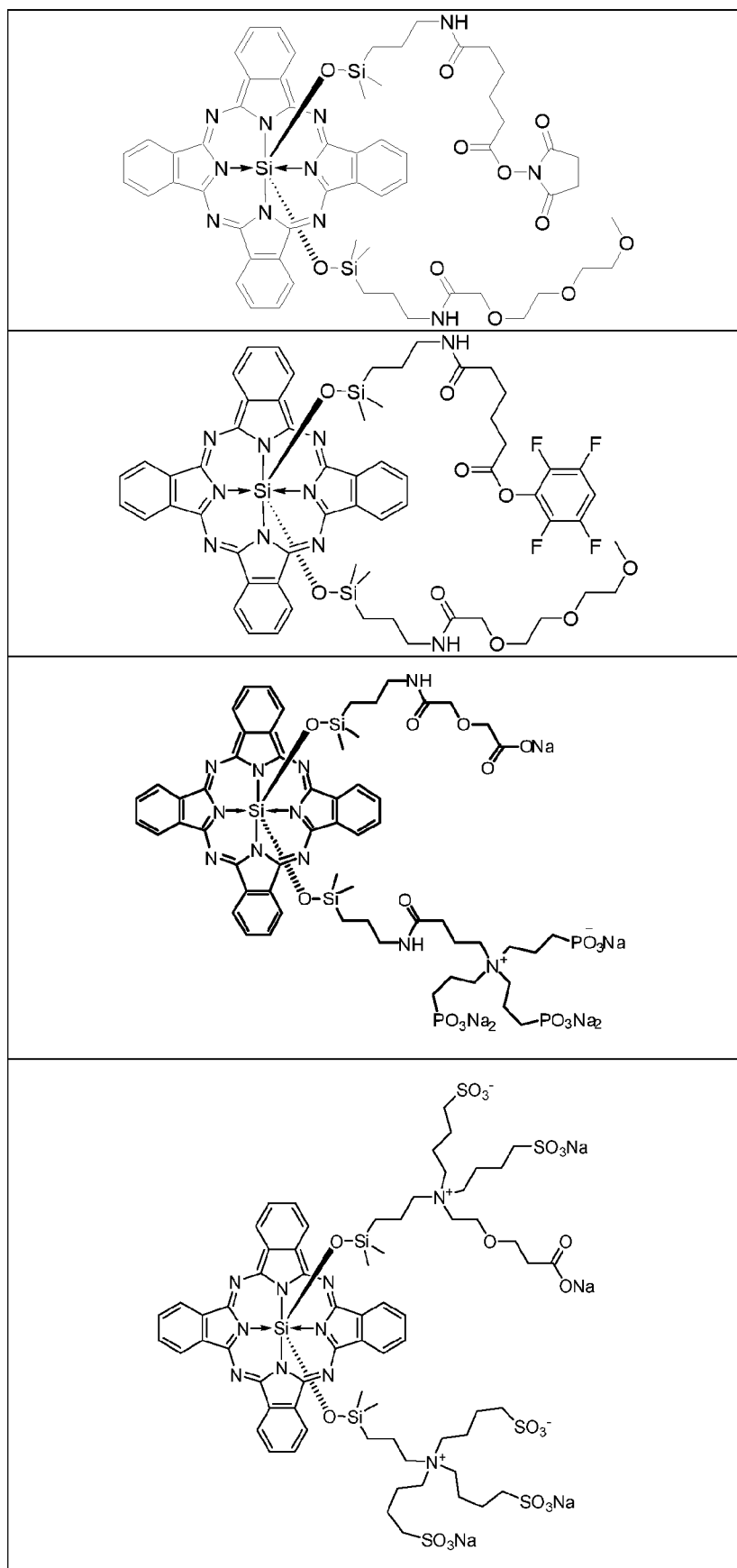
Ex. No.	Structure Name
24	 Sodium 4,4',4''-((3-(((19-((18-((2,5-dioxopyrrolidin-1-yl)oxy)-2-methyl-18-oxo-6,6-bis(4-sulfonatobutyl)-9,12,15-trioxa-6-aza-2-silaoctadecan-6-ium-2-yl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)ammonio)tris(butane-1-sulfonate)
25	 Sodium 3,3',3''-((3-(((19-((15-((2,5-dioxopyrrolidin-1-yl)oxy)-2-methyl-15-oxo-6,6-bis(3-sulfonatopropyl)-9,12-dioxa-6-aza-2-silapentadecan-6-ium-2-yl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)ammonio)tris(propane-1-sulfonate)

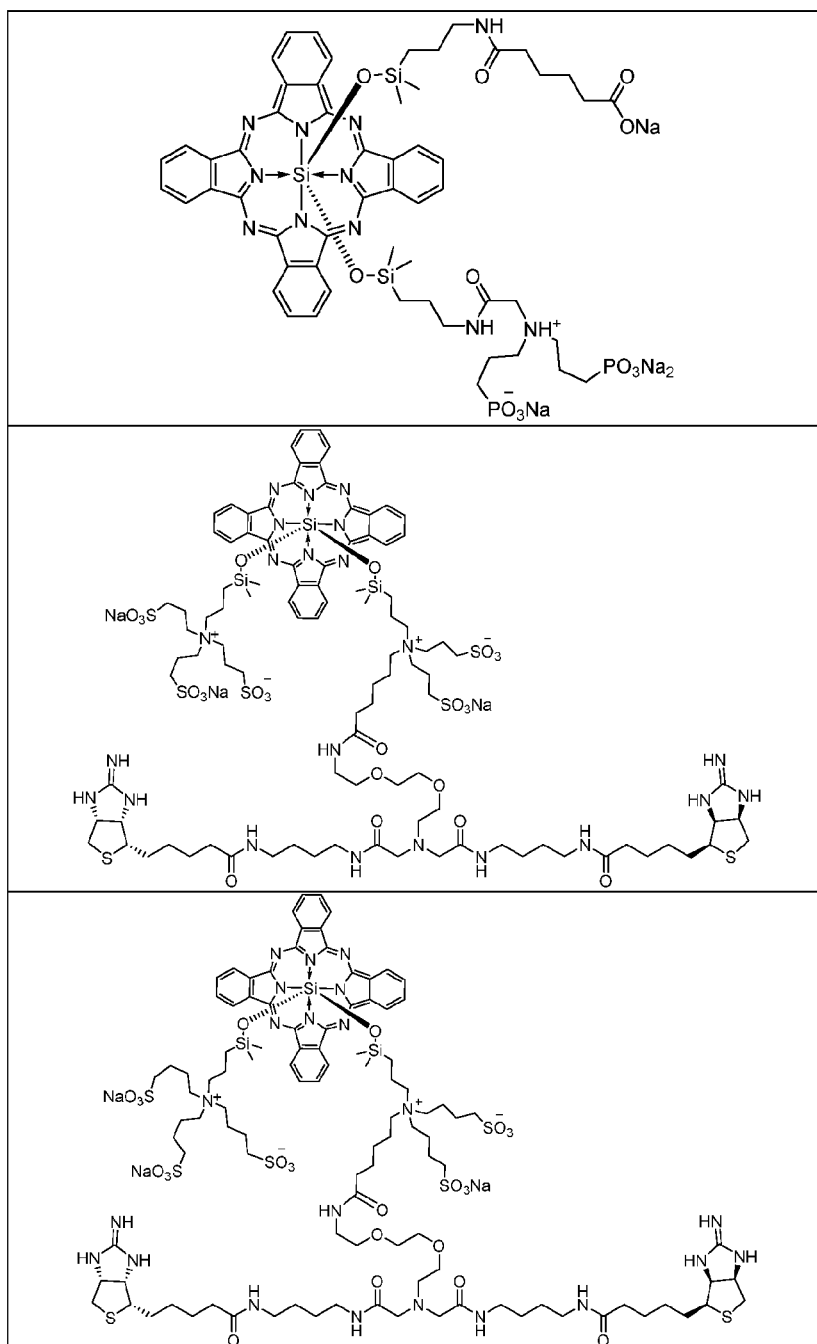
Ex. No.	Structure Name
26	 Sodium 4,4',4''-((3-(((19-((dimethyl(3-((6-oxo-6-(perfluorophenoxy)hexyl)bis(4-sulfonatobutyl)ammonio)propyl)silyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)ammonio)tris(butane-1-sulfonate)
27	 Sodium 4,4',4''-((3-(((19-(((3-((6-((2-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)ethyl)amino)-6-oxohexyl)bis(4-sulfonatobutyl)ammonio)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)ammonio)tris(butane-1-sulfonate)

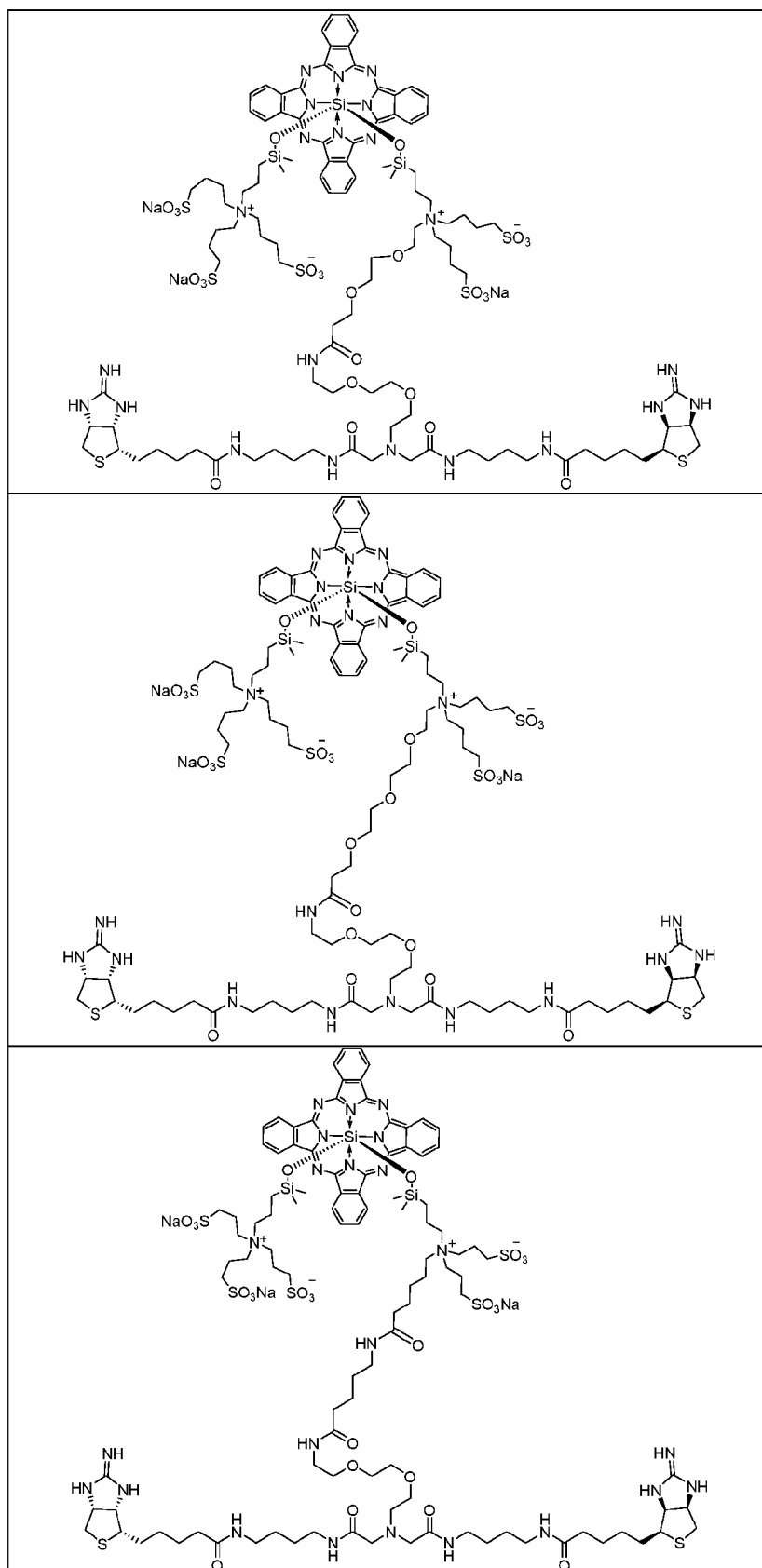
[00070] In yet certain embodiments, provided herein are compounds selected from Table 2A.

Table 2A

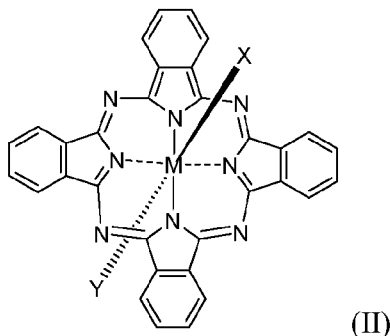






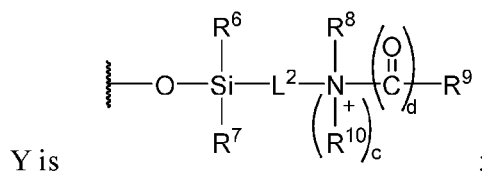
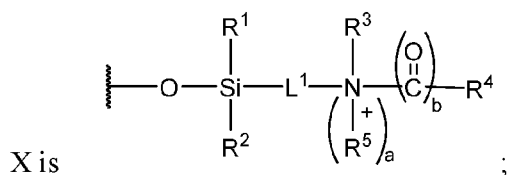


[00071] One embodiment provides a compound, or a salt, stereoisomer, or tautomer thereof, having the structure of Formula (II):



wherein,

M is a metal or metalloid;



R¹ and R² are each independently optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl or optionally substituted heteroaralkyl;

R³, R⁴ or R⁵ are selected from substituent group (a) or substituent group (b) wherein,

(a) R³ is hydrogen, -L³-H, -L³-A, or -L³-Z;

R⁴ is -L⁴-H, -(NH)_m-L⁴-A, -(NH)_m-L⁴-Z, -(O)_m-L⁴-A, or -(O)_m-L⁴-Z;

R⁵ is -L⁵-H, or -L⁵-A; and

(b) R³ and R⁴ are connected with a bond to form a heterocyclyl substituted with -L⁴-A, and

R⁵ is -L⁵-H or -L⁵-A;

provided at least one of R³, R⁴ and R⁵ is a group containing A;

A is a reactive group capable of forming a covalent bond with a second moiety, or a protected form thereof or a reacted form thereof;

R⁶ and R⁷ are each methyl;

R⁸ is -L⁸-Z;

R^9 is $-L^9-Z$;

R^{10} is $-L^{10}-Z$; and

Z is a water soluble group optionally substituted with A, or $L'-A$;

L^1 is selected from optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, or optionally substituted heteroalkenylene;

L^2 is propylene;

L^3 , L^4 , and L^5 are each independently selected from optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkylene, optionally substituted heterocyclene, optionally substituted arylene, optionally substituted aralkylene, optionally substituted heteroaralkylene, or optionally substituted heteroarylene where the carbon atom of the alkylene, heteroalkylene, alkenylene, heteroalkenylene, cycloalkylene, heterocyclene, arylene, aralkylene, heteroaralkylene, or optionally substituted heteroarylene is further optionally substituted with a Z, and each nitrogen atom of the heteroalkylene or heteroalkenylene is optionally substituted with one or two $L'-Z$;

L' is each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkylene, optionally substituted heterocyclene, optionally substituted arylene, optionally substituted aralkylene, optionally substituted heteroaralkylene, or optionally substituted heteroarylene;

L^8 , L^9 and L^{10} are each propylene;

a is 0 or 1;

b is 0 or 1;

c is 0 or 1;

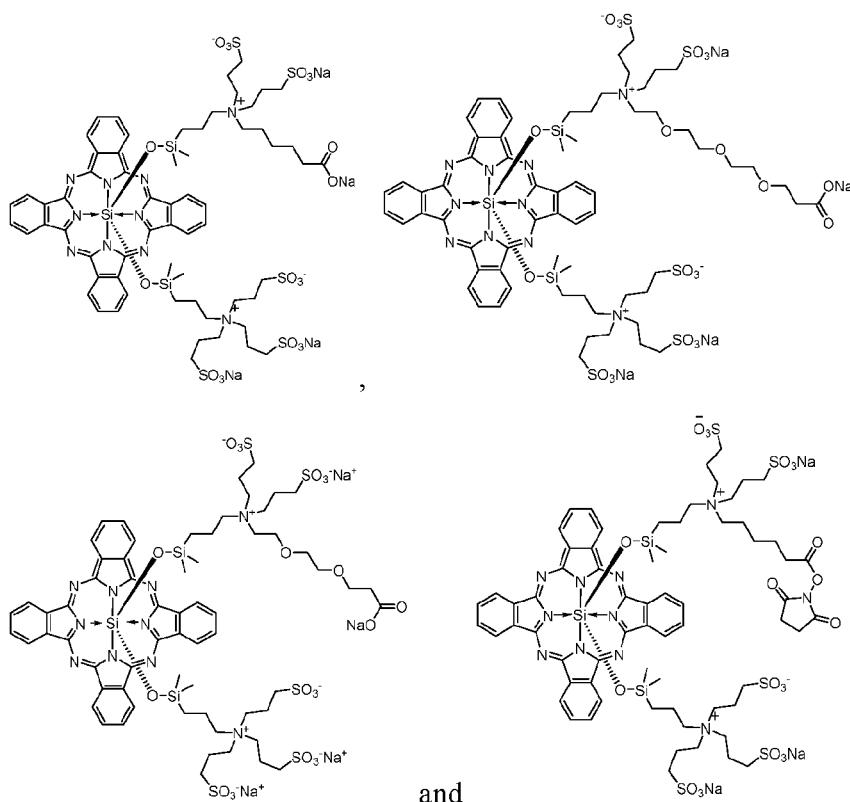
d is 0 or 1;

m is 0 or 1;

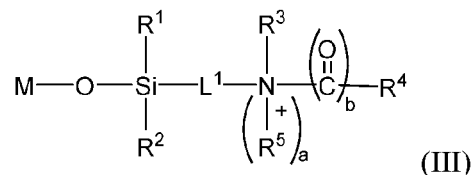
n is 0 or 1;

provided that if b is 1, then a is 0; if d is 1, then c is 0; if m is 1, then b is 1; and if n is 1, then c is 1.

[00072] Another embodiment provides the compound of Formula (II), or salt, stereoisomer, or tautomer thereof, selected from the group consisting of:



[00073] One embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, having the structure:



wherein M is a metal or metalloid selected from Si, Ge, Sn, Al, or Zn, optionally further ligated on the metal or metalloid;

R¹ and R² are each independently optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted heterocycl, optionally substituted heterocyclalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl or optionally substituted heteroaralkyl;

R³, R⁴ or R⁵ are selected from substituent group (a) or substituent group (b) wherein,

(a) R³ is hydrogen, -L³-H, -L³-A, or -L³-Z;

R⁴ is -L⁴-H, -(NH)_m-L⁴-A, -(NH)_m-L⁴-Z, -(O)_m-L⁴-A or -(O)_m-L⁴-Z;

R⁵ is -L⁵-H or -L⁵-A; and

(b) R³ is -L³-H, or -L³-A;

R⁴ is -L⁴-H, -(NH)_m-L⁴-A, or -(O)_m-L⁴-A; wherein R³ and R⁴ are connected with a bond to form a heterocycl substituted with -L⁴-A; and

R^5 is $-L^5-H$ or $-L^5-A$;

provided at least one of R^3 , R^4 and R^5 is a group containing A;

A is a reactive group capable of forming a covalent bond with a thiol, hydroxyl, carboxyl or amino group of a second moiety, or a protected form thereof or a reacted form thereof;

L^1 is optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene or optionally substituted heteroalkenylene;

Z is a water soluble group optionally substituted with A or $L'-A$;

L^3 , L^4 , and L^5 are each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkylene, optionally substituted heterocyclene, optionally substituted arylene, optionally substituted aralkylene, optionally substituted heteroaralkylene, or optionally substituted heteroarylene where the carbon atom of the alkylene, heteroalkylene, alkenylene, heteroalkenylene, cycloalkylene, heterocyclene, arylene, aralkylene, heteroaralkylene, or heteroarylene is further optionally substituted with Z and each nitrogen atom of the heteroalkylene or heteroalkenylene is optionally substituted with one or two $L'-Z$;

L' is each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkylene, optionally substituted heterocyclene, optionally substituted arylene, optionally substituted aralkylene, optionally substituted heteroaralkylene, or optionally substituted heteroarylene;

a is 0 or 1;

b is 0 or 1;

m is 0 or 1;

provided that if b is 1, then a is 0; and

if m is 1, b is 1.

[00074] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein L^3 , L^4 , L^5 , are each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene or optionally substituted heteroalkenylene, where each nitrogen atom of the heteroalkylene or heteroalkenylene is further optionally substituted with one or two $L'-Z$; and L' is independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene or optionally substituted heteroalkenylene.

[00075] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein L^1 and L^2 , are each independently optionally substituted C_{1-10} alkylene, optionally substituted hetero C_{1-10} alkylene, optionally substituted C_{2-10} alkenylene or hetero C_{2-10} alkenylene.

[00076] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein L^1 and L^2 , are each independently C_{2-4} alkylene, hetero C_{2-4} alkylene, optionally substituted C_{2-4} alkenylene or optionally substituted hetero C_{2-4} alkenylene.

[00077] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein L^1 and L^2 are each optionally substituted C_{2-4} alkylene.

[00078] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein the reactive group A is each independently selected from:

-C(O)OR¹¹,
 -NR¹²R¹³,
 -NHC(O)R¹⁴,
 -C(O)R¹⁵,
 -OR¹⁶,
 -SR¹⁶,
 -OS(O)₂R¹⁷,
 -OP(OR¹⁸)(NR¹⁹R²⁰),
 -N=C=O;
 -N=C=S,
 -S-C≡N,
 -SO₂-F,
 -SO₂-Cl,
 -SO₂-Br,
 -S-SR²¹; or

5- or 6- membered dioxo-substituted heterocyclyl;

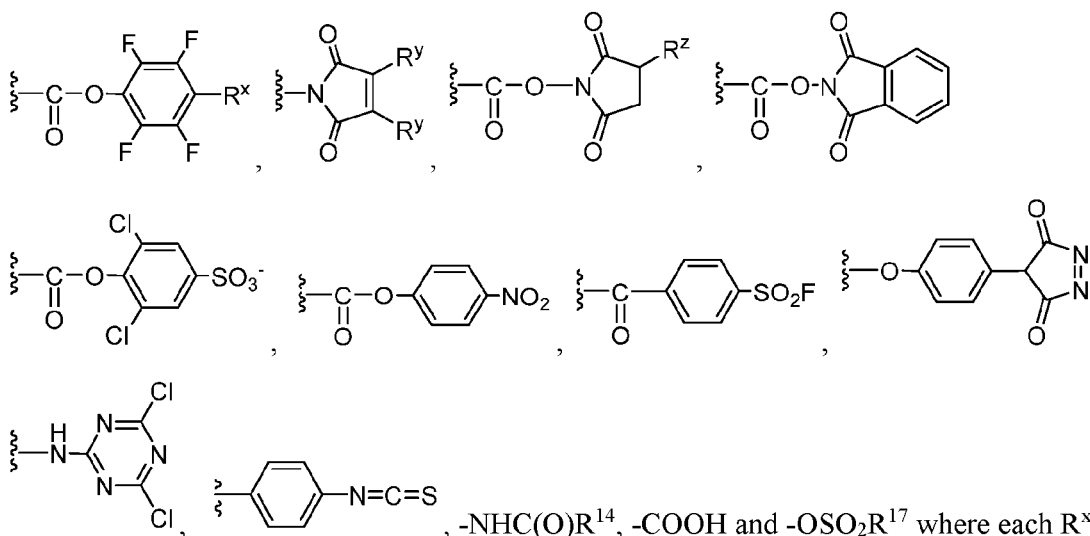
each R¹¹ is independently hydrogen, alkyl, haloalkyl, alkenyl, heterocyclyl, aryl or heteroaryl, wherein each R¹¹ is independently optionally substituted with one to five groups each independently selected from halo, -SO₃⁻ and -SO₂F;

each R¹² is independently hydrogen, alkyl or haloalkyl;

each R¹³ is aryl or heteroaryl, each R¹³ independently optionally substituted with one to five groups each independently selected from halo, -SO₃⁻ and -SO₂F; or optionally R¹² and R¹³, together with the nitrogen to which they are attached, form a cyclic imide;

each R^{14} is independently optionally substituted haloalkyl or optionally substituted aralkyl;
 each R^{15} is independently aryl optionally substituted with one to five groups each independently halo, heterocyclyl, $-\text{SO}_3^-$ or $-\text{SO}_2\text{F}$;
 each R^{16} is independently aryl optionally substituted with one to five groups each independently halo or heterocyclyl;
 each R^{17} is independently optionally substituted alkyl, optionally substituted haloalkyl, optionally substituted alkenyl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, optionally substituted aryl or optionally substituted heteroaryl, wherein the heterocyclyl, aryl or heteroaryl is optionally substituted with one to five groups each independently selected from halo, $-\text{SO}_3^-$, $-\text{SO}_2\text{F}$ and $-\text{C}(\text{O})\text{OR}^c$;
 each R^c is independently optionally substituted alkyl, optionally substituted haloalkyl, optionally substituted cycloalkyl or optionally substituted aryl;
 R^{18} , R^{19} and R^{20} are each independently optionally substituted alkyl or optionally substituted haloalkyl; and
 R^{21} is heteroaryl.

[00079] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein the reactive group A is selected from the group consisting of:



R^y are independently hydrogen or halo, and R^z is hydrogen or $-\text{SO}_3^-$;

R^{14} is optionally substituted haloalkyl or optionally substituted aralkyl; and

R^{17} is independently optionally substituted alkyl, optionally substituted haloalkyl, optionally substituted alkenyl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, optionally substituted aryl or optionally substituted heteroaryl, wherein the heterocyclyl, aryl or heteroaryl is optionally substituted with one to five groups each independently selected from halo, $-\text{SO}_3^-$, $-\text{SO}_2\text{F}$ and $-\text{C}(\text{O})\text{OR}^c$; and

each R^c is independently optionally substituted alkyl, optionally substituted haloalkyl, optionally substituted cycloalkyl or optionally substituted aryl.

[00080] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein the reactive group is each independently $-C(O)OR^{11}$ or $-NR^{12}R^{13}$.

[00081] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein the water soluble group Z is

$-C(O)OH$,
 $-(CH_2)_q(OCH_2CH_2)_v(CH_2)_qC(O)OH$,
 $-(CH_2CH_2O)_v(CH_2)_pC(O)OH$,
 $-(CH_2)_q(OCH_2CH_2)_vOR^{22}$,
 $-(CH_2CH_2O)_v(CH_2)_pOR^{22}$,
 $-(CH_2)_q(OCH_2CH_2)_vSR^{22}$,
 $-(CH_2CH_2O)_v(CH_2)_pSR^{22}$,
 $-O(CH_2)_vN[(CH_2CH_2O)_nCH_2CH_2OR^{22}]_t$,
 $-(CH_2)_q(OCH_2CH_2)_vN[(CH_2CH_2O)_wCH_2CH_2OR^{22}]_t$,
 $-(CH_2CH_2O)_m(CH_2)_pN[(CH_2CH_2O)_wCH_2CH_2OR^{22}]_t$,
 $-NH_2$,
 $-(CH_2)_qN[(CH_2CH_2O)_vCH_2CH_2OR^{22}]_t$,
 $-(CH_2)_qNR^b[(CH_2CH_2O)_wCH_2CH_2OR^{22}]_u$,
 $-(CH_2)_qN[(CH_2)_p(OCH_2CH_2)_vOR^{22}]_t$,
 $-(CH_2)_qN[(CH_2)_pSO_3^-]_t$,
 $-(CH_2)_qNR^b[(CH_2)_pSO_3^-]_u$,
 $-(CH_2)_qNR^b(CH_2)_pCH(SO_3^-)_2$,
 $-(CH_2)_qN[(CH_2)_pS(O)_uOH]_t$,
 $-(CH_2)_qN[(CH_2)_pOSO_3^{2-}]_t$,
 $-(CH_2)_q(OCH_2CH_2)_v(CH_2)_qSO_3^-$,
 $-(CH_2)_q(OCH_2CH_2)_v(CH_2)_qS(O)_uOH$,
 $-(CH_2)_q(OCH_2CH_2)_v(CH_2)_qOSO_3^{2-}$,
 $-SO_3^-$,
 $-CH(SO_3^-)_2$,
 $-OSO_3^{2-}$,
 $-S(O)_uOH$,
 $-PO_3^{2-}$,
 $-CH(PO_3^{2-})_2$,

$-(\text{CH}_2)_q\text{N}[(\text{CH}_2)_p\text{PO}_3^-]_t$,
 $-(\text{CH}_2)_q(\text{OCH}_2\text{CH}_2)_v(\text{CH}_2)_q\text{PO}_3^-$,
 $-(\text{CH}_2)_q\text{N}[(\text{CH}_2)_p\text{OPO}_3^-]_t$,
 $-\text{OPO}_3^-$,
 $-(\text{CH}_2)_q(\text{OCH}_2\text{CH}_2)_v(\text{CH}_2)_q\text{P}(\text{O})(\text{OH})_2$,
 $-(\text{CH}_2)_q\text{N}[(\text{CH}_2)_p\text{P}(\text{O})(\text{OH})_2]_t$,
 $-\text{P}(\text{O})(\text{OH})_2$,
 glutamate,
 aspartate,
 histidine,
 1,3-beta-glucan, or
 1,4-beta-glucan;

each R^{22} is independently alkyl, haloalkyl, cycloalkyl or aryl;

each R^b is independently hydrogen, alkyl optionally substituted with $-\text{CO}_2\text{H}$, heteroalkylene optionally substituted with $-\text{CO}_2\text{H}$, haloalkyl or cycloalkyl;

each v , w and p are independently an integer from 1 to 10;

each q is independently an integer from 0 to 10;

t is 2 or 3; and

u is 1 or 2.

[00082] Another embodiment provides a compound of Formula (III) or a salt, stereoisomer, tautomer thereof, wherein the water soluble group Z is

$-(\text{CH}_2)_q(\text{OCH}_2\text{CH}_2)_v\text{OR}^{22}$,
 $-(\text{CH}_2)_q\text{O}(\text{CH}_2)_v\text{N}[(\text{CH}_2\text{CH}_2\text{O})_w\text{CH}_2\text{CH}_2\text{OR}^{22}]_t$,
 $-(\text{CH}_2)_q\text{N}[(\text{CH}_2)_p(\text{OCH}_2\text{CH}_2)_v\text{OR}^{22}]_t$,
 $-(\text{CH}_2)_q\text{N}[(\text{CH}_2)_p\text{SO}_3^-]_t$,
 $-(\text{CH}_2)_q\text{NR}^b[(\text{CH}_2)_p\text{SO}_3^-]_u$,
 $-(\text{CH}_2)_q\text{NR}^b[(\text{CH}_2)_p\text{CH}(\text{SO}_3^-)_2]_u$,
 $-\text{SO}_3^-$,
 $-\text{CH}(\text{SO}_3^-)_2$,
 $-\text{PO}_3^{2-}$,
 $-(\text{CH}_2)_q\text{N}[(\text{CH}_2)_p\text{PO}_3^-]_t$,
 $-(\text{CH}_2)_q\text{NR}^b[(\text{CH}_2)_p\text{PO}_3^-]_u$ or
 $-(\text{CH}_2)_q\text{NR}^b(\text{CH}_2)_p\text{CH}(\text{PO}_3^-)_2$;

each R^{22} is independently alkyl, haloalkyl, cycloalkyl or aryl;

each R^b is independently hydrogen, alkyl optionally substituted with $-CO_2H$, heteroalkylene optionally substituted with $-CO_2H$, haloalkyl or cycloalkyl;

each v , w and p are independently an integer from 1 to 10;

each q is independently an integer from 0 to 10;

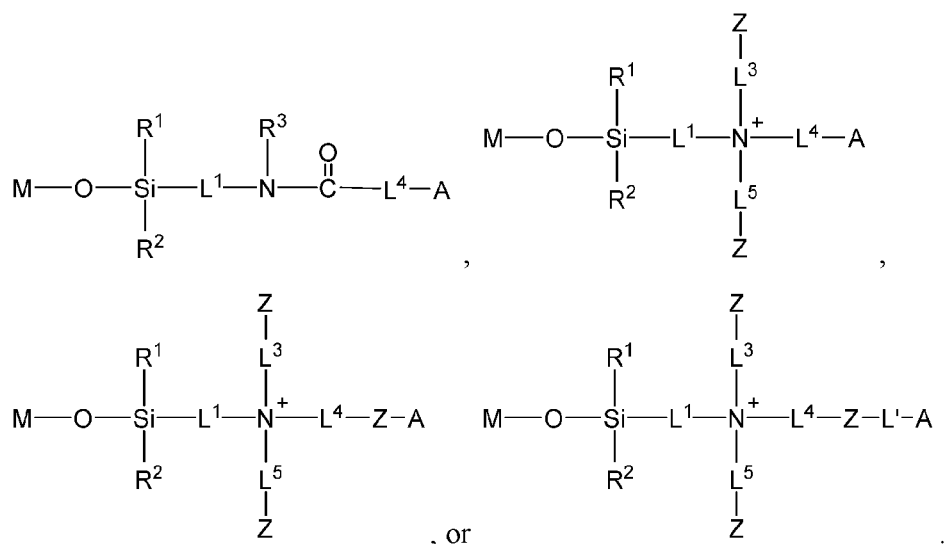
t is 2 or 3; and

u is 1 or 2.

[00083] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein a is 0, and b is 1.

[00084] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein a is 1, and b is 0.

[00085] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein the compound of Formula (III) has the structure:



[00086] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein L^1 is selected from $-(CH_2)_2-$, $-(CH_2)_3-$ or $-(CH_2)_4-$.

[00087] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein L^1 is $-(CH_2)_3-$.

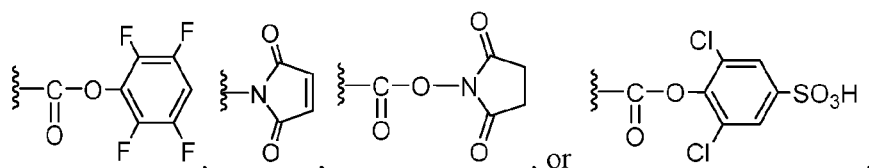
[00088] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein L^4 is selected from $-(CH_2)-$, $-(CH_2)_2-$, $-(CH_2)_3-$, $-(CH_2)_4-$, or $-(CH_2)_5-$. Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein L^4 is $-(CH_2)-$ or $-(CH_2)_2-$. Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein L^4 is $-(CH_2)_3-$. Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein L^4 is $-(CH_2)_4-$. Another embodiment provides a

compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein L^4 is $-(CH_2)_5-$

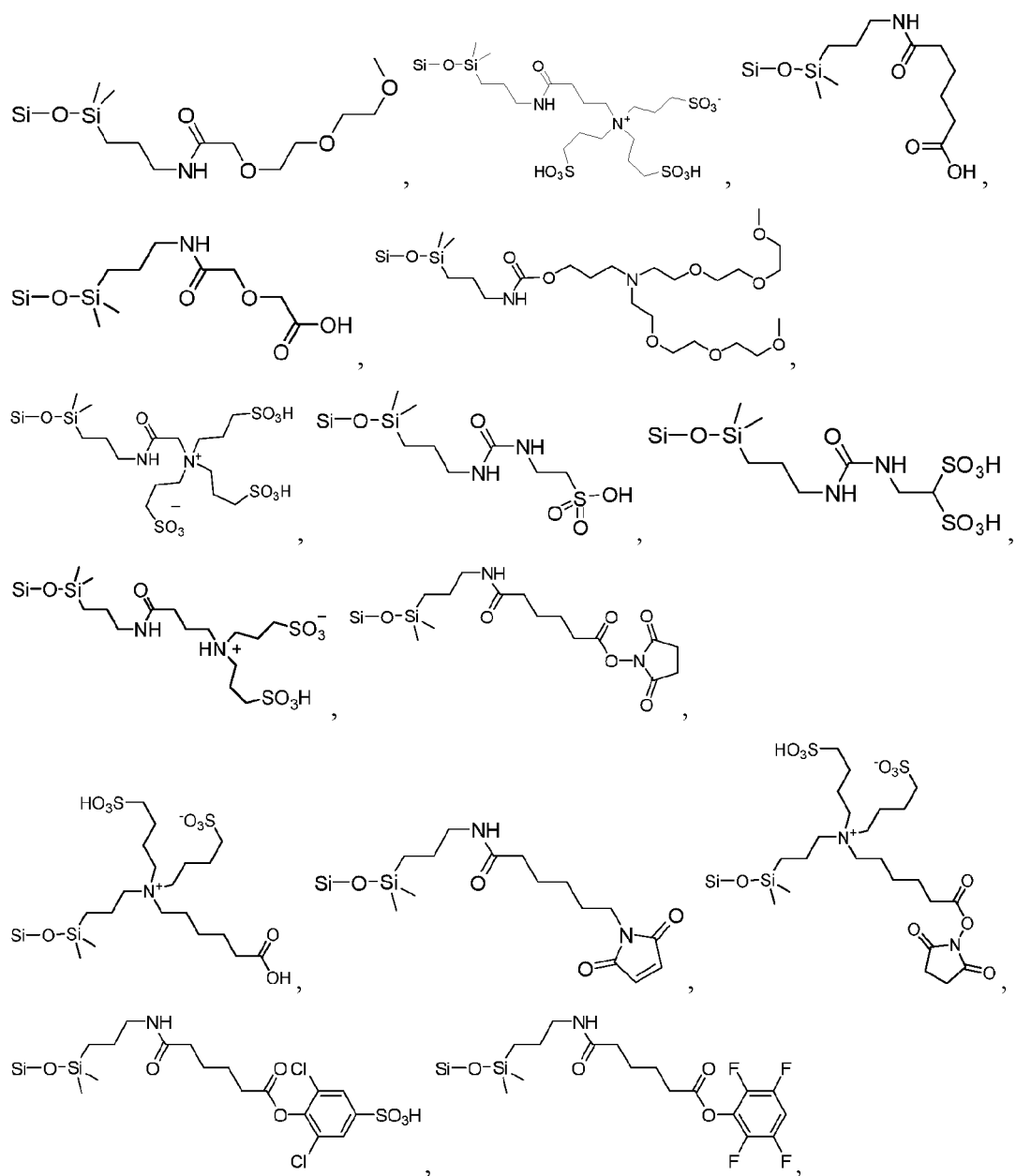
- [00089] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein L^5 is selected from $-(CH_2)_3-$, $-(CH_2)_4-$ or $-(CH_2)_5-$. Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein L^5 is $-(CH_2)_3-$. Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein L^5 is $-(CH_2)_4-$. Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein L^5 is $-(CH_2)_5-$.
- [00090] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein R^3 , R^4 or R^5 are selected from substituent group (a).
- [00091] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein R^3 is hydrogen. Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein R^3 is hydrogen, a is 0, and b is 1.
- [00092] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein R^3 is $-L^3-Z$.
- [00093] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein R^4 is $-(NH)_m-L^4-Z$. Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein R^4 is $-(O)_m-L^4-Z$.
- [00094] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein m is 0.
- [00095] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein L^4 is alkylene, and the carbon atom of the alkylene is further substituted with a second Z. Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein the L^4 alkylene is a C_{2-5} alkylene. Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein said second Z is $-(CH_2)_qN[(CH_2)_pSO_3^-]_t$.
- [00096] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein t is 3, q is 2-6, and p is 2-4.
- [00097] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein R^5 is $-L^5-A$.
- [00098] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein R^3 , R^4 or R^5 are selected from substituent group (b).

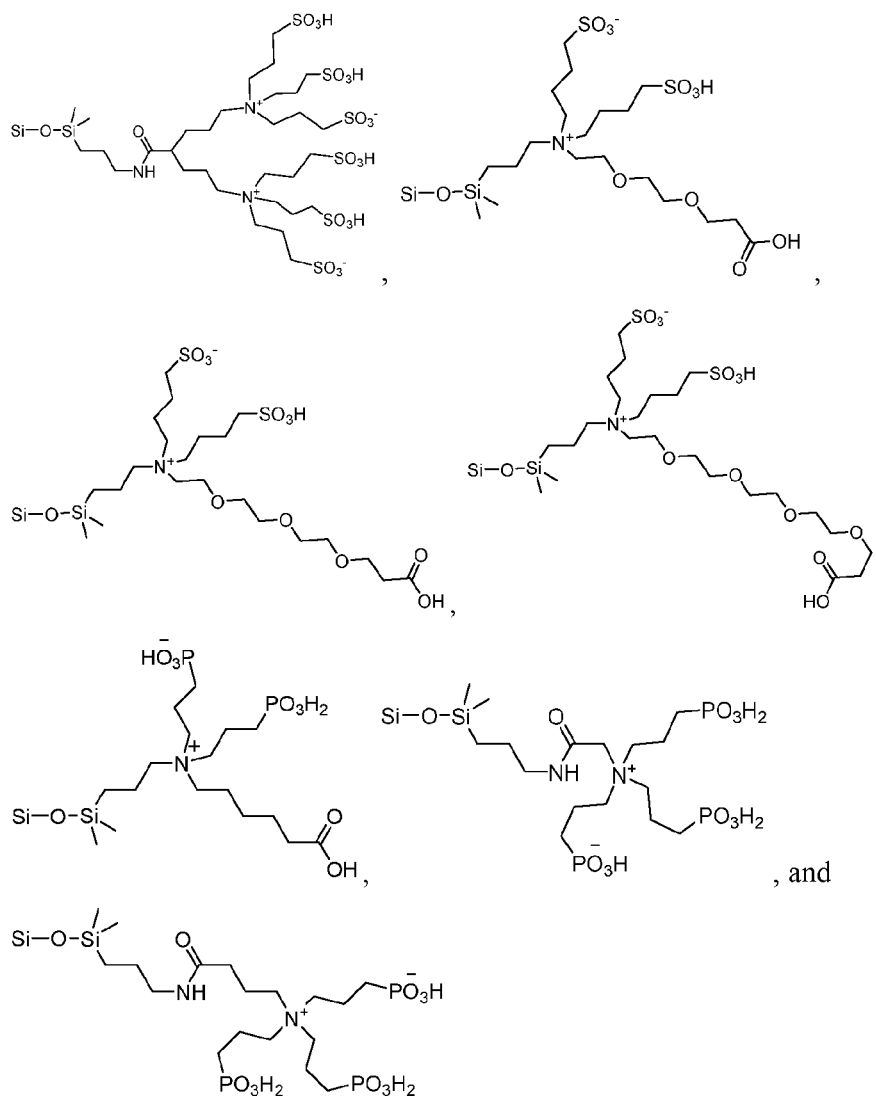
- [00099]** Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein L^4 is C_{2-5} alkylene, and Z is $-(CH_2)_qN[(CH_2)_pSO_3^-]_t$, wherein q is 0.
- [000100]** Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein p is 2-5. Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein p is 3. Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein p is 4.
- [000101]** Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein L^4 is C_{2-5} alkylene, and Z is $-(CH_2)_qN[(CH_2)_pPO_3^-]_t$, wherein q is 0. Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein p is 2-5, and t is 3. Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein p is 3. Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein p is 4.
- [000102]** Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein L^4 is C_{2-5} alkylene, and Z is $-(CH_2)_qNR^b(CH_2)_pCH(SO_3^-)_2$, wherein q is 0.
- [000103]** Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein R^b is alkyl optionally substituted with $-CO_2H$, or heteroalkylene optionally substituted with $-CO_2H$.
- [000104]** Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein R^b is hydrogen.
- [000105]** Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein p is 2-5.
- [000106]** Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein L^4 is C_{2-5} alkylene, and Z is $-(CH_2)_qNR^b[(CH_2)_pPO_3^-]_2$, wherein q is 0.
- [000107]** Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein R^b is alkyl optionally substituted with $-CO_2H$, or heteroalkylene optionally substituted with $-CO_2H$.
- [000108]** Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein R^b is hydrogen.
- [000109]** Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein p is 2-5.

- [000110] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein L^4 is C_{1-5} alkylene or heteroalkylene, and Z is $-C(O)OH$, or $-(CH_2)_q(OCH_2CH_2)_vOR^{22}$,
- [000111] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein q is 1-3 and v is 1-3.
- [000112] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein m is 1.
- [000113] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein L^4 is C_{1-5} alkylene, and Z is $-SO_3^-$, or $-CH(SO_3^-)_2$.
- [000114] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein L^4 is C_{2-5} alkylene, and Z is $-(CH_2)_qN[(CH_2CH_2O)_vCH_2CH_2OR^{22}]_2$ wherein q is 0, and v is 1-3.
- [000115] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein R^4 is $-(NH)_m-L^4-A$.
- [000116] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein R^4 is $-(O)_m-L^4-A$.
- [000117] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein m is 0.
- [000118] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein L^4 is C_{1-5} alkylene or heteroalkylene.
- [000119] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein A is selected from the group consisting of:



- [000120] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, wherein M is Si or Ge.
- [000121] Another embodiment provides a compound of Formula (III), or a salt, stereoisomer, tautomer thereof, selected from the group consisting of:

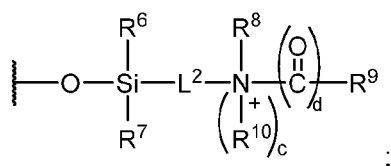




[000122] In certain embodiments, provided herein is a compound of Formula (0) comprising a silicon atom coordinated by (a) an unsubstituted phthalocyanine, (b) an axial silicon-containing ligand having a conjugatable group A'; and (c) an axial silicon-containing ligand having a water-solubilizing group Z that is not a conjugatable group.

[000123] One embodiment provides a compound, or salt, stereoisomer, or tautomer thereof, comprising a silicon atom coordinated by (a) an unsubstituted phthalocyanine, (b) a first axial silicon-containing ligand comprising a conjugatable group; and (c) a second axial silicon-containing ligand comprising a water-solubilizing group, but not a conjugatable group; and wherein the chemical structures of the first and second axial ligands are different. Another embodiment provides the compound, or salt, stereoisomer, or tautomer thereof, wherein the axial silicon-containing ligand having a conjugatable group further comprises a water-solubilizing group. Another embodiment provides the compound, or salt, stereoisomer, or tautomer thereof, wherein the water-solubilizing group is a group comprising one or more

polar and/or ionic substituents. Another embodiment provides the compound, or salt, stereoisomer, or tautomer thereof, wherein the one or more polar and/or ionic substituents on the water-solubilizing group are selected from carboxylate ($-\text{CO}_2$), poly(ethylene glycol), sulfonate ($-\text{SO}_3\text{H}$) group, a sulfonyl ($-\text{SO}_2\text{H}$) group, a sulfate ($-\text{SO}_4$) group, a hydroxyl ($-\text{OH}$) group, a phosphate ($-\text{OPO}_3\text{H}$) group, a phosphonate ($-\text{PO}_3\text{H}$) group, an amine ($-\text{NH}_2$) group and an optionally substituted quaternized nitrogen. Another embodiment provides the compound, or salt, stereoisomer, or tautomer thereof, wherein the one or more polar and/or ionic substituents on the water-solubilizing group are selected from a trivalent or tetravalent nitrogen-containing group, tris-sulfoalkyl quaternary ammonium, tris-sulfonate quaternary ammonium, bis-sulfoalkyl amine, bis-sulfonate amine, or bis-alkoxypolyethylene glycol amine. Another embodiment provides the compound, or salt, stereoisomer, or tautomer thereof, wherein the axial silicon-containing ligand having a water-solubilizing group has the structure of



R^6 and R^7 are each independently optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl or optionally substituted heteroaralkyl;

R^8 , R^9 or R^{10} are selected from substituent group (a) or substituent group (b) wherein,

(a) R^8 is hydrogen, $-\text{L}^8\text{-H}$ or $-\text{L}^8\text{-Z}$;

R^9 is $-\text{L}^9\text{-H}$, $-(\text{NH})_n\text{-L}^9\text{-Z}$ or $-(\text{O})_n\text{-L}^9\text{-Z}$;

R^{10} is $-\text{L}^{10}\text{-Z}$; and

(b) R^8 and R^9 are connected with a bond to form a heterocyclyl substituted with $-\text{L}^9\text{-Z}$ and R^{10} is $-\text{L}^{10}\text{-H}$ or $-\text{L}^{10}\text{-Z}$; provided at least one of R^8 , R^9 and R^{10} is a group containing Z; Z is a water-solubilizing group;

L^2 is an optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene or optionally substituted heteroalkenylene;

L^8 , L^9 and L^{10} are each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkylene, optionally substituted heterocyclene, optionally substituted arylene, optionally substituted aralkylene, optionally substituted heteroaralkylene, or optionally substituted heteroarylene, where the carbon atom of the alkylene,

heteroalkylene, alkenylene, heteroalkenylene, cycloalkylene, heterocyclene, arylene aralkylene, optionally substituted heteroaralkylene, or optionally substituted heteroarylene, is further optionally substituted with Z and each nitrogen atom of the heteroalkylene or heteroalkenylene is optionally substituted with one or two L'-Z;

L' is each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkylene, optionally substituted heterocyclene, optionally substituted arylene, optionally substituted aralkylene, optionally substituted heteroaralkylene, or optionally substituted heteroarylene;

c is 0 or 1;

d is 0 or 1;

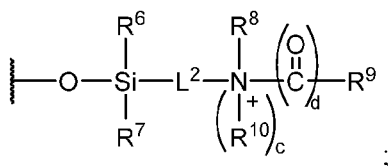
n is 0 or 1;

if d is 1, then c is 0;

if n is 1, c is 1 and

provided that when R⁶ and R⁷ are both methyl, and L² is propylene, c is 1 and d is 0, then L⁸, L⁹ and L¹⁰ are each not propylene.

[000124] Another embodiment provides the compound, or salt, stereoisomer, or tautomer thereof, wherein the axial silicon-containing ligand having a water-solubilizing group has the structure of



R⁶ and R⁷ are each independently optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl or optionally substituted heteroaralkyl;

R⁸, R⁹ or R¹⁰ are selected from substituent group (a) or substituent group (b) wherein,

(a) R⁸ is hydrogen, -L⁸-H or -L⁸-Z;

R⁹ is -L⁹-H, -(NH)_n-L⁹-Z or -(O)_n-L⁹-Z;

R¹⁰ is -L¹⁰-Z; and

(b) R⁸ and R⁹ are connected with a bond to form a heterocyclyl substituted with -L⁹-Z and R¹⁰ is -L¹⁰-H or -L¹⁰-Z; provided at least one of R⁸, R⁹ and R¹⁰ is a group containing Z; Z is a water-solubilizing group;

L^2 is an optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene or optionally substituted heteroalkenylene;

L^8 , L^9 and L^{10} are each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkylene, optionally substituted heterocyclene, optionally substituted arylene, optionally substituted aralkylene, optionally substituted heteroaralkylene, or optionally substituted heteroarylene, where the carbon atom of the alkylene, heteroalkylene, alkenylene, heteroalkenylene, cycloalkylene, heterocyclene, arylene, aralkylene, optionally substituted heteroaralkylene, or optionally substituted heteroarylene, is further optionally substituted with Z and each nitrogen atom of the heteroalkylene or heteroalkenylene is optionally substituted with one or two $L'-Z$;

L' is each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkylene, optionally substituted heterocyclene, optionally substituted arylene, optionally substituted aralkylene, optionally substituted heteroaralkylene, or optionally substituted heteroarylene;

c is 0 or 1;

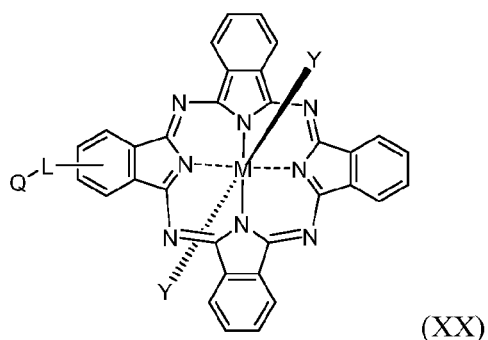
d is 0 or 1;

n is 0 or 1;

if d is 1, then c is 0; and

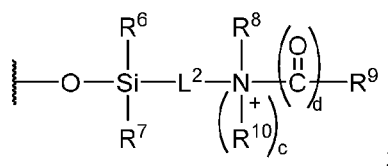
if n is 1, c is 1.

[000125] Another embodiment provides a phthalocyanine dye having the Formula (XX):



or a salt, stereoisomer, or tautomer thereof, wherein,

M is a metal or metalloid;



each Y is independently selected and Y is

L is a member selected from the group consisting of a direct link, or a covalent linkage, wherein said covalent linkage is linear or branched, cyclic or heterocyclic, saturated or unsaturated, having 1–60 atoms selected from the group consisting of C, N, P, O, and S, wherein L can have additional hydrogen atoms to fill valences, and wherein said linkage contains any combination of ether, thioether, amine, ester, carbamate, urea, thiourea, oxy or amide bonds; or single, double, triple or aromatic carbon-carbon bonds; or phosphorus-oxygen, phosphorus-sulfur, nitrogen-nitrogen, nitrogen-oxygen, or nitrogen-platinum bonds; or aromatic or heteroaromatic bonds;

Q is a reactive or an activatable group;

R⁶ and R⁷ are each independently optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl or optionally substituted heteroaralkyl;

R⁸, R⁹ or R¹⁰ are selected from substituent group (a) or substituent group (b) wherein,

(a) R⁸ is hydrogen, -L⁸-H, -L⁸-A or -L⁸-Z;

R⁹ is -L⁹-H, -L⁹-A, -(NH)_n-L⁹-Z or -(O)_n-L⁹-Z;

R¹⁰ is -L¹⁰-A -L¹⁰-Z; and

(b) R⁸ and R⁹ are connected with a bond to form a heterocyclyl substituted with -L⁹-Z and R¹⁰ is -L¹⁰-H or -L¹⁰-Z;

provided at least one of R⁸, R⁹ and R¹⁰ is a group containing Z;

Z is a water soluble group optionally substituted with A or L'-A;

L⁸, L⁹ and L¹⁰ are each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkylene, optionally substituted heterocyclene, optionally substituted arylene, optionally substituted aralkylene, optionally substituted heteroaralkylene, or optionally substituted heteroarylene, where the carbon atom of the alkylene, heteroalkylene, alkenylene, heteroalkenylene, cycloalkylene, heterocyclene, arylene, aralkylene, heteroaralkylene, or optionally substituted heteroarylene is further optionally substituted with Z and each nitrogen atom of the heteroalkylene or heteroalkenylene is optionally substituted with one or two L'-Z;

L' is each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkylene, optionally substituted heterocyclene, optionally

substituted arylene, optionally substituted aralkylene, optionally substituted heteroaralkylene, or optionally substituted heteroarylene;

A is a reactive group capable of forming a covalent bond with a thiol, hydroxyl, carboxyl or amino group of a second moiety, or a protected form thereof or a reacted form thereof;

c is 0 or 1;

d is 0 or 1;

n is 0 or 1;

provided that if d is 1, then c is 0; and if n is 1, then c is 0.

[000126] In some embodiments, M is Si or Ge.

[000127] In some embodiments, each group Z is independently selected from:

-C(O)OH,
 -(CH₂)_q(OCH₂CH₂)_v(CH₂)_qC(O)OH,
 -(CH₂CH₂O)_v(CH₂)_pC(O)OH,
 -(CH₂)_q(OCH₂CH₂)_vOR²²,
 -(CH₂CH₂O)_v(CH₂)_pOR²²,
 -(CH₂)_q(OCH₂CH₂)_vSR²²,
 -(CH₂CH₂O)_v(CH₂)_pSR²²,
 -O(CH₂)_vN[(CH₂CH₂O)_nCH₂CH₂OR²²]_t,
 -(CH₂)_q(OCH₂CH₂)_vN[(CH₂CH₂O)_wCH₂CH₂OR²²]_t,
 -(CH₂CH₂O)_m(CH₂)_pN[(CH₂CH₂O)_wCH₂CH₂OR²²]_t,
 -NH₂,
 -(CH₂)_qN[(CH₂CH₂O)_vCH₂CH₂OR²²]_t,
 -(CH₂)_qNR^b[(CH₂CH₂O)_wCH₂CH₂OR²²]_u,
 -(CH₂)_qN[(CH₂)_p(OCH₂CH₂)_vOR²²]_t,
 -(CH₂)_qN[(CH₂)_pSO₃H]_t,
 -(CH₂)_qNR^b[(CH₂)_pSO₃H]_u,
 -(CH₂)_qNR^b(CH₂)_pCH(SO₃H)₂,
 -(CH₂)_qN[(CH₂)_pS(O)_uOH]_t,
 -(CH₂)_qN[(CH₂)_pOSO₃H]_t,
 -(CH₂)_q(OCH₂CH₂)_v(CH₂)_qSO₃H,
 -(CH₂)_q(OCH₂CH₂)_v(CH₂)_qS(O)_uOH,
 -(CH₂)_q(OCH₂CH₂)_v(CH₂)_qOSO₃H,
 -SO₃H,
 -CH(SO₃H)₂,

$-\text{OSO}_3\text{H}$,
 $-\text{S}(\text{O})_u\text{OH}$,
 $-\text{PO}_3\text{H}$,
 $-\text{CH}(\text{PO}_3\text{H})_2$,
 $-(\text{CH}_2)_q\text{N}[(\text{CH}_2)_p\text{PO}_3^-]_t$,
 $-(\text{CH}_2)_q(\text{OCH}_2\text{CH}_2)_v(\text{CH}_2)_q\text{PO}_3\text{H}$,
 $-(\text{CH}_2)_q\text{N}[(\text{CH}_2)_p\text{OPO}_3\text{H}]_t$,
 $-\text{OPO}_3\text{H}$,
 $-(\text{CH}_2)_q(\text{OCH}_2\text{CH}_2)_v(\text{CH}_2)_q\text{P}(\text{O})(\text{OH})_2$,
 $-(\text{CH}_2)_q\text{N}[(\text{CH}_2)_p\text{P}(\text{O})(\text{OH})_2]_t$,
 $-\text{P}(\text{O})(\text{OH})_2$,

glutamate, aspartate, histidine, 1,3-beta-glucan and 1,4-beta-glucan;

each R^{22} is independently alkyl, haloalkyl, cycloalkyl or aryl;

each R^b is independently hydrogen, alkyl optionally substituted with $-\text{CO}_2\text{H}$, heteroalkylene optionally substituted with $-\text{CO}_2\text{H}$, haloalkyl or cycloalkyl;

each v , w and p are independently an integer from 1 to 10;

each q is independently an integer from 0 to 10;

t is 2 or 3; and

u is 1 or 2.

[000128] In some embodiments, each group Z is independently selected from:

$(\text{CH}_2)_q(\text{OCH}_2\text{CH}_2)_v\text{OR}^{22}$,
 $(\text{CH}_2)_q\text{O}(\text{CH}_2)_v\text{N}[(\text{CH}_2\text{CH}_2\text{O})_w\text{CH}_2\text{CH}_2\text{OR}^{22}]_t$,
 $-(\text{CH}_2)_q\text{N}[(\text{CH}_2)_p(\text{OCH}_2\text{CH}_2)_v\text{OR}^{22}]_t$,
 $-(\text{CH}_2)_q\text{N}[(\text{CH}_2)_p\text{SO}_3\text{H}]_t$,
 $-(\text{CH}_2)_q\text{NR}^b[(\text{CH}_2)_p\text{SO}_3\text{H}]_u$,
 $-(\text{CH}_2)_q\text{NR}^b[(\text{CH}_2)_p\text{CH}(\text{SO}_3\text{H})_2]_u$,
 $-\text{SO}_3\text{H}$,
 $-\text{CH}(\text{SO}_3\text{H})_2$,
 $-\text{PO}_3\text{H}$,
 $-(\text{CH}_2)_q\text{N}[(\text{CH}_2)_p\text{PO}_3\text{H}]_t$,
 $-(\text{CH}_2)_q\text{NR}^b[(\text{CH}_2)_p\text{PO}_3\text{H}]_u$, or
 $-(\text{CH}_2)_q\text{NR}^b(\text{CH}_2)_p\text{CH}(\text{PO}_3\text{H})_2$,

each R^{22} is independently alkyl, haloalkyl, cycloalkyl or aryl;

each R^b is independently hydrogen, alkyl, haloalkyl or cycloalkyl;

each v, w and p are independently an integer from 1 to 10;

each q is independently an integer from 0 to 10;

t is 2 or 3; and

u is 1 or 2.

[000129] In some embodiments, each group A is independently selected from:

-C(O)OR¹¹,

-NR¹²R¹³,

-NHC(O)R¹⁴,

-C(O)R¹⁵,

-OR¹⁶,

-SR¹⁶,

-OS(O)₂R¹⁷,

-OP(OR¹⁸)(NR¹⁹R²⁰),

-N=C=O;

-N=C=S,

-S-C≡N,

-SO₂-F,

-SO₂-Cl,

-SO₂-Br,

-S-SR²¹, or

a 5- or 6- membered dioxo-substituted heterocyclyl;

wherein each R¹¹ is independently hydrogen, alkyl, haloalkyl, alkenyl, heterocyclyl, aryl or heteroaryl, and each R¹¹ is independently optionally substituted with one to five groups each independently selected from halo, -SO₃H and -SO₂F;

each R¹² is independently hydrogen, alkyl or haloalkyl;

each R¹³ is aryl or heteroaryl, and each R¹³ is independently optionally substituted with one to five groups each independently selected from halo, -SO₃H and -SO₂F; or optionally R¹² and R¹³, together with the nitrogen to which they are attached, form a cyclic imide;

each R¹⁴ is independently optionally substituted haloalkyl or optionally substituted aralkyl;

each R¹⁵ is independently aryl optionally substituted with one to five groups each independently halo, heterocyclyl, -SO₃H or -SO₂F;

each R¹⁶ is independently aryl optionally substituted with one to five groups each independently halo or heterocyclyl;

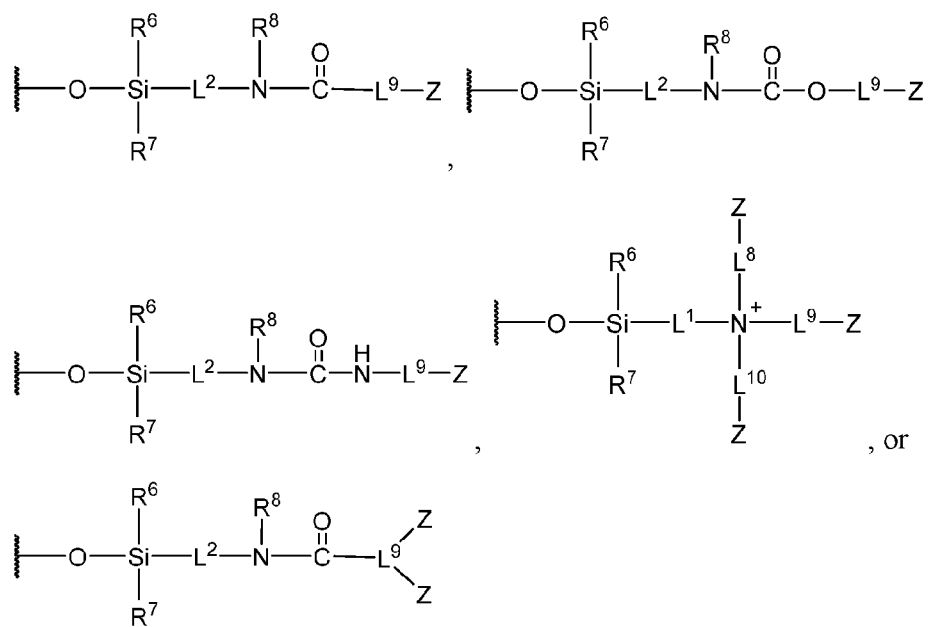
each R^{17} is independently optionally substituted alkyl, optionally substituted haloalkyl, optionally substituted alkenyl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, optionally substituted aryl or optionally substituted heteroaryl, wherein the heterocyclyl, aryl or heteroaryl is optionally substituted with one to five groups each independently selected from halo, $-SO_3H$, $-SO_2F$, and $-C(O)OR^c$;

each R^c is independently optionally substituted alkyl, optionally substituted haloalkyl, optionally substituted cycloalkyl or optionally substituted aryl;

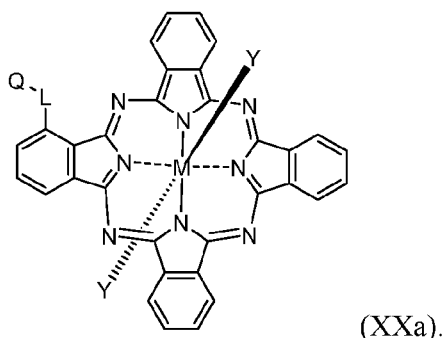
R^{18} , R^{19} and R^{20} are each independently optionally substituted alkyl or optionally substituted haloalkyl; and

R^{21} is heteroaryl.

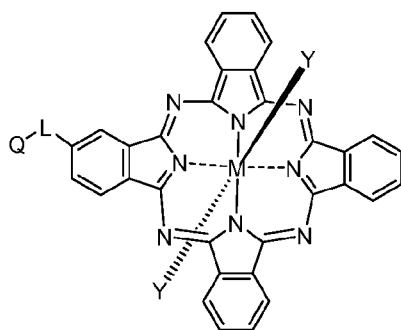
[000130] In some embodiments, each group Y is independently selected from:



[000131] One embodiment provides a phthalocyanine dye having the regiochemistry indicated with Formula (XXa):

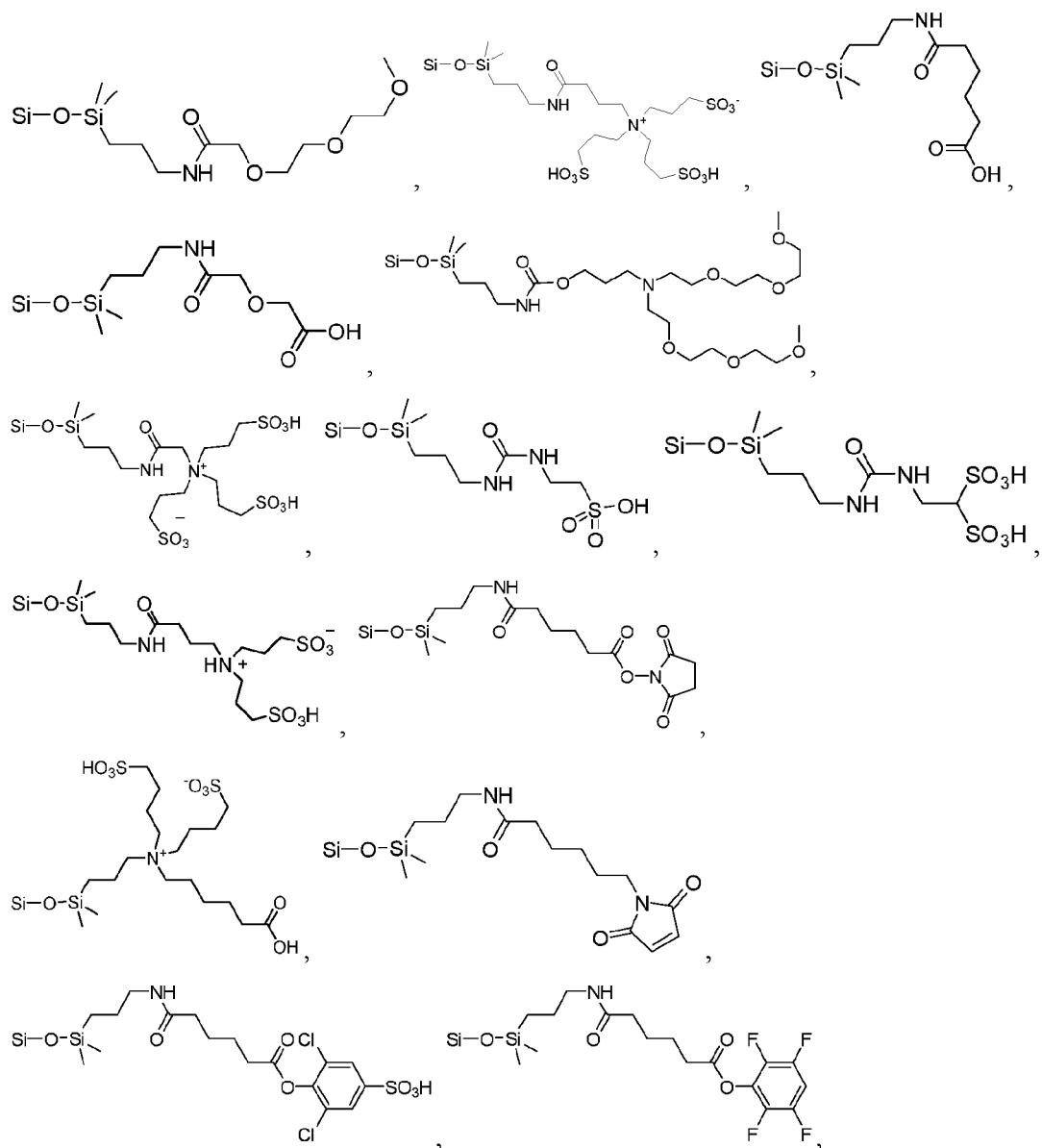


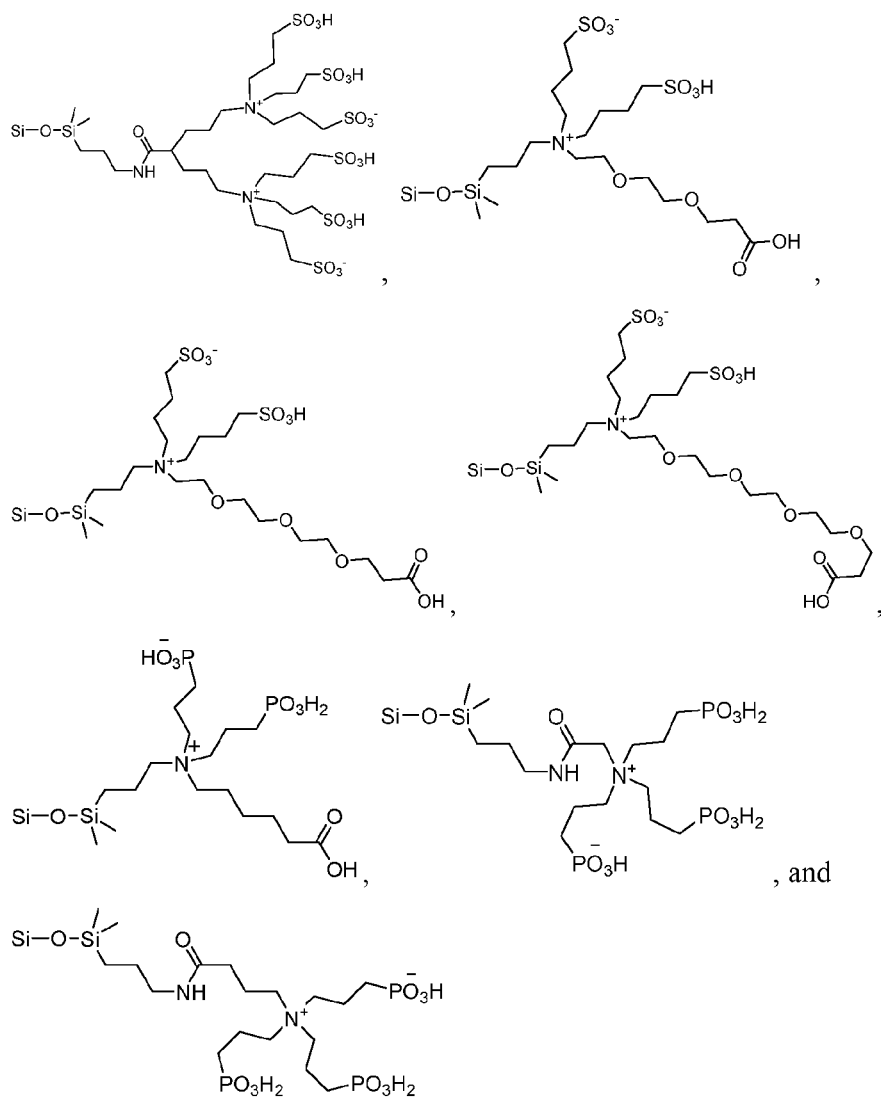
[000132] One embodiment provides a phthalocyanine dye having the Formula (XXb):



(XXb)

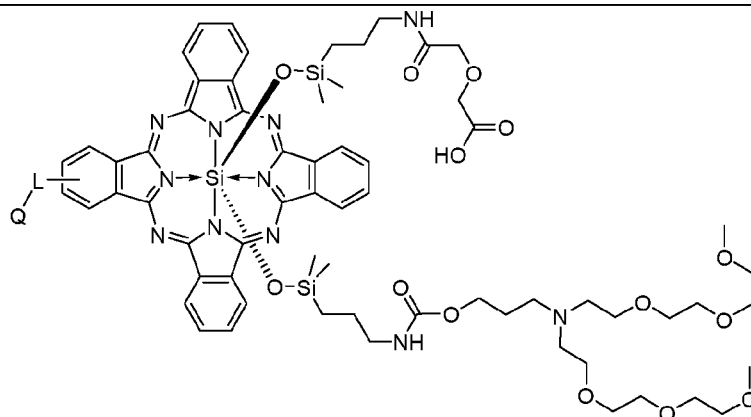
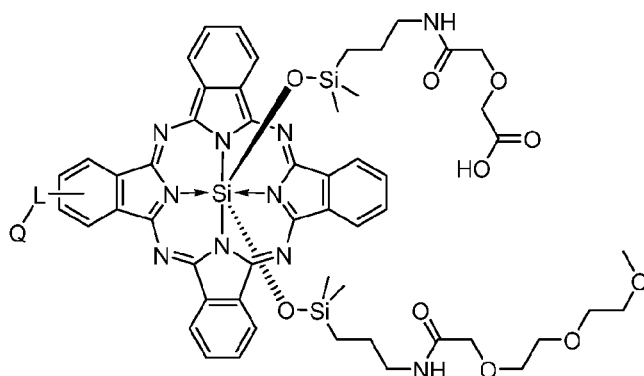
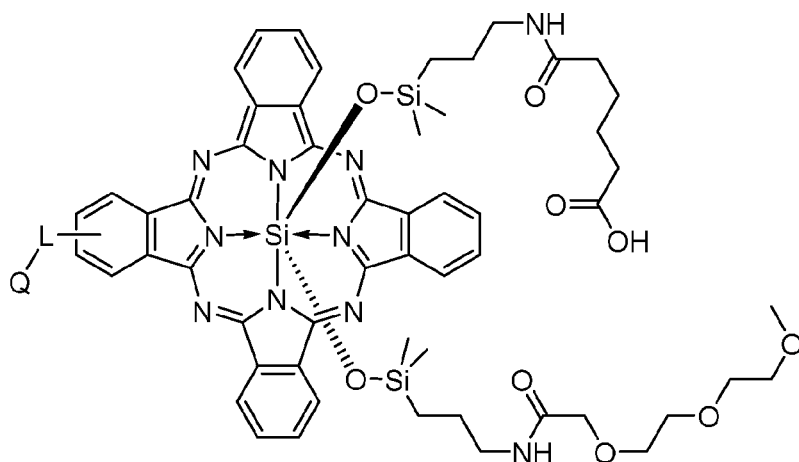
[000133] Another embodiment provides a compound of Formula (XX), wherein the M-Y group is independently selected from the group consisting of:



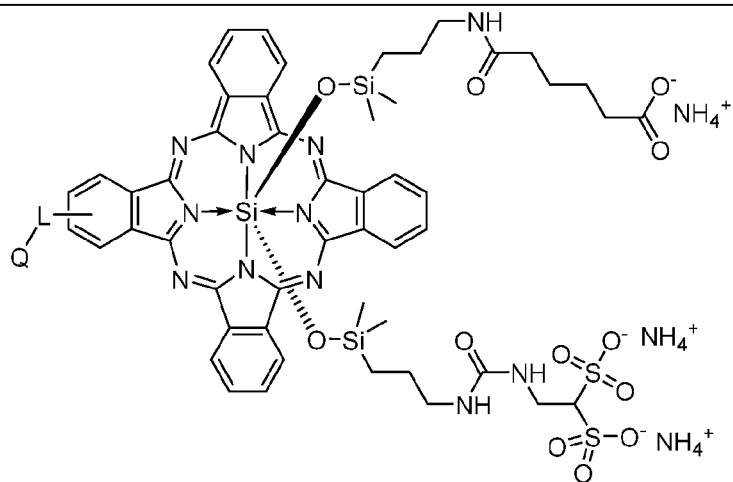
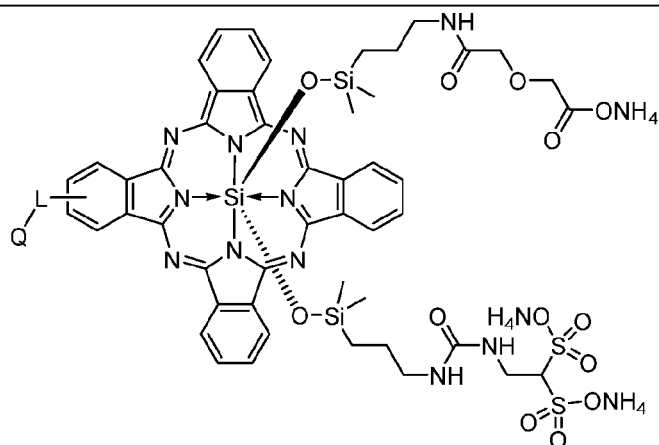
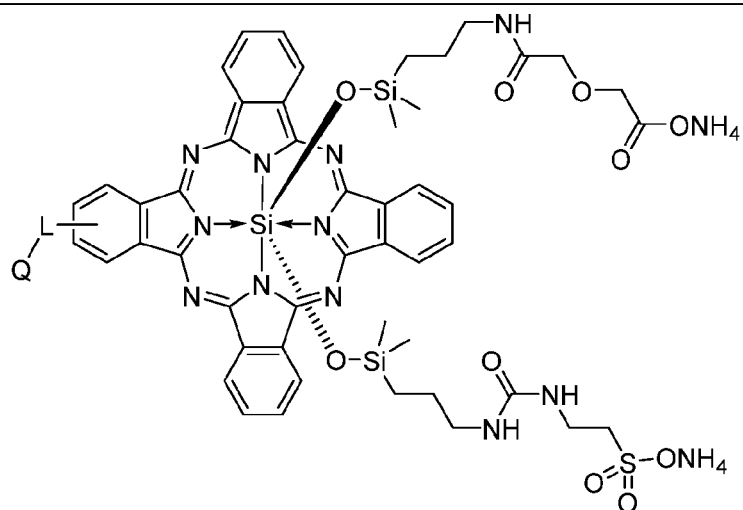


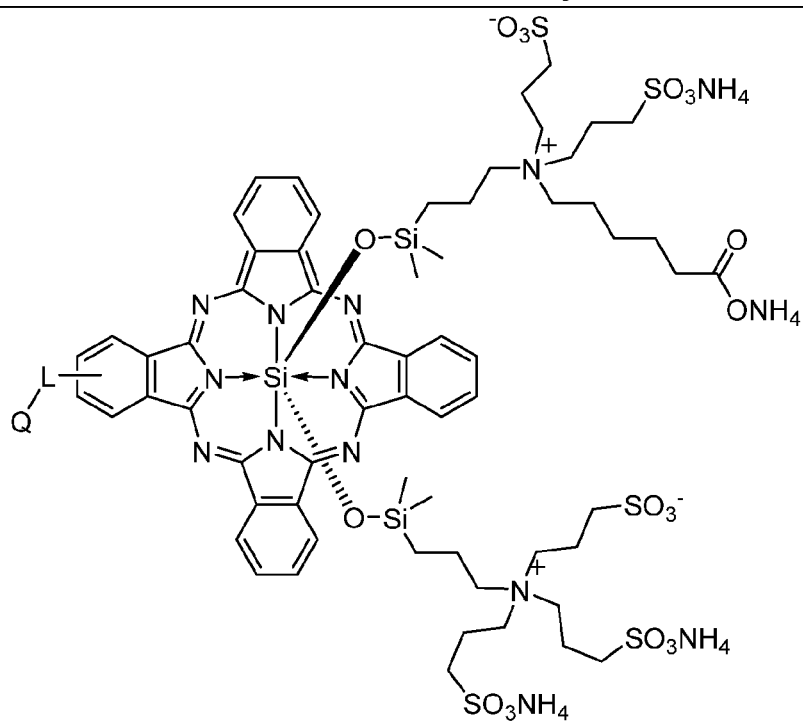
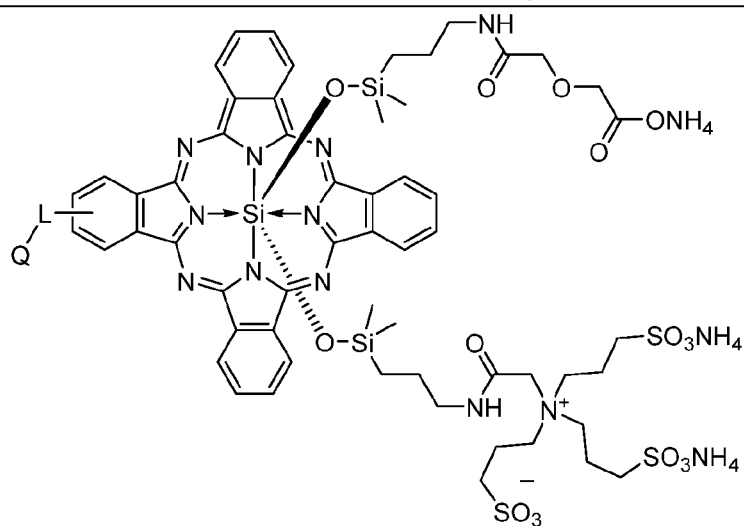
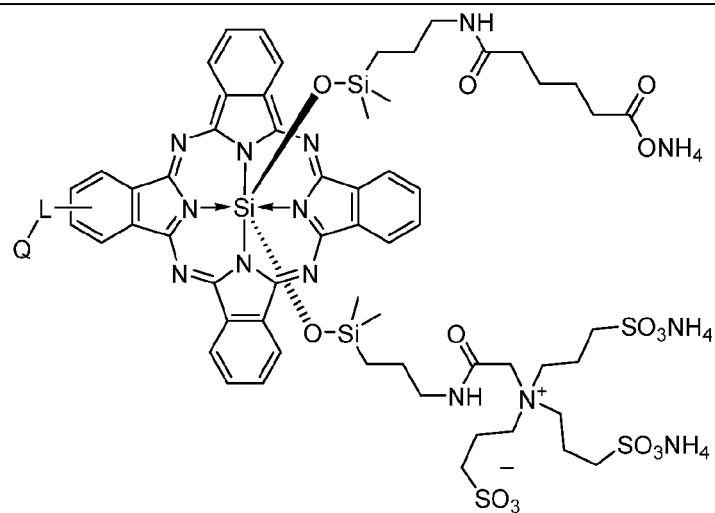
[000134] In some embodiments, the compound of Formula (XX) is selected from a compound in Table 2B.

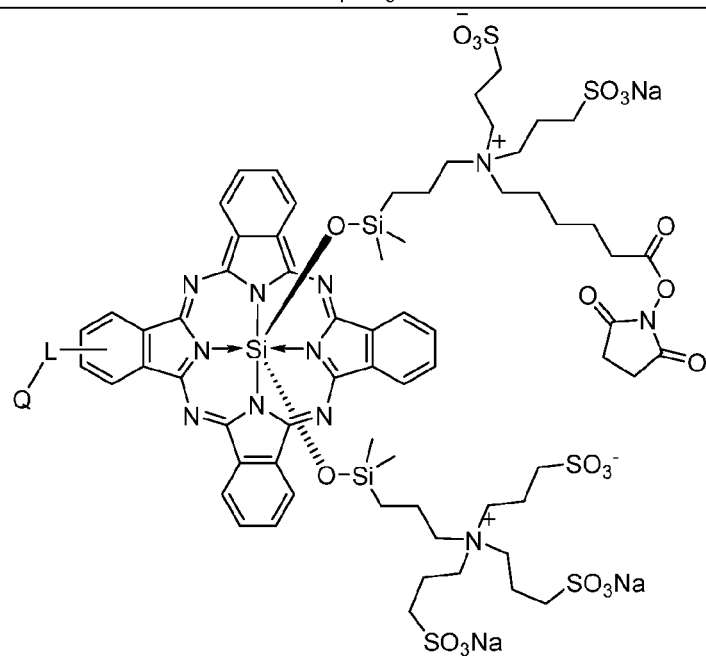
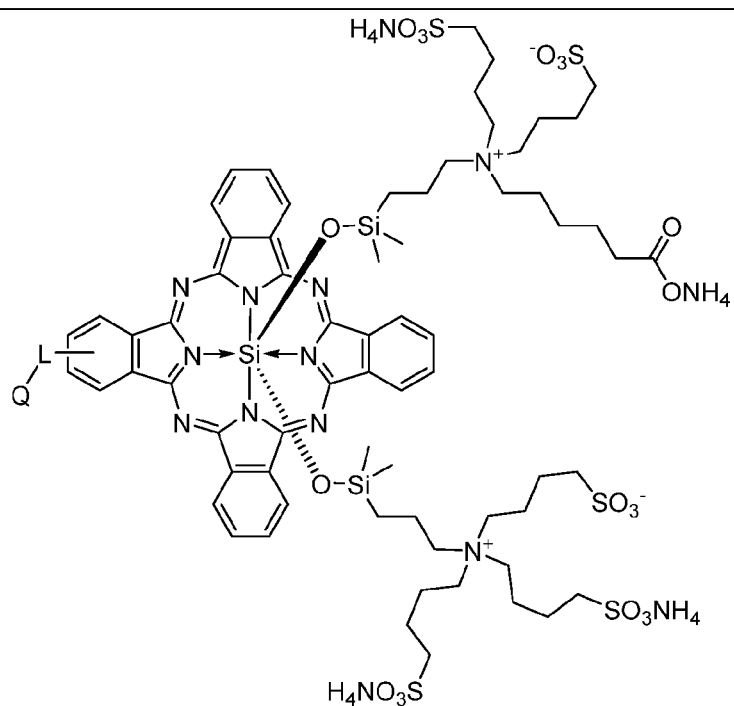
Table 2B

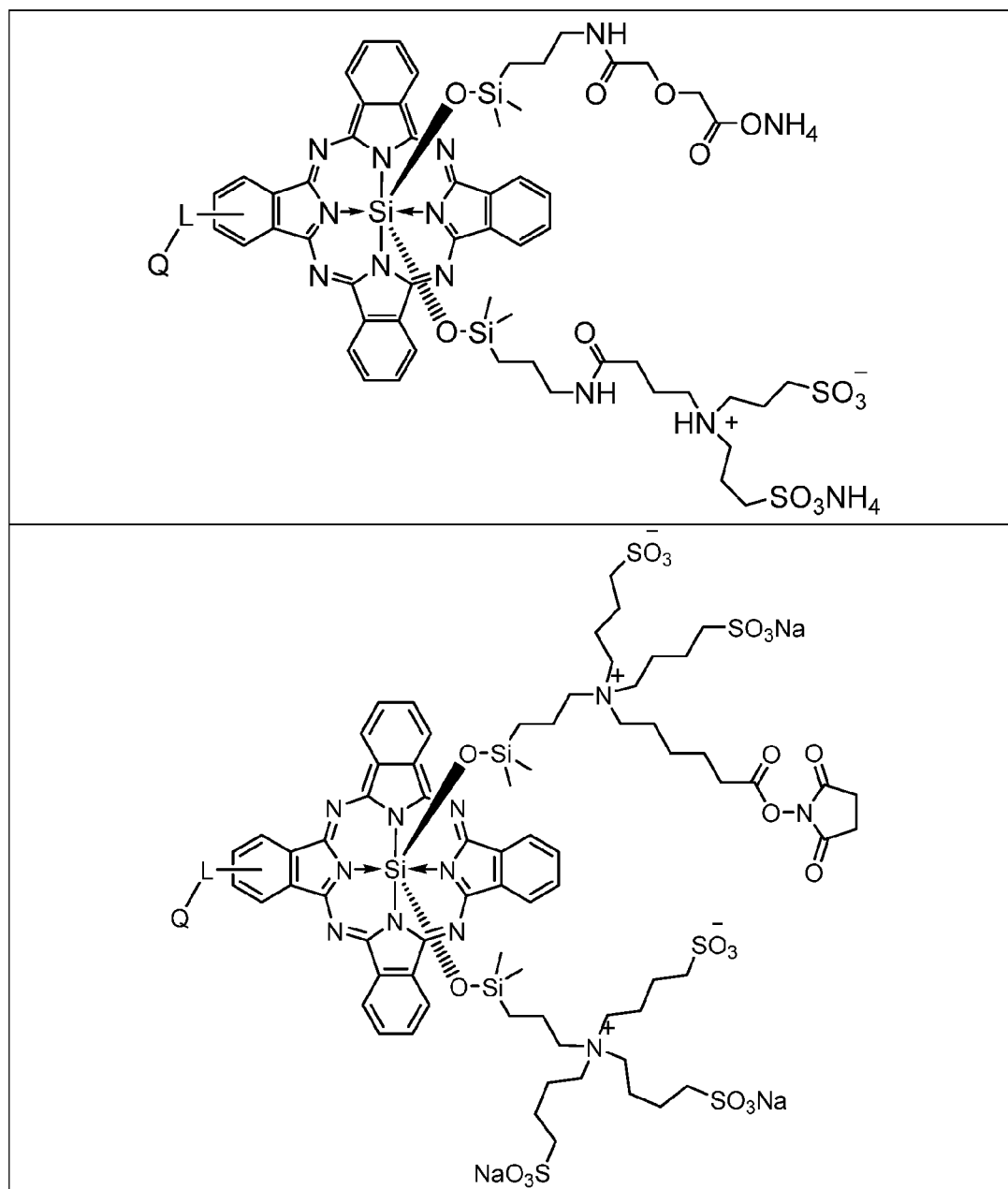


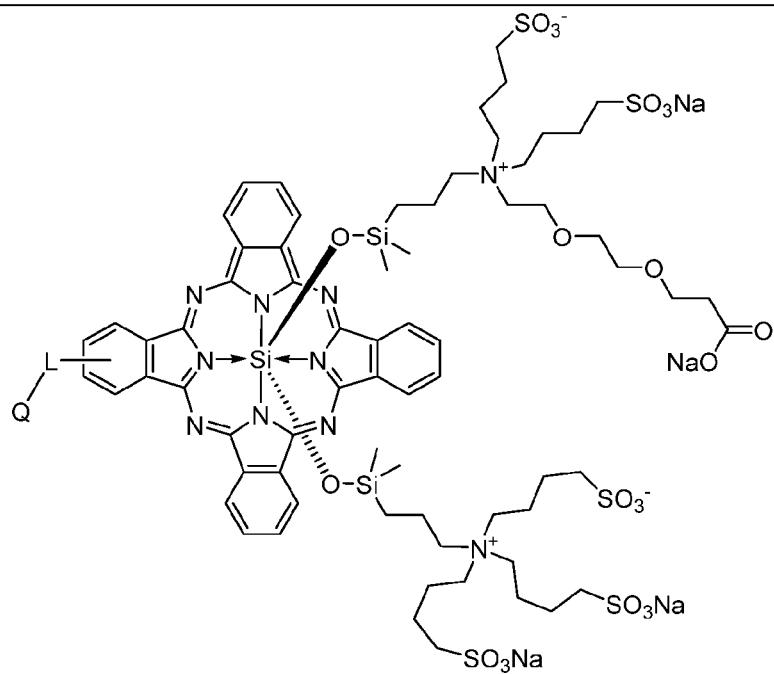
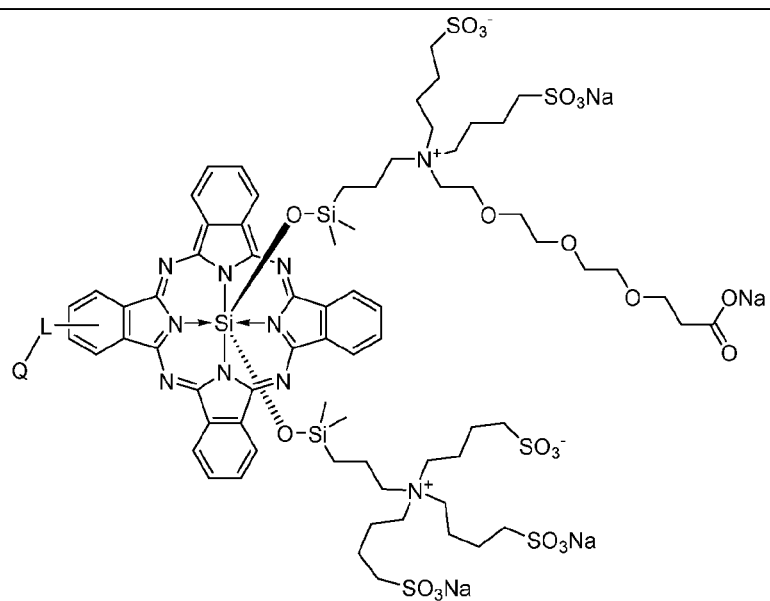


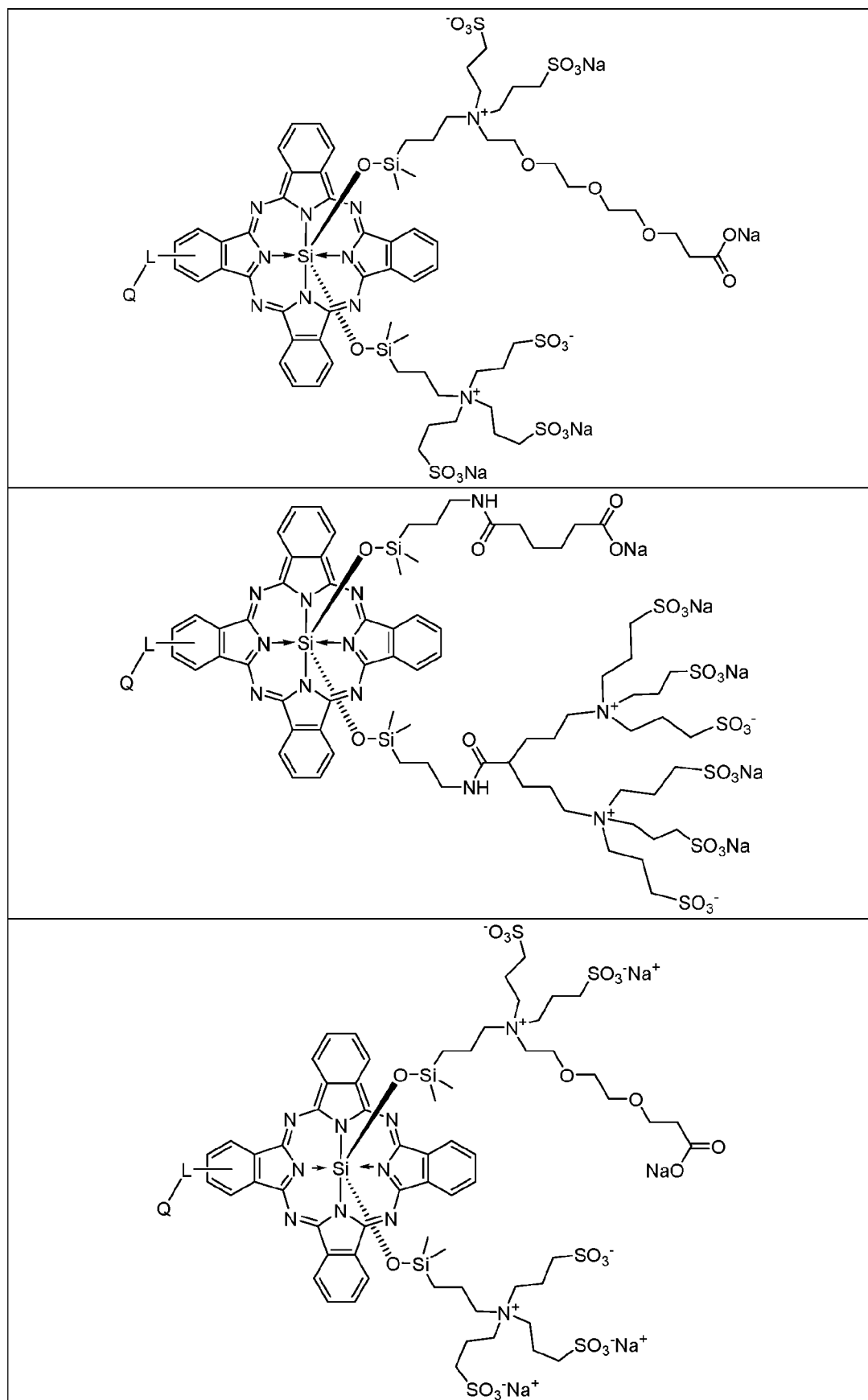


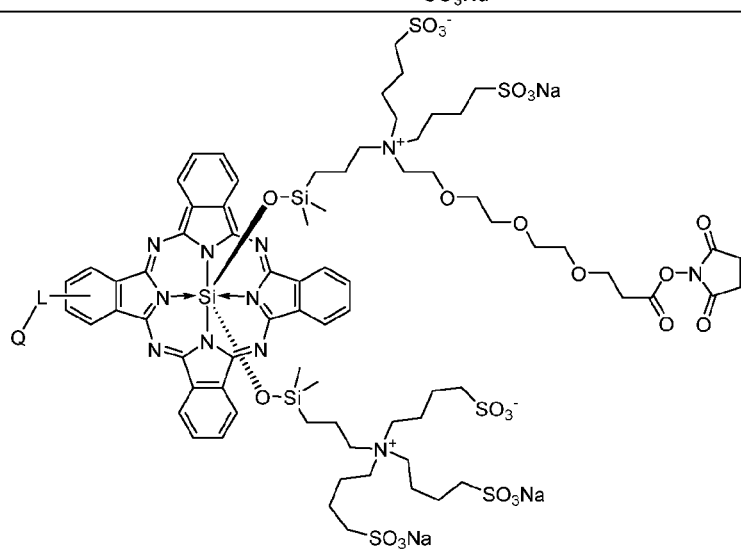
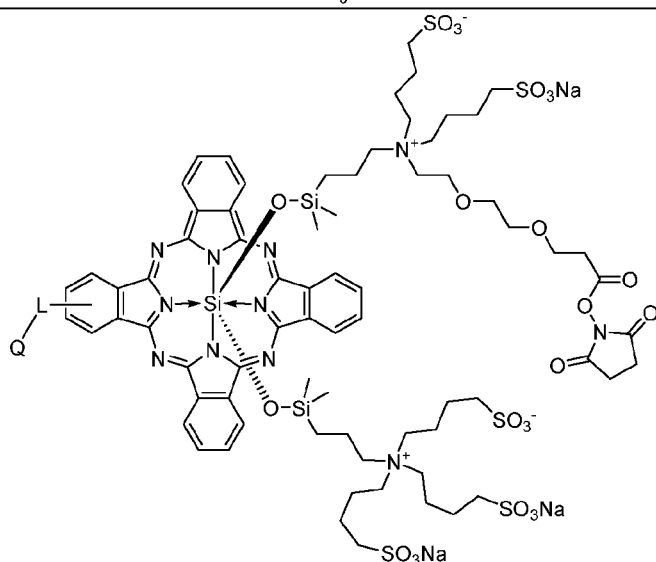
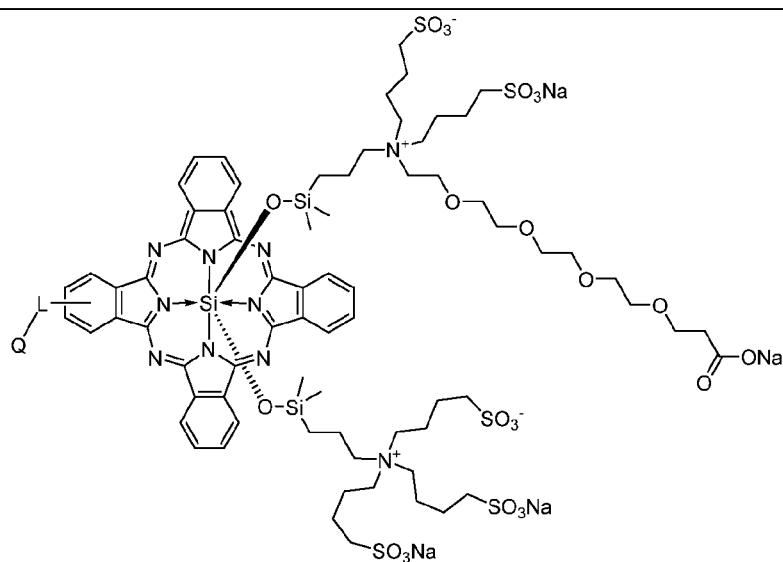


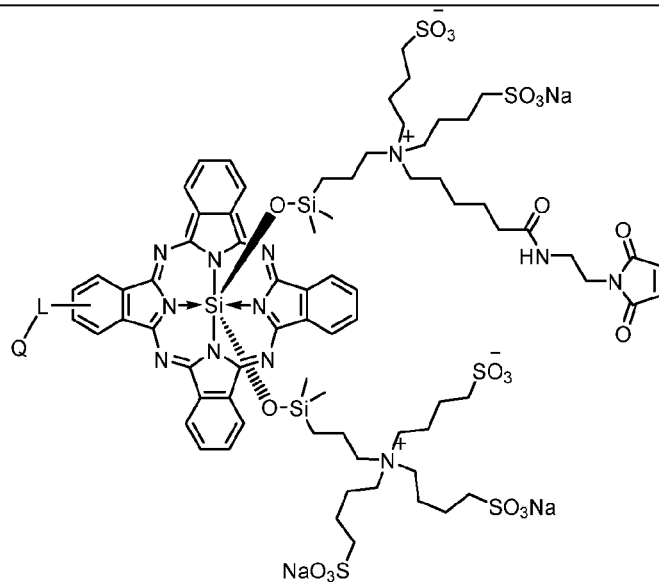
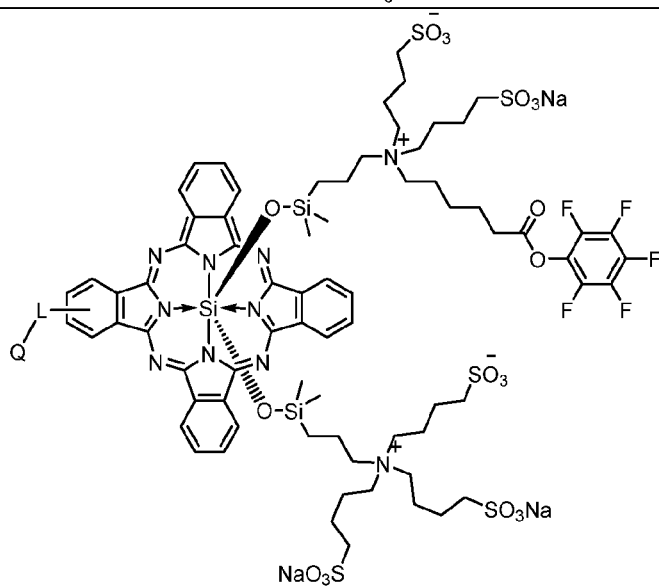
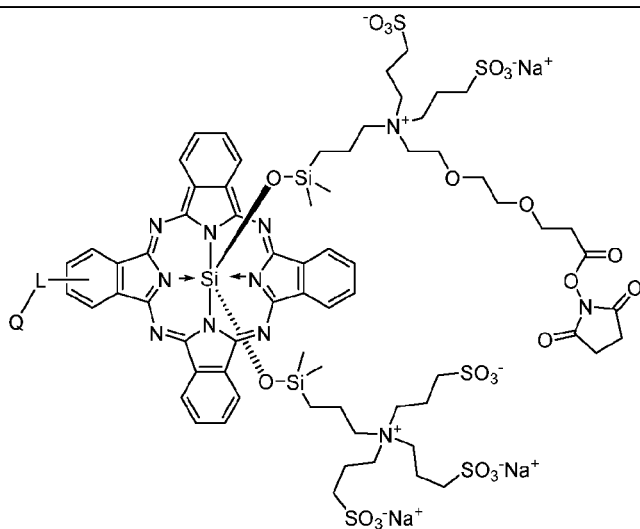












[000135] The compounds of this disclosure may contain one or more stereogenic centers and thus occur as racemates and racemic mixtures, enantiomerically enriched mixtures, single enantiomers, individual diastereomers and diastereomeric mixtures. The compounds of the present disclosure may, either by nature of stereogenic centers or by restricted rotation, be present in the form of isomers (e.g., enantiomers, diastereomers).

[000136] It will also be appreciated that when two or more stereogenic centers are present in the compounds of the disclosure, several diastereomers and enantiomers of the exemplified structures will often be possible. It is intended that pure stereoisomers, pure diastereomers, pure enantiomers, and mixtures thereof, are within the scope of the disclosure. When compounds contain stereochemistry, the compounds are designated as ‘(racemic)’ or “rac” if the stereoisomers have not been separated and ‘(R) or (S)’ if the stereoisomers have been resolved.

[000137] All isomers, whether separated, pure, partially pure, or in racemic mixture, of the compounds of this disclosure are encompassed within the scope of this disclosure. The purification of said isomers and the separation of said isomeric mixtures may be accomplished by various methods. For example, diastereomeric mixtures can be separated into the individual isomers by chromatographic processes or crystallization, and racemates can be separated into the respective enantiomers either by chromatographic processes on chiral phases or by resolution.

[000138] The compounds of the present disclosure include all cis, trans, syn, anti, entgegen (*E*), and zusammen (*Z*) isomers as well as mixtures thereof. The compounds of the present disclosure may also be represented in multiple tautomeric forms, in such instances, the present disclosure expressly includes all tautomeric forms of the compounds described herein, even though only a single tautomeric form may be represented. In addition, where a term used in the present disclosure encompasses a group that may tautomerize, all tautomeric forms are expressly included thereunder. For example, hydroxy substituted heteroaryl includes 2-hydroxypyridine as well as 2-pyridone, 1-hydroxyisoquinoline as well as 1-oxo-1,2-dihydroisoquinoline, and the like. All such isomeric forms of such compounds are expressly included in the present disclosure.

[000139] The compounds of the present disclosure include the compounds themselves, as well as their salts, solvate, solvate of the salt and their prodrugs, if applicable. Salts for the purposes of the present disclosure are preferably pharmaceutically acceptable salts of the compounds according to the present disclosure. Salts which are not themselves suitable for pharmaceutical uses but can be used, for example, for isolation or purification of the

compounds according to the disclosure are also included. A salt, for example, can be formed between an anion and a positively charged substituent (e.g., amino) on a compound described herein. Suitable anions include chloride, bromide, iodide, sulfate, nitrate, phosphate, citrate, methanesulfonate, trifluoroacetate, and acetate. Likewise, a salt can also be formed between a cation and a negatively charged substituent (e.g., carboxylate) on a compound described herein. Suitable cations include sodium ion, potassium ion, magnesium ion, calcium ion, and an ammonium cation such as tetramethylammonium ion.

[000140] The present disclosure also encompasses all suitable isotopic variants of the compounds according to the present disclosure, whether radioactive or not. An isotopic variant of a compound according to the present disclosure is understood to mean a compound in which at least one atom within the compound according to the present disclosure has been exchanged for another atom of the same atomic number, but with a different atomic mass than the atomic mass which usually or predominantly occurs in nature. Examples of isotopes which can be incorporated into a compound according to the present disclosure are those of hydrogen, carbon, nitrogen, oxygen, fluorine, chlorine, bromine and iodine, such as ^2H (deuterium), ^3H (tritium), ^{13}C , ^{14}C , ^{15}N , ^{17}O , ^{18}O , ^{18}F , ^{36}Cl , ^{82}Br , ^{123}I , ^{124}I , ^{125}I , ^{129}I and ^{131}I . Particular isotopic variants of a compound according to the present disclosure, especially those in which one or more radioactive isotopes have been incorporated, may be beneficial, for example, for the examination of the mechanism of action or of the active compound distribution in the body. Compounds labelled with ^3H , ^{14}C and/or ^{18}F isotopes are suitable for this purpose. In addition, the incorporation of isotopes, for example of deuterium, can lead to particular therapeutic benefits as a consequence of greater metabolic stability of the compound, for example an extension of the half-life in the body or a reduction in the active dose required. In some embodiments, hydrogen atoms of the compounds described herein may be replaced with deuterium atoms. In certain embodiments, “deuterated” as applied to a chemical group and unless otherwise indicated, refers to a chemical group that is isotopically enriched with deuterium in an amount substantially greater than its natural abundance. Isotopic variants of the compounds according to the present disclosure can be prepared by various, including, for example, the methods described below and in the working examples, by using corresponding isotopic modifications of the particular reagents and/or starting compounds therein.

[000141] In certain embodiments, the phthalocyanine dye compound of Formula (I) is unconjugated or used as a free dye for biomedical imaging, including, but not limited to, magnetic resonance imaging (MRI), fluorescence imaging, positron emission tomography

(PET) and photoacoustic imaging. In certain embodiments, provided herein are kits comprising the phthalocyanine dye compound of Formula (I) and instructions for its use. In certain embodiments, provided herein are kits comprising the phthalocyanine dye compounds of Formula (I) and an additional reagent, such as an additional detection reagent, reference or standards, luminescence standards, enzymes, antibodies, enzyme inhibitors, or solvents.

[000142] The phthalocyanine dye compounds provided herein are photoactivatable dyes, that absorb at a wavelength generally between 600 nm and 810 nm. In some embodiments, the wavelengths at which the phthalocyanine dye compounds absorb and are excited is between about 600 nm and 810 nm, between about 640 nm and 750 nm, or between about 660 and 710 nm. In some embodiments, the wavelengths at which the phthalocyanine dye compounds absorb and are excited is about 650 nm, 660 nm, 670 nm, 680 nm, 690 nm, or 700 nm. In some embodiments, the maximum wavelength for absorption is no more than about 690 nm, about 680 nm, about 675 nm, or about 670 nm.

B. CONJUGATES OF PHTHALOCYANINE DYE COMPOUNDS

[000143] Provided are compositions and combinations containing the phthalocyanine dye compounds described herein conjugated to a targeting molecule that binds to a target molecule, such as a target molecule on the surface of a cell or pathogen. In some embodiments, the conjugates contain the phthalocyanine dye compounds described herein conjugated to a biomolecule, such an antibody, antibody fragment, antibody-like molecule, DNA probe, avidin, streptavidin, lipid, biochemical analog, polymer, peptide, or drug. In some embodiments, the provided conjugates and combinations are to be employed in methods and uses described herein.

[000144] In some embodiments, conjugates of the phthalocyanine dye compounds described herein, such as a Formula (X), Formula (0), Formula (I), or Formula (II) compound conjugated to a targeting molecule are used in methods of treatment, such as to inhibit growth and/or kill cells, such as cancer tumor cells. In some embodiments, conjugates of the phthalocyanine dye compounds described herein, such as a Formula (X), Formula (0), Formula (I), or Formula (II) compound conjugated to a targeting molecule are used in methods of imaging, whereby the conjugates as a result of the targeting molecule bind to a target, such as on a cell (e.g., a specific type of tumor cell) or on a pathogen, and the Formula (X), Formula (0), Formula (I), or Formula (II) compound of the conjugate, when exposed to an appropriate wavelength of light permits imaging of the targeted cell type. Such imaging can be used in conjunction with treatment with the conjugate or separately.

[000145] In some embodiments, the targeting molecule of the conjugate binds to a target molecule expressed on the surface of a cell or pathogen, such as a proliferating cell, a cancer cell, a cell in hyperplasia, a tumor cell, a cell in the tumor microenvironment (TME), a cell of the immune system, a neuron, or a pathogen. In some embodiments, the cell is a stem cell, a proliferating cell, a cell in a hyperplasia, or a pathogen-infected cell. In some embodiments, the pathogen is selected from among viruses, bacteria, fungi, biofilms, and other prokaryote cell systems. In some examples, the targeting molecule in the provided compositions binds to a target molecule on the surface of a certain cancer or tumor cell or a cell in the TME. In some embodiments, the cell of the immune system is a leukocyte, such as a neutrophil, an eosinophil, a basophil, a lymphocyte, or a monocyte. In some embodiments, the targeting molecule bind to a target molecule expressed on the surface of one or more immune cells, such as lymphocytes (T-cells, B-cells, and NK cells), neutrophils, and/or monocytes or macrophages. In some examples, the targeting molecule in the provided compositions binds a target molecule expressed on the surface of immunosuppressive cells, e.g., TAMs, tDCs, MDSCs, TANs, CAFs, and/or regulatory T cells (Tregs). In some of the provided compositions, the targeting molecule binds an immune checkpoint inhibitor on the surface of immunosuppressive cells. In some embodiments, the targeting molecule bind to a target molecule on the surface of a neuron, such as a peripheral nervous system neuron or a central nervous system neuron. In some embodiments, the neuron is a nociceptor such as a thermal nociceptor, mechanical nociceptor, chemical nociceptor, or polymodal nociceptor. In some embodiments, the targeting molecule binds to a pathogen, such as a virus, bacterium, fungus, biofilm, or other prokaryote cell system. In some embodiments, the pathogen is a gram-negative or gram-positive bacterium.

[000146] In some embodiments, the target molecule to which the targeting molecule of the stable conjugate binds includes an antigen, a polypeptide, a peptide, a lipid, or a carbohydrate, or a combination thereof. In some embodiments, the target molecule is a cell surface molecule.

[000147] In some embodiments, the one or more target molecule(s) is/are selected from among cell membrane phospholipids, prokaryotic peptidoglycans, bacterial cell envelop proteins, viral capsid proteins, 1-40- β -amyloid, 1AR, 2AR, 4-1BB (CD137), 5AC, 5'-nucleotidase, 5T4, ACTHR, activated factor IX, activin receptor-like kinase 1, ACVR2B, adenocarcinoma antigen, ALK, alpha-4-integrin, alpha-5-beta-3 integrin, alpha-5-beta-5 integrin, alpha-fetoprotein (AFP), aminopeptidase N, amyloid, Ang-2, angiopoietin 2, angiopoietin 3, ANPA, ANPB, anthrax protective antigen, anthrax toxin, Anti-alpha 1

Fetoprotein, AOC3, AOC3 (VAP-1), APA, APN, APP, AT1, AXL, B1, B2, B7-DC, B7-H3, Bacillus anthracis anthrax, bacterial cell envelop proteins, BAFF, BAFF-R, BAGE1, BAGE2, B-cell receptor BB1, BB2, BB4, BCMA, BCR complex, Bcr-Abl, beta amyloid, B1, B-lymphoma cell, Bombesin receptor, BRAF, BRAF(V600E), BRCA, BTK, C1s, C242 antigen, C5, CAIX, calcitonin gene-related peptide (CGRP), calcitonin gene-related peptide alpha, calcitonin receptor, cancer antigen 125 (CA125), Canis lupus familiaris IL31, Caprin-1, carbonic anhydrase 9 (CA-IX), cardiac myosin, CCK1, CCK2, CCL11 (eotaxin-1), CCR2, CCR4, CCR5, CD2, CD3, CD3 epsilon, CD3 T cell co-receptor, CD4, CD5, CD6, CD7, CD10, CD11, CD11a, CD13, CD14, CD15, CD18, CD19, CD20, CD22, CD23 (IgE receptor), CD25, CD27, CD28, CD30 (TNFRSF8), CD33, CD34, CD37, CD38, CD40, CD41 (integrin alpha-IIb), CD44, CD44 v6, CD45, CD47, CD51, CD52, CD68, CD70, CD74, CD79B, CD80, CD90, CD97B, CD123, CD125, CD133, CD134/OX40/TNFRSF4, CD147 (Basigin), CD154 (CD40L), CD200, CD206, CD271, CD276, CD276/B7-H3, CD278 (aka ICOS), CD319, CDK 4/6, CDS, CEA (Carcinoembryonic Antigen), CEACAM1, CEACAM3, CEACAM5, CEACAM6, CEA-related antigen, cell membrane phospholipids, cell surface plectin-1, cell-surface annexin-1, CFD, chemokine receptors, c-KIT, Claudin 18 Isoform 2, CLDN18.2, Clostridium difficile, clumping factor A, c-Met, coagulation factor III, complement C5a., Cripto-1, CRLR, CSF1, CSF1R, CSF2, CTGF, CTLA-4, CXCR2, CXCR4 (CD184), CXCR4 antagonist, cytomegalovirus, cytomegalovirus glycoprotein B, dabigatran, DCC, dendritic cell-associated lectin 2, DLL3, DLL4, DPP4, DR5, E. coli shiga toxin type-1, E. coli shiga toxin type-2, E2 glycoprotein, ebolavirus glycoprotein, EGFL7, EGFR/ERBB1/HER1, EGFR extracellular domain III, EGFRvIII, EML4-ALK, EMR1, endoglin, Endosialin, endothelial cell Anxa-1, endotoxin, EP2, EP4, EpCAM, EphA2, Ephrin ligands, Ephrin receptor, ephrin receptor A3, Escherichia coli, ET receptors, F protein of respiratory syncytial virus, Factor X, FAP, FAS-ligand, FCGRT, FGF 23, FGFR, FGFR2, fibrin II, beta chain, Fibronectin, Fibronectin ED-B, fibronectin extra domain-B, folate hydrolase, folate receptor 1, folate receptor alpha, folate-binding protein, frizzled receptors, G protein coupled receptors of the Family B (Secretin receptor-like) like), GAGE1, GAGE2, GAGE3, GAGE4, GAGE6, gangliosides (such as GD2, GD3, GM1 and GM2), GARP/inactive TGF- β complex, GCGR, GD2 ganglioside, GD3 ganglioside, GDF-8, gelatinase B, GPCR (glucocorticoid-induced tumor necrosis factor receptor), GLP-1 receptor, Glypican-3, GMCSF receptor α -chain, GP120, gp72, gpA33, GP100, GPNMB, G-protein coupled receptors of the Family A (Rhodopsin-like), G-protein coupled receptors of the Family C (Metabotropic Glutamate Receptor-like), growth differentiation factor 8, GUCY2C,

hemagglutinin (HA), Heparin sulfates, hepatitis B surface antigen, hepatitis B virus, HER1/EGFR, HER2/ERBB2/neu, HER2/neu, HER3/ERBB3, HER4, HGF receptor, histone complex, HIV-1, HLA-DR 10 β , HLA-DR antigen, HMFG, HNGF, HPV 16/18 and E6/E7 antigens, Hsp90, hTERT, human scatter factor receptor kinase, human TNF, human beta-amyloid, ICAM-1, ICAM-1 (CD54), ICOSL, IgE, IgE Fc region, IGF-1 receptor (CD221), IGHE, ILGF2, ILT3, influenza A virus hemagglutinin, integrin α 4 β 7, integrin α 5 β 1, integrin α V β 3, integrin α 4, integrin α 4 β 7, integrin α 5 β 1, integrin α Ib β 3, integrin α V β 3, integrin β 7, interferon receptor, interferon α / β receptor, interferon gamma-induced protein, interleukin-1 (IL-1), interleukin-1 alpha, interleukin-1 β , interleukin-2 (IL-2), interleukin-3 (IL-3), interleukin-4 (IL-4), interleukin-5 (IL-5), interleukin-6 (IL-6), interleukin-7 (IL-7), interleukin-8 (IL-8), interleukin-9 (IL-9), interleukin-10 (IL-10), interleukin-11 (IL-11), interleukin-12 (IL-12), interleukin-13 (IL-13), interleukin-15 (IL-15), interleukin-17 (IL-17), interleukin-17A (IL-17A), interleukin-17F (IL-17F), interleukin-19 (IL-19), interleukin-20, interleukin-22, interleukin-23, interleukin-23 (IL-23), interleukin-23A, interleukin receptor (e.g., IL-2R, IL-3R, IL-4R α , IL-6R, IL-11R, IL-13R, IL-31RA), ITGA2 (CD49b), ITGAM, ITGB2 (CD18), JAK1, JAK2, Kalikrien-9, kallikrein, KIR, KIR2D, KIT, LAG-3, Lewis-Y antigen, LFA-1 (CD11a), LH receptor (LHR), luteinizing-releasing hormone receptor, LINGO-1, lipoteichoic acid, LIV-1, LOXL2, LPA1, LRRC15, L-selectin (CD62L), LTA, LYPD3, MAC-1, MAGE 1, MAGE 2, MAGE 3, MAGE 4, MART1, MASP-2, MCAM, MC1R, MCP-1, MCSF, MEK1, MEK2, member 1 (SLITRK1), member 2 (SLITRK2), member 3 (SLITRK3), member 4 (SLITRK4), member 5 (SLITRK5), member 6 (SLITRK6), Mesothelin, MET, metalloproteinases, MIF, MS4A1, MSLN, MST1R (aka RON), mTOR, MUC1 (episialin), MUC16, mucin CanAg, mucins, mucosal addressin cell adhesion molecule 1 (MAdCAM-1), mutant p53, mutant Ras, myelin-associated glycoprotein, myostatin, NACP, NCA-90 (granulocyte antigen), nectin-4, Nepriylisin, Neu (cell-surface Nucleolin), neural apoptosis-regulated proteinase 1, Neuropilin-1 (NRP1), Neuropilin-2, NG2, NGNA ganglioside, NK1, NK2, NK3, NKG2A, NMB-R, NOGO-A, Notch receptor, Notch-1, NRP1, NTR2, NTR3, nuC242, NY-ESO-1, OT-R, OX40, oxLDL, *P. aeruginosa* type III secretion system, p32 (p32/gC1qR/HABP1), p75, p97 melanoma antigen, PAC1, PAR1, Patched (PTCH), PCDC1, PCSK9, PD-1, PDFG receptors, PDGF receptor, PDGF-R α , PD-L1, PDT, PEM antigen, phosphate-sodium co-transporter, phosphatidylserine, platelet-derived growth factor receptor beta, plexins, PMSA, prohibitin, prokaryotic peptidoglycans, prostatic carcinoma cells, Protease- cleaved collagen IV, protein tyrosine kinase 7, proteinase 3, PSA, *Pseudomonas aeruginosa*, PSMA, PTK7, purinergic P2X family (e.g. P2X1-5), rabies virus G

glycoprotein, rabies virus glycoprotein, RAMP1, RAMP2, RAMP3 patched, RANKL, RBB3, respiratory syncytial virus, RET, RET receptor, RGMA, RHD, Rhesus factor, root plate-specific spondin 3, ROR1, ROS, ROS1, RSVFR, RTN4, *S. aureus* alpha toxin, *S. aureus* bi-component leukocidin, sclerostin, SDC1, selectin P, serum amyloid A protein, serum amyloid P component, SK1 antigen, SLAMF7, SMO, smoothened, SOST, sphingosine-1-phosphate, SRC, sst1, sst2A, sst2B, sst3, sst4, sst5, *Staphylococcus aureus*, *Staphylococcus aureus* alpha toxin, STEAP1, TAG-72, tau protein, T-cell receptor (TCR), TEM1, TEMs, tenascin C, tenascin glycoproteins, TFPI, TGFBR2, TGFBR1, TGF- β , Tie-1, Tie-2, TIGIT, TIM-3, TNF, TNFR superfamily member 4, TNF- α , TR1, TRAIL-R1, TRAIL-R2, TRAP, Trk-A, Trk-B, Trk-C, TROP-2, TRPA, TRPC, TRPM, TRPML, TRPP (e.g. TRPV1-6, TRPA1, TRPC1-7, TRPM1-8, TRPP1-5, TRPML1-3), TRPV, TSC1, TSC2, TSH receptor, TSLP, tumor antigen CTA16.88, tumor necrosis factor alpha (TNF- α), tumor specific glycosylation of MUC1, tumor-associated glycoprotein 72 (TAG72), TWEAK receptor, TYRP1 (glycoprotein 75), VEGF receptors (VEGFR1 or Flt-1, VEGFR2 or FLK-1/KDR and VEGF-3 or FLT-4), VEGFA, vimentin, viral capsid proteins, voltage-gated ion channels, VPAC1, VPAC2, VSIR, VWF, Wilms tumor 1, Y1 receptor, Y2 receptor, Y4 receptor, Y5 receptor, and Zaire ebolavirus glycoprotein.

[000148] In some embodiments, the one or more target molecule(s), such as a cell surface target molecule, is/are selected from among HER1/EGFR, HER2/ERBB2, CD20, CD25 (IL-2Ra receptor), CD33, CD52, CD133, CD206, CEA, CEACAM1, CEACAM3, CEACAM5, CEACAM6, cancer antigen 125 (CA125), alpha-fetoprotein (AFP), Lewis Y, TAG72, Caprin-1, mesothelin, PDGF receptor, PD-1, PD-L1, CTLA-4, IL-2 receptor, vascular endothelial growth factor (VEGF), CD30, EpCAM, EphA2, Glypican-3, gpA33, mucins, CAIX, PSMA, folate-binding protein, gangliosides (such as GD2, GD3, GM1 and GM2), VEGF receptor (VEGFR), VEGFR2, VEGF-A, integrin α V β 3, integrin α 5 β 1, ERBB3, MET, IGF1R, EPHA3, TRAILR1, TRAILR2, RANKL, FAP, tenascin, AFP, BCR complex, CD3, CD18, CD44, CTLA-4, gp72, HLA-DR 10 β , HLA-DR antigen, IgE, MUC-1, nuC242, PEM antigen, metalloproteinases, Ephrin receptor, Ephrin ligands, HGF receptor, CXCR4, CXCR4, Bombesin receptor, SK1 antigen, Bcr-Abl, RET, MET, TRKB, TIE2, ALK, ROS, EML4-ALK, ROS1, BRAFV600E, SRC, c-KIT, PDGFR, mTOR, TSC1, TSC2, BTK, KIT, BRCA, CDK 4/6, JAK1, JAK2, BRAF, FLT-3, MEK1, MEK2, and SMO. In some embodiments, the one or more cell surface target molecule(s) is/are HER1/EGFR, HER2, PD-L1, CD25, EpCAM, EphA2, FAP, CD206, CD20, CD44, CD133, Mesothelin, MUC1, PSMA, Glypican-3, and carcinoembryonic antigen (CEA). In some embodiments, the cell surface target

molecule is one or more of CD25, CEA, FAP, HER1/EGFR, HER2, MUC1, PD-L1, or PSMA.

[000149] A “dye-containing conjugate” or a “conjugate” as used herein has a targeting molecule linked to a phthalocyanine dye compound provided herein, such as the phthalocyanine dye compound of Formula (X), Formula (0), Formula (I), or Formula (II). In some embodiments, at least part of the targeting molecule is or is a combination of a protein, a glycoprotein, an antibody, an antibody fragment, an affibody, an antigen, an antigen binding fragment, a peptide, a polypeptide, a tissue homing peptide, a small molecule, a polymeric synthetic molecule, a polymeric nanoparticle, a liposome, an enzyme substrate, a hormone, a neurotransmitter, a cell metabolite, a viral particle, a viral capsid, a viral nanoparticle, a bacterial particle, a marker, a cell, a hapten, an avidin, a streptavidin, a monomeric streptavidin, a biotin, a carbohydrate, an oligosaccharide, a polysaccharide, a nucleic acid, a deoxy nucleic acid, a fragment of DNA, a fragment of RNA, an aptamer, nucleotide triphosphates, acyclo terminator triphosphates, PNA. In some instances, the targeting molecule can include an antigen binding molecule, such as an antibody or antibody fragment (e.g., antigen-binding fragment), or other protein, peptide or small molecule that binds to a target molecule, such as a target molecule on the surface of a cell. In some aspects, an exemplary conjugate contains a targeting molecule that is an antibody or an antibody fragment. In some aspects, and exemplary conjugate contains a targeting molecule that is an antigen-binding fragment derived from an antibody, a functional equivalent thereof, or an antibody fragment. In some examples, the targeting molecule in the provided conjugates contains a bispecific antibody, an scFv, a single domain antibody (sdAb) or nanobody, a VHH, an isolated single variable domain, an affibody, or a z-domain structure, a DARPin, a monobody, an anticalin, an affilin, an affimer type 1 molecule, an affimer type 2 molecule, an affitin, an alphabody, an anticalin, an avimer, a fynomer, a kunitz domain peptide, or a nanoclamp.

[000150] In some embodiments, the targeting molecule binds to the target molecule, such as an antigen or protein, directly or indirectly. For example, in some embodiments, the targeting molecule is a second binding molecule that binds to a first binding molecule which is capable of binding to the target molecule, such as an antigen or protein. For example, the targeting molecule can be a secondary antibody, which binds to a first binding molecule, e.g., a primary antibody, capable of binding the protein or antigen, e.g., a cell surface protein or a cell surface receptor. Thus, in some embodiments, the phthalocyanine dye is conjugated to a secondary antibody.

[000151] In some embodiments, the targeting molecule is an RGD polypeptide, an iRGD polypeptide, a Lyp-1 polypeptide, a cripto-1 binding polypeptide, a somatostatin receptor binding polypeptide, a prohibitin binding polypeptide, an NGR polypeptide, an iNGR polypeptide, or an activatable cell penetrating peptide (ACPP) comprised of a polycationic cell penetrating peptide (CPP) connected via a cleavable linker to a neutralizing polyanion.

[000152] In some embodiments, the targeting molecule is a viral particle, such as a virus-like particle, a viral-like nanoparticle, or a viral capsid. In some embodiments, the targeting molecule is a viral-like nanoparticle. In some embodiments, the viral-like nanoparticle is assembled from L1 capsid proteins. In some embodiments, the viral-like nanoparticle is assembled from a combination of L1 and L2 capsid proteins. In some embodiments, the targeting molecule and bind to and infect cells. In some embodiments, the targeting molecule is one such as described in WO2015042325.

[000153] In some embodiments, a virus-like particle (VLP) refers to an organized capsid-like structure, such as roughly spherical or cylindrical in shape, that comprises self-assembling ordered arrays of L1 or L1 and L2 capsomers and does not include a viral genome. In some embodiments, virus-like particles are morphologically and antigenically similar to authentic virions, but they lack viral genetic material, such as viral nucleic acid, rendering the particles noninfectious. A VLP may be used to deliver to a recipient cell an agent, such as prophylactic agent, therapeutic agent or diagnostic agent, or an enclosed circular or linear DNA or RNA molecule.

[000154] In some embodiments, VLPs may have modified immunogenicity and/or antigenicity with respect to the wild type VLPs. The VLPs may, for example, be assembled from capsomers having a variant capsid protein with modified immunogenicity and/or antigenicity. In some embodiments, a variant capsid protein with modified immunogenicity and/or antigenicity is one that is modified naturally or synthetically, such as mutated, substituted, deleted, pegylated or inserted, at an amino acid to reduce or prevent recognition of the capsid protein by pre-existing, such as endogenous, viral serotype-specific antibodies. A variant capsid protein may be a human papillomavirus (HPV) L1 variant, a non-human papillomavirus L1 variant, or a papillomavirus L1 variant based on a combination of amino acids from different HPV serotypes.

[000155] In some embodiments, a VLP is a papilloma virus VLP. The VLP may be a human papilloma virus VLP, such as derived from a virus that can infect human, while in other embodiments, the VLP may be a non-human papilloma virus VLP. Examples of nonhuman VLPs include those derived from, without limitation, bovine papilloma viruses, murine

papilloma viruses, cotton-rabbit papilloma viruses and macaque or rhesus papilloma virus particles. In some embodiments, the VLPs are bovine papilloma virus viral-like nanoparticles, such as type 1 viral-like nanoparticles, such as assembled from BPV L1 capsid proteins or a combination of BPV L1 and BPV L2 capsid proteins. In some embodiments, a capsid protein refers to a protein monomer, several of which form a capsomer oligomer. In some embodiments, a capsomer refers to the basic oligomeric structural unit of a viral capsid, which is an outer covering of protein that protects the genetic material of a virus. Capsid proteins may include in some embodiments, papillomavirus L1 major capsid proteins and papillomavirus L2 minor capsid proteins. In some embodiments, the VLPs contain only L1 capsid proteins, while in other embodiments, the VLPs contain a mixture, or combination, of L1 and L2 capsid proteins.

[000156] In some embodiments, the percentage of L1 capsid proteins in a virus-like particle is greater than the percentage of L2 capsid proteins in the virus-like particle. For example, in some embodiments, the percentage of L1 capsid proteins in a virus-like particle is 80% to 100% of the total number of capsid proteins in the virus-like particle. In some embodiments, the percentage of L1 capsid proteins in a virus-like particle is at least or is about 80%, 85%, 90%, 91 %, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100%. In some embodiments, the percentage of L2 capsid proteins in a virus-like particle is 1 % to 25% of the total number of capsid proteins in the virus-like particle. For example, in some embodiments, the percentage of L2 capsid proteins in a virus-like particle is at least or about 1 %, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 11 %, 12%, 13%, 14%, 15%, 16%, 17%, 18%, 19% or 20%.

[000157] In some embodiments, a virus-like particle contains 12 to 72 L2 proteins. In some embodiments, a virus-like particle contains 360 L1 proteins and 12 to 72 L2 proteins. In some embodiments, capsid proteins assemble into viral-like nanoparticles having a diameter of 20 to 60 nm. For example, capsid proteins may assemble into viral-like nanoparticles having a diameter of at least or about 20, 25, 30, 35, 40, 45, 50, 55 or 60 nm.

[000158] In some embodiments, the targeting molecule is a DARPIn (designed ankyrin repeat protein). Typically, DARPins are derived from natural ankyrin repeat proteins and bind to proteins including e.g., human receptors, cytokines, kinases, human proteases, viruses and membrane proteins (Molecular Partners AG Zurich Switzerland; see Chapter 5. "Designed Ankyrin Repeat Proteins (DARPins): From Research to Therapy", Methods in Enzymology, vol 503: IOC134 (2012); and "Efficient Selection of DARPins with Sub-nanomolar Affinities using SRP Phage Display", J. Mol. Biol. (2008) 382, 1211-1227, the entire disclosures of which are hereby incorporated by reference. In some embodiments, the DARPIn is an

antibody mimetic protein having high specificity and high binding affinity to a target protein, which is prepared via genetic engineering. In some embodiments, DARPins have a structure comprising at least 2 ankyrin repeat motifs, for example, comprising at least 3, 4 or 5 ankyrin repeat motifs. The DARPins can have any suitable molecular weight depending on the number of repeat motifs. For example, the DARPins including 3, 4 or 5 ankyrin repeat motifs may have a molecular weight of about 10 kDa, about 14 kDa, or about 18 kDa, respectively.

[000159] In some embodiments, the DARPin includes a core part that provides structure and a target binding portion that resides outside of the core and binds to a target. In some embodiments, the structural core includes a conserved amino acid sequence and the target binding portion includes an amino acid sequence that differs depending on the target.

[000160] In some embodiments, the targeting molecule is an affibody molecule. An “affibody” refers to a protein engineered to bind a target protein or peptide with high affinity. In some examples, an affibody mimics an antibody. Typically, an affibody molecule is composed alpha helices, such as three alpha helices, that confer binding to the target molecule. In some examples the affibody protein scaffold is based on the B or Z domain of staphylococcal protein A or an amino acid-substituted protein scaffold thereof. Affibodies can be engineered and synthesized, and molecules with desired binding properties can be identified and selected, for example, using phage display. Affibody molecules are reviewed in Lofblom et al. (2010), FEBS Letters 584(12):2670-2680, which is incorporated by reference.

[000161] In some embodiments, the targeting molecule is selected from among adrenocorticotrophic hormone (ACTH), angiotensin II, atrial natriuretic factor (ANF), bombesin, bradykinin, brain derived neurotrophic factor (BDNF), bone morphogenetic protein 2 (BMP-2), bone morphogenetic protein 6 (BMP-6), bone morphogenetic protein 7 (BMP-7), bone morphogenetic protein 2 (BMP-2), calcitonin, cardiotrophin 1 (CT-1), CD22, CD40, cholecystokinin (CCK), ciliary neurotrophic factor (CNTF), CCL1-CCL28, CXCL1-CXCL17, XCL1, XCL2, CX3CL1, crypto-1 binding peptide, vascular endothelial cell growth factor (VEGF), epidermal growth factor (EGF), endothelin 1, endothelin 1/3, FAS-ligand, fibroblast growth factor 1 (FGF-1), fibroblast growth factor 2 (FGF-2), fibroblast growth factor 4 (FGF-4), fibroblast growth factor 5 (FGF-5), fibroblast growth factor 6 (FGF-6), fibroblast growth factor 1 (FGF-7), fibroblast growth factor 1 (FGF-10), Flt-3, gastrin, gastrin releasing peptide (GRP), granulocyte colony-stimulating factor (G-CSF), granulocyte macrophage stimulating factor (GM-CSF), glucagon like peptide (GLP-1), hepatocyte growth factor (HGF), interferon alpha (IFN-a), interferon beta (IFN-b), interferon gamma (IFN γ), insulin-like growth factor I (IGF-1), insulin-like growth factor 2 (IGF-2), interleukin 1 (IL-1),

interleukin 2 (IL-2), interleukin 3 (IL-3), interleukin 4 (IL-4), interleukin 5 (IL-5), interleukin 6 (IL-6), interleukin 7 (IL-7), interleukin 8 (IL-8), interleukin 9 (IL-9), interleukin 10 (IL-10), interleukin 11 (IL-11), interleukin 12 (IL-12), interleukin 13 (IL-13), interleukin 15 (IL-15), interleukin 17 (IL-17), interleukin 19 (IL-19), luteinizing hormone (LH), luteinizing-releasing hormone (LHRH), macrophage colony-stimulating factor (M-CSF), monocyte chemotactic protein 1 (MCP-1), macrophage inflammatory protein 3a (MIP-3a), macrophage inflammatory protein 3b (MIP-3b), nerve growth factor (NGF), neuromedin B, neurotrophin 3 (NT-3), neurotrophin 4 (NT-4), neurotensin, neuropeptide Y, oxytocin, pituitary adenylate cyclase activating peptide (PACAP), platelet derived growth factor AA (PDGF-AA), platelet derived growth factor AB (PDGF-AB), platelet derived growth factor BB (PDGF-BB), platelet derived growth factor CC (PDGF-CC), platelet derived growth factor DD (PDGF-DD), netrin-1 (NTN1), netrin-2 (NTN2), netrin-4 (NTN4), netrin-G1 (NTNG1) and netrin-G2 (NTNG2), ephrin A1 (EFNA1), ephrin A2 (EFNA2), ephrin A3 (EFNA3), ephrin A4 (EFNA4), ephrin A5 (EFNA5), semaphorin 3A (SEMA3A), semaphorin 3B (SEMA3B), semaphorin 3C (SEMA3C), semaphorin 3D (SEMA3D), semaphorin 3F (SEMA3F), semaphorin 3G (SEMA3G), semaphorin 4A (SEMA4A), semaphorin 4B (SEMA4B), semaphorin 4C (SEMA4C), semaphorin 4D (SEMA4D), semaphorin 4F (SEMA4F), semaphorin 4G (SEMA4G), semaphorin 5A (SEMA5A), semaphorin 5B (SEMA5B), semaphorin 6A (SEMA6A), semaphorin 6B (SEMA6B), semaphorin 6D (SEMA6D), semaphorin 7 A (SEMA7A), SLIT1, SLIT2, SLIT3, SLIT and NTRK-like family, member 1 (SLITRK1), SLIT and NTRK-like family, member 2 (SLITRK2), SLIT and NTRK-like family, member 3 (SLITRK3), SLIT and NTRK-like family, member 4 (SLITRK4), SLIT and NTRK-like family, member 5 (SLITRK5), SLIT and NTRK-like family, member 6 (SLITRK6), prostaglandin E2 (PGE2), RANTES, Somatostatin-14, Somatostatin-28, stem cell factor (SCF), stromal cell derived factor 1 (SDF-1), substance P, thyroid stimulating hormone (TSH), transforming growth factor alpha (TGF- α), transforming growth factor beta (TGF- β), tumor necrosis factor alpha (TNF- α), thrombin, vasoactive intestinal peptide (VIP), Wnt1, Wnt2, Wnt2b/13, Wnt3, Wnt3a, Wnt4, Wnt5a, Wnt5b, Wnt6, Wnt7a, Wnt7b, Wnt7c, Wnt8, Wnt8a, Wnt8b, Wnt8c, Wnt10a, Wnt10b, Wnt11, Wnt14, Wnt15, or Wnt16, Sonic hedgehog, Desert hedgehog, and Indian hedgehog.

[000162] In some embodiments, the targeting molecule is an antibody, an antibody fragment, or a functional equivalent of an antibody or antibody fragments (e.g., an affibody) that specifically binds to an antigen, such as a cell surface molecule on a tumor cell or immune cell(s). Included among such antibodies are antibodies, affibodies, or antigen-binding

antibody fragments capable of binding to a cell surface molecule, such as a cell surface protein, e.g., cell surface receptor, described herein. In some cases, the antibody can bind to an antigen of a protein expressed on a cell in a tumor, including a tumor-specific protein. In some cases, the antibody can bind to an antigen of a protein expressed on an immune cell, such as lymphocyte (T-cell, B-cell, and NK cell), neutrophil, and/or monocyte or macrophage.

[000163] An "antibody" is a polypeptide ligand comprising at least a light chain or heavy chain immunoglobulin variable region that specifically recognizes and binds an epitope of an antigen, such as a tumor-specific protein. Generally, antibodies are composed of a heavy and a light chain, each of which has a variable region, termed the variable heavy (VH) region and the variable light (VL) region. Together, the VH region and the VL region are responsible for binding the antigen recognized by the antibody.

[000164] Antibodies include intact immunoglobulins and fragments of antibodies that exhibit antigen-binding, such as Fab fragments, Fab' fragments, F(ab)'₂ fragments, single chain Fv proteins ("scFv"), and disulfide stabilized Fv proteins ("dsFv"). An scFv protein is a fusion protein in which a light chain variable region of an immunoglobulin and a heavy chain variable region of an immunoglobulin are bound by a linker, while in dsFvs, the chains have been mutated to introduce a disulfide bond to stabilize the association of the chains. The term also includes genetically engineered forms such as chimeric antibodies, for example, humanized murine antibodies, and heteroconjugate antibodies, such as bispecific antibodies. See also, Pierce Catalog and Handbook, 1994-1995 (Pierce Chemical Co., Rockford, Ill.); Kuby, J. Immunology, 3rd Ed., W.H. Freeman & Co., New York, 1997.

[000165] Typically, a naturally occurring immunoglobulin has heavy (H) chains and light (L) chains interconnected by disulfide bonds. There are two types of light chain, lambda (λ) and kappa (κ). There are five main heavy chain classes, or isotypes, which determine the functional activity of an antibody molecule: IgM, IgD, IgG, IgA and IgE.

[000166] Each heavy and light chain contains a constant region and a variable region, also known as "domains." In combination, the heavy and the light chain variable regions generally specifically bind the antigen. Light and heavy chain variable regions may contain a "framework" region interrupted by three hypervariable regions, also called "complementarity-determining regions" or "CDRs." The precise amino acid sequence boundaries of a given CDR or framework regions (FR, the non-CDR portions of the variable regions of the heavy and light chains) can be determined using any of a number of known schemes, including those described by Kabat et al. (1991), "Sequences of Proteins of Immunological Interest," 5th Ed.

Public Health Service, National Institutes of Health, Bethesda, MD ("Kabat" numbering scheme); Al-Lazikani et al., (1997) JMB 273,927-948 ("Chothia" numbering scheme); MacCallum et al., J. Mol. Biol. 262:732-745 (1996), "Antibody-antigen interactions: Contact analysis and binding site topography," J. Mol. Biol. 262, 732-745." ("Contact" numbering scheme); Lefranc MP et al., "IMGT unique numbering for immunoglobulin and T cell receptor variable domains and Ig superfamily V-like domains," Dev Comp Immunol, 2003, 27(1):55-77 ("IMGT" numbering scheme); Honegger A and Plückthun A, "Yet another numbering scheme for immunoglobulin variable domains: an automatic modeling and analysis tool," J Mol Biol, 2001, 309(3):657-70, ("Aho" numbering scheme); and Martin et al., "Modeling antibody hypervariable loops: a combined algorithm," PNAS, 1989, 86(23):9268-9272, ("AbM" numbering scheme). The sequences of the framework regions of different light or heavy chains are relatively conserved within a species, such as humans. The framework region of an antibody, that is the combined framework regions of the constituent light and heavy chains, serves to position and align the CDRs in three-dimensional space.

[000167] The CDRs are typically responsible for binding to an epitope of an antigen. The CDRs of each chain are typically referred to as CDR1, CDR2, and CDR3, numbered sequentially starting from the N-terminus, and are also generally identified by the chain in which the particular CDR is located. Thus, a VH CDR3 is located in the variable domain of the heavy chain of the antibody in which it is found, whereas a VL CDR1 is the CDR1 from the variable domain of the light chain of the antibody in which it is found. Antibodies with different specificities, such as different combining sites for different antigens, have different CDRs. Although it is the CDRs that vary from antibody to antibody, only a limited number of amino acid positions within the CDRs are directly involved in antigen binding. These positions within the CDRs are called specificity determining residues (SDRs).

[000168] References to "VH" or "VH" refer to the variable region of an immunoglobulin heavy chain, including that of an Fv, scFv, dsFv or Fab. References to "VL" or "VL" refer to the variable region of an immunoglobulin light chain, including that of an Fv, scFv, dsFv or Fab.

[000169] Among the provided antibodies are antibody fragments. An "antibody fragment" refers to a molecule other than an intact antibody that comprises a portion of an intact antibody that binds the antigen to which the intact antibody binds. Examples of antibody fragments include but are not limited to Fv, Fab, Fab', Fab'-SH, F(ab')₂; diabodies; linear antibodies; single-chain antibody molecules (e.g., scFv); and multispecific antibodies formed from antibody fragments. Other antibody fragments or multispecific antibodies formed from

antibody fragments include a multivalent scFv, a bispecific scFv or an scFv-CH3 dimer. Antibody fragments can be made by various techniques, including but not limited to proteolytic digestion of an intact antibody as well as production by recombinant host cells.

[000170] A "monoclonal antibody" is an antibody produced by a single clone of B lymphocytes or by a cell into which the light and heavy chain genes of a single antibody have been transfected. Monoclonal antibodies are produced by methods known to those of skill in the art, for instance by making hybrid antibody-forming cells from a fusion of myeloma cells with immune spleen cells. Monoclonal antibodies include humanized monoclonal antibodies.

[000171] A "chimeric antibody" has framework residues from one species, such as human, and CDRs, which generally confer antigen binding, from another species, such as a murine antibody that specifically binds mesothelin.

[000172] A "humanized" immunoglobulin is an immunoglobulin including a human framework region and one or more CDRs from a non-human (for example a mouse, rat, or synthetic) immunoglobulin. The non-human immunoglobulin providing the CD Rs is termed a "donor," and the human immunoglobulin providing the framework is termed an "acceptor." In some embodiments, the CDRs are from the donor immunoglobulin in a humanized immunoglobulin. Constant regions need not be present, but if they are, they may be substantially identical to human immunoglobulin constant regions, such as at least about 85-90%, such as about 95% or more identical. Hence, parts of a humanized immunoglobulin, except possibly the CDRs, are substantially identical to corresponding parts of natural human immunoglobulin sequences. A "humanized antibody" is an antibody comprising a humanized light chain and a humanized heavy chain immunoglobulin. A humanized antibody binds to the same antigen as the donor antibody that provides the CDRs. The acceptor framework of a humanized immunoglobulin or antibody may have a limited number of substitutions by amino acids taken from the donor framework. Humanized or other monoclonal antibodies can have additional conservative amino acid substitutions which have substantially no effect on antigen binding or other immunoglobulin functions. Humanized immunoglobulins can be constructed by means of genetic engineering (see for example, U.S. Pat. No. 5,585,089).

[000173] A "human" antibody (also called a "fully human" antibody) is an antibody that includes human framework regions and CD Rs from a human immunoglobulin. In some embodiments, the framework and the CDRs are from the same originating human heavy and/or light chain amino acid sequence. However, frameworks from one human antibody can be engineered to include CDRs from a different human antibody. Parts of a human

immunoglobulin may be substantially identical to corresponding parts of natural human immunoglobulin sequences.

[000174] "Specifically binds" refers to the ability of a molecule, such as an antibody or antigen-binding fragment, to specifically bind an antigen, such as a tumor-specific antigen, relative to binding to unrelated proteins, such as non-tumor proteins, for example β -actin. In some embodiments, a molecule, such as an antibody or fragment, including a molecule, such as an antibody or fragment, attached to a phthalocyanine dye molecule, specifically binds to a target, such as a cell surface protein.

[000175] In some embodiments, the phthalocyanine dye molecule, such as the phthalocyanine dye of Formula (X), Formula (0), Formula (I), or Formula (II) is conjugated to an antibody or an antigen-binding antibody fragment. For example, in some aspects, the conjugate is a phthalocyanine dye of Formula (X) and an antibody or an antigen-binding antibody fragment. In some aspects, the conjugate is a phthalocyanine dye of Formula (0) and an antibody or an antigen-binding antibody fragment. In some aspects, the conjugate is a phthalocyanine dye of Formula (I) and an antibody or an antigen-binding antibody fragment. In some aspects, the conjugate is a phthalocyanine dye of Formula (II) and an antibody or an antigen-binding antibody fragment. Exemplary antibodies which can be conjugated to one or more dyes of Formula (X), Formula (0), Formula (I), and/or Formula (II) provided herein include 3F8, 8H9, AB122, ab75705, Abagovomab, Abciximab, Abituzumab, Abrezekimab, Abrilumab, Actoxumab, Adalimumab, Adecatumumab, ADG116, ADU-1604, Aducanumab, Afasevikumab, Afelimomab, Afutuzumab, AGEN1181, AGEN1884, AGX-115, AK104, AK105, Alacizumab pegol, Alemtuzumab, Alirocumab, Altumomab pentetate, Amatuximab, AMG 404, AMP-224, AMP-514, Anatumomab mafenatox, Andecaliximab, Anetumab ravtansine, Anifrolumab, Anrukinzumab, anti-CD133, Apolizumab, Aprutumab ixadotin, Arcitumomab, arcitumomab Fab fragment, Ascrinvacumab, Aselizumab, Atezolizumab, Atidortoxumab, Atinumab, Atlizumab (Tocilizumab), ATOR-1015, Atorolimumab, Avelumab, Azintuxizumab vedotin, B72.3, Bapineuzumab, Basiliximab, Bavituximab, BCD-100, BCD-135, BCD-145, BCD-217, Bectumomab, Begelomab, Belantamab mafodotin, Belimumab, Bemarituzumab, Benralizumab, Berlimatoxumab, Bermekimab, Bersanlimab, Bertilimumab, Besilesomab, Bevacizumab, Bezlotoxumab, BGB-A333, BI 754091, Biciromab, Bimagrumab, Bimekizumab, Birtamimab, Bivatuzumab, Bivatuzumab mertansine, BL-8040, Bleselumab, Blinatumomab, Blontuvetmab, Blosozumab, BMS-936559, BMS-986218, Bococizumab, Brazikumab, Brentuximab vedotin, Briakinumab, Brodalumab, Brolucizumab, Brontictuzumab, Burosumab, Cabiralizumab, Camidanlumab

tesirine, Camrelizumab, Canakinumab, Cantuzumab mertansine, Cantuzumab ravtansine, Caplacizumab, Capromab, Capromab pendetide, Carlumab, Carotuximab, Catumaxomab, cBR96-doxorubicin immunoconjugate, CBT-502, CC-90002, CDC-022, Cedelizumab, Cemiplimab, Cergutuzumab amunaleukin, Certolizumab pegol, Cetrelimab, Cetuximab, Cibisatamab, Cirmutuzumab, Citatuzumab bogatox, Cixutumumab, Clazakizumab, Clenoliximab, Clivatuzumab tetraxetan, CMAB302, Codrituzumab, Cofetuzumab pelidotin, Coltuximab ravtansine, Conatumumab, Concizumab, Cosfroviximab, Cosibelimab, CP-870,893, CR6261, Crenezumab, Crizanlizumab, Crotedumab, CS1001, CS1003, Cusatuzumab, CX-188, Dacetuzumab, Daclizumab, Dalotuzumab, Dapirolizumab pegol, Daratumumab, Dectrekumab, Demcizumab, Denintuzumab mafodotin, Denosumab, Depatuxizumab mafodotin, Derlotuximab biotin, Detumomab, Dezamizumab, Dinutuximab, Diridavumab, Domagrozumab, Dorlimomab aritox, Dostarlimab, Drozitumab, DS-8201, Duligotumab, Duligotuzumab, Dupilumab, Durvalumab, Dusigitumab, Duvortuxizumab, Echromeximab, Eculizumab, Edobacomab, Edrecolomab, Efalizumab, Eftilagimod alpha, Efungumab, Eldelumab, Elezanumab, Elgemtumab, Elotuzumab, Elsilimomab, Emaetuzumab, Emapalumab, Emibetuzumab, Emicizumab, Enapotamab vedotin, Enavatuzumab, Enfortumab vedotin, Enlimomab pegol, Enoblituzumab, Enokizumab, Enoticumab, Ensituximab, Epitumomab cituxetan, Epratuzumab, Eptinezumab, Erenumab, Erlizumab, Ertumaxomab, Etaracizumab, Etigilimab, Etrolizumab, Evinacumab, Evolocumab, Exbivirumab, F3, F520, Fanolesomab, Faralimomab, Faricimab, Farletuzumab, Fasinumab, FAZ053, FBTA05, Felvizumab, Fezakinumab, Fibatuzumab, Ficlatuzumab, Figitumumab, Firivumab, Flanvotumab, Fletikumab, Flotetuzumab, Fontolizumab, Foralumab, Foravirumab, Fremanezumab, Fresolimumab, Frovocimab, Frunevetmab, Fulranumab, Futuximab, Galcanezumab, Galiximab, Gancotamab, Ganitumab, Gantenerumab, Gatipotuzumab, Gavilimomab, GB221, Gedivumab, Gemtuzumab ozogamicin, genolimzumab, Gevokizumab, Gilvetmab, Gimsilumab, Girentuximab, Glembatumumab vedotin, GLS-010, Golimumab, Gomiliximab, Gosuranemab, Guselkumab, HD201, Hervycta, HLX02, HLX10, HLX20, HLX22, HX008, HX009, Ianalumab, Ibalizumab, IBI308, Ibritumomab tiuxetan, Icrucumab, Idarucizumab, Ieramilimab, Ifabotuzumab, Igovomab, Iladatuzumab vedotin, IMAB362, Imalumab, Imaprelimab, Imciromab, Imgatuzumab, INBRX-105, Inclacumab, Indatuximab ravtansine, Indusatumab vedotin, Inebilizumab, Infliximab, Inolimomab, Inotuzumab ozogamicin, Intetumumab, Iomab-B, IPH2101, Ipilimumab, Iratumumab, Isatuximab, Iscalimab, Istiratumab, Itolizumab, Ixekizumab, JTX-4014, Keliximab, KN035, KN046, Labetuzumab, Lacnotuzumab,

Ladiratuzumab vedotin, Lambrolizumab (Pembrolizumab), Lampalizumab, Lanadelumab, Landogrozumab, Laprituximab emtansine, Larcaviximab, LDP, Lebrikizumab, Lemalesomab, Lendalizumab, Lenvervimab, Lenzilumab, Lerdelimumab, Leronlimab, Lesofavumab, Letolizumab, Lexatumumab, Libivirumab, Lifestuzumab vedotin, Ligelizumab, Lilotomab satetraxetan, Lintuzumab, Lirilumab, Lodelcizumab, Lokivetmab, Loncastuximab tesirine, Lorvotuzumab mertansine, Losatuxizumab vedotin, Lucatumumab, Lulizumab pegol, Lumiliximab, Lumretuzumab, Lupartumab, Lupartumab amadotin, Lutikizumab, LY3300054, LY3415244, LZM009, mAb114, Mapatumumab, Margetuximab, Marstacimab, Maslimomab, Matuzumab, Mavrilumab, MCLA-145, MED16469, MEDI6383, Mepolizumab, Metelimumab, MGA012, MGD013, MGD019, Milatuzumab, Minretumomab, Mirikizumab, Mirvetuximab soravtansine, Mitumomab, MK-1308, MK-4166, MNRP1685A, Modotuximab, Mogamulizumab, Monalizumab, Morolimumab, Mosunetuzumab, Motavizumab, Moxetumomab pasudotox, MOXR0916, MSB2311, Muromonab-CD3, Nacolomab tafenatox, Namilumab, Naptumomab estafenatox, Naratuximab emtansine, Narnatumab, Natalizumab, Navicixizumab, Navivumab, Naxitamab, Nebacumab, Necitumumab, Nemolizumab, NEOD001, Nerelimomab, Nesvacumab, Netakimab, Nimotuzumab, Nirsevimab, Nivolumab, NM-01, Nofetumomab merpentan, Obiltoxaximab, Obinutuzumab, OC125 monoclonal antibody, Ocaratuzumab, Ocrelizumab, Odulimomab, Ofatumumab, Olaratumab, Oleclumab, Olendalizumab, Olokizumab, Omalizumab, Omburtamab, OMS721, Onartuzumab, Ontuxizumab, Onvatilimab, Opicinumab, Oportuzumab monatox, Oregovomab, Orticumab, Otelixizumab, Otilimab, Otlertuzumab, Oxelumab, Ozanezumab, Ozoralizumab, Pagibaximab, Palivizumab, Pamrevlumab, Panitumumab, Pankomab, Panobacumab, Parsatuzumab, Pascolizumab, Pasotuxizumab, Pateclizumab, Patritumab, PDR001, Pembrolizumab, Pentumomab, Perakizumab, Pertuzumab, Pexelizumab, PF-05280014, PF-06801591, Pidilizumab, Pinatuzumab vedotin, Pintumomab, Placulumab, Plozalizumab, Pogalizumab, Polatuzumab vedotin, Ponezumab, Porgaviximab, Prasinezumab, Prezalizumab, Prezalumab, Priliximab, Pritoxaximab, Pritumumab, PRO 140, Quilizumab, Racotumomab, Radretumab, Rafivirumab, Ralpancizumab, Ramucirumab, Ranevetmab, Ranibizumab, Ravagalimab, Ravulizumab, Raxibacumab, Refanezumab, Regavirumab, REGN2810, REGN3504, REGN4659, REGN-EB3, Relatlimab, Remtolumab, Reslizumab, rHlgM12B7, Rilotumumab, Rinucumab, Risankizumab, Rituximab, Rituximab, Rivabazumab pegol, Rmab, RO7121661, Robatumumab, Roledumab, Romilkimab, Romosozumab, Rontalizumab, Rosmantuzumab, Rovalpituzumab tesirine, Rovelizumab, Rozanolixizumab, Ruplizumab, SA237, Sacituzumab,

Sacituzumab govitecan, Samalizumab, Samrotamab vedotin, Sarilumab, Satralizumab, Satumomab pendetide, SB3, SCT-II0A, SEA-CD40, Secukinumab, Selicrelumab, Seribantumab, Setoxaximab, Setrusumab, Sevirumab, SG001, SGN-CD19A, SHP647, SHR-1316, SIBP-01, Sibrotuzumab, Sifalimumab, Siltuximab, Simtuzumab, Sintilimab, Siplizumab, Sirtratumab vedotin, Sirukumab, Sofituzumab vedotin, Solanezumab, Solitomab, Sonepcizumab, Sontuzumab, Spartalizumab, Stamulumab, STI-3031, Sulesomab, Suptavumab, Sutimlimab, Suvizumab, Suvratouxumab, Sym021, Tabalumab, Tacatuzumab tetraxetan, Tadcocizumab, Talacotuzumab, Talizumab, Tamtuvetmab, Tanezumab, Taplitumomab paptox, Tarextumab, Tavolimab, Tefibazumab, Telimomab aritox, Telisotuzumab, Telisotuzumab vedotin, Tenatumomab, Teneliximab, Teplizumab, Tepoditamab, Teprotumumab, Tesidolumab, Tetulomab, Tezepelumab, TG-1501, TGN1412, Tibulizumab, Ticilimumab, Tigatuzumab, Tildrakizumab, Timigutuzumab, Timolumab, Tiragolumab, Tiragotumab, Tislelizumab, Tisotumab vedotin, TNX-650, Tocilizumab, Tocilizumab, Tomuzotuximab, Toralizumab, Toripalimab, Tosatoxumab, Tositumomab, Tositumomab, Tovetumab, Tralokinumab, Trastuzumab, Trastuzumab deruxtecan, Trastuzumab-anns, trastuzumab-dkst, Trastuzumab emtansine, TRBS07, Tregalizumab, Tremelimumab, Trevogrumab, TRX385, TRX518, TSR-042, Tucotuzumab celmoleukin, Tuvirumab, TX05, Ublituximab, Ulocuplumab, Urelumab, Urtoxazumab, Ustekinumab, Utomilumab, Vadastuximab talirine, Vanalimab, Vandortuzumab vedotin, Vantictumab, Vanucizumab, Vapaliximab, Varisacumab, Varlilumab, Vatelizumab, Vedolizumab, Veltuzumab, Vepalimomab, Vesencumab, Visilizumab, Vobarilizumab, Volociximab, Vonlerolizumab, Vopratelimab, Vorsetuzumab mafodotin, Votumumab, Vunakizumab, Xentuzumab, XmAb20717, XmAb22841, XMAB-5574, Zalutumumab, Zanolimumab, Zatuximab, Zenocutuzumab, Ziralimumab, ZKAB001, Zolbetuximab, and Zolimomab aritox.

[000176] In some embodiments, the antibody is Cetuximab (ERBITUX), panitumumab, zalutumumab, nimotuzumab, trastuzumab, Ado-trastuzumab emtansine, Tositumomab (Bexxar®), Rituximab (Rituxan, MabThera), Ibritumomab tiuxetan (Zevalin), Basiliximab, Daclizumab (Zenapax), Gemtuzumab (Mylotarg), Alemtuzumab, CEA-scan Fab fragment, OC125 monoclonal antibody, ab75705, B72.3, Bevacizumab (Avastin®), Afatinib, Axitinib, Bosutinib, Cabozantinib, Ceritinib, Crizotinib, Dabrafenib, Dasatinib, Erlotinib, Everolimus, Ibrutinib, Imatinib, Lapatinib, Lenvatinib, Nilotinib, Olaparib, Palbociclib, Pazopanib, Pertuzumab, Ramucirumab, Regorafenib, Ruxolitinib, Sorafenib, Sunitinib, Temsirolimus, Vandetanib, Vemurafenib, Vismodegib, Basiliximab, Ipilimumab, Nivolumab,

pembrolizumab, lambrolizumab, MPDL3280A, Pidilizumab (CT-011), MS BOO 1078C, BMS-935559 or MEDI4736, AMP-224, or is an antigen-binding fragment thereof.

[000177] In some embodiments, the antibody is AB122, ADG116, ADU-1604, AGEN1181, AGEN1884, AK105, AMG 404, AMP-224, AMP-514 (MEDI0680), Atezolizumab (TECENTRIQ, MPDL3280A, RG7446), Avelumab (BAVENCIO; MSB0010718C; M7824), Basiliximab (SIMULECT), BCD-100, BCD-135, BCD-145, BGB-A333, BI 754091, BMS-936559 (MDX-1105), BMS-986218, Camidanlumab tesirine, Camrelizumab (SHR1210), Cantuzumab ravtansine, CBT-502 (TQB-2450), Cemiplimab (LIBTAYO; REGN2810), Cetrelimab (hPAM4-Cide), Cetuximab (ERBITUX), Clivatuzumab tetraxetan, Cosibelimab (CK-301), CS1001 (WPB3155), CS1003, CX-188, Daclizumab (ZINBRYTA, ZENAPAX), Depatuxizumab mafodotin, Dostarlimab, Durvalumab (IMFINZI), F520, FAZ053, Futuximab, Gatipotuzumab, Genolimzumab (APL-501; GB226; CBT-501), GLS-010, HLX10, HLX20, HX008, IBI308, Imgatuzumab, Inolimomab, Ipilimumab (YERVOY), JTX-4014, KN035, Laprituximab emtansine, LDP, LY3300054, LZM009, Matuzumab, MGA012 (INCMGA0012), MK-1308, Modotuximab, MSB2311, Necitumumab (PORTRAZZA), Nimotuzumab (THERACIM, THERALOC), Nivolumab (OPDIVO), NM-01, Panitumumab (VECTIBIX; ABX-EGF), PDR001, Pembrolizumab (KEYTRUDA; lambrolizumab; MK-3475), Pemtumomab (THERAGYN), PF-06801591, RA8, REGN2810, REGN3504, REGN4659, SCT-I10A, SG001, SHR-1316, Sibrotuzumab, Sintilimab (TYVYT), Spartalizumab (PDR001), STI-003, STI-3031 (IMC-001; STI-A1015), Sym021, TG-1501, Tislelizumab, Tomuzotuximab, Toripalimab, Tremelimumab (Ticilimumab), TSR-042, Xenopax, Zalutumumab (HuMax-EGFR), ZKAB001 (STI-A1014), or is a binding fragment thereof.

[000178] In some embodiments, the targeting molecule of the conjugate binds to EGFR. For example, in some aspects, the conjugate is a phthalocyanine dye of Formula (X), or Formula (0) and an antibody or an antigen-binding fragment that binds to EGFR. In some aspects, the antibody of the conjugate that targets or binds to EGFR includes, but is not limited to, Alacizumab pegol, Cetuximab, Depatuxizumab mafodotin, Futuximab, Icrucumab, Imgatuzumab, Laprituximab emtansine, Matuzumab, Modotuximab, Necitumumab, Nimotuzumab, Panitumumab, Ramucirumab, Tomuzotuximab, Zalutumumab, or an EGFR-binding fragment thereof. In some aspects, the conjugate is a phthalocyanine dye of Formula (X), or Formula (0) and cetuximab or an antigen-binding fragment of cetuximab. In some aspects, the conjugate is a phthalocyanine dye of Formula (X), or Formula (0) and a polypeptide or small peptide that binds to EGFR. In some aspects, the conjugate is a

phthalocyanine dye of Formula (I) and an antibody or an antigen-binding fragment that binds to EGFR. In some aspects, the conjugate is a phthalocyanine dye of Formula (I) and cetuximab or an antigen-binding fragment of cetuximab. In some aspects, the conjugate is a phthalocyanine dye of Formula (I) and a polypeptide or small peptide that binds to EGFR.

[000179] In some embodiments, the targeting molecule of the conjugate binds to CD25. For example, in some aspects, the conjugate is a phthalocyanine dye of Formula (X), or Formula (0) and an antibody or an antigen-binding fragment that binds to CD25. In some aspects, the antibody of the conjugate that targets or binds to CD25 includes, but is not limited to, Basiliximab, Camidanlumab tesirine, daclizumab, Inolimomab, RA8, STI-003, Xenopax, or a CD25-binding fragment thereof. In some aspects, the conjugate is a phthalocyanine dye of Formula (X), or Formula (0) and basiliximab or an antigen-binding fragment of basiliximab. In some aspects, the conjugate is a phthalocyanine dye of Formula (X), or Formula (0) and daclizumab or an antigen-binding fragment of daclizumab. In some aspects, the conjugate is a phthalocyanine dye of Formula (X), or Formula (0) and an IL-2 non-blocking CD25 antibody, such as an antibody disclosed in WO2018167104 and WO2019008386. In some aspects, the conjugate is a phthalocyanine dye of Formula (I) and an antibody or an antigen-binding fragment that binds to CD25. In some aspects, the conjugate is a phthalocyanine dye of Formula (I) and basiliximab or an antigen-binding fragment of basiliximab. In some aspects, the conjugate is a phthalocyanine dye of Formula (I) and daclizumab or an antigen-binding fragment of daclizumab. In some aspects, the conjugate is a phthalocyanine dye of Formula (I) and an IL-2 non-blocking CD25 antibody, such as an antibody disclosed in WO2018167104 and WO2019008386.

[000180] In some embodiments, the targeting molecule of the conjugate is an antibody or antigen-binding fragment thereof that targets or binds PD-L1, such as an anti-PD-L1 antibody or an antigen-binding fragment thereof and the phthalocyanine dye has the Formula (X), Formula (0), Formula (I), or Formula (II). In some aspects, the antibody of the conjugate that targets or binds to PD-L1 includes, but is not limited to, Atezolizumab (MPDL3280A, TECENTRIQ), Avelumab (BAVENCIO), Durvalumab (MEDI4736, IMFINZI), LDP, NM-01, STI-3031, KN035, LY3300054, M7824 (MSB0011359C), BMS-936559, MSB2311, BCD-135, BGB-A333, CBT-502, Cosibelimab (CK-301), CS1001, FAZ053, MDX-1105, SHR-1316, TG-1501, ZKAB001, INBRX-105, MCLA-145, KN046, LY3415244, REGN3504, and HLX20. Exemplary anti-PD-L1 antibodies include MEDI4736 (Medimmune) MPDL3280A (Genentech), BMS-935559 (Bristol-Myers Squibb) and MSB0010718C and an antigen-binding fragment of any of the foregoing.

[000181] In some embodiments, the targeting molecule of the conjugate is an antibody or antigen-binding fragment thereof that targets or binds PD1, such as an anti-PD1 antibody or an antigen-binding fragment thereof and the phthalocyanine dye has the Formula (X), Formula (0), Formula (I), or Formula (II). In some aspects, the antibody of the conjugate that targets or binds to PD1 includes, but is not limited to, pembrolizumab (MK-3475, Keytruda), nivolumab (Opdivo), cemiplimab (Libtayo), toripalimab (JS001), HX008, SG001, GLS-010, dostarlimab (TSR-042), tislelizumab (BGB-A317), cetrelimab (JNJ-63723283), pidilizumab (CT-011), genolimzumab (APL-501, GB226), BCD-100, cemiplimab (REGN2810), F520, sintilimab (IBI308), GLS-010, CS1003, LZM009, camrelizumab (SHR-1210), SCT-I10A, MGA012, AK105, PF-06801591, AMP-224, AB122, AMG 404, BI 754091, HLX10, JTX-4014, MEDI0680, Sym021, MGD019, MGD013, AK104, XmAb20717, RO7121661, CX-188, and spartalizumab.

[000182] In some embodiments, the targeting molecule of the conjugate is an antibody or antigen-binding fragment thereof that targets or binds CTLA-4, such as an anti-CTLA-4 antibody or an antigen-binding fragment thereof and the phthalocyanine dye has the Formula (X), Formula (0), Formula (I), or Formula (II). In some aspects, the antibody of the conjugate that targets or binds to CTLA-4 includes, but is not limited to, ipilimumab (Yervoy®), tremelimumab (ticilimumab), AGEN1181, AGEN1884, ADU-1064, BCD-145, and BCD-217.

[000183] In some embodiments, the targeting molecule of the conjugate is an antibody or antigen-binding fragment thereof that targets or binds HER2, such as an anti-HER2 antibody or an antigen-binding fragment thereof and the phthalocyanine dye has the Formula (X), Formula (0), Formula (I), or Formula (II). In some aspects, the antibody of the conjugate that targets or binds to HER2 includes, but is not limited to, CDC-022 (HERtiCAD), CMAB302 (Cipterbin), DS-8201, Gancotamab, GB221, HD201, Hervycta, HLX02, HLX22, Margetuximab, Pertuzumab (Perjeta), PF-05280014 (Trazimera), SB3, SIBP-01, Timigutuzumab, Trastuzumab (Herceptin), trastuzumab deruxtecan (ENHERTU), Trastuzumab emtansine (Kadcyla), trastuzumab-anns (Kanjinti), trastuzumab-dkst (Ogivri), and TX05.

[000184] In some embodiments, the targeting molecule of the conjugate is an antibody or antigen-binding fragment thereof that targets or binds MUC1, such as an anti-MUC1 antibody or an antigen-binding fragment thereof and the phthalocyanine dye has the Formula (X), Formula (0), Formula (I), or Formula (II). In some aspects, the antibody of the conjugate that

targets or binds to MUC1 includes, but is not limited to, Cantuzumab ravtansine, Clivatuzumab tetraxetan, Gatipotuzumab, and Pentumomab.

[000185] In some embodiments, the targeting molecule of the conjugate is an antibody or antigen-binding fragment thereof that targets or binds PSMA, such as an anti-PSMA antibody or an antigen-binding fragment thereof and the phthalocyanine dye has the Formula (X), Formula (0), Formula (I), or Formula (II). In some aspects, the antibody of the conjugate that targets or binds to PSMA includes, but is not limited to, Capromab pendetide.

[000186] In some embodiments, the targeting molecule of the conjugate is an antibody or antigen-binding fragment thereof that targets or binds CEA, such as an anti-CEA antibody or an antigen-binding fragment thereof and the phthalocyanine dye has the Formula (X), Formula (0), Formula (I), or Formula (II). In some aspects, the antibody of the conjugate that targets or binds to CEA includes, but is not limited to, Altumomab pentetate, Arcitumomab, arcitumomab Fab fragment, Besilesomab, Cibisatamab, F3, and Labetuzumab. In some embodiments, the targeting molecule of the conjugate in an antibody or antibody fragment, such as an antibody fragment disclosed in EP1505076 or a full-length antibody with the antigen binding domains of an antibody fragment disclosed in EP1505076.

[000187] In some embodiments, the targeting molecule of the conjugate is an antibody or antigen-binding fragment thereof that targets or binds FAP, such as an anti-FAP antibody or an antigen-binding fragment thereof and the phthalocyanine dye has the Formula (X), Formula (0), Formula (I), or Formula (II). In some aspects, the antibody of the conjugate that targets or binds to FAP includes, but is not limited to, Sibrotuzumab.

[000188] In some embodiments, the targeting molecule of the conjugate is a biosimilar, interchangeable or biobetter of any of the targeting molecules described herein.

[000189] In some embodiments, the conjugate contains a number of dye residues per targeting molecule that is from or from about 1 to about 1000, such as from or from about 1 to about 100, from or from about 1 to about 50, from or from about 1 to about 25, from or from about 1 to about 10, from or from about 1 to about 5. In some embodiments, the ratio of dye molecules to targeting molecule is or is about 1:1, 2:1, 3:1, 4:1, 5:1, 10:1, 15:1, 20:1, 25:1, 50:1, 75:1, 100:1, 150:1, 200:1, 250:1, 300:1, 350:1, 400:1, 450:1, 500:1, 550:1, 600:1, 650:1, 700:1, 750:1, 800:1, 850:1, 900:1, 950:1 or 1000:1, or is between or between about any two of such values. In some embodiments, the targeting molecule may contain up to 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 50, 75, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950 or 1000 dye molecules.

[000190] In some embodiments, such as when the targeting molecule is a polypeptide, such as an antibody or antigen-binding fragment, the number of dye molecule per targeting molecule can be from or from about 1 to 5, such as from or from about 1 to 4, for example at or about 1, at or about 2, or at or about 3. In some embodiments, the number of dye residues per targeting molecule is about 3:1. In some embodiments, the number of dye residues per targeting molecule is about 4:1. In some embodiments, the number of dye residues per targeting molecule is about 2:1. In some embodiments, the number of dye residues per targeting molecule is about 1:1. In some embodiments, the number of dye residues per targeting molecule is between about 2:1 and about 3:1. In some embodiments, the number of dye residues per targeting molecule is between about 1:1 to about 2:1. In some embodiments, the number of dye residues per targeting molecule is between about 1.5:1 to about 2:1. In some embodiments, the number of dye residues per targeting molecules is between about 3:1 and about 4:1.

C. FORMULATIONS AND ADMINISTRATION

[000191] Also provided herein are compositions, such as pharmaceutical compositions, containing any of the conjugates provided herein. In some aspects, the compositions contain the phthalocyanine dye conjugate, such as a targeting molecule and a phthalocyanine dye of Formula (X), Formula (0), Formula (I), or Formula (II), and a pharmaceutically acceptable carrier. In some embodiments, the composition containing the conjugate is for use in treatment or therapy, in accordance with any of the provided embodiments, such as for administration to a subject having a disease or condition, for the treatment of the disease or condition. The dosages of phthalocyanine dye conjugate to be administered to a subject are not subject to absolute limits but will depend on the nature of the composition; its active ingredients; and its unwanted side effects, such as immune response against the agent, the subject being treated, and the type of condition being treated and the manner of administration. Generally, the dose will be a therapeutically effective amount, such as an amount sufficient to achieve a desired biological effect, for example an amount that is effective to decrease the size, such as volume and/or weight, of the tumor, or attenuate further growth of the tumor, or decrease undesired symptoms of the tumor.

[000192] In some embodiments, the compositions used for administration of the phthalocyanine dye conjugate contain an effective amount of the agent along with conventional pharmaceutical carriers and excipients appropriate for the type of administration contemplated. For example, in some embodiments, parenteral formulations may contain a sterile aqueous solution or suspension of the conjugate. In some embodiments, compositions

for enteral administration may contain an effective amount of the phthalocyanine dye conjugate in aqueous solution or suspension that may optionally include buffers, surfactants, thixotropic agents, and flavoring agents.

[000193] In some embodiments, the phthalocyanine dye conjugate or conjugate in combination with an additional therapeutic agent, can be formulated in a pharmaceutically acceptable buffer, such as that containing a pharmaceutically acceptable carrier or vehicle. Generally, the pharmaceutically acceptable carriers or vehicles, such as those present in the pharmaceutically acceptable buffer, can be any known in the art. Remington's Pharmaceutical Sciences, by E. W. Martin, Mack Publishing Co., Easton, Pa., 19th Edition (1995), describes compositions and formulations suitable for pharmaceutical delivery of one or more therapeutic compounds. Pharmaceutically acceptable compositions generally are prepared in view of approvals for a regulatory agency or other agency prepared in accordance with generally recognized pharmacopeia for use in animals and in humans.

[000194] Pharmaceutical compositions can include carriers such as a diluent, adjuvant, excipient, or vehicle with which the compound is administered. Examples of suitable pharmaceutical carriers are described in "Remington's Pharmaceutical Sciences" by E. W. Martin. Such compositions will contain a therapeutically effective amount of the compound, generally in purified form, together with a suitable amount of carrier so as to provide the form for proper administration to the patient. Such pharmaceutical carriers can be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, and sesame oil. Water is a typical carrier when the pharmaceutical composition is administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions also can be employed as liquid carriers, particularly for injectable solutions. Compositions can contain along with an active ingredient: a diluent such as lactose, sucrose, dicalcium phosphate, or carboxymethylcellulose; a lubricant, such as magnesium stearate, calcium stearate and talc; and a binder such as starch, natural gums, such as gum acacia, gelatin, glucose, molasses, polyvinylpyrrolidone, celluloses and derivatives thereof, povidone, crospovidones and other such binders known to those of skill in the art. Suitable pharmaceutical excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, and ethanol. A composition, if desired, also can contain minor amounts of wetting or emulsifying agents, or pH buffering agents, for example, acetate, sodium citrate, cyclodextrin derivatives, sorbitan monolaurate, triethanolamine sodium acetate, triethanolamine oleate, and other such agents.

[000195] In some embodiments, pharmaceutical preparation can be in liquid form, for example, solutions, syrups or suspensions. Such liquid preparations can be prepared by conventional means with pharmaceutically acceptable additives such as suspending agents (e.g., sorbitol syrup, cellulose derivatives or hydrogenated edible fats); emulsifying agents (e.g., lecithin or acacia); non-aqueous vehicles (e.g., almond oil, oily esters, or fractionated vegetable oils); and preservatives (e.g., methyl or propyl-p-hydroxybenzoates or sorbic acid). In some cases, pharmaceutical preparations can be presented in lyophilized form for reconstitution with water or other suitable vehicle before use.

[000196] In some embodiments, the nature of the pharmaceutically acceptable buffer, or carrier, depends on the particular mode of administration being employed. For instance, in some embodiments, parenteral formulations may comprise injectable fluids that include pharmaceutically and physiologically acceptable fluids such as water, physiological saline, balanced salt solutions, aqueous dextrose, or glycerol as a vehicle. In some embodiments, for solid compositions, for example powder, pill, tablet, or capsule forms, non-toxic solid carriers can include, for example, pharmaceutical grades of mannitol, lactose, starch, or magnesium stearate. In addition to biologically-neutral carriers, pharmaceutical compositions to be administered can in some embodiments contain minor amounts of non-toxic auxiliary substances, such as wetting or emulsifying agents, preservatives, and pH buffering agents, for example sodium acetate or sorbitan monolaurate.

[000197] The compounds can be formulated into suitable pharmaceutical preparations such as solutions, suspensions, tablets, dispersible tablets, pills, capsules, powders, sustained release formulations or elixirs, for oral administration, as well as transdermal patch preparation and dry powder inhalers. Typically, the compounds are formulated into pharmaceutical compositions using techniques and procedures well known in the art (see e.g., Ansel Introduction to Pharmaceutical Dosage Forms, Fourth Edition, 1985, 126). Generally, the mode of formulation is a function of the route of administration.

[000198] Compositions can be formulated for administration by any route known to those of skill in the art including intramuscular, intravenous, intradermal, intralesional, intraperitoneal injection, subcutaneous, intratumoral, epidural, nasal, oral, vaginal, rectal, topical, local, otic, inhalational, buccal (e.g., sublingual), and transdermal administration or any route. Other modes of administration also are contemplated. Administration can be local, topical or systemic depending upon the locus of treatment. Local administration to an area in need of treatment can be achieved by, for example, but not limited to, local infusion during surgery,

topical application, e.g., in conjunction with a wound dressing after surgery, by injection, by means of a catheter, by means of a suppository, or by means of an implant.

[000199] Parenteral administration, generally characterized by injection, either subcutaneously, intramuscularly, intratumorally, intravenously or intradermally is contemplated herein. Injectables can be prepared in conventional forms, either as liquid solutions or suspensions, solid forms suitable for solution or suspension in liquid prior to injection, or as emulsions. Suitable excipients are, for example, water, saline, dextrose, glycerol or ethanol. In addition, if desired, the pharmaceutical compositions to be administered may also contain an activator in the form of a solvent such as pH buffering agents, metal ion salts, or other such buffers. The pharmaceutical compositions also may contain other minor amounts of non-toxic auxiliary substances such as wetting or emulsifying agents, pH buffering agents, stabilizers, solubility enhancers, and other such agents, such as for example, sodium acetate, sorbitan monolaurate, triethanolamine oleate and cyclodextrins. Implantation of a slow-release or sustained-release system, such that a constant level of dosage is maintained (see, e.g., U.S. Pat. No. 3,710,795) also is contemplated herein. The percentage of active compound contained in such parenteral compositions is highly dependent on the specific nature thereof, as well as the activity of the compound and the needs of the subject.

[000200] Injectables are designed for local and systemic administration. Preparations for parenteral administration include sterile solutions ready for injection, sterile dry soluble products, such as lyophilized powders, ready to be combined with a solvent just prior to use, including hypodermic tablets, sterile suspensions ready for injection, sterile dry insoluble products ready to be combined with a vehicle just prior to use and sterile emulsions. The solutions may be either aqueous or non-aqueous. If administered intravenously, suitable carriers include physiological saline or phosphate buffered saline (PBS), and solutions containing thickening and solubilizing agents, such as glucose, polyethylene glycol, and polypropylene glycol and mixtures thereof.

[000201] Pharmaceutically acceptable carriers used in parenteral preparations include aqueous vehicles, non-aqueous vehicles, antimicrobial agents, isotonic agents, buffers, antioxidants, local anesthetics, suspending and dispersing agents, emulsifying agents, sequestering or chelating agents and other pharmaceutically acceptable substances. Examples of aqueous vehicles include Sodium Chloride Injection, Ringers Injection, Isotonic Dextrose Injection, Sterile Water Injection, Dextrose and Lactated Ringers Injection. Non-aqueous parenteral vehicles include fixed oils of vegetable origin, cottonseed oil, corn oil, sesame oil and peanut

oil. Antimicrobial agents in bacteriostatic or fungistatic concentrations can be added to parenteral preparations packaged in multiple-dose containers, which include phenols or cresols, mercurials, benzyl alcohol, chlorobutanol, methyl and propyl p-hydroxybenzoic acid esters, thimerosal, benzalkonium chloride and benzethonium chloride. Isotonic agents include sodium chloride and dextrose. Buffers include phosphate and citrate.

[000202] If administered intravenously, suitable carriers include physiological saline or phosphate buffered saline (PBS), and solutions containing thickening and solubilizing agents, such as glucose, polyethylene glycol, and polypropylene glycol and mixtures thereof.

[000203] The composition can be formulated for single dosage administration or for multiple dosage administration. The agents can be formulated for direct administration. The composition can be provided as a liquid or lyophilized formulation. Where the composition is provided in lyophilized form it can be reconstituted just prior to use by an appropriate buffer, for example, a sterile saline solution.

[000204] Compositions also can be administered with other biologically active agents, either sequentially, intermittently or in the same composition. Administration also can include controlled release systems including controlled release formulations and device-controlled release, such as by means of a pump.

[000205] The most suitable route in any given case depends on a variety of factors, such as the nature of the disease, the progress of the disease, the severity of the disease and the particular composition which is used. For example, compositions are administered systemically, for example, via intravenous administration. Subcutaneous methods also can be employed, although increased absorption times can be necessary to ensure equivalent bioavailability compared to intravenous methods.

[000206] Pharmaceutical compositions can be formulated in dosage forms appropriate for each route of administration. Pharmaceutically and therapeutically active compounds and derivatives thereof are typically formulated and administered in unit dosage forms or multiple dosage forms. Each unit dose contains a predetermined quantity of therapeutically active compound sufficient to produce the desired therapeutic effect, in association with the required pharmaceutical carrier, vehicle or diluent. Unit dosage forms include, but are not limited to, tablets, capsules, pills, powders, granules, sterile parenteral solutions or suspensions, and oral solutions or suspensions, and oil water emulsions containing suitable quantities of the compounds or pharmaceutically acceptable derivatives thereof. Unit dose forms can be contained ampoules and syringes or individually packaged tablets or capsules. Unit dose forms can be administered in fractions or multiples thereof. A multiple dose form is a

plurality of identical unit dosage forms packaged in a single container to be administered in segregated unit dose form. Examples of multiple dose forms include vials, bottles of tablets or capsules or bottles of pints or gallons. Hence, multiple dose form is a multiple of unit doses that are not segregated in packaging. Generally, dosage forms or compositions containing active ingredient in the range of 0.005% to 100% with the balance made up from non-toxic carrier can be prepared. Pharmaceutical compositions can be formulated in dosage forms appropriate for each route of administration.

[000207] The concentration of the pharmaceutically active compound is adjusted so that an injection provides an effective amount to produce the desired pharmacological effect. The exact dose depends on the age, weight and condition of the patient or animal as is known in the art. The unit-dose parenteral preparations are packaged in an ampoule, a vial or a syringe with a needle. The volume of liquid solution or reconstituted powder preparation, containing the pharmaceutically active compound, is a function of the disease to be treated and the particular article of manufacture chosen for package. All preparations for parenteral administration must be sterile, as is known and practiced in the art. In some embodiments, the compositions can be provided as a lyophilized powder, which can be reconstituted for administration as solutions, emulsions and other mixtures. They may also be reconstituted and formulated as solids or gels. The lyophilized powders can be prepared from any of the solutions described above.

[000208] The sterile, lyophilized powder can be prepared by dissolving a phthalocyanine dye-targeting molecule conjugate in a buffer solution. The buffer solution may contain an excipient which improves the stability of other pharmacological components of the powder or reconstituted solution, prepared from the powder.

[000209] In some embodiments, subsequent sterile filtration of the solution followed by lyophilization under standard conditions known to those of skill in the art provides the desired formulation. Briefly, the lyophilized powder is prepared by dissolving an excipient, such as dextrose, sorbitol, fructose, corn syrup, xylitol, glycerin, glucose, sucrose or other suitable agent, in a suitable buffer, such as citrate, sodium or potassium phosphate or other such buffer known to those of skill in the art. Then, a selected enzyme is added to the resulting mixture, and stirred until it dissolves. The resulting mixture is sterile filtered or treated to remove particulates and to ensure sterility and apportioned into vials for lyophilization. Each vial can contain a single dosage (1 mg-1 g, generally 1-100 mg, such as 1-5 mg) or multiple dosages of the compound. The lyophilized powder can be stored under appropriate conditions, such as at about 4 °C. to room temperature. Reconstitution of this lyophilized powder with a buffer

solution provides a formulation for use in parenteral administration. The precise amount depends upon the indication treated and selected compound. Such amount can be empirically determined.

[000210] In some embodiments, the pH of the composition is between or between about 6 and 10, such as between or between about 6 and 8, between or between about 6.9 and 7.3, such as about pH 7.1. In some embodiments, the pH of the pharmaceutically acceptable buffer is at least or about 5, at least or about 6, at least or about 7, at least or about 8, at least or about 9 or at least or about 10, or is 7.1.

[000211] The compositions can be formulated for single dosage administration or for multiple dosage administration. The agents can be formulated for direct administration.

[000212] In some embodiments, the compositions provided herein are formulated in an amount for direct administration of the provided conjugates, in a range from at or about 0.01 mg to at or about 3000 mg, from at or about 0.01 mg to at or about 1000 mg, from at or about 0.01 mg to at or about 500 mg, from at or about 0.01 mg to at or about 100 mg, from at or about 0.01 mg to at or about 50 mg, from at or about 0.01 mg to at or about 10 mg, from at or about 0.01 mg to at or about 1 mg, from at or about 0.01 mg to at or about 0.1 mg, from at or about 0.1 mg to at or about 2000 mg, from at or about 0.1 mg to at or about 1000 mg, from at or about 0.1 mg to at or about 500 mg, from at or about 0.1 mg to at or about 100 mg, from at or about 0.1 mg to at or about 50 mg, from at or about 0.1 mg to at or about 10 mg, from at or about 0.1 mg to at or about 1 mg, from at or about 1 mg to at or about 2000 mg, from at or about 1 mg to at or about 1000 mg, from at or about 1 mg to at or about 500 mg, from at or about 1 mg to at or about 100 mg, from at or about 1 mg to at or about 10 mg, from at or about 10 mg to at or about 2000 mg, from at or about 10 mg to at or about 1000 mg, from at or about 10 mg to at or about 500 mg, from at or about 10 mg to at or about 100 mg, from at or about 100 mg to at or about 2000 mg, from at or about 100 mg to at or about 1000 mg, from at or about 100 mg to at or about 500 mg, from at or about 500 mg to at or about 2000 mg, from at or about 500 mg to at or about 1000 mg, and from about 1000 mg to at or about 3000 mg. In some embodiments, the volume of the composition can be 0.5 mL to 1000 mL, such as 0.5 mL to 100 mL, 0.5 mL to 10 mL, 1 mL to 500 mL, 1 mL to 10 mL, such as at least or about at least or about or 0.5 mL, 1 mL, 2 mL, 3 mL, 4 mL, 5 mL, 6 mL, 7 mL, 8 mL, 9 mL, 10 mL, 15 mL, 20 mL, 30 mL, 40 mL, 50 mL or more. For example, the composition is formulated for single dosage administration of an amount between at or about 100 mg and at or about 500 mg, or between at or about 200 mg and at or about 400 mg. In some embodiments, the composition is formulated for single dosage administration of an amount

between at or about 500 mg and at or about 1500 mg, at or about 800 mg and at or about 1200 mg or at or about 1000 mg and at or about 1500 mg. In some embodiments, the volume of the composition is between at or about 10 mL and at or about 1000 mL or at or about 50 mL and at or about 500 mL; or the volume of the composition is at least at or about 10 mL, 20 mL, 30 mL, 40 mL, 50 mL, 75 mL, 100 mL, 150 mL, 200 mL, 250 mL, 300 mL, 400 mL, 500 mL or 1000 mL.

[000213] In some embodiments, the entire vial contents of the formulations can be withdrawn for administration or can be divided up into a plurality of dosages for multiple administrations. Upon withdrawal of an amount of drug for administration, the formulation can be further diluted if desired, such as diluted in water, saline (e.g., 0.9%) or other physiological solution.

[000214] In some embodiments, also provided are compositions containing an additional therapeutic agent, such as an immunomodulatory agent or anti-cancer agent, for use in combination with the provided conjugates, in accordance with the provided embodiments. In some aspects, the additional therapeutic agent can be prepared in accord with known or standard formulation guidelines, such as described above. In some embodiments, the immunomodulatory agent, anti-cancer agent and/or provided conjugate are formulated as separate compositions. In some embodiments, the immunomodulatory agent is provided as a separate composition from the provided conjugate, and the two compositions are administered separately. In some embodiments, the anti-cancer agent is provided as a separate composition from the provided conjugate, and the two compositions are administered separately. The compositions can be formulated for parenteral delivery (i.e., for systemic delivery). For example, the compositions or combination of compositions are formulated for subcutaneous delivery or for intravenous delivery. The agents, such as a provided conjugate and an immunomodulatory agent and/or an anti-cancer agent can be administered by different routes of administration.

[000215] The compositions comprising the provided conjugate can be administered locally or systemically using any method known in the art, for example to subjects having a tumor, such as a cancer, or who has had a tumor previously removed, for example via surgery. Although specific examples are provided, one skilled in the art will appreciate that alternative methods of administration of the disclosed agents can be used. Such methods may include for example, the use of catheters or implantable pumps to provide continuous infusion over a period of several hours to several days into the subject in need of treatment.

[000216] In some embodiments, the provided conjugate is administered by parenteral means, including direct injection or infusion into a tumor, such as intratumorally. In some embodiments, the conjugate is administered to the tumor by applying the agent to the tumor, for example by bathing the tumor in a solution containing the conjugate, or by pouring the agent onto the tumor.

[000217] In addition, or alternatively, the conjugate can be administered systemically, for example intravenously, intramuscularly, subcutaneously, intradermally, intraperitoneally, subcutaneously, or orally, to a subject having a tumor, such as cancer.

[000218] In some embodiments, the conjugate can be administered ex vivo, for example by obtaining cells from a subject, treating such cells with a conjugate in conjunction with illumination, and administering the treated cells either to the same subject or a different subject.

[000219] In some embodiments, the composition contains an average number of dye residues per targeting molecule (e.g., DAR) that is from or from about 0.5 to about 1000, such as from or from about 0.5 to about 100, from or from about 0.5 to about 50, from or from about 0.5 to about 25, from or from about 0.5 to about 10, from or from about 0.5 to about 5. In some embodiments, the average ratio of dye molecules to targeting molecules in the composition is greater than 0.5 or greater than about 0.5, such as 0.6, 0.7, 0.8, 0.9, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more. In some embodiments, the ratio of dye molecules to targeting molecules in the composition is or is about 0.5:1, 0.7:1, 0.8:1, 1:1, 2:1, 3:1, 4:1, 5:1, 10:1, 15:1, 20:1, 25:1, 50:1, 75:1, 100:1, 150:1, 200:1, 250:1, 300:1, 350:1, 400:1, 450:1, 500:1, 550:1, 600:1, 650:1, 700:1, 750:1, 800:1, 850:1, 900:1, 950:1 or 1000:1, or is between or between about any two of such values.

[000220] In some embodiments, such as when the targeting molecule is a polypeptide, such as an antibody, antigen-binding fragment, or nanobody, the average number of dye molecules per targeting molecule in the composition can be from or from about 0.5 to 5, such as from or from about 0.5 to 4, for example at or about 0.5, at or about 0.6, at or about 0.7, at or about 0.8, at or about 0.9, at or about 1, at or about 2, or at or about 3. In some embodiments, the average number of dye residues per targeting molecule in the composition is about 3:1. In some embodiments, the average number of dye residues per targeting molecule in the composition about 4:1. In some embodiments, the average number of dye residues per targeting molecule in the composition about 2:1. In some embodiments, the average number of dye residues per targeting molecule in the composition is about 1:1. In some embodiments, the average number of dye residues per targeting molecule in the composition is between

about 2:1 and about 3:1. In some embodiments, the average number of dye residues per targeting molecule in the composition is between about 1:1 to about 2:1. In some embodiments, the average number of dye residues per targeting molecule in the composition is between about 1.5:1 to about 2:1. In some embodiments, the average number of dye residues per targeting molecule in the composition is between about 3:1 and about 4:1. In some embodiments, the average number of dye residues per targeting molecule in the composition is between about 0.5:1 to about 1:1.

D. DEVICES AND ILLUMINATION METHODS FOR USE WITH CONJUGATES

[000221] In some aspects, devices that can be used with the provided embodiments include light diffusing devices that provide illumination (in some cases, also referred to as irradiation) at a wavelength (or wavelengths) of light suitable for use with the dye conjugate composition, such as a phthalocyanine dye conjugates of Formula (X), Formula (0), Formula (I), or Formula (II) and a targeting molecule described herein. Illumination devices can include a light source (for example, a laser), and a means of conveying the light to the area of interest (for example, one or more fibers to illuminate an isolated area of a subject or an isolated lesion or tumor). Exemplary illumination devices are described in Patent Nos. US 10,295,719; US 10,527,771; and US 10,416,366, incorporated herein by reference. Such devices deliver light to a target region of a subject using a light diffusing device, containing, a non-circular core optic fiber that is operably connected to a laser. In some embodiments, the core optic fiber is circular and is coiled or bent prior to interfacing with a light diffusing device. In particular aspects, the device delivers a “top hat” core irradiance distribution to deliver uniform light to the illuminated area. The light diffusing device can be as cylindrical diffuser for use, for example, for intratumor or intratissue irradiation. In some embodiments, the light diffusing device is a frontal diffuser, with a lens, where the illumination is projected through the lens of the frontal diffuser at the end of the optic fiber. The projected light can be a collimated or dispersing beam of light.

[000222] In some embodiments, the target area, such as a tumor, the vicinity of a tumor, a lymph node, the vicinity of the lymph node, is illuminated with light at a wavelength within a range from at or about 400 nm to at or about 900 nm, such as from or from at or about 500 nm to at or about 900 nm, such as from or from at or about 600 nm to at or about 850 nm, such as from or from at or about 600 nm to at or about 740 nm, such as from at or about 660 nm to at or about 740 nm, from at or about 660 nm to at or about 710 nm, from at or about 660 nm to at or about 700 nm, from at or about 660 to at or about 685, from at or about 665 to at or about 680, from at or about 670 to at or about 685, from at or about 670 nm to at or about 690

nm, from at or about 670 to at or about 680, from at or about 680 nm to at or about 740 nm, or from at or about 690 nm to at or about 710 nm. In some embodiments, the target area, such as a tumor, the vicinity of a tumor, a lymph node, the vicinity of the lymph node, or the tumor microenvironment, is illuminated with light at a wavelength of at or about 600 nm to at or about 850 nm, such as at or about 660 nm to at or about 740 nm. In some embodiments, the target area, such as a tumor, the vicinity of a tumor, a lymph node, the vicinity of the lymph node, or the tumor microenvironment, is illuminated with light at wavelength of at least at or about 600 nm, 620 nm, 640 nm, 660 nm, 680, nm, 700 nm, 720 nm or 740 nm, such as at or about 670 ± 50 nm, or at or about 670 ± 40 nm, for example at or about 670 nm or at or about 670 nm. In some embodiments, the target area, such as a tumor, the vicinity of a tumor, a lymph node, the vicinity of the lymph node, or the tumor microenvironment, is illuminated with light at a wavelength of less than or less than about 685 nm or 680 nm.

[000223] In some embodiments of the methods and uses provided herein, illumination is carried out using cylindrical diffusing fibers that includes a diffuser length of at or about 0.5 cm to at or about 10 cm and spaced at or about 1.8 ± 0.2 cm apart. In some embodiments, the light illumination dose is from at or about 20 J/cm fiber length to at or about 500 J/cm fiber length. In some embodiments, the tumor is greater than at or about 10 mm deep or is a subcutaneous tumor.

[000224] In some embodiments, the provided methods include illuminating a target area that is an interstitial tumor in a subject with cylindrical diffusing fibers that includes a diffuser length of at or about 0.5 cm to at or about 10 cm and spaced at or about 1.8 ± 0.2 cm apart with a light dose of at or about 100 J/cm fiber length or with a fluence rate of at or about 400 mW/cm. In some embodiments, the target area is a tumor that is greater than at or about 10 mm deep or is a subcutaneous tumor. In some embodiments, the cylindrical diffusing fibers are placed in a catheter positioned in the tumor at or about 1.8 ± 0.2 cm apart. In some embodiments, the catheter is optically transparent.

[000225] In some embodiments, the target area, such as a tumor, the vicinity of a tumor, a lymph node, the vicinity of the lymph node, or the tumor microenvironment, is illuminated with light dose of at least at or about 1 J/cm^2 , such as at least at or about 10 J/cm^2 , at least at or about 30 J/cm^2 , at least at or about 50 J/cm^2 , at least at or about 75 J/cm^2 , at least at or about 100 J/cm^2 , at least at or about 150 J/cm^2 , or at least at or about 500 J/cm^2 . In some embodiments, the dose of illumination is from at or about 1 to at or about J/cm^2 , from at or about 1 to at or about 500 J/cm^2 , from at or about 5 to at or about 200 J/cm^2 , from at or about 10 to at or about 100 J/cm^2 , from at or about 10 to at or about 50 J/cm^2 , from at or about 30 to

at or about 200 J/cm², from at or about 30 to at or about 150 J/cm², or from at or about 30 J/cm² to at or about 100 J/cm². In some embodiments, the target area is illuminated at a dose of at least at or about 2 J/cm², 5 J/cm², 10 J/cm², 25 J/cm², 50 J/cm², 75 J/cm², 100 J/cm², 150 J/cm², 200 J/cm², 300 J/cm², 400 J/cm², or 500 J/cm².

[000226] In some embodiments, the target area is a tumor that is a superficial tumor. In some embodiments, the tumor is less than 10 mm thick. In some embodiments, illumination is carried out using a microlens-tipped fiber for surface illumination. In some embodiments, the light illumination dose is from at or about 5 J/cm² to at or about 200 J/cm².

[000227] In some embodiments, the target area, such as a tumor, the vicinity of a tumor, a lymph node, the vicinity of the lymph node, or the tumor microenvironment, are illuminated at a dose of at least at or about 1 J/cm fiber length, such as at least at or about 10 J/cm fiber length, at least at or about 50 J/cm fiber length, at least at or about 100 J/cm fiber length, at least at or about 250 J/cm fiber length, or at least at or about 500 J/cm fiber length. In some embodiments, the dose of illumination is from at or about 1 to at or about 1000 J/cm fiber length, from at or about 1 to at or about 500 J/cm fiber length, from at or about 2 to at or about 500 J/cm fiber length, from at or about 50 to at or about 300 J/cm fiber length, from at or about 10 to at or about 100 J/cm fiber length, or from at or about 10 to at or about 50 J/cm fiber length. In some embodiments, the target area, such as a tumor, the vicinity of a tumor, a lymph node, the vicinity of the lymph node, or the tumor microenvironment, are illuminated at a dose of at least at or about 2 J/cm fiber length, 5 J/cm fiber length, 10 J/cm fiber length, 25 J/cm fiber length, 50 J/cm fiber length, 75 J/cm fiber length, 100 J/cm fiber length, 150 J/cm fiber length, 200 J/cm fiber length, 250 J/cm fiber length, 300 J/cm fiber length, 400 J/cm fiber length or 500 J/cm fiber length.

[000228] In some embodiments, the provided methods include illuminating a target area that is a superficial tumor in a subject with a microlens-tipped fiber for surface illumination with a light dose of from at or about 5 J/cm² to at or about 200 J/cm². In some embodiments, the light illumination dose is at or about 50 J/cm².

[000229] In some embodiments, the dose of illumination following administration of the composition comprising the phthalocyanine dye-targeting molecule conjugate is at least at or about 1 J/cm² or at least at or about 1 J/cm of fiber length at a wavelength of at or about 600-800 nm, for example, at least at or about 1 J/cm² or at least at or about 1 J/cm of fiber length at a wavelength of at or about 620-720 nm, at least at or about 10 J/cm² or at least at or about 10 J/cm of fiber length at a wavelength of at or about 620-720 nm, at least at or about 50 J/cm² or at least at or about 50 J/cm of fiber length at a wavelength of at or about 620-720 nm,

or at least at or about 100 J/cm² or at least at or about 100 J/cm of fiber length at a wavelength of at or about 620-720 nm. In some embodiments, the wavelength is 640-700 nm. In some embodiments, the dose of illumination following administration of the composition comprising the phthalocyanine dye-targeting molecule conjugate is at least at or about 1.0 J/cm² or at least at or about 1 J/cm of fiber length, at a wavelength of at or about 670 nm, for example, at least at or about 10 J/cm² or at least at or about 10 J/cm of fiber length, at a wavelength of at or about 670 nm, at least at or about 50 J/cm² or at least at or about 50 J/cm of fiber length, at a wavelength of at or about 670 nm, or at least at or about 100 J/cm² or at least at or about 100 J/cm of fiber length, at a wavelength of at or about 670 nm, for example 1.0 to 500 J/cm² or 1.0 to 500 J/cm of fiber length, at a wavelength of at or about 670 nm. Exemplary illumination after administration of the conjugates or compositions provided herein include illuminating the target area at a wavelength of at or about 620 nm to at or about 720 nm at a dose of at least at or about 1 J/cm² or at least at or about 1 J/cm of fiber length.

[000230] In some embodiments, illuminating is carried out at a wavelength of at or about 580 nm to at or about 830 nm and at a dose of from at or about 25 J/cm² to at or about 400 J/cm² or from at or about 2 J/cm fiber length to at or about 500 J/cm fiber length. In some embodiments, the target area is illuminated at a wavelength of 670 ± 40 nm. In some embodiments, target area is illuminated at a dose of at or about 50 J/cm² or at or about 100 J/cm of fiber length.

[000231] In some embodiments, a light or laser may be applied to the conjugate, such as cells containing the conjugate, for a duration from at or about 5 seconds to at or about 5 minutes. For example, in some embodiments, the light or laser is applied for at or about 5, 10, 15, 20, 25, 30, 35, 40, 45, 50 or 55 seconds, or for within a range between any of two such values, to activate the dye molecule(s) of the conjugate. In some embodiments, the light or laser is applied for at or about 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5 or 5 minutes, or more, or within a range between any two of such values. In some embodiments, the length of time a light or laser is applied can vary depending, for example, on the energy, such as wattage, of the light or laser. For example, lights or lasers with a lower wattage may be applied for a longer period of time.

[000232] In some embodiments, a light or laser may be applied for at or about 30 minutes to at or about 96 hours after administering the conjugate. For example, in some embodiments, the light or laser is applied at or at about 30, 35, 40, 45, 50 or 55 minutes after administering the conjugate, or within a range between any two of such values. In some embodiments, the light or laser is applied at or at about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 hours after administering the conjugate, or is

administered within a range between about any two of such values, such as, for example between at or about 20 hours to at or about 28 hours, or about 24 hours $\pm$ 4 hours. In some embodiments, the light or laser is applied between or between about 1 and 24 hours, such as between at or about 1 and at or about 12 hours, at or about 12 and at or about 24 hours, at or about 6 and at or about 12 hours, or may be administered more than at or about 24 hours following administration of the conjugate. In some embodiments, the light or laser is applied at or about 36, 48, 72 or 96 hours after administering the conjugate. In some embodiments, the light or laser is applied at or at about 24 hours $\pm$ 4 hours after administering the conjugate.

[000233] In some embodiments, the target area, such as a tumor, the vicinity of a tumor, a lymph node, the vicinity of the lymph node, or the tumor microenvironment, or subjects, can be illuminated one or more times. Thus, illumination can be completed in a single day, or can be done repeatedly on multiple days with the same or a different dosage, such as illumination at least at or about 2 different times, 3 different times, 4 different times 5 different times or 10 different times. In some embodiments, repeated illuminations may be done on the same day, on successive days, or every 1-3 days, every 3-7 days, every 1-2 weeks, every 2-4 weeks, every 1-2 months, or at even longer intervals. In some embodiments, multiple illuminations are performed, such as at least 2, at least 3, or at least 4 illuminations, such as 2, 3, 4, 5, 6, 7, 8, 9 or 10 separate administrations.

[000234] In some embodiments, the dose or method of illumination differs depending on the type or morphology of the target area, such as a tumor, the vicinity of a tumor, a lymph node, the vicinity of the lymph node. For example, in some embodiments, the illumination employs a device with “top hat” irradiance distribution profile, such as those described in published applications WO2018/080952 and US20180239074.

[000235] In some embodiments of the methods and uses provided herein, the illumination is administered after administration of the conjugate. In some embodiments, the illumination or illumination is carried out or effected between or between about 30 minutes and 96 hours after administering the phthalocyanine dye-targeting molecule conjugate, such as between 30 minutes and 48 hours, 30 minutes and 24 hours or 12 hours and 48 hours, such as generally at least 30 minutes, 1 hour, 2 hours, 3 hours, 4 hours, 5 hours, 6 hours, 7 hours, 8 hours, 9 hours, 10 hours, 11 hours, 12 hours, 13 hours, 14 hours, 15 hours, 16 hours, 17 hours, 18 hours, 19 hours, 20 hours, 21 hours, 22 hours, 23 hours, 24 hours or more after administering the conjugate. In some embodiments, the illumination is performed within about 24 hours after administering the conjugate or within 24 hours $\pm$ 4 hours after administering the conjugate, or within about 20, 21, 22, 23, 24, 24, 26, 27, or 28 hours after administering the conjugate.

E. COMBINATION THERAPY

[000236] In some embodiments, also provided are methods and uses that include combination therapies, and combinations, such as combinations for use in accordance with the combination therapy. In some aspects, the combination includes a conjugate provided herein and an additional therapeutic agent, such as an immunomodulatory agent or an anti-cancer agent. In some embodiments, the targeting molecule used for the conjugate in such combination therapies is an antibody, or an antibody fragment, that binds to a target molecule, linked to a phthalocyanine dye provided herein. In some aspects, the combination therapy includes administration of the conjugate and the additional therapeutic, e.g., an immunomodulatory agent, an immune checkpoint inhibitor, and anti-cancer agent, a therapeutic agent that acts against suppressor cells, or a combination thereof. In such methods, the primary tumors, newly arising tumors, invasive tumor cells, and metastatic tumor cells can be sensitized to the treatment with the additional therapeutic agent, such as an immunomodulatory agent, an immune checkpoint inhibitor, therapeutic agent, or an anti-cancer agent. In such methods, the growth of primary tumors, newly arising tumors, invasive tumor cells, and metastatic tumor cells can be inhibited, reduced or eliminated, and/or the volume of one or more tumors is reduced.

[000237] The increase in sensitivity as a result of such combination treatments can include, but is not limited to, a reduction of inhibition of tumor growth, a reduction in tumor cell invasion and/or metastasis, an increase in tumor cell killing, an increase in systemic immune response, an increase in new T cell priming, an increase in the diversity of intratumoral CD8⁺ T cells, an increase in the number and/or activity of intratumoral CD8⁺ T effector cells, a decrease in the number and/or activity of intratumoral regulatory T cells, a decrease in the number and/or activity of intratumoral myeloid derived suppressor cells, a decrease in the number and/or activity of intratumoral tumor associated fibroblasts or cancer associated fibroblasts (CAFs), or any combination thereof.

[000238] In some embodiments the additional therapeutic agent is an anticancer agent. In some embodiments, the anticancer agent can be one or more of a chemotherapeutic agent, an antibody treatment and/or a radiotherapeutic agent. In some embodiments, the additional therapeutic agent is an anti-cancer agent selected from a checkpoint inhibitor, an immune adjuvant, a therapeutic that acts against suppressor cells, a chemotherapeutic agent, radiation, and a biologic comprising an anti-cancer targeting molecule that binds to a tumor cell.

[000239] In some aspects, the additional therapeutic agent is an immunomodulatory agent (also called immune modulating agent), such as an immune checkpoint inhibitor. In some

aspects, such combination is employed for treatment of the tumor, lesion or cancer. In some embodiments, the methods include the administration of the immunomodulatory agent, such as an immune checkpoint inhibitor, prior to, concurrent with or subsequent to the administration of a provided conjugate.

[000240] In some embodiments, the additional therapeutic agent, such as an immunomodulatory agent, used in such combination therapies herein can include an adjuvant, immune checkpoint inhibitor, cytokine or any combination thereof. A cytokine for use in the combinations can be, for example, Aldesleukin (PROLEUKIN), Interferon alfa-2a, Interferon alfa-2b (Intron A), Peginterferon Alfa-2b (SYLATRON/PEG-Intron), IL-15, IL-18, or a cytokine that targets the IFNAR1/2 pathway, the IL-2/IL-2R pathway. An adjuvant for use in the combinations can be, for example, Poly ICLC (HILTONOL / Imiquimod), 4-1BB (CD137; TNFRS9), OX40 (CD134) OX40-Ligand (OX40L), Toll-Like Receptor 2 Agonist SUP3, Toll-Like Receptor TLR3 and TLR4 agonists and adjuvants targeting the Toll-like receptor 7 (TLR7) pathway, other members of the TNFR and TNF superfamilies, other TLR2 agonists, TLR3 agonists and TLR4 agonists.

[000241] In some embodiments, the additional therapeutic agent is an immune checkpoint inhibitor that is a PD-1 inhibitor, such as a small molecule, antibody or antigen binding fragment that inhibits PD-1 activity. Exemplary antibodies that target PD-1 include, but are not limited to, AB122, AK104, AK105, AMG 404, AMP-224, AMP-514 (MEDI0680), BCD-100, BCD-217, BI 754091, Camrelizumab (SHR1210), Cemiplimab (LIBTAYO; REGN2810), Cetrelimab (JNJ-63723283), CS1003, CX-188, Dostarlimab (TSR-042), F520, Genolimzumab (APL-501; GB226, CBT-501), GLS-010, HLX10, HX008, HX009, IBI308, JTX-4014, LZM009, MGA012 (INCMGA0012), MGD013, MGD019, Nivolumab (OPDIVO, BMS-936558), PDR001, Pembrolizumab (KEYTRUDA, Lambrolizumab, MK-3475), PF-06801591, Pidilizumab (CT-011), REGN2810, RO7121661, SCT-I10A, SG001, Sintilimab (TYVYT, IBI308), Spartalizumab (PDR001), Sym021, Tislelizumab (BGB-A317), Toripalimab (JS 001), TSR-042 (ANB011), and XmAb20717.

[000242] In some embodiments, the additional therapeutic agent is an immune checkpoint inhibitor that is a PD-L1 inhibitor, such as a small molecule, antibody or antigen binding fragment that inhibits PD-L1 activity. Exemplary antibodies that target PD-L1 include but are not limited to, Atezolizumab (TECENTRIQ, MPDL3280A, RG7446), Avelumab (BAVENCIO, MSB0010718C; M7824), BCD-135, BGB-A333, BMS-936559 (MDX-1105), CBT-502 (TQB-2450), Cosibelimab (CK-301), CS1001 (WPB3155), Durvalumab (IMFINZI; MEDI4736), FAZ053, HLX20, INBRX-105, KN035, KN046, LDP, LY3300054,

LY3415244, MCLA-145, MSB2311, NM-01, REGN3504, SHR-1316 (HTI-1088), STI-3031 (IMC-001; STI-A1015), TG-1501, and ZKAB001 (STI-A1014).

[000243] In some embodiments, the additional therapeutic agent is an immune checkpoint inhibitor that is a CTLA-4 inhibitor, such as a small molecule, antibody or antigen binding fragment that inhibits CTLA-4 activity. In some of any embodiments, the antibody that targets CTLA-4 is selected from the group consisting of ADG116, ADU-1604, AGEN1181, AGEN1884, AK104, ATOR-1015, BCD-145, BCD-217, BMS-986218, Ipilimumab (YERVOY), KN046, MGD019, MK-1308, REGN4659, Tremelimumab (Ticilimumab, CP-675,206), XmAb20717, and XmAb22841.

[000244] In some embodiments, the additional therapeutic agent is a CD25 inhibitor, such as a small molecule, antibody or antigen binding fragment that inhibits CD25 activity. In some of any embodiments, the anti-CD25 antibody is selected from the group consisting of Basiliximab (SIMULECT), Camidanlumab tesirine, daclizumab (Zinbryta; Zenapax), Inolimomab, RA8, STI-003, and Xenopax.

[000245] The administration of an additional therapeutic agent, such as a checkpoint inhibitor, adjuvant or cytokine, can be administered prior to, concurrent with, or subsequent to the administration of the provided conjugates. For example, the methods can include administering one or more doses of an immune checkpoint inhibitor, administering a conjugate, and after administration of the conjugate, illuminating with a suitable wavelength of light a target area. The methods can include first administering the conjugate, and after administration of the conjugate, illuminating a target area, and then administering an additional therapeutic agent, such as an immune checkpoint inhibitor, subsequently either to administration of the conjugate or subsequently to the illumination step. The methods can also include the administration of an additional therapeutic agent, such as an immune checkpoint inhibitor, concurrently with administration of the conjugate, followed by illuminating a target area. In some embodiments, an additional therapeutic agent, such as an immune checkpoint inhibitor, adjuvant or cytokine, is administered one or more times, prior to when a provided conjugate is administered, followed by illuminating a target area, and then one or more additional administrations of an additional therapeutic agent (the same or a different additional therapeutic agent).

F. OTHER USES

[000246] Also provided are other methods and uses for the conjugates provided herein. In some embodiments, the provided conjugates are used for purposes associated with diagnostics, monitoring, or research, such as laboratory research. For example, in some

embodiments, the provided conjugates are used for visualizing or detecting a target molecule or interaction of interest. Such applications include, but are not limited to, imaging, DNA sequencing, DNA microarray, immunoblotting (e.g., Western blotting), flow cytometry analysis, protein microarray, and fluorescence resonance imaging transfer (FRET). In some embodiments the provided conjugates are used for detection of enzyme activity, screening in high throughput applications, detection of protein interactions (e.g., ligand-receptor interactions), and nucleic acid hybridizations.

[000247] For example, in some embodiments, the provided conjugates are used as in vitro, in vivo, or ex vivo imaging agents of cells, tissues or organs in various biomedical applications including, but not limited to, tomographic imaging of organs, monitoring of organ functions, coronary angiography, fluorescence endoscopy, imaging of tumors, laser guided surgery, photoacoustic and sonofluorescence methods, and other similar methods.

[000248] In some embodiments, the conjugates are administered to a subject for visualization or detection in vivo. In such embodiments, the compositions are administered in doses effective to achieve the desired optical image of a tumor, tissue, or organ. Such doses may vary widely, depending upon the particular dye compound or conjugate employed, the tumor, tissue, or organ subjected to the imaging procedure, the imaging equipment being used, and other factors. In some embodiments, the provided conjugates are used for the visualization of a disease or condition. The equipment for such visualization is selected as appropriate for the disease or condition to be visualized, such as by direct microscopic imaging, endoscopic visualization, or 2D or 3D image reconstruction. Exemplary diseases or conditions for which the provided conjugates can be used to visualize include, but are not limited to, ocular diseases or conditions, skin diseases or conditions; vascular disorders, such as atherosclerotic plaques or other vascular abnormalities; gastrointestinal, oral, bronchial, cervical, and urinary diseases and tumors; and other tumors, such as breast or brain tumors.

[000249] In some aspects, the provided conjugates are used for visualization by immunofluorescence of formalin-fixed cells or tissue, or live-cell imaging, in vitro or ex vivo.

G. DEFINITIONS

[0001] Unless defined otherwise, all terms of art, notations and other technical and scientific terms or terminology used herein are intended to have the same meaning as is commonly understood by one of ordinary skill in the art to which the claimed subject matter pertains. In some cases, terms with commonly understood meanings are defined herein for clarity and/or for ready reference, and the inclusion of such definitions herein should not

necessarily be construed to represent a substantial difference over what is generally understood in the art.

[0002] As used herein, the singular forms “a,” “an,” and “the” include plural referents unless the context clearly dictates otherwise. For example, “a” or “an” means “at least one” or “one or more.” It is understood that aspects and variations described herein include “consisting” and/or “consisting essentially of” aspects and variations.

[0003] Throughout this disclosure, various aspects of the claimed subject matter are presented in a range format. It should be understood that the description in range format is merely for convenience and brevity and should not be construed as an inflexible limitation on the scope of the claimed subject matter. Accordingly, the description of a range should be considered to have specifically disclosed all the possible sub-ranges as well as individual numerical values within that range. For example, where a range of values is provided, it is understood that each intervening value, between the upper and lower limit of that range and any other stated or intervening value in that stated range is encompassed within the claimed subject matter. The upper and lower limits of these smaller ranges may independently be included in the smaller ranges, and are also encompassed within the claimed subject matter, subject to any specifically excluded limit in the stated range. Where the stated range includes one or both of the limits, ranges excluding either or both of those included limits are also included in the claimed subject matter. This applies regardless of the breadth of the range.

[0004] The term “about” as used herein refers to the usual error range for the respective value readily known to the skilled person in this technical field. Reference to “about” a value or parameter herein includes (and describes) embodiments that are directed to that value or parameter per se. For example, description referring to “about X” includes description of “X”.

[0005] As used herein, a “conjugate” refers to a targeting molecule linked directly or indirectly to a photoactivatable dye described herein, in particular a phthalocyanine dye of Formula (0), Formula (I), or Formula (II), produced by chemical conjugation and those produced by any other methods. For example, a conjugate can refer to a phthalocyanine dye provided herein linked directly or indirectly to one or more targeting molecules, such as to a polypeptide that binds to or targets to a cell surface protein. A targeting molecule can be, for example, a protein, a glycoprotein, an antibody, an antibody fragment, an affibody, an antigen, an antigen binding fragment, a peptide, a polypeptide, a tissue homing peptide, a small molecule, a polymeric synthetic molecule, a polymeric nanoparticle, a liposome, an enzyme substrate, a hormone, a neurotransmitter, a cell metabolite, a viral particle, a viral capsid, a viral nanoparticle, a bacterial particle, a marker, a cell, a hapten, an avidin, a

streptavidin, a monomeric streptavidin, a biotin, a carbohydrate, an oligosaccharide, a polysaccharide, a nucleic acid, a deoxy nucleic acid, a fragment of DNA, a fragment of RNA, an aptamer, nucleotide triphosphates, acyclo terminator triphosphates, PNA, or a chemical moiety.

[0006] As used herein, “protein” and “polypeptide” are used interchangeably. Proteins may include moieties other than amino acids (e.g., may be glycosylated, etc.) or may be otherwise processed or modified. Those of ordinary skill in the art will appreciate that a “protein” can be a complete protein chain as produced by a cell (with or without a signal sequence) or can be a protein portion thereof. A protein can sometimes include more than one protein chain, for example, non-covalently or covalently attached, e.g., linked by one or more disulfide bonds or associated by some other means. Polypeptides may contain l-amino acids, d-amino acids, or both and may contain any of a variety of amino acid modifications or analogs known in the art. Useful modifications include, e.g., terminal acetylation, amidation, methylation. In some embodiments, proteins may comprise natural amino acids, non-natural amino acids, synthetic amino acids, and combinations thereof. In some embodiments, proteins are antibodies, antibody fragments, biologically active portions thereof and/or characteristic portions thereof.

[0007] As used herein, an “antibody” refers to a polypeptide comprising at least a light chain or heavy chain immunoglobulin variable region which specifically recognizes and binds an epitope of an antigen, such as a tumor-specific protein. Antibodies are composed of a heavy and a light chain, each of which has a variable region, termed the variable heavy (V_H) region and the variable light (V_L) region. Together, the V_H region and the V_L region are responsible for binding the antigen recognized by the antibody. The term “antibody” also includes intact antibodies and antigen-binding antibody fragments that exhibit antigen binding, such as Fab fragments, Fab' fragments, $F(ab)_2$ fragments, Fab'-SH fragments, single chain Fv proteins (“scFv”), single domain antibodies (sdAb), such as heavy chain variable region only (VHH) single domain antibodies, scFv fragments, and disulfide stabilized Fv proteins (“dsFv”); diabodies; linear antibodies; and multispecific antibodies formed from antibody fragments. Other antibody fragments or multispecific antibodies formed from antibody fragments include a multivalent scFv, a bispecific scFv or an scFv-CH3 dimer. An scFv protein is a fusion protein in which a light chain variable region of an immunoglobulin and a heavy chain variable region of an immunoglobulin are bound by a linker, while in dsFvs, the chains have been mutated to introduce a disulfide bond to stabilize the association of the chains. The term “antibody” also includes genetically engineered forms such as

modified forms of immunoglobulins, chimeric antibodies, for example, humanized murine antibodies, and heteroconjugate antibodies, such as bispecific antibodies. See also, *Pierce Catalog and Handbook*, 1994-1995 (Pierce Chemical Co., Rockford, Ill.); Kuby, J., *Immunology*, 3rd Ed., W.H. Freeman & Co., New York, 1997.

[0008] An “antibody-like” molecule as used herein includes molecules that specifically bind to an antigen but are not structurally related to antibodies. Exemplary anti-body like molecules include, but are not limited to, affibodies, z-domain structures, DARPin, monobodies, anticalins, affilins, affimers (e.g, affimer type 1 molecules and affimer type 2 molecules), affitins, alphabodies, anticalins, avimers, fynomers, kunitz domain peptides, and nanoclamps that specifically bind to an antigen.

[0009] References to “V_H” or “VH” refer to the variable region of an immunoglobulin heavy chain, including that of an Fv, scFv, dsFv or Fab. References to “V_L” or “VL” refer to the variable region of an immunoglobulin light chain, including that of an Fv, scFv, dsFv or Fab.

[0010] A “monoclonal antibody” is an antibody produced by a single clone of B lymphocytes or by a cell into which the light and heavy chain genes of a single antibody have been transfected. Monoclonal antibodies are produced by methods known to those of skill in the art, for instance by making hybrid antibody-forming cells from a fusion of myeloma cells with immune spleen cells. Monoclonal antibodies include humanized monoclonal antibodies.

[0011] “Specifically binds” refers to the ability of individual antibodies to specifically immunologically react with an antigen relative to binding to unrelated proteins. For example, a PD-L1-specific binding agent binds substantially only the PD-L1 protein *in vitro* or *in vivo*. As used herein, the term “tumor-specific binding agent” includes tumor-specific antibodies and other agents that bind substantially only to a tumor-specific protein in that preparation.

[0012] “Antibody-dye molecule” or “antibody-dye conjugate” refers to a molecule that includes both an antibody, such as a tumor-specific antibody, conjugated to a dye molecule provided herein. In some examples the antibody is a humanized antibody (such as a humanized monoclonal antibody) that specifically binds to a surface protein on a cancer cell.

[0013] “Antigen” refers to a compound, composition, or substance that can stimulate the production of antibodies or a T cell response in an animal, including compositions (such as one that includes a tumor-specific protein) that are injected or absorbed into an animal. An antigen reacts with the products of specific humoral or cellular immunity, including those induced by heterologous antigens, such as the disclosed antigens. “Epitope” or “antigenic determinant” refers to the region of an antigen to which B and/or T cells respond. For

example, an epitope is the piece of an antigen to which an antibody binds. In one embodiment, T cells respond to the epitope, when the epitope is presented in conjunction with an MHC molecule. Epitopes can be formed from contiguous amino acids or noncontiguous amino acids juxtaposed by tertiary folding of a protein. Epitopes formed from contiguous amino acids are typically retained on exposure to denaturing solvents whereas epitopes formed by tertiary folding are typically lost on treatment with denaturing solvents. An epitope typically includes at least 3, and more usually, at least 5, about 9, or about 8-10 amino acids in a unique spatial conformation. Methods of determining spatial conformation of epitopes include, for example, x-ray crystallography and nuclear magnetic resonance.

[00014] Examples of antigens include, but are not limited to, peptides, lipids, carbohydrates, polysaccharides, and nucleic acids containing antigenic determinants, such as those recognized by an immune cell. In some examples, an antigen includes a tumor-specific peptide (such as one found on the surface of a cancer cell) or immunogenic fragment thereof.

[00015] “Immunomodulatory agent” and “immune modulatory therapy” refer to a therapeutic agent and treatment with such agent, respectively that modulates the immune system, such as a cytokine, an adjuvant and an immune checkpoint inhibitor.

[00016] “Immune checkpoint inhibitor” refers to a type of drug that blocks certain proteins made by some types of immune system cells, such as T cells, and some cancer cells. These proteins help keep immune responses in check and can keep T cells from killing cancer cells. When these proteins are blocked, the “brakes” on the immune system are released and T cells are able to kill cancer cells better. Examples of checkpoint proteins found on T cells or cancer cells include PD-1/PD-L1 and CTLA-4/B7-1/B7-2. Some immune checkpoint inhibitors are used to treat cancer.

[00017] As used herein, a combination refers to any association between or among two or more items. The combination can be two or more separate items, such as two compositions or two collections, can be a mixture thereof, such as a single mixture of the two or more items, or any variation thereof. The elements of a combination are generally functionally associated or related.

[00018] As used herein, “combination therapy” refers to a treatment in which a subject is given two or more therapeutic agents, such as at least two or at least three therapeutic agents, for treating a single disease. In some embodiments, each therapy can result in an independent pharmaceutical effect, and together can result in an additive or synergistic pharmaceutical effect.

- [00019]** As used herein, “treating” a subject with a disease or condition means that the subject's symptoms are partially or totally alleviated or remain static following treatment. Hence treating encompasses prophylaxis, therapy and/or cure. Prophylaxis refers to prevention of a potential disease and/or a prevention of worsening of symptoms or progression of a disease.
- [00020]** As used herein, “treatment” means any manner in which the symptoms of a condition, disorder or disease or other indication, are ameliorated or otherwise beneficially altered.
- [00021]** As used herein, “therapeutic effect” means an effect resulting from treatment of a subject that alters, typically improves or ameliorates the symptoms of a disease or condition or that cures a disease or condition.
- [00022]** As used herein, amelioration of the symptoms of a particular disease or disorder by a treatment, such as by administration of a pharmaceutical composition or other therapeutic, refers to any lessening, whether permanent or temporary, lasting or transient, of the symptoms that can be attributed to or associated with administration of the composition or therapeutic.
- [00023]** As used herein, the term “subject” refers to an animal, including a mammal, such as a human being.
- [00024]** As used herein, “optional” or “optionally” means that the subsequently described event or circumstance does or does not occur, and that the description includes instances where said event or circumstance occurs and instances where it does not. For example, an optionally substituted group means that the group is unsubstituted or is substituted.
- [00025]** As used herein, a “tumor” refers to an abnormal mass of tissue that results when cells divide more than they should or do not die when they should. Tumors may be benign (not cancer), or malignant (cancer).
- [00026]** As used herein, a “lesion” refers to an area of abnormal tissue. A lesion may be benign (not cancer) or malignant (cancer).
- [00027]** As used herein, an “anti-cancer agent” refers to any molecules that are used for treatment to stop or prevent cancer. Examples may include, but are not limited to, small chemical molecules, antibodies, antibody conjugates, immunomodulators, or any combination thereof.
- [00028]** As used herein, a “suppressor cell” or an “immunosuppressor cell” refers to cells that are able to decrease or inhibit the function of immune effector cells such as CD8⁺ T effector cells. Example for suppressor cells may include, but are not limited to, regulatory T

cells, M2 macrophages, myeloid derived suppressor cells, tumor associated fibroblasts, or cancer associated fibroblasts.

[00029] As used herein, an “immunosuppressive agent” refers to an agent that decreases the body’s immune responses. It reduces the body’s ability to fight infections and other diseases, such as cancer.

[00030] As used herein, “resistant to treatment” refers to that a disease or a pathological condition that is not responsive to a treatment, so that this treatment is not effective or does not show efficacy in treating this disease or pathological condition.

[00031] As used herein, “systemic immune response” refers to the ability of a subject’s immune system to respond to an immunologic challenge or immunologic challenges, including those associated with a tumor, a lesion or a cancer, in a systemic manner. Systemic immune response can include systemic response of the subject’s adaptive immune system and/or innate immune system. Systemic immune response includes an immune response across different tissues, including the blood stream, lymph node, bone marrow, spleen and/or the tumor microenvironment, and in some cases, includes a coordinated response among the tissues and organs and various cells and factors of the tissues and organs.

[00032] As used herein, “local immune response” refers to the immune response in a tissue or an organ to an immunologic challenge or immunologic challenges including those associated with a tumor, a lesion or a cancer. Local immune response can include the adaptive immune system and/or innate immune system. Local immunity includes immune response concurrently occurring at different tissues, including the blood stream, lymph node, bone marrow, spleen and/or the tumor microenvironment.

[00033] As used herein, a “protected form” of the reactive group means certain functional groups of the reactive group or the reactive group itself, including hydroxyl, amino, mercapto and carboxylic acid groups, are protected by a suitable protecting group, using standard techniques which are well-known to those in the art and as described herein. Suitable protecting groups for hydroxy include trialkylsilyl or diarylalkylsilyl (e.g., *t*-butyldimethylsilyl, *t*-butyldiphenylsilyl or trimethylsilyl), tetrahydropyranyl, benzyl and the like. Suitable protecting groups for amino, amidino and guanidino include *t*-butoxycarbonyl, benzyloxycarbonyl and the like. Suitable protecting groups for mercapto include -C(O)R (where R is alkyl, aryl or aralkyl), *p*-methoxybenzyl, trityl and the like. Suitable protecting groups for carboxylic acid include alkyl, aryl or aralkyl esters. The use of protecting groups is described in detail in Peter G. M. Wutz, *Greene’s Protective Groups in Organic Synthesis*, (2014) 5th Edition, John Wiley & Sons, Inc.

[00034] In some embodiments, the axial silicon-containing ligand is described as having a conjugatable group. In some embodiments, the axial silicon-containing ligand is described as having a reactive group. The terms “conjugatable” and “reactive”, as used in this disclosure, are synonymous and interchangeable, and no distinction between the two terms shall be construed.

[00035] As used herein, the terms “reactive group” and “conjugatable group” are used interchangeably and are intended to be construed as a moiety that is capable of chemically reacting with a functional group on a different molecule (e.g., targeting molecule) to form a linkage, such as a covalent linkage. Typically, the reactive group is an electrophile or nucleophile that can form a covalent linkage through exposure to the corresponding functional group that is a nucleophile or electrophile, respectively. Alternatively, the reactive group is a photoactivatable group, and becomes chemically reactive only after illumination with light of an appropriate wavelength. Typically, the conjugation reaction between the reactive dye and the targeting molecule to be conjugated results in one or more atoms of the reactive group A incorporated into a new linkage attaching the dye to the conjugated targeting molecule.

[00036] In some embodiments, A is a reactive group that is reactive with a carboxyl group, an amine, or a thiol group on the targeting molecule. Suitable reactive groups include, but are not limited to, an activated ester, an acyl halide, an alkyl halide, an anhydride, a carboxylic acid, a carbodiimide, a carbonate, a carbamate, a haloacetamide (e.g., iodoacetamide), an isocyanate, an isothiocyanate, a maleimide, an NHS ester, a phosphoramidite, a platinum complex, a sulfonate ester and a thiocyanate for optional attachment to the targeting molecule. In some embodiments, the reactive groups are reactive with a carboxyl group, an amine, or a thiol group on a targeting molecule. In some embodiments, the reactive group is a sulfhydryl-reactive chemical group such as maleimide, haloacetyl, pyridyl disulfide, aziridines, acryloyl, arylating agents, vinylsulfones, pyridyl di-sulfides and the like. In some embodiments, the reactive group is amine-reactive. In some embodiments, the reactive group is an NHS ester.

[00037] As used herein, a “reacted form” of the reactive group means that the reactive group has undergone chemical reaction resulting in covalent linkage with another molecule.

[00038] As used herein, “water soluble group” refers to a group comprising one or more polar and/or ionic substituents that improves the solubility of the overall molecule in aqueous media. Water soluble groups include, but are not limited to a carboxylate (—CO_2) group, poly(ethylene glycol), sulfonate (—SO_3) group, a sulfonyl (—SO_2) group, a sulfate (—SO_4) group, a hydroxyl (—OH) group, a phosphate (—OPO_3^{2-}) group, a phosphonate ($\text{—$

PO_3^{2-}) group, an amine (—NH_2) group and an optionally substituted quaternized nitrogen with each having an optional counter ion.

[00039] In certain embodiments, the water soluble group is a trivalent or tetravalent nitrogen-containing group. In yet certain embodiments, the water soluble group is tris-sulfoalkyl or tris-sulfonate quaternary ammonium, bis-sulfoalkyl or bis-sulfonate amine, or bis-alkoxypolyethylene glycol amine.

[00040] As used herein, “alkenylene” refers to a straight or branched divalent unsaturated hydrocarbon chain consisting of carbon and hydrogen atoms, having one to twelve carbon atoms, wherein the unsaturation is present only as double bonds and wherein the double bond can exist between any two carbon atoms in the chain, e.g., ethenylene, prop-1-enylene, but-2-enylene and the like. The alkenylene chain may be attached to the rest of the molecule through any two carbons within the chain.

[00041] The term “alkoxy” as used herein and unless otherwise indicated, refers to a group of formula O(alkyl) . Alkoxy can be, for example, methoxy, ethoxy, *n*-propoxy, isopropoxy, *n*-butoxy, iso-butoxy, *sec*-butoxy, *n*-pentoxy, 2-pentoxy, 3-pentoxy, or hexyloxy.

[00042] The term “alkenyl” as used herein and unless otherwise indicated, refers to a straight or branched hydrocarbon chain radical containing the indicated number of carbon atoms or otherwise having from two to ten, two to eight or two to six carbon atoms, having one or more carbon-carbon double bonds and which is attached to the rest of the molecule by a single bond or a double bond. Alkenyl groups can include, e.g., vinyl, allyl, 1-butenyl, and 2-hexenyl. In some embodiments, an alkenyl is a $\text{C}_2\text{--C}_6$ alkenyl.

[00043] The term “alkyl” as used herein and unless otherwise indicated, refers to a saturated hydrocarbon chain radical that may be a straight chain or branched chain, containing the indicated number of carbon atoms or otherwise having from one to ten, one to eight, one to six or one to four carbon atoms, and which is attached to the rest of the molecule by a single bond. In certain embodiments, the hydrocarbon chain is optionally deuterated. For example, C_1C_6 alkyl indicates that the group may have from 1 to 6 (inclusive) carbon atoms in it. In some embodiments, an alkyl is a $\text{C}_1\text{--C}_6$ alkyl which represents a straight-chain or branched saturated hydrocarbon radical having 1 to 6 carbon atoms. Examples of alkyl include without limitation methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, isobutyl, *sec*-butyl, and *tert*-butyl.

[00044] As used herein, “alkylene” refers to a straight or branched divalent hydrocarbon chain consisting of carbon and hydrogen, containing no unsaturation, and having from one to twelve carbon atoms, e.g., methylene, ethylene, propylene or *n*-butylene. The alkylene chain may be attached to the rest of the molecule through any two carbons within the chain.

- [00045]** The term “alkynyl” as used herein and unless otherwise indicated, refers to a straight or branched hydrocarbon chain radical containing the indicated number of carbon atoms or otherwise having from two to ten, two to eight or two to six carbon atoms and having one or more carbon-carbon triple bonds. Alkynyl groups can include, e.g., ethynyl, propargyl, 1-butynyl, and 2-hexynyl. In some embodiments, an alkynyl is a C₂-C₆ alkynyl.
- [00046]** The term “amino” refers to a radical having the formula -NR'R'' wherein R' and R'' are each independently hydrogen, alkyl or haloalkyl.
- [00047]** The term “aralkyl” as used herein and unless otherwise indicated, refers to an alkyl radical in which an alkyl hydrogen atom is replaced by an aryl group. One of the carbons of the alkyl moiety serves as the point of attachment of the aralkyl group to another moiety. Non-limiting examples of “aralkyl” include benzyl, 2-phenylethyl, and 3-phenylpropyl groups.
- [00048]** The term “aryl” as used herein and unless otherwise indicated, is intended to mean any stable monocyclic or bicyclic carbon ring radical of up to 6 members in each ring, wherein at least one ring is aromatic. Examples of aryl include phenyl, naphthyl, tetrahydronaphthyl, indanyl, or biphenyl.
- [00049]** As used herein, “arylene” refers to a divalent aryl group having six to fourteen carbon atoms, that may be attached to the rest of the molecule through any two carbons within the carbocyclic group. For example, six-membered arylene includes 1,2-phenylene, 1,3-phenylene and 1,4-phenylene linkers wherein the attachment points of the phenylene are in the ortho, meta or para configuration, respectively.
- [00050]** The term “aralkylene” as used herein and unless otherwise indicated, refers to an aralkyl radical attached to the rest of the molecule through any two carbons within the moiety. Non-limiting examples of “aralkylene” include -(C₆H₄)-(CH₂)-, -(CH₂)-(C₆H₄)-(CH₂)-, and -(CH₂)-(C₆H₄)- groups. The aryl portion of an aralkylene group may have six to fourteen carbon atoms, that may be attached to the rest of the molecule through any two carbons within the aralkylene group. For example, the six-membered arylene includes 1,2-phenylene, 1,3-phenylene and 1,4-phenylene linkers wherein the attachment points of the phenylene are in the ortho, meta or para configuration, respectively.
- [00051]** The term “cycloalkyl” as used herein and unless otherwise indicated, refers to a monocyclic, bicyclic, tricyclic or other polycyclic hydrocarbon radical having the indicated number of ring carbon atoms or otherwise having three to ten carbon atoms and which are fully saturated or partially unsaturated. Multicyclic cycloalkyl may be fused, bridged or spiro-ring systems. Cycloalkyl groups include, but are not limited to, cyclopropyl,

cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, norbornyl, and partially unsaturated hydrocarbon rings such as cyclobutylene, cyclopentene and cyclohexene. In some embodiments, cycloalkyl is a monocyclic C₃-C₈ cycloalkyl.

[00052] As used herein, “cycloalkylene” refers to a divalent saturated or partially saturated carbocycle group having three to eight carbon atoms, that may be attached to the rest of the molecules through any two carbons of the cycloalkyl. Cycloalkylene groups include but are not limited to cyclopropylene, cyclobutylene, cyclopentylene and cyclooctylene.

[00053] The term “halo”, “halogen” or “halide” as used herein and unless otherwise indicated, refers to any radical of fluorine, chlorine, bromine or iodine.

[00054] The term “haloalkyl” as used herein and unless otherwise indicated, refers to an alkyl radical in which at least one hydrogen atom is replaced by a halogen. In some embodiments, more than one hydrogen atom (e.g., 2, 3, 4, 5 or 6) are replaced by halogens. In these embodiments, the hydrogen atoms can each be replaced by the same halogen (e.g., fluoro) or the hydrogen atoms can be replaced by a combination of different halogens (e.g., fluoro and chloro). “Haloalkyl” also includes alkyl moieties in which all hydrogens have been replaced by halogens (sometimes referred to herein as perhaloalkyl, e.g., perfluoroalkyl, such as trifluoromethyl).

[00055] As used herein “heteroalkylene” refers to an alkylene group, as defined above, wherein the at least one carbon atom of the alkylene chain is replaced with a heteroatom including -NR^d, -O-, -OP(R^e)(R^f)O-, -S-, -S(O)-, -S(O)₂-, -C(O)-, -C(S)-, or -C(NOR^d)- where R^d is R^e, and R^f are both =O; or one of R^e and R^f is =O and the other of R^e and R^f is OR^a; where R^a is alkyl as defined herein. In some embodiments, the heteroatom is within the alkylene chain (i.e., the heteroalkylene comprises at least one carbon-Z-carbon bond where Z is -NR^g- and R^g is hydrogen or alkyl, -O-, -OP(R^e)(R^f)O-, -S-, -S(O)- or -S(O)₂-).

[00056] The term “heteroaryl” as used herein, and unless otherwise indicated, is intended to mean any stable monocyclic or bicyclic aromatic ring radical of up to 10 members in each ring, containing at least one heteroatom selected from N, O, S, S(O) and S(O)₂. Examples of heteroaryl include furan, pyrrole, oxazole, thiazole, imidazole, pyrazole, isoxazole, isothiazole, pyridine, pyridazine, pyrimidine, pyrazine, triazine, indolizine, indole, isoindole, benzofuran, benzothiophene, indazole, benzimidazole, benzthiazole, purine, quinoline, isoquinoline, cinnoline, phthalazine, quinazoline, quinoxaline, or naphthyridine.

[00057] The term “heteroaralkylene” as used herein and unless otherwise indicated, refers to an heteroaralkyl radical attached to the rest of the molecule through any two atoms within the moiety. Non-limiting examples of “heteroaralkylene” include -(heteroarylene)-(CH₂)-, -

(CH₂)-(heteroarylene)-(CH₂)-, and -(CH₂)-(heteroarylene)- groups. The heteroaryl portion of a heteroaralkylene group may have five to ten ring atoms, that may be attached to the rest of the molecule through any two atoms within the heteroaralkylene group. For example, the heteroaralkylene group may comprise a six-membered heteroarylene comprising includes 1,2-pyridine, 1,3- pyridine and 1,4- pyridine linkers wherein the attachment points of the pyridine are in the ortho, meta or para configuration, respectively.

[00058] As used herein, “heteroarylene” refers to a divalent radical heteroaryl group containing at least one heteroatom selected from N, O, S, S(O) and S(O)₂, which heteroaryl group may be attached to the rest of the molecule through any two atoms of the heteroaryl.

[00059] As used herein, “heterocycloalkylene” refers to a divalent six-membered saturated or partially saturated heterocyclyl group containing at least one heteroatom selected from N, O, S, S(O) and S(O)₂ and wherein each carbon atom of the heterocyclyl may be optionally substituted with oxo; which heterocyclyl group may be attached to the rest of the molecules through any two carbon and/or nitrogen atoms of the heterocycle.

[00060] The term “heterocycle”, “heterocyclyl” or “heterocyclic” as used herein and unless otherwise indicated, represents a stable 4-, 5-, 6- or 7-membered monocyclic- or a stable 6-, 7-, 8-, 9-, 10-, 11-, or 12-membered bicyclic heterocyclic ring system which comprises at least one non-aromatic (i.e. saturated or partially unsaturated) ring which consists of carbon atoms and from one to four, preferably up to three, heteroatoms selected from the group consisting of N, O and S, wherein the carbon, nitrogen and sulfur atoms may optionally be oxidized as carbonyl, *N*-oxide, or sulfoxide/sulfone, respectively, and wherein the nitrogen atom may optionally be quaternized. A heterocycle can be bonded via a ring carbon atom or, if available, via a ring nitrogen atom. Bicyclic heterocyclic ring systems may be fused, bridged, or spiro-bicyclic heterocyclic ring system(s). In some embodiments, heterocyclyl is monocyclic having 4 to 7 or 4 to 6, ring atoms, of which 1 or 2 are heteroatoms independently selected from the group consisting of N, O and S. In some embodiments, a heterocyclyl group is bicyclic, and in which case, the second ring may be an aromatic or a non-aromatic ring which consists of carbon atoms and from one to four, preferably up to three, heteroatoms independently selected from the group consisting of N, O and S, or the second ring may be a benzene ring, or a “cycloalkyl”, or a “cycloalkenyl”, as defined herein. Examples of such heterocyclic groups include, but are not limited to azetidine, chroman, dihydrofuran, dihydropyran, dioxane, dioxolane, hexahydroazepine, imidazolidine, imidazoline, indoline, isochroman, isoindoline, isothiazoline, isothiazolidine, isoxazoline, isoxazolidine, morpholine, oxazoline, oxazolidine, oxetane, piperazine, piperidine, dihydropyridine,

tetrahydropyridine, dihydropyridazine, pyran, pyrazolidine, pyrazoline, pyrrolidine, pyrroline, tetrahydrofuran, tetrahydropyran, thiamorpholine, tetrahydrothiophene, thiazoline, thiazolidine, thiomorpholine, thietane, thiolane, sulfolane, 1,3-dioxolane, 1,3-oxazolidine, 1,3-thiazolidine, tetrahydrothiopyran, tetrahydrotriazine, 1,3-dioxane, 1,4-dioxane, hexahydrotriazine, tetrahydro-oxazine, tetrahydropyrimidine, perhydroazepine, perhydro-1,4-diazepine, perhydro-1,4-oxazepine, 7-azabicyclo[2.2.1]heptane, 3-azabicyclo[3.2.0]heptane, 7-azabicyclo[4.1.0]heptane, 2,5-diazabicyclo[2.2.1]heptane, 2-oxa-5-azabicyclo[2.2.1]heptane, tropane, 2-oxa-6-azaspiro[3.3]heptane, dihydrobenzofuran, dihydrobenzimidazolyl, dihydrobenzoxazole, and dihydrobenzothiazolyl, and *N*-oxides or sulfones or sulfoxides thereof.

[00061] As used herein, “metalloid” refers to a chemical element with properties intermediate between those of typical metals and nonmetals. Metalloids include the chemical elements boron, silicon, germanium, arsenic, antimony, tin, aluminium, zinc and tellurium. In some embodiments, the metal or metalloid is silicon. In some embodiments, the metal or metalloid is germanium. In some embodiments, the metal or metalloid is aluminium. In some embodiments, the metal or metalloid is tin. In some embodiments, the metal or metalloid is zinc. In some embodiments, the metal or metalloid is tellurium.

[00062] As used herein, in certain embodiments unless specified otherwise, “optionally substituted alkyl”, “optionally substituted alkylene”, “optionally substituted heteroalkylene”, “optionally substituted alkenylene”, “optionally substituted heteroalkenylene” and “optionally substituted alkynyl” refers to alkyl, alkylene, heteroalkylene, alkenylene, heteroalkenylene and alkynyl radicals, respectively, that may optionally be substituted with one or more substituents independently selected from the group consisting of halo, oxo, haloalkyl, hydroxyl, hydroxyalkyl, alkoxy, alkoxyalkyl, haloalkoxy, haloalkoxyalkyl, amino, aminoalkyl, sulfonate, and cyano.

[00063] As used herein, in certain embodiments unless specified otherwise, “optionally substituted cycloalkyl”, “optionally substituted aryl”, “optionally substituted heterocyclyl” and “optionally substituted heteroaryl” refers to cycloalkyl, aryl, heterocyclyl and heteroaryl radicals, respectively, that are optionally substituted with one or more substituents selected from the group consisting of halo, oxo, alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, hydroxyl, hydroxyalkyl, alkoxy, alkoxyalkyl, haloalkoxy, haloalkoxyalkyl, amino, aminoalkyl, sulfonate, cyano and nitro.

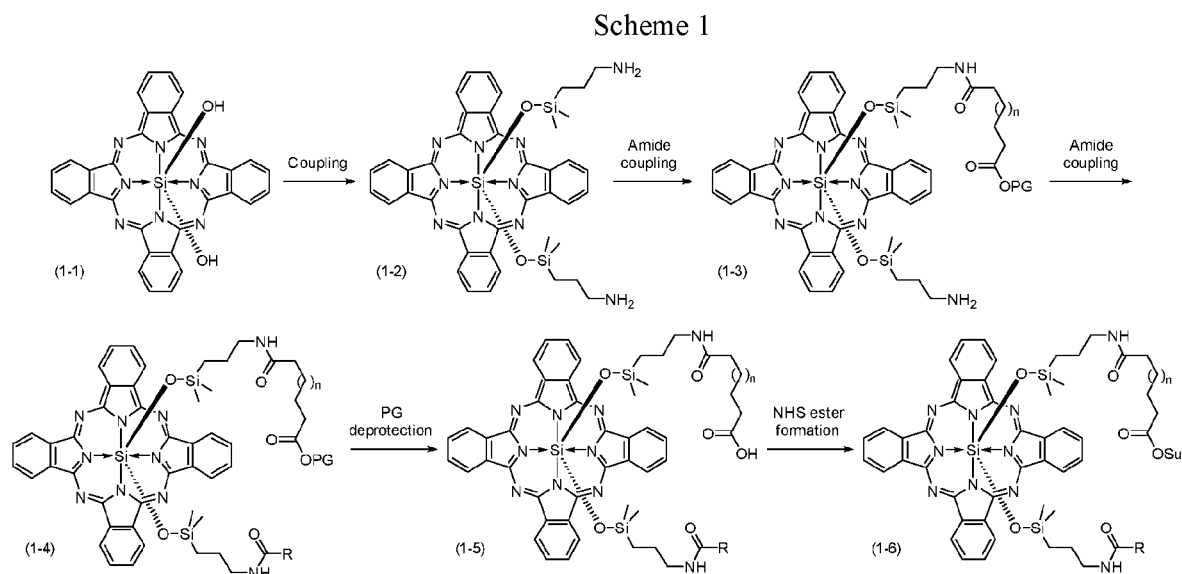
[00064] As used herein, “protein” and “polypeptide” are used interchangeably. Proteins may include moieties other than amino acids (e.g., may be glycosylated, etc.) or may be otherwise

processed or modified. Those of ordinary skill in the art will appreciate that a “protein” can be a complete protein chain as produced by a cell (with or without a signal sequence) or can be a protein portion thereof. Those of ordinary skill will appreciate that a protein can sometimes include more than one protein chain, for example, non-covalently or covalently attached, e.g., linked by one or more disulfide bonds or associated by some other means. Polypeptides may contain l-amino acids, d-amino acids, or both and may contain any of a variety of amino acid modifications or analogs known in the art. Useful modifications include, e.g., terminal acetylation, amidation, methylation. In some embodiments, proteins may comprise natural amino acids, non-natural amino acids, synthetic amino acids, and combinations thereof. In some embodiments, proteins are antibodies, antibody fragments, biologically active portions thereof and/or characteristic portions thereof.

H. PREPARATION OF PHTHALOCYANINE DERIVATIVE COMPOUNDS

[00065] In some embodiments, the phthalocyanine compounds disclosed herein are prepared by the general synthetic routes described below in Schemes 1-3. These schemes are intended to be exemplary to one of skill in the art and are not limiting. Additional methods for the synthesis of the phthalocyanine compounds disclosed herein are readily available to one of skill in the art.

[00066] A method for preparing phthalocyanine compounds disclosed herein is provided in Scheme 1:

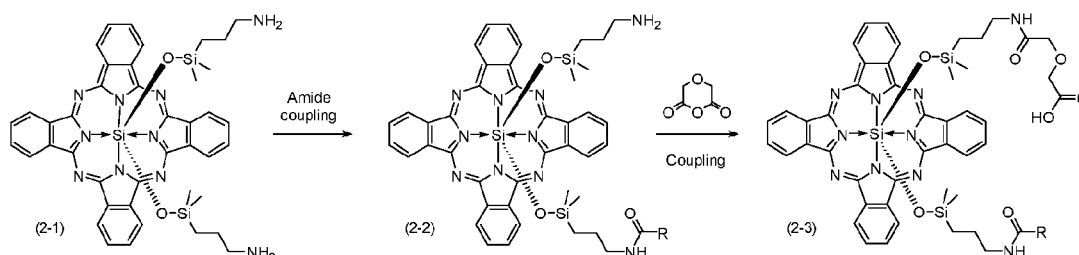


[00067] According to Scheme 1, the compound silicon phthalocyanine dihydroxide (1-1) is treated with 3-(ethoxydimethylsilyl)propan-1-amine to afford the axially disubstituted compound (1-2). Amide coupling of (1-2) with a suitable carboxylic acid derivative provides compound (1-3). Further amide coupling with a substituted carboxylic acid derivative affords

compound (1-4). Removal of the protective group of (1-4) followed by activation of the generated carboxylic acid, such as by formation of its NHS ester, provides the desired product (1-6).

[00068] A method for preparing phthalocyanine compounds disclosed herein is provided in Scheme 2:

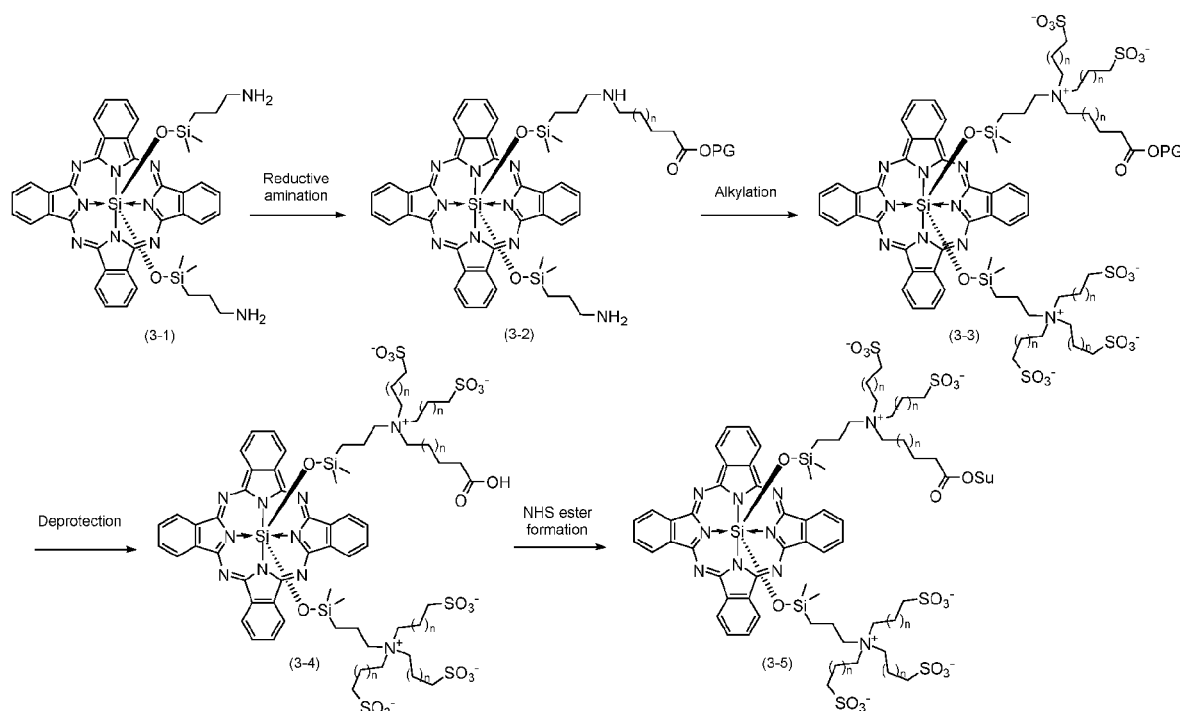
Scheme 2



[00069] According to the method provided in Scheme 2, compound (2-1) is treated with a substituted carboxylic acid derivative to afford compound (2-2). Further amide coupling with a suitable carboxylic acid derivative provides compound (2-3).

[00070] Phthalocyanine compounds disclosed herein may also be prepared by the process outlined in Scheme 3:

Scheme 3



[00071] According to Scheme 3, the axially disubstituted compound (3-1) was submitted to reductive alkylation with the corresponding aldehyde to afford the mono-substituted derivative (3-2). Alkylation with the appropriate sulfonate-substituted haloalkyl provides

compound (3-3). Removal of the protective group of (3-3) followed by activation of the generated carboxylic acid (3-4), such as by formation of its NHS ester, provides the desired product (3-5).

[00072] The subject matter has been described in an illustrative manner, and it is to be understood that the terminology used is intended to be in the nature of description rather than of limitation. Thus, it will be appreciated by those of skill in the art that conditions of solvent, temperature of reaction, volumes, reaction time may vary while still producing the desired compounds. In addition, one of skill in the art will also appreciate that many of the reagents provided in the following examples may be substituted with other suitable reagents. *See, e.g.,* Smith & March, *Advanced Organic Chemistry*, 5th ed. (2001). Such changes and modifications, including without limitation those relating to the chemical structures, substituents, derivatives, intermediates, syntheses, formulations and/or methods of use provided herein, may be made without departing from the spirit and scope thereof. U.S. patents and publications references herein are incorporated by reference.

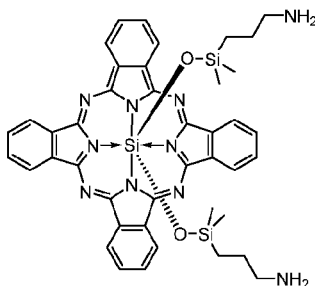
EXAMPLES

I. Chemical Synthesis

Example 1

Preparation of 6-((3-(dimethyl((19-((15-methyl-10-oxo-2,5,8-trioxa-11-aza-15-silahexadecan-15-yl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)silyl)propyl)amino)-6-oxohexanoic acid.

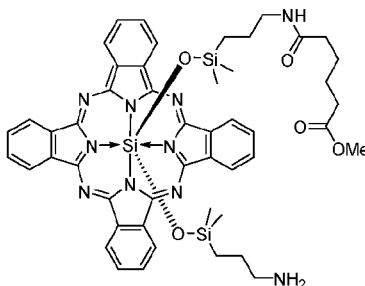
[00073] Step 1: 3,3'-(((19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindole-19,19-diyl)bis(oxy))bis(dimethylsilanediyl))bis(propan-1-amine):



[00074] To a suspension of silicon (IV) phthalocyanine dihydroxide (0.5 g, 0.87 mmol) in dry pyridine (40 mL) under a nitrogen atmosphere was added 3-aminopropyldimethylethoxysilane (4.2 g, 26.1 mmol). The resulting mixture was heated at 140 °C for 3h. Reaction progress was monitored by TLC on neutral alumina (10% MeOH/CH₂Cl₂). Upon reaction completion, the mixture was filtered and the mother liquor

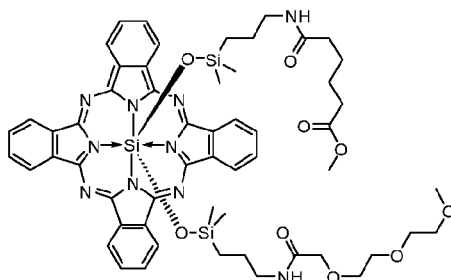
evaporated to dryness under reduced pressure. The resulting residue was suspended in hexane (50 mL), filtered and further washed with diethyl ether (2 x 10 mL) to afford the Step 1 intermediate (0.4 g, 57% yield) as a dark blue solid. ¹H-NMR (400 MHz, CDCl₃) δ 9.70 (m, 8H), 8.39 (m, 8H), 1.23 (m, 4H), -1.22 (m, 4H), -2.26 (m, 4H), -2.81 (s, 12H).

[00075] Step 2: methyl 6-((3-(((19-(((3-aminopropyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-6-oxohexanoate.dimethylsilyl)propyl)amino)-6-oxohexanoate.



[00076] To a solution of 6-methoxy-6-oxohexanoic acid (33 mg, 0.8 eq), HOBt (39 mg, 0.96 eq) and EDCI (46 mg, 0.96 eq) in CH₂Cl₂ (7 mL) under nitrogen at room temperature was added DMAP (cat.). The reaction was stirred for 1.1 h. This mixture was added dropwise over 24 minutes to a solution of the title compound from Step 1 (200 mg, 0.25 mmol) and DIPEA (82 uL, 1.9 eq) in CH₂Cl₂ (23 mL). The reaction was stirred for 24 h at room temperature. The mixture was diluted with CH₂Cl₂ (20 mL) and washed with aqueous saturated NaHCO₃ (25 mL). The aqueous phase was separated and extracted with CH₂Cl₂ (3 x 8 mL). The combined organic layers were dried over Na₂SO₄, filtered and concentrated under reduced pressure. The blue residue was purified by silica gel column chromatography (CombiFlash, 24 g column, 0 to 90% MeOH/CH₂Cl₂) to afford the title compound (74 mg, 31% yield). LCMS: 969 (M+23)⁺.

[00077] Step 3: methyl 6-((3-(dimethyl((19-((15-methyl-10-oxo-2,5,8-trioxa-11-aza-15-silahexadecan-15-yl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)silyl)propyl)amino)-6-oxohexanoate.



[00078] A solution of 2-(2-(2-methoxyethoxy)ethoxy)acetic acid (14.5 mg, 1.3 eq), HOBt (14.5 mg, 1.5 eq) and EDCI (17 mg, 1.5 eq) in CH₂Cl₂ (7 mL) under nitrogen at room temperature was stirred for 1 h. A solution of the intermediate from Step 2 (56 mg, 0.059 mmol) in CH₂Cl₂ (3 mL) was added dropwise followed by ⁱPr₂NEt (20 uL, 2 eq). The reaction mixture was stirred for 21 h at room temperature. It was then diluted with CH₂Cl₂ (7 mL) and sequentially washed with 0.1 N HCl (10 mL), NaHCO₃ (10 mL) and brine (10 mL). Each of the aqueous layers was back-extracted with CH₂Cl₂ (3 mL). The combined organic layers were dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (CombiFlash 12 g, 0-60% CH₂Cl₂/MeOH) to afford the Step 3 intermediate (47 mg, 72% yield) as a solid. ¹H NMR (CD₂Cl₂, 500 MHz) δ 9.68 (m, 8H), 8.39 (m, 8H), 3.67 (s, 3H), 3.63 (s, 2H), 3.51 (m, 2H), 3.47 (m, 1H), 3.45 (m, 2H), 3.34 (m, 1H), 3.31 (m, 2H), 3.13 (s, 3H), 2.31 (dd, J=7.5, 7.5 Hz, 2H), 1.88 (dd, J=7.5, 7.5 Hz, 2H), 1.81 (m, 2H), 1.74 (m, 2H), 1.58 (m, 2H), 1.47 (m, 2H), -1.04 (m, 2H), -1.25 (m, 2H), -2.28 (m, 4H), -2.85 (s, 3H), -2.87 (s, 3H).

[00079] Step 4: 6-((3-(dimethyl((19-((15-methyl-10-oxo-2,5,8-trioxa-11-aza-15-silahexadecan-15-yl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)silyl)propyl)amino)-6-oxohexanoic acid: To a solution of the intermediate from Step 3 (46 mg, 0.04 mmol) in THF (19 mL) cooled with an ice/water bath was added 0.01N NaOH (12.5 mL, 3 eq) dropwise. The reaction was warmed up to room temperature and stirred for 22 h. The reaction mixture was diluted with EtOAc (20 mL) and washed with saturated aqueous NH₄Cl (15 mL). The aqueous phase was separated and extracted with CH₂Cl₂ (2 x 5 mL). The combined organic layers were dried over Na₂SO₄, filtered and concentrated under reduced pressure. The blue residue was purified by silica gel column chromatography (CombiFlash 12 g, 0-60% MeOH/ CH₂Cl₂) to afford the title compound (37.2 mg, 82% yield) as a solid. ¹H NMR (CD₂Cl₂, 500 MHz) δ 9.68 (m, 8H), 8.39 (m, 8H), 3.75 (s, 2H), 3.50 (dd, J=5.5, 2.5 Hz, 2H), 3.45 (m, 4H), 3.29 (dd, J=5.8, 3.8 Hz, 2H), 3.12 (s, 3H), 2.47 (dd, J=6.5, 6.5 Hz, 2H), 2.01 (dd, J=7.0, 7.0 Hz, 2H), 1.85 (m, 2H), 1.68 (m, 6H), -1.08 (m, 2H), -1.31 (m, 2H), -2.23 (m, 2H), -2.29 (m, 2H), -2.85 (s, 3H), -2.86 (s, 3H). LCMS: 1115 (M+23)⁺.

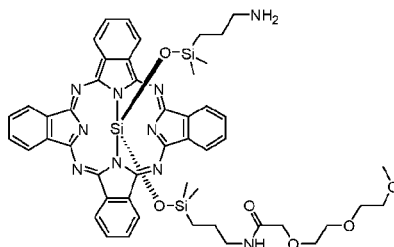
Example 2

Preparation of 2-(2-((3-(dimethyl((19-((15-methyl-10-oxo-2,5,8-trioxa-11-aza-15-silahexadecan-15-yl)oxy)-19H-6,11-(azeno)-17,21-

(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)silyl)propyl)amino)-2-oxoethoxy)acetic acid.

[00080] Step 1: Synthesis of N-(3-(((19-(((3-aminopropyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-

(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)-2-(2-(2-methoxyethoxy)ethoxy)acetamide.



[00081] To a mixture of 2-(2-(2-methoxyethoxy)ethoxy)acetic acid (5 mg, 0.026 mmol), HOBt (4.3 mg, 1 eq) and EDCI (5 mg, 1 eq) in CH₂Cl₂ (1.5 mL) under nitrogen at room temperature was added DMAP (cat.). The reaction was stirred for 1 h and then added dropwise over 15 minutes to a solution of the title compound from Example 1, Step 1, (25 mg, 0.031 mmol) and Pr₂NEt (9 uL, 2 eq) in CH₂Cl₂ (3 mL). The reaction was stirred for 24 h at room temperature. It was then diluted with CH₂Cl₂ (3 mL) and washed with saturated aqueous NaHCO₃ (5 mL). The aqueous phase was separated and extracted with CH₂Cl₂ (2 x 3 mL). The combined organic layers were dried over Na₂SO₄, filtered and concentrated under reduced pressure. The blue residue was purified by silica gel column chromatography (CombiFlash Isco, 4 g Gold column, 0 to 90% MeOH/CH₂Cl₂). ¹H-NMR (CD₂Cl₂, 500 MHz) δ 9.67 (m, 8H), 8.38 (m, 8H), 3.63 (s, 2H), 3.52 (m, 2H), 3.46 (m, 4H), 3.31 (m, 2H), 3.13 (s, 3H), 1.81 (dd, J = 14.0, 7.0, 2H), 1.11 (m, 2H), -1.05 (m, 2H), -1.24 (m, 2H), -2.30 (m, 4H), -2.85 (s, 6H), -2.88 (s, 6H). LCMS: 965 (M+1)⁺.

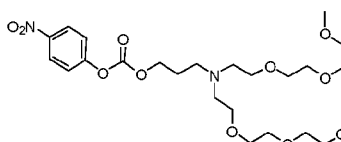
[00082] Step 2: Synthesis of 2-(2-((3-(dimethyl((19-((15-methyl-10-oxo-2,5,8-trioxa-11-aza-15-silahexadecan-15-yl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)silyl)propyl)amino)-2-oxoethoxy)acetic acid: A solution of the intermediate compound from Step 1 (4.5 mg, 0.005 mmol) and diglycolic anhydride (2.4 mg, 4.3 eq) in DMF (0.5 mL) was stirred at room temperature for 2.5 hours. The reaction mixture was diluted with EtOAc (1 mL) and washed with aqueous NH₄Cl (1 mL). The aqueous phase was separated and extracted with EtOAc (3x1 mL). The combined organic layers were dried over Na₂SO₄, filtered and concentrated under reduced pressure. The blue residue was purified by silica gel column chromatography (CombiFlash 4 g, 0-90% MeOH/CH₂Cl₂) to afford the title compound (3.5 mg, 69% yield). ¹H NMR (CD₂Cl₂, 500 MHz) δ 9.60 (m, 8H), 8.24 (m,

8H), 3.68 (bs, 2H), 3.62 (s, 2H), 3.60 (bs, 2H), 3.47 (m, 2H), 3.42 (m, 4H), 3.27 (m, 2H), 1.81 (m, 2H), 1.26 (m, 2H), -1.06 (m, 2H), -1.34 (m, 2H), -2.31 (m, 2H), -2.50 (m, 2H), -2.85 (s, 6H), -3.00 (s, 6H). LCMS: 1080 (M+1)⁺.

Example 3

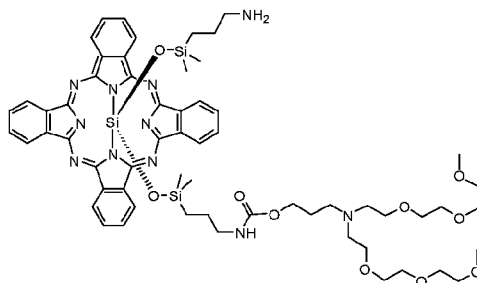
Preparation of 2-(2-(((19-(((11-(2-(2-(2-methoxyethoxy)ethoxy)ethyl)-21-methyl-16-oxo-2,5,8,15-tetraoxa-11,17-diaza-21-siladocosan-21-yl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-2-oxoethoxy)acetic acid.

[00083] Step 1: 11-(2-(2-(2-methoxyethoxy)ethoxy)ethyl)-2,5,8-trioxa-11-azatetradecan-14-yl (4-nitrophenyl) carbonate



[00084] To a solution of 11-(2-(2-(2-methoxyethoxy)ethoxy)ethyl)-2,5,8-trioxa-11-azatetradecan-14-ol (1 g, 2.72 mmol) and TEA (0.75 mL, 5.44 mmol) in dichloromethane (25 mL) cooled to 0 °C was added 4-nitrophenyl chloroformate (0.821 g, 4.09 mmol) portion wise over a 15 min period. The reaction was stirred at room temperature for 6 h. It was then poured over water (50 mL) and extracted with CH₂Cl₂ (3×50 mL). The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure to afford the crude Step 1 intermediate compound (1.8 g) that was used in the following step without further purification.

[00085] Step 2: 11-(2-(2-(2-methoxyethoxy)ethoxy)ethyl)-2,5,8-trioxa-11-azatetradecan-14-yl (3-(((19-(((3-aminopropyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)carbamate.



[00086] To a solution of the intermediate compound from Example 1, Step 1, (0.4 g, 0.49 mmol) in THF (8 mL) was added TEA (0.14 mL, 0.99 mmol). The reaction was cooled to 0 °C and a solution of the title compound from Step 1 (0.26 g, 0.50 mmol) in THF (2 mL) was added drop wise. The resulting mixture was allowed to warm to room temperature and stirred for 1 h. The reaction mixture was poured over water (30 mL) and extracted with CH₂Cl₂

(3×30 mL). The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on basic alumina (3% MeOH in CH₂Cl₂) to afford the Step 2 intermediate compound (0.2 g, 34% yield). LCMS: 1199 (M+1)⁺.

[00087] Step 3: Synthesis of 2-(2-((3-(((19-((11-(2-(2-(2-methoxyethoxy)ethoxy)ethyl)-21-methyl-16-oxo-2,5,8,15-tetraoxa-11,17-diaza-21-siladocosan-21-yl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-2-oxoethoxy)acetic acid: To a solution of the intermediate compound from Step 2 (0.08 g, 0.07 mmol) in DMF (2 mL) at room temperature was added 1,4-dioxane-2,6-dione (0.010 g, 0.08 mmol). The reaction was stirred for 30 min and then filtered. The filtrate was diluted with ACN and lyophilized. The residue was sequentially triturated with diethyl ether (2×3 mL), hexane (2×3 mL) and dried under reduced pressure to afford the title compound (0.025 g, 34% yield). LCMS: 1314 (M+1)⁺.

Example 4

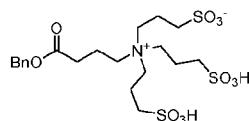
Preparation of 6-((3-(((19-((11-(2-(2-(2-methoxyethoxy)ethoxy)ethyl)-21-methyl-16-oxo-2,5,8,15-tetraoxa-11,17-diaza-21-siladocosan-21-yl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-6-oxohexanoic acid.

[00088] The title compound was synthesized in a manner similar to Example 3, Step 3, by replacing 1,4-dioxane-2,6-dione for oxepane-2,7-dione (15.4 mg, 1.2 eq). LCMS: 1326 (M+1)⁺.

Example 5

Preparation of Ammonium 3-((4-((3-(((19-((3-(2-(carboxymethoxy)acetamido)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-4-oxobutyl)bis(3-sulfopropyl)ammonio)propane-1-sulfonate

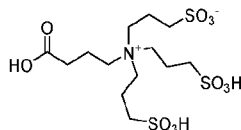
[00089] Step 1: Synthesis of 3-((4-(benzyloxy)-4-oxobutyl)bis(3-sulfopropyl)ammonio)propane-1-sulfonate.



[00090] To a solution of benzyl 4-aminobutanoate hydrochloride (1 g, 4.4 mmol) in DMF (5 mL) was added DIPEA (4 mL, 43.7 mmol) followed by 1,2-oxathiolane 2,2-dioxide (2.1 g, 43.7 mmol) at room temperature under nitrogen atmosphere. The reaction mixture was stirred at 150 °C for 16 h. Upon completion, the reaction was cooled to room temperature, poured

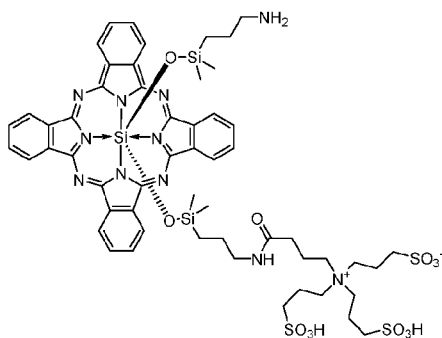
over a saturated aqueous NaHCO_3 solution (8 mL) and stirred for 1h. The mixture was washed with ethyl acetate (2 x 15 mL). Lyophilization of the aqueous layer yielded a gummy mass that was triturated with THF (12 mL) to afford a sticky solid (8 g). A gram out of this crude was further purified by preparative HPLC to afford the Step 1 intermediate (310 mg) as its ammonium salt. LCMS: $[\text{M}+\text{H}]^+$ 560

[00091] Step 2: Synthesis of 3-((3-carboxypropyl)bis(3-sulfopropyl)ammonio)propane-1-sulfonate.



[00092] A stirred solution of the intermediate from Step 1 (310 mg, 0.56 mmol) in methanol:water (1:1, 8 mL) was purged with nitrogen for 5 min. 10% palladium on carbon was added and the resulting mixture was stirred under a hydrogen atmosphere for 30 min. Upon reaction completion, the mixture was filtered and washed with methanol:water (1:1, 10 mL). Solvent from the combined filtrates was removed under reduced pressure and the resulting aqueous phase was lyophilized to afford the Step 2 intermediate (271 mg) as a sticky solid. $^1\text{H-NMR}$ (400 MHz, D_2O) δ 3.93 (m, 1H), 3.40 – 3.25 (m, 5H), 2.88-2.81 (m, 4H), 2.37 (m, 1H), 2.14-2.02 (m, 4H), 1.91 (bs, 1H), 1.34 (m, 6H), 1.23 (m, 2H). LCMS: $[\text{M}-\text{H}]^-$ 468.

[00093] Step 3: 3-((4-(((19-(((3-aminopropyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno) benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl) propyl)amino)-4-oxobutyl)bis(3-sulfopropyl)ammonio)propane-1-sulfonate.



[00094] To a solution of the intermediate from Step 2 (0.187 g, 0.40 mmol) in DMF (10 mL) was added DIPEA (0.192 g, 1.49 mmol), EDC.HCl (0.143 g, 0.75 mmol) and HOBt (0.114 g, 0.75 mmol) at room temperature under nitrogen atmosphere. The reaction was stirred for 2 h followed by addition of the title compound from Example 1, Step 1 (400 mg, 0.5 mmol). The resulting mixture was stirred at room temperature for 48 h. It was then poured over water (150

mL). The precipitate was collected after centrifugation and purified by preparative HPLC to afford the title compound (30 mg, 5%) as a blue solid. LCMS: $[M+H]^+$ 1256

[00095] Step 4: Synthesis of ammonium 3-((4-((3-(((19-(((3-(2-(carboxymethoxy)acetamido)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-4-oxobutyl)bis(3-sulfopropyl)ammonio)propane-1-sulfonate: To a solution of the intermediate from Step 3 (10 mg, 0.008 mmol) in DMF (2 mL) at room temperature under a nitrogen atmosphere was added 1,4-dioxane-2,6-dione (2.8 mg, 0.024 mmol). The reaction mixture was stirred for 5 h and directly submitted to preparative HPLC purification. Appropriate fractions were combined and lyophilized to afford the title compound (3.2 mg, 29%) as a blue solid. ^1H NMR (400 MHz, DMSO- d_6) δ 9.71 (m, 8H), 8.50 (m, 8H), 7.04 (bs, 9H), 6.82 (s, 2H), 3.92 (m, 3H), 3.62 (s, 3H), 3.02 (m, 3H), 1.87 (m, 7H), 1.75 (m, 3H), 1.58 (m, 11H), -1.15 (m, 4H), -2.35 (m, 4H), -2.92 (s, 12H). MS: $[M+H]^+$ 1372.

Example 6

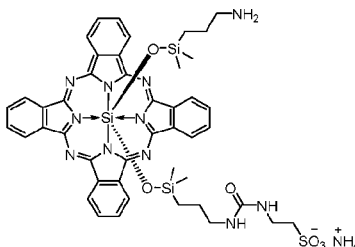
Preparation of 3-((4-((3-(((19-(((3-(6-((λ^5 -azaneyl)oxy)-6-oxohexanamido)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-4-oxobutyl)bis(3-((λ^5 -azaneyl)oxy)sulfonyl)propyl)ammonio)propane-1-sulfonate.

[00096] The title compound was synthesized in a manner similar to Example 5, Step 4, by replacing 1,4-dioxane-2,6-dione for oxepane-2,7-dione. LCMS: 1385 ($M+1$) $^+$.

Example 7

Preparation of Ammonium 2-(2-((3-(((19-((dimethyl(3-(3-(2-sulfonatoethyl)ureido)propyl)silyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-2-oxoethoxy)acetate.

[00097] Step 1: Synthesis of Ammonium 2-(3-(3-(((19-(((3-(aminopropyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)ureido)ethane-1-sulfonate.



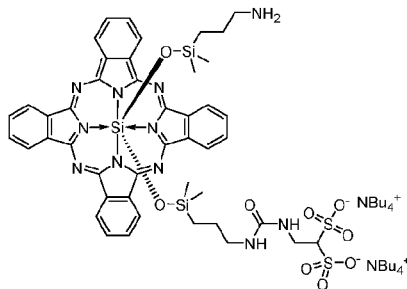
[00098] To a stirred solution of the title compound from Example 1, Step 1 (0.150 g, 0.186 mmol) in DCM (10 ml) under nitrogen atmosphere was added DIPEA (0.072 g, 0.560 mmol). The reaction mixture was cool at 0 °C and a solution of tetrabutylammonium 2-(((4-nitrophenoxy)carbonyl)amino)ethane-1-sulfonate (0.079 g, 0.149 mmol) in DCM (3.3 ml) was added dropwise. The reaction was allowed to warm up to room temperature and stirred for 16 h. The reaction mixture was concentrated under reduced pressure and triturated with DCM (3 x 5 ml) to obtain a crude material that was further purified by preparative HPLC. Pure fractions were lyophilized to afford the intermediate as a blue solid (6 mg, 4% yield). LCMS: [M-H]⁻ 954.

[00099] Step 2: Synthesis of ammonium 2-(2-(((3-(((19-((dimethyl(3-(3-(2-sulfonatoethyl)ureido)propyl)silyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-2-oxoethoxy)acetate: To a solution of the intermediate from Step 1 (6 mg, 0.0063 mmol) in DMF (1 mL) at room temperature under a nitrogen atmosphere was added 1,4-dioxane-2,6-dione (2.2 mg, 0.0188 mmol). The reaction was stirred for 5 h. It was then directly purified by preparative HPLC. Appropriate fractions were combined and lyophilized to afford the title compound (2 mg, 29%) as a blue solid. ¹H NMR (400 MHz, DMSO-d₆) δ 9.71 (bs, 8H), 8.51 (bs, 8H), 7.06 (bs, 4H), 5.45 (s, 1H), 5.10 (s, 1H), 3.85 (s, 2H), 3.61 (s, 2H), 3.03 (m, 2H), 2.34 (m, 2H), 1.60 (m, 2H), 1.53 (m, 2H), -1.14 (m, 2H), -1.17 (m, 2H), -2.37 (bs, 4H), -2.91 (s, 6H), -2.92 (s, 6H). LCMS: [M-H]⁻ 1070

Example 8

Preparation of Ammonium 2-(2-(((3-(((19-((3-(3-(2,2-disulfonatoethyl)ureido)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-2-oxoethoxy)acetate.

[000100] Step 1: Synthesis of tetrabutylammonium 2-(3-(3-(((19-(((3-aminopropyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)ureido)ethane-1,1-disulfonate.



[000101] To a solution of the title compound from Example 1, Step 1, (0.2 g, 0.25 mmol) in CH₂Cl₂ (20 mL) under inert atmosphere at 0 °C was sequentially added DIPEA (0.096 g, 0.75 mmol) and a solution of bis(tetrabutyl-λ⁵-azaneyl) 2-(((4-nitrophenoxy)carbonyl)amino)ethane-1,1-disulfonate (0.2 mmol) in CH₂Cl₂ (7.5 mL). The reaction mixture was stirred at room temperature for three hours. A blue precipitate formed. The reaction mixture was concentrated to dryness under reduced pressure and washed with CH₂Cl₂ to afford the Step 1 intermediate (0.17 g, 45%). LCMS: [M-H]⁻ 1034.

[000102] Step 2: Synthesis of ammonium 2-(2-((3-(((19-(((3-(3-(2,2-disulfonatoethyl)ureido)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-2-oxoethoxy)acetate: To a stirred solution of the intermediate from Step 1 (38 mg, 0.025 mmol) in DMF (4 mL) under nitrogen was added 1,4-dioxane-2,6-dione (8.7 mg, 0.075 mmol). The reaction mixture was stirred for two hours at room temperature and directly purified by preparative HPLC. Appropriate fractions were combined and lyophilized to afford the title compound (4.3 mg, 14%). ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.71 (bs, 8H), 8.50 (bs, 8H), 7.51 (bs, 2H), 7.02 (bs, 8H), 5.52 (bs, 2H), 5.25 (bs, 2H), 3.76 (bs, 2H), 1.60 (m, 2H), 1.53 (m, 2H), -1.13 (m, 2H), -1.23 (m, 2H), -2.38 (m, 4H), -2.91 (s, 6H), -2.93 (s, 6H). LCMS: [M-H]⁻ 1150.

Example 9

Preparation of Ammonium 6-(((3-(((19-(((3-(3-(2,2-disulfonatoethyl)ureido)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-6-oxohexanoate.

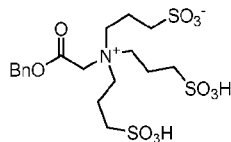
[000103] To a solution of the intermediate from Example 8, Step 1, (45 mg, 0.03 mmol) in DMF (4.5 mL) at room temperature under a nitrogen atmosphere was added adipic anhydride (11 mg, 0.088 mmol). The reaction mixture was stirred for two hours and directly purified by preparative HPLC. Appropriate fractions were combined and lyophilized to afford the title compound (8.5 mg, 24% yield). ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.69 (bs, 8H), 8.49 (bs, 8H), 6.68 (m, 2H), 5.50 (m, 2H), 5.25 (m, 2H), 3.16 (m, 2H), 2.67 (bs, 1H), 2.06 (m, 2H), 1.63 (m, 2H), 1.55 (m, 2H), 1.51 (m, 2H), 1.23 (m, 4H), -1.18 (m, 2H), -1.26 (m, 2H), -2.39 (m, 4H), -2.94 (s, 6H), -2.95 (s, 6H). LCMS: [M-H]⁻ 1162.

Example 10

Preparation of 3-((2-((3-(((19-(((3-(6-((λ⁵-azaneyl)oxy)-6-oxohexanamido)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-

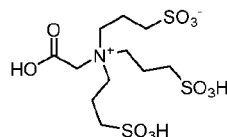
a' [diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-2-oxoethyl)bis(3-((λ⁵-azanevl)oxy)sulfonyl)propyl)ammonio)propane-1-sulfonate

[000104] Step 1: Synthesis of 3-((2-(benzyloxy)-2-oxoethyl)bis(3-sulfopropyl)ammonio)propane-1-sulfonate



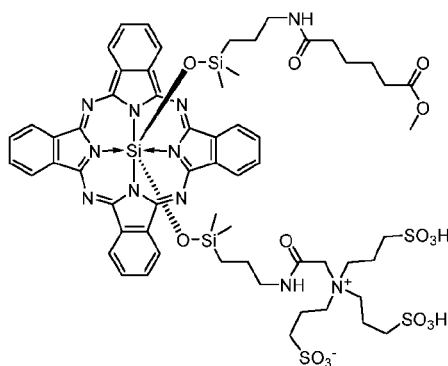
[000105] To a suspension of benzyl glycinate hydrochloride (0.5 g, 2.5 mmol) in sulfolane (8 mL) was added DIPEA (4.75 mL, 27.3 mmol). The mixture was stirred at room temperature for 15 min to obtain a clear solution. 1,2-oxathiolane 2,2-dioxide (3 g, 24.8 mmol) was added and the reaction was stirred at 140 °C for 16 h. It was then cooled to room temperature, diluted with water (15 mL) and washed with DCM (2 x 10 mL). The aqueous layer was separated and lyophilized to afford 3.5 g of a sticky solid residue. 900 mg of this crude were further purified by preparatory HPLC to afford the Step 1 intermediate (400 mg) as a sticky solid. LCMS: 532.7 [M+H]⁺.

[000106] Step 2: 3-((carboxymethyl)bis(3-sulfopropyl)ammonio)propane-1-sulfonate.



[000107] A stirred solution of the intermediate from Step 1 (350 mg, 0.66 mmol) in water (10 mL) was purged with N₂ for 5 min. 10% palladium on carbon was added and the resulting mixture was stirred under a hydrogen atmosphere for 2 h. The reaction was filtered and the residue was washed with water (5 mL). The combined filtrates were partially distilled under reduced pressure. The remaining solution was lyophilized to afford the Step 2 intermediate as a sticky solid. LCMS: 440 [M-H]⁻.

[000108] Step 3: Synthesis of 3-((2-((3-(((19-(((3-(6-methoxy-6-oxohexanamido)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy) dimethylsilyl)propyl)amino)-2-oxoethyl)bis(3-sulfopropyl)ammonio)propane-1-sulfonate.



[000109] To a stirred solution of the intermediate from Step 2 (9 mg, 0.021 mmol) in DMF (1 mL) under a nitrogen atmosphere were sequentially added EDC.HCl (6 mg, 0.03 mmol), HOBt (2.8 mg, 0.02 mmol) and DIPEA (11 μ L, 0.06 mmol). The mixture was stirred at room temperature for 1 h and then added to a solution of the title compound from Example 1, Step 2 (20 mg, 0.02 mmol) in DMF (0.5 mL) at 0 °C. The reaction was stirred at room temperature for 8 h. Water (0.5 mL) was added and the resulting mixture was lyophilized. The residue was washed with hexanes (5 mL) and diethyl ether (2 x 3 mL) to afford the Step 3 intermediate (18 mg) as a blue solid that was used in the next step without further purification. LCMS: 1369 [M]⁺.

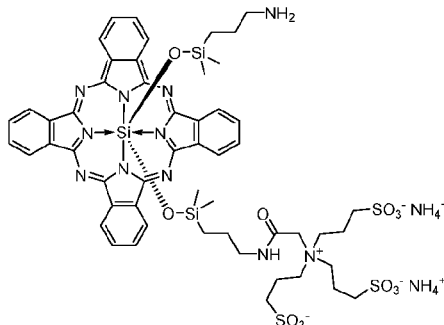
[000110] Step 4: Synthesis of 3-((2-((3-(((19-(((3-(6-((λ^5 -azaneyl)oxy)-6-oxohexanamido)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-2-oxoethyl)bis(3-(((λ^5 -azaneyl)oxy)sulfonyl)propyl)ammonio)propane-1-sulfonate. To a solution of the intermediate from Step 3 (18 mg, 0.01 mmol) in a 1:2 MeOH:H₂O mixture (2 mL) was added K₂CO₃ (6 mg, 0.04 mmol). The resulting mixture was stirred at room temperature for 16 h. The reaction was directly purified by preparatory HPLC (mobile phases: 5 mM ammonium bicarbonate + 0.1% NH₃ in water; 100% ACN; X-Bridge C18). Selected fractions were combined and lyophilized to afford the title compound (0.4 mg, 3% yield) as a blue solid. LCMS: 1354 [M-H]⁻.

Example 11

Preparation of 3-((2-((3-(((19-(((3-(2-(2-((λ^5 -azaneyl)oxy)-2-oxoethoxy)acetamido)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-2-oxoethyl)bis(3-(((λ^5 -azaneyl)oxy)sulfonyl)propyl)ammonio)propane-1-sulfonate

[000111] Step 1: Ammonium 3,3',3''-((2-((3-(((19-(((3-aminopropyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-

(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-2-oxoethyl)ammonio)tris(propane-1-sulfonate)



[000112] To a stirred solution of the intermediate from Example 10, Step 2 (54 mg, 0.12 mmol) in DMF (2 mL) at 0 °C under a nitrogen atmosphere was sequentially added T₃P (0.16 mL of 50% solution in EtOAc, 0.25 mmol) and DIPEA (0.11 mL, 0.62 mmol). The reaction mixture was stirred at room temperature for 1 h. A solution of the title compound from Example 1, Step 1 (0.1 g, 0.12 mmol) in DMF (1 mL) was added dropwise at 0 °C. The resulting mixture was stirred at room temperature for 8 h. The reaction mixture was purified by preparative HPLC (A: 5 mM ammonium bicarbonate + 0.1% NH₃ in water; B: 100% ACN) to afford the Step 1 intermediate compound (6 mg, 4%) as a blue solid. LCMS: 1227 [M]⁺

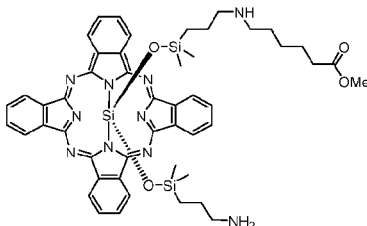
[000113] Step 2: 3-((2-(((19-(((3-(2-(2-((λ⁵-azaneyl)oxy)-2-oxoethoxy)acetamido)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-2-oxoethyl)bis(3-(((λ⁵-azaneyl)oxy)sulfonyl)propyl)ammonio)propane-1-sulfonate. The title compound was prepared in a manner similar to Example 2, Step 2 by replacing the intermediate compound from Example 2, Step 1 with the intermediate compound from Step 1. The reaction mixture was directly purified by preparative HPLC to afford the title compound as a blue solid (1.2 mg, 49%). ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.70 (m, 8H), 8.51 (m, 8H), 7.03 (bs, 6H), 3.90 (bs, 2H), 3.62 (s, 2H), 3.53 (s, 2H), 3.44 (s, 2H), 2.67-2.61 (m, 4H), 2.34 (m, 8H), 1.83 (bs, 6H), 1.57 (m, 4H), -1.15 (m, 4H), -2.23 (m, 4H), -2.92 (s, 12H). LCMS: 1342 [M-H]⁺.

Example 12

Preparation of 3-((6-((λ⁵-azaneyl)oxy)-6-oxohexyl)(3-(((λ⁵-azaneyl)oxy)sulfonyl)propyl)(3-(((19-(((3-(bis(3-(((λ⁵-azaneyl)oxy)sulfonyl)propyl)(3-sulfonatopropyl)ammonio)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-

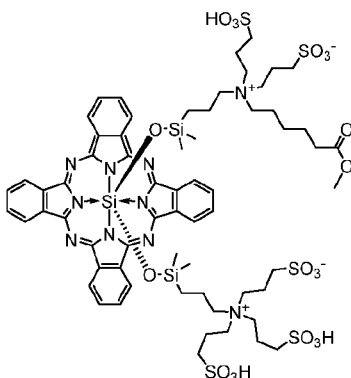
(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)ammonio)propane-1-sulfonate.

[000114] Step 1: Methyl 6-((3-(((19-(((3-aminopropyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)hexanoate.



[000115] To a solution of the intermediate compound from Example 1, Step 1 (0.3 g, 0.37 mmol) in THF (50 mL) was added a solution of methyl-6-oxohexanoate (0.08 g, 0.56 mmol) in THF (2 mL) and a catalytic amount of AcOH. The solution was stirred at room temperature for one hour. It was then added to a suspension of NaBH(OAc)₃ (0.237 g, 1.12 mmol) in THF (10 mL) and stirred for 16 h. The reaction was quenched with saturated aqueous NaHCO₃ (50 mL) and extracted with DCM (3 x 70 mL). The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The residue was purified by basic alumina column chromatography to afford the Step 1 intermediate (0.10 g, 29%) as a blue solid. LCMS: 933[M+H]⁺

[000116] Step 2: 3-((3-(((19-(((dimethyl(3-((3-sulfonatopropyl)bis(3-sulfopropyl)ammonio)propyl)silyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)(6-methoxy-6-oxohexyl)(3-sulfopropyl)ammonio)propane-1-sulfonate.



[000117] 1,3-Propane sultone (0.654 g, 5.4 mmol) and DIPEA (1.4 mL, 8 mmol) were sequentially added to a solution of the intermediate compound from Step 1 (0.10 g, 0.107 mmol) in sulfolane (10 mL) under a nitrogen atmosphere followed by irradiation under

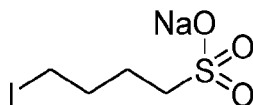
microwave at 120 °C for 2h. The reaction mixture was added drop-wise to THF (30 mL) and stirred for 30 min. The supernatant was removed. The precipitate was sequentially washed with THF (2 x 10 mL) and dried under reduced pressure to afford the Step 2 intermediate (0.24 g) as a blue solid. LCMS: 1542 [M]⁺.

[000118] Step 3: 3-((6-((λ5-azaneyl)oxy)-6-oxohexyl)(3-(((λ5-azaneyl)oxy)sulfonyl)propyl)(3-(((19-(((3-(bis(3-((λ5-azaneyl)oxy)sulfonyl)propyl)(3-sulfonatopropyl)ammonio)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)ammonio)propane-1-sulfonate. To a solution of the intermediate from Step 2 (120 mg, 0.08 mmol) in a 1:2 MeOH:water mixture (5 mL) was added K₂CO₃ (32 mg, 0.23 mmol). The reaction was stirred at room temperature for 16 h and directly purified by preparatory HPLC (mobile phases: 5 mM ammonium bicarbonate + 0.1% NH₃ in water; 100% ACN; X-Bridge C18). Appropriate fractions were combined and lyophilized to afford the title compound (23 mg, 18%) as a blue solid. ¹H NMR (400 MHz, DMSO-d₆) δ 9.76 (m, 8H), 8.52 (m, 8H), 7.12 (bs, 8H), 3.49 (m, 2H), 3.42 (m, 2H), 2.64 (m, 12H), 2.27 (m, 10H), 1.88 (m, 4H), 1.43 (m, 10H), 1.11 (m, 4H), -0.89 (m, 2H), -1.03 (m, 2H), -2.30 (m, 2H), -2.37 (m, 2H), -2.89 (s, 12H). LCMS: 764 [M/2]⁺.

Example 13

Preparation of 4-((6-((λ5-azaneyl)oxy)-6-oxohexyl)(4-(((λ5-azaneyl)oxy)sulfonyl)butyl)(3-(((19-(((3-(bis(4-(((λ5-azaneyl)oxy)sulfonyl)butyl)(4-sulfonatobutyl)ammonio)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)ammonio)butane-1-sulfonate.

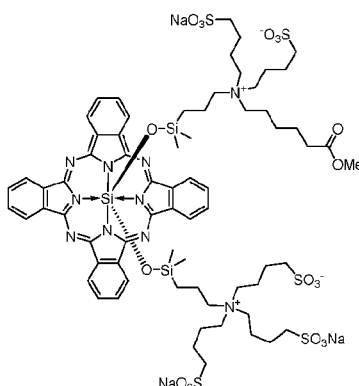
[000119] Step 1: Sodium 4-iodobutane-1-sulfonate



[000120] To a solution of 1,2-oxathiolane 2,2-dioxide (0.5 g, 3.7 mmol) in MeOH (5 mL) at room temperature in a sealed tube was added sodium iodide (550 mg, 3.7 mmol). The reaction mixture was heated at 80 °C for 6 h. It was then allowed to cool down to room temperature. The precipitate was filtered, washed with cold MeOH (5 mL) and dried under reduced pressure to afford the Step 1 intermediate (270 mg, 26%) as a white solid. ¹H NMR (400 MHz, Chloroform-d) δ 3.33-3.29 (m, 2H), 2.42-2.48 (m, 2H), 1.90-1.83 (m, 2H), 1.71-1.64 (m, 2H).

[000121] Step 2: Sodium 4,4',4''-((3-(((19-(((3-((6-methoxy-6-oxohexyl)bis(4-sulfonatobutyl)ammonio)propyl) dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-

(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2] silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)ammonio)tris(butane-1-sulfonate).



[000122] To a solution of the intermediate from Example 12, Step 1 (25 mg, 0.03 mmol) in sulfolane (3 mL) under nitrogen were added the intermediate from Step 1 (0.115 g, 0.4 mmol) and DIPEA (0.093 mL, 0.54 mmol). The reaction was irradiated under microwave at 120 °C for 4 h. The reaction mixture was added drop-wise to THF (5 mL) and stirred for 30 min. The supernatant was removed, and the residue was washed with THF (2 x 3 mL). The residue was dried under reduced pressure to afford the crude Step 2 intermediate (50 mg) that was used in the following step without further purification. LCMS: 805 [M/2-1]⁺

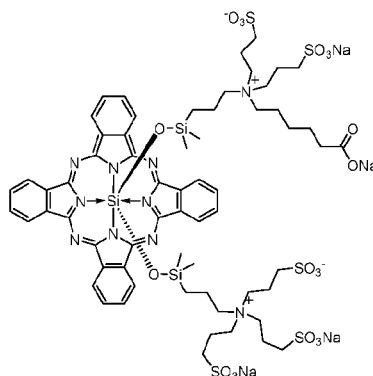
[000123] Step 3: 4-(((6-((λ5-azaneyl)oxy)-6-oxohexyl)(4-(((λ5-azaneyl)oxy)sulfonyl)butyl)(3-(((19-(((3-(bis(4-(((λ5-azaneyl)oxy)sulfonyl)butyl)(4-sulfonatobutyl)ammonio)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)ammonio)butane-1-sulfonate: The title compound was prepared in a manner similar to Example 12, Step 3 by replacing the intermediate from Example 12, Step 3 with the intermediate from Step 2 to afford the title compound (12 mg, 24%) as blue solid. ¹H NMR (400 MHz, DMSO-d₆) δ 9.77 (m, 8H), 8.54 (m, 8H), 7.12 (bs, 8H), 2.40-2.33 (m, 22H), 2.23 (m, 2H), 1.79 (m, 4H), 1.50 (m, 10H), 1.40 (m, 2H), 1.20 (m, 10H), 1.06 (m, 4H), -1.20 (m, 4H), -2.24 (m, 4H), -2.89 (s, 12H). LCMS: 798 [M-1/2]⁺.

Example 14

Preparation of sodium 3,3',3''-((3-(((19-(((3-(((6-((2,5-dioxopyrrolidin-1-yl)oxy)-6-oxohexyl)bis(3-sulfonatopropyl)ammonio)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)ammonio)tris(propane-1-sulfonate)

[000124] Step 1: Tetrasodium mono(6-(((3-(((19-((dimethyl(3-(tris(3-sulfonatopropyl)ammonio)propyl)silyl)oxy)-19H-6,11-(azeno)-17,21-

(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)bis(3-sulfonatopropyl)ammonio)hexanoate)



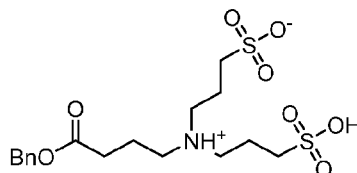
[000125] Dowex® 50WX8 hydrogen form resin (4 g, 50-100 mesh) was loaded into a column and converted to its sodium form by passing through a 1N NaCl solution (50 ml) until the pH of the eluent became neutral. The column was further washed with water to remove excess NaCl. The process was continued until no precipitate was observed upon treatment of the eluent with silver nitrate. A solution of the title compound from Example 12 (33 mg, 0.02 mmol) in water (3 ml) was passed through the column. The blue-colored fractions were collected and lyophilized to afford the Step 1 intermediate (29 mg, 91%). ¹H NMR (400 MHz, DMSO-d₆) δ 9.75 (m, 8H), 8.52 (m, 8H), 3.49 (m, 2H), 3.42 (m, 2H), 2.64 (m, 12H), 2.29 (m, 10H), 1.89 (m, 4H), 1.42 (m, 10H), 1.11 (m, 4H), -0.88 (m, 2H), -1.04 (m, 2H), -2.30 (m, 2H), -2.38 (m, 2H), -2.89 (s, 12H). LCMS: 764 [M/2]⁺.

[000126] Step 2: Sodium 3,3',3''-(((3-(((19-(((3-(((6-((2,5-dioxopyrrolidin-1-yl)oxy)-6-oxohexyl)bis(3-sulfonatopropyl)ammonio)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)ammonio)tris(propane-1-sulfonate): To a solution of the intermediate from Step 1 (1.3 mg) in DMSO (0.3 mL) under nitrogen in an amber vial was sequentially added DIPEA (32 μL of 0.1 M DMSO solution, 4 eq) and N,N'-disuccinimidyl carbonate (64 μL of 0.1 M DMSO solution, 8 eq). The resulting mixture was stirred at room temperature overnight. The reaction was diluted with DMF (0.3 mL), filtered through a 0.45 μm filter and added dropwise to vigorously stirred MTBE (5 mL) over 20 minutes. The reaction vial was washed with DMF (0.2 mL). A blue precipitate forms. The suspension was allowed to settle, and the clear supernatant was removed. MTBE (2.5 mL) was added and the process was repeated twice. The residue after the final wash was dried under reduced pressure to afford the title compound (0.5 mg, 37%). LCMS: 812 [M-1/2]⁺.

Example 15

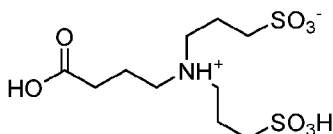
Preparation of Ammonium 2-(2-((3-(((19-(((3-(4-(bis(3-sulfonatopropyl)ammonio)butanamido)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-2-oxoethoxy)acetate.

[000127] Step 1: 3-((4-(benzyloxy)-4-oxobutyl)(3-sulfopropyl)ammonio)propane-1-sulfonate



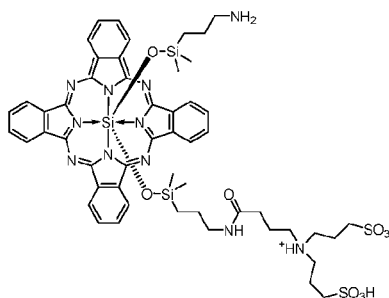
[000128] To a solution of benzyl 4-aminobutanoate hydrochloride (1 g, 4.4 mmol) in DMF (5 ml) at room temperature under a nitrogen atmosphere was added DIPEA (4 ml, 17.5 mmol) followed by 1,2-oxathiolane 2,2-dioxide (2.1 g, 44 mmol). The reaction mixture was stirred at 100 °C for 16 h. It was then cooled to room temperature, treated with a saturated aqueous NaHCO₃ solution (8 ml) and stirred for 1h. The mixture was washed with ethyl acetate (2x15 ml). The aqueous layer was lyophilized to yield a residue that was triturated with THF (12 ml). A gram out of the three-gram crude was further purified by preparative HPLC to afford the Step 1 intermediate (260 mg). LCMS: 438 [M+H]⁺

[000129] Step 2: 3-((3-carboxypropyl)(3-sulfopropyl)ammonio)propane-1-sulfonate



[000130] A solution of the intermediate from Step 1 (260 mg, 0.59 mmol) in a methanol:water mixture (6 ml, 1:1) was purged with nitrogen for 5 min. 10% palladium on carbon (140 mg) was added and the mixture was stirred under a hydrogen atmosphere for 30 min. The reaction mixture was filtered and the residue washed with methanol:water (10 ml, 1:1). The combined filtrates were partially rotavaped and lyophilized to afford the Step 2 intermediate (210 mg). ¹H-NMR (400 MHz, Deuterium Oxide) δ 3.25 – 3.21 (m, 4H), 3.09 – 3.13 (m, 2H), 2.86 (t, *J* = 7.2 Hz, 4H), 2.27 (t, *J* = 6.9 Hz, 2H), 2.04 (m, 4H), 1.85 (m, 2H). MS: 348 [M+H]⁺

[000131] Step 3: 3-((4-((3-(((19-(((3-(4-(bis(3-sulfonatopropyl)ammonio)butanamido)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-4-oxobutyl)(3-sulfopropyl)ammonio)propane-1-sulfonate



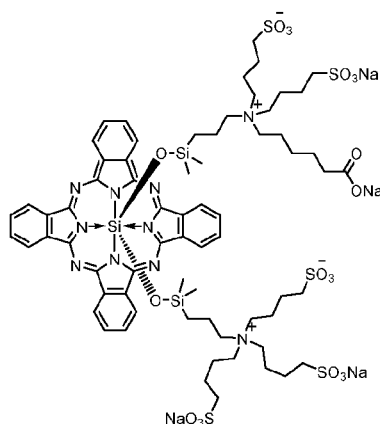
[000132] To a solution of the intermediate from Step 2 (69 mg, 0.18 mmol) in DMF (4 ml) at room temperature under a nitrogen atmosphere were added HOBt (57 mg, 0.37 mmol), DIPEA (96 mg, 0.75 mmol) and EDC.HCl (71 mg, 0.37 mmol). The reaction mixture was stirred for 2 h followed by addition of the title compound from Example 1, Step 1 (0.200 g, 0.25 mmol). The reaction was stirred at room temperature for 48 h. Its contents were poured over water (100 mL). The precipitate was separated by centrifugation to yield 210 mg of crude material that was purified by preparative HPLC to afford the Step 3 intermediate (10 mg, 4%) as a blue solid. LCMS: 1134 [M+H]⁺

[000133] Step 4: Ammonium 2-(2-((3-(((19-(((3-(4-(bis(3-sulfonatopropyl)ammonio)butanamido)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-2-oxoethoxy)acetate: The title compound was prepared in a manner similar to Example 2, Step 2 by replacing the intermediate from Example 2, Step 1 with the intermediate from Step 3 (8 mg, 0.007 mmol) to afford the title compound (3.2 mg, 35%) as a blue solid. ¹H NMR (400 MHz, DMSO-d₆) δ 9.71 (bs, 8H), 8.52 (bs, 8H), 6.82 (m, 2H), 3.98 (s, 2H), 3.64 (s, 2H), 3.12 (m, 3H), 1.89 (m, 7H), 1.77 (m, 2H), 1.59 (m, 8H), -1.15 (m, 4H), -2.34 (m, 4H), -2.92 (s, 12H). LCMS: 1248 [M-H]⁻.

Example 16

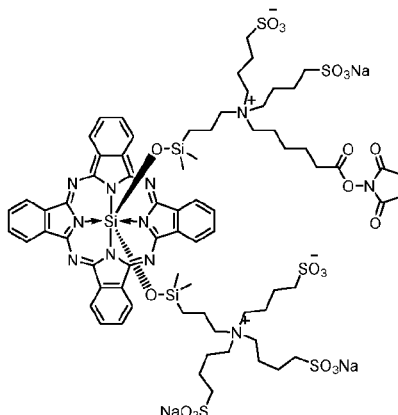
Preparation of sodium 4,4',4''-(((3-(((19-(((3-(((2,5-dioxopyrrolidin-1-yl)oxy)-6-oxohexyl)bis(4-sulfonatobutyl)ammonio)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)ammonio)tris(butane-1-sulfonate)

[000134] Step 1: Sodium 6-(((3-(((19-(((dimethyl(3-(tris(4-sulfonatobutyl)ammonio)propyl)silyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)bis(4-sulfonatobutyl)ammonio)hexanoate



[000135] The title compound was prepared in a manner similar to Example 14, Step 1 by replacing Example 12 for Example 13 (38 mg, 0.02 mmol) to afford the title compound (34 mg, 88%). ¹H NMR (400 MHz, DMSO-d₆) δ 9.77 (m, 8H), 8.54 (m, 8H), 2.39-2.33 (m, 22H), 2.21 (m, 2H), 1.79 (m, 4H), 1.50 (m, 10H), 1.39 (m, 2H), 1.18 (m, 10H), 1.05 (m, 4H), -1.20 (m, 4H), -2.24 (m, 4H), -2.89 (s, 6H), -2.90 (s, 6H). LCMS: 799 [M/2]⁺

[000136] Step 2: Sodium 4,4',4''-(((3-(((19-(((3-(((6-((2,5-dioxopyrrolidin-1-yl)oxy)-6-oxohexyl)bis(4-sulfonatobutyl)ammonio)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)ammonio)tris(butane-1-sulfonate)

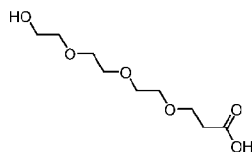


[000137] The title compound was prepared in a manner similar to Example 14, Step 2 by replacing the title compound from Example 14, Step 1 for the title compound from Step 1 (1.4 mg, 0.0008 mmol) to afford the title compound (0.0005 mmol). LCMS: 847 [M-1/2]⁻

Example 17

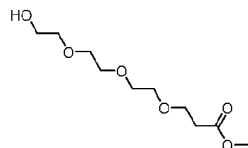
Preparation of Sodium 2-((19-((dimethyl(3-(tris(4-sulfonatobutyl)ammonio)propyl)silyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)-2-methyl-6,6-bis(4-sulfonatobutyl)-9,12,15-trioxa-6-aza-2-silaoctadecan-6-ium-18-oate

[000138] Step 1: 3-(2-(2-(2-Hydroxyethoxy)ethoxy)ethoxy)propanoic acid



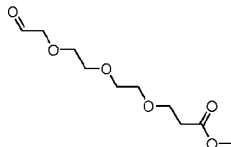
[000139] Tert-butyl 3-(2-(2-(2-hydroxyethoxy)ethoxy)ethoxy)propanoate (2.0 g, 7.2 mmol) was dissolved in trifluoroacetic acid (20 mL) at 0 °C. The reaction mixture was stirred at room temperature for 16 h. Upon completion, solvents were removed under reduced pressure to obtain the crude title compound that was used in the following step without further purification.

[000140] Step 2: Methyl 3-(2-(2-(2-hydroxyethoxy)ethoxy)ethoxy)propanoate



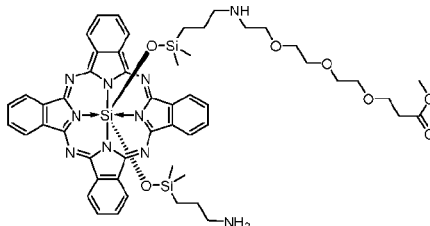
[000141] To a solution of the title compound from Step 1 (1.5 g, 6.7 mmol) in MeOH (20 mL) was added concentrated H₂SO₄ (0.3 mL) at room temperature. The solution was stirred at 60 °C for 3 h. The reaction mixture was concentrated under reduced pressure. The crude material was purified by column chromatography on neutral alumina to afford the title compound (1.1 g, 69%) as a liquid. ¹H NMR (400 MHz, D₂O) δ 3.69 (m, 2H), 3.60-3.56 (m, 15H), 2.57 (m, 2H).

[000142] Step 3: Methyl 3-(2-(2-(2-oxoethoxy)ethoxy)ethoxy)propanoate



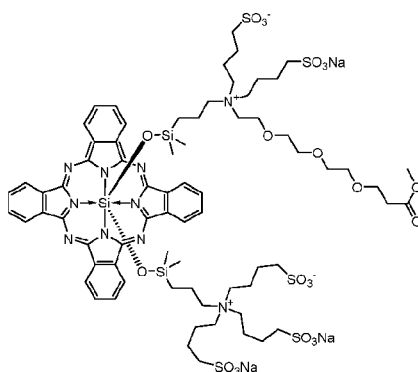
[000143] To a stirred solution of Dess–Martin periodinane (4.04 g, 9.5 mmol) and pyridine (0.92 mL, 11.4 mmol) in dichloromethane (10 mL) under nitrogen was added a solution of the title compound from Step 2 (0.9 g, 3.8 mmol) in dichloromethane (5 mL). The reaction was stirred at room temperature for 4 h. Upon completion, the reaction mixture was diluted with dichloromethane (5 mL) and treated with a saturated solution of NaHCO₃ (5 mL) and a 10% Na₂S₂O₃ solution (5 mL). The resulting mixture was stirred at room temperature for 30 min and extracted with dichloromethane (3 x 30 mL). The combined organic layers were dried over sodium sulphate, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on neutral alumina to afford the title compound (0.45 g, 50%) that was promptly used in the next step. LCMS: 235 [M+1]⁺

[000144] Step 4: Methyl 2-((19-(((3-aminopropyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno) benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)-2-methyl-9,12,15-trioxa-6-aza-2-silaoctadecan-18-oate.



[000145] To a stirred solution of the title compound from Example 1, Step 1 (200 mg, 0.25 mmol) in THF (100 mL) at room temperature was added a solution of the title compound from Step 3 (72 mg, 0.3 mmol) in THF (2 mL) followed by a catalytic amount of AcOH (0.1 mL of a 15 mg/mL solution of AcOH in THF, 0.025 mmol). The solution was stirred at room temperature for 1 h and then added to a suspension of NaBH(OAc)₃ (0.16 g, 0.75 mmol) in THF (10 mL). The resulting mixture was stirred at room temperature for 4 h. The reaction contents were poured over a saturated NaHCO₃ aqueous solution (50 mL) and extracted with DCM (3 x 50 mL). The combined organic layers were dried over sodium sulphate, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on basic alumina to afford the title compound (70 mg, 27%) as a blue solid. LCMS: 1023 [M+H]⁺.

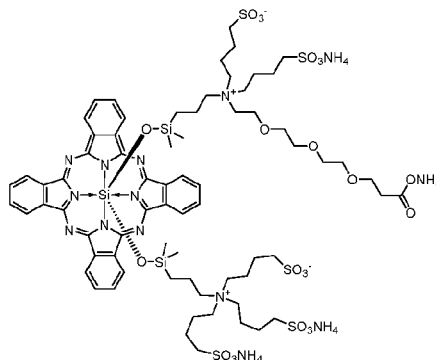
[000146] Step 5: Sodium 4,4',4''-((3-(dimethyl((19-((2-methyl-18-oxo-6,6-bis(4-sulfonatobutyl)-9,12,15,19-tetraoxa-6-aza-2-silaicosan-6-ium-2-yl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno) benzo[7,8][1,3,5,10] tetraaza [2] silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)silyl) propyl)ammonio)tris (butane-1-sulfonate)



[000147] To a solution of the title compound from Step 4 (35 mg, 0.034 mmol) in sulfolane (5 mL) under nitrogen was added the title compound from Example 13, Step 1 (0.196 g, 0.68 mmol) and DIPEA (0.18 mL, 1.02 mmol). The reaction was irradiated at 120 °C in a microwave for 5 h. Upon completion, the reaction mixture was added dropwise to THF (50 mL) and stirred for 30 min. The precipitate was separated by centrifugation, washed with

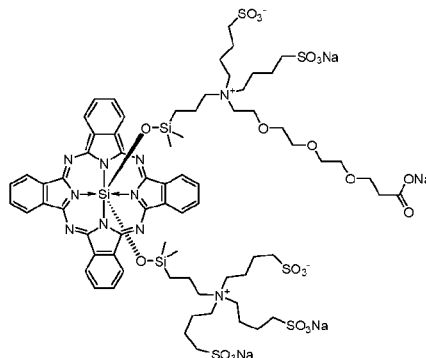
THF (2 x 10 mL) and dried under reduced pressure to afford the title compound (100 mg crude) that was used in the following step without further purification. LCMS: 853 [M+2/2]⁺.

[000148] Step 6: Ammonium 2-((19-((dimethyl(3-(tris(4-sulfonatobutyl)ammonio)propyl)silyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)-2-methyl-6,6-bis(4-sulfonatobutyl)-9,12,15-trioxa-6-aza-2-silaoctadecan-6-ium-18-oate



[000149] To a solution of the title compound from Step 5 (200 mg, 0.11 mmol) in MeOH: water (2:1, 7.5 mL) was added K₂CO₃ (94 mg, 0.68 mmol). The reaction was stirred at room temperature for 16 h. The reaction mixture was directly purified by preparative HPLC. Appropriate fractions were lyophilized to afford the title compound (41 mg, 34% over two steps) as a blue solid. LCMS: 844 [M-1/2]⁻.

[000150] Step 7: Sodium 2-((19-((dimethyl(3-(tris(4-sulfonatobutyl)ammonio)propyl)silyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)-2-methyl-6,6-bis(4-sulfonatobutyl)-9,12,15-trioxa-6-aza-2-silaoctadecan-6-ium-18-oate.



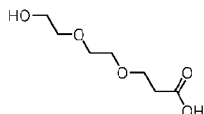
[000151] The title compound of Step 6 (41 mg, 0.027 mmol) was submitted to the ion exchange procedure described in Example 14, Step 1 to afford the title compound (39 mg, 94%). ¹H NMR (400 MHz, DMSO-d₆) δ 9.78 (m, 8H), 8.55 (m, 8H), 3.39 (m, 6H), 3.17 (m,

2H), 3.07 (m, 4H), 2.95 (m, 2H), 2.84 (m, 2H), 2.61 (m, 2H), 2.40 (m, 20H), 2.04 (m, 2H), 1.94 (m, 2H), 1.78 (m, 2H), 1.51 (m, 4H), 1.41 (m, 4H), 1.25 (m, 8H), -1.18 (m, 2H), -1.28 (m, 2H), -2.22 (m, 4H), -2.89 (s, 12H). LCMS: 844 [M-1/2]⁺.

Example 18

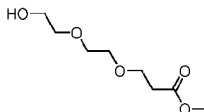
Preparation of Sodium 2-((19-((dimethyl(3-(tris(4-sulfonatobutyl)ammonio)propyl)silyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)-2-methyl-6,6-bis(4-sulfonatobutyl)-9,12-dioxa-6-aza-2-silapentadecan-6-ium-15-oate

[000152] Step 1: 3-(2-(2-hydroxyethoxy)ethoxy)propanoic acid



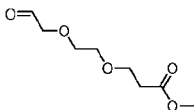
[000153] The title compound was prepared in a manner similar to Example 17, Step 1 by replacing tert-butyl 3-(2-(2-(2-hydroxyethoxy)ethoxy)ethoxy)propanoate for tert-butyl 3-(2-(2-hydroxyethoxy)ethoxy)propanoate (4.5 g, 19.21 mmol) to afford the crude title compound that was used in the following step without further purification.

[000154] Step 2: Methyl 3-(2-(2-hydroxyethoxy)ethoxy)propanoate



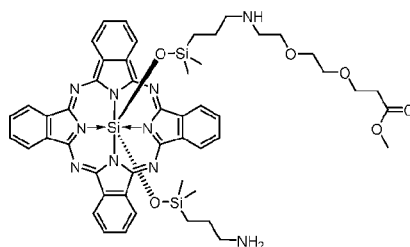
[000155] The title compound was prepared in a manner similar to Example 17, Step 2 by replacing 3-(2-(2-(2-Hydroxyethoxy)ethoxy)ethoxy)propanoic acid for the title compound from Step 1 (3.7 g, 20.8 mmol) to afford the title compound (2.8 g, 70%) as a liquid. ¹H NMR (400 MHz, CDCl₃) δ 3.79 (m, 2H), 3.74 (m, 2H), 3.71 (s, 3H), 3.64 (m, 6H), 2.63 (t, J = 5.6 Hz, 2H).

[000156] Step 3: Methyl 3-(2-(2-oxoethoxy)ethoxy)propanoate



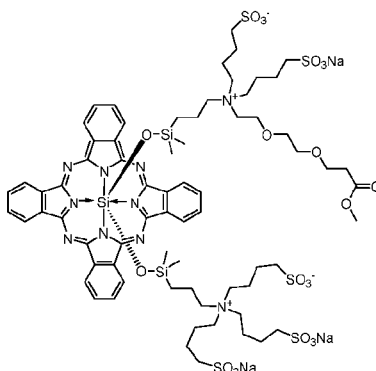
[000157] The title compound was prepared in a manner similar to Example 17, Step 3 by replacing methyl 3-(2-(2-(2-hydroxyethoxy)ethoxy)ethoxy)propanoate for the title compound from Step 2 (1 g, 5.2 mmol) to afford the title compound (470 mg, 47%) as a liquid.

[000158] Step 4: Methyl 2-((19-(((3-aminopropyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)-2-methyl-9,12-dioxa-6-aza-2-silapentadecan-15-oate.



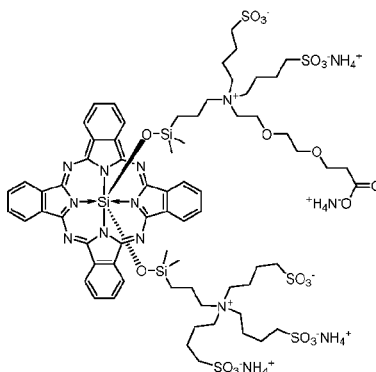
[000159] The title compound was prepared in a manner similar to Example 17, Step 4 by replacing methyl 3-(2-(2-(2-oxoethoxy)ethoxy)ethoxy)propanoate for the title compound from Step 3 (59 mg, 0.31 mmol) to afford the title compound (95 mg, 39%) as a blue solid. LCMS: 980 $[M+1]^+$.

[000160] Step 5: Sodium 4,4',4''-((3-(dimethyl((19-((2-methyl-15-oxo-6,6-bis(4-sulfonatobutyl)-9,12,16-trioxa-6-aza-2-silaheptadecan-6-ium-2-yl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)silyl)propyl)ammonio)tris(butane-1-sulfonate)



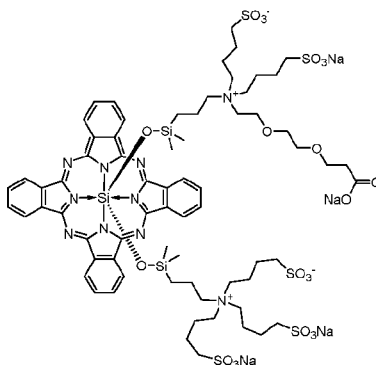
[000161] The title compound was prepared in a manner similar to Example 17, Step 5 by replacing the title compound from Example 17, Step 4 for the title compound from Step 4 (75 mg, 0.08 mmol) to afford the title compound (190 mg crude) as a blue solid. LCMS: 828 $[M-2/2]^-$.

[000162] Step 6: Ammonium 2-((19-((dimethyl(3-(tris(4-sulfonatobutyl)ammonio)propyl)silyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)-2-methyl-6,6-bis(4-sulfonatobutyl)-9,12-dioxa-6-aza-2-silapentadecan-6-ium-15-oate.



[000163] The title compound was prepared in a manner similar to Example 17, Step 6 by replacing the title compound from Example 17, Step 5 for the title compound from Step 5 (380 mg, 0.22 mmol) to afford the title compound (60 mg, 23% over two step) as a blue solid. LCMS: 822 [M-1/2]⁻.

[000164] Step 7: Sodium 2-((19-((dimethyl(3-(tris(4-sulfonatobutyl)ammonio)propyl)silyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)-2-methyl-6,6-bis(4-sulfonatobutyl)-9,12-dioxa-6-aza-2-silapentadecan-6-ium-15-oate.

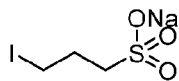


[000165] The title compound of Step 6 (70 mg, 0.04 mmol) was submitted to the ion exchange procedure described in Example 14, Step 1 to afford the title compound (66 mg, 93%). ¹H NMR (400 MHz, D₂O) δ 9.66 (m, 8H), 8.46 (m, 8H), 3.29 (bs, 2H), 2.82 (m, 4H), 2.74 (m, 6H), 2.68 (m, 8H), 2.48 (bs, 2H), 2.32 (m, 6H), 2.20 (m, 2H), 1.92 (m, 2H), 1.73 (dd, J = 6.8, 6.8 Hz, 4H), 1.59 (m, 8H), 1.45 (m, 2H) 1.31 (m, 4H), 1.16 (m, 6H), -1.49 (m, 2H), -1.66 (m, 2H), -2.04 (m, 4H), -2.91 (s, 6H), -2.92 (s, 6H). LCMS: 822 [M-1/2]⁻.

Example 19

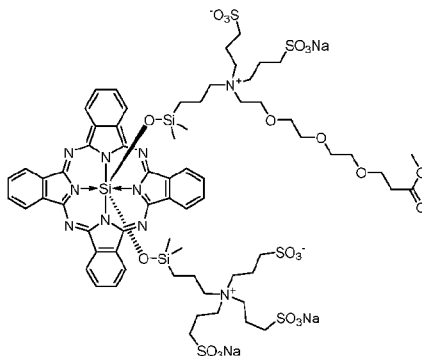
Preparation of sodium 2-((19-((dimethyl(3-(tris(3-sulfonatopropyl)ammonio)propyl)silyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)-2-methyl-6,6-bis(3-sulfonatopropyl)-9,12,15-trioxa-6-aza-2-silaoctadecan-6-ium-18-oate

[000166] Step 1: Sodium 3-iodopropane-1-sulfonate



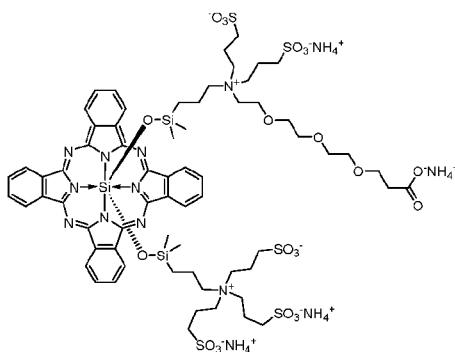
[000167] To a solution of sodium iodide (24.5 g, 164 mmol) in dry methanol (200 mL) was added 1,3-propanesultone (20 g, 164 mmol). The sealed tube was heated at 80 °C and stirred for 1 h. The reaction mixture was cooled to room temperature and filtered through a Buchner funnel. The residue was washed with DCM (50 mL) and dried under reduced pressure to afford the title compound as an off-white powder (27 g, 61%). ¹H NMR (400 MHz, D₂O) δ 3.27 (t, *J* = 6.8 Hz, 2H), 2.94 (t, *J* = 7.2 Hz, 2H), 2.16 (q, *J* = 7.6 Hz, 2H).

[000168] Step 2: Sodium 3,3',3''-(((3-(dimethyl((19-((2-methyl-18-oxo-6,6-bis(3-sulfonatopropyl)-9,12,15,19-tetraoxa-6-aza-2-silaicosan-6-ium-2-yl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)silyl)propyl)ammonio)tris(propane-1-sulfonate).



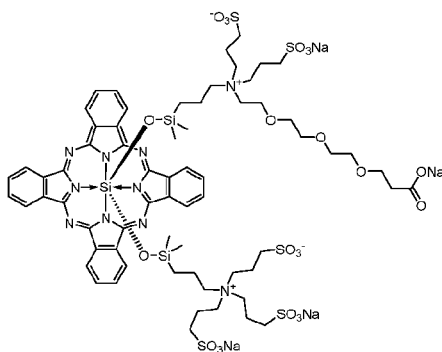
[000169] The title compound was prepared in a manner similar to Example 17, Step 5 by replacing sodium 4-iodobutane-1-sulfonate for the title compound from Step 1 (345 mg, 1.2 mmol) to afford the title compound (0.275 g, crude) as a blue solid. LCMS: 816 [M-1/2]⁺.

[000170] Step 3: Ammonium 2-(((19-((dimethyl(3-(tris(3-sulfonatopropyl)ammonio)propyl)silyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)-2-methyl-6,6-bis(3-sulfonatopropyl)-9,12,15-trioxa-6-aza-2-silaooctadecan-6-ium-18-oate.



[000171] The title compound was prepared in a manner similar to Example 17, Step 6 by replacing the title compound from Example 17, Step 5 for the title compound from Step 2 (275 mg, 0.16 mmol) to afford the title compound (62 mg, 60% over two steps) as a blue solid. LCMS: 809 [M-1/2]⁻.

[000172] Step 4: Sodium 2-((19-((dimethyl(3-(tris(3-sulfonatopropyl)ammonio)propyl)silyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)-2-methyl-6,6-bis(3-sulfonatopropyl)-9,12,15-trioxa-6-aza-2-silaooctadecan-6-ium-18-oate.

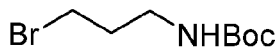


[000173] The title compound of Step 3 (62 mg, 0.04 mmol) was submitted to the ion exchange procedure described in Example 14, Step 1 to afford the title compound (58 mg, 92%). ¹H NMR (400 MHz, D₂O) δ 9.66 (m, 8H), 8.47 (m, 8H), 3.30 (m, 2H), 3.23 (m, 2H), 2.87 (m, 8H), 2.72 (s, 6H), 2.60-2.39 (m, 16H), 2.09-2.07 (m, 4H), 1.91 (m, 2H), 1.67-1.50 (m, 10H), -1.56 (m, 2H), -1.67 (m, 2H), -2.02 (m, 4H), -2.89 (s, 6H), -2.93 (s, 6H). LCMS: 809 [M-1/2]⁻.

Example 20

Preparation of sodium 6-(((3-(((19-((dimethyl(3-(5-(tris(3-sulfonatopropyl)ammonio)-2-(3-(tris(3-sulfonatopropyl) ammonio)propyl)pentanamido)propyl)silyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-6-oxohexanoate)

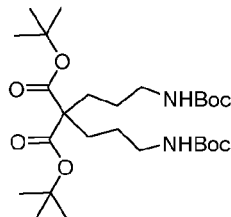
[000174] Step 1: *tert*-Butyl (3-bromopropyl)carbamate



[000175] To a solution of *tert*-butyl (3-hydroxypropyl)carbamate (2.0 g, 11.4 mmol) in THF (30 mL) under nitrogen was added CBr₄ (5.68 g, 17.1 mmol) and PPh₃ (4.49 g, 17.1 mmol). The reaction was stirred at room temperature for 1h. It was then diluted with an aqueous saturated NaHCO₃ solution (30 mL) and extracted with ethyl acetate (3x30 mL). The combined organic layers were dried over sodium sulphate, filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography to afford the title

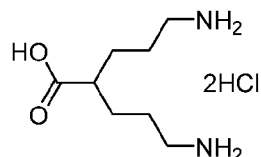
compound (2 g, 74% yield) as a white solid. $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 4.67 (bs, 1H), 3.46 (t, $J = 6.4$ Hz, 2H), 3.29 (m, 2H), 2.06 (t, $J = 6.4$ Hz, 2H), 1.45 (s, 9H).

[000176] Step 2: Di-*tert*-utyl 2,2-bis(3-(((*tert*-butoxycarbonyl)amino)propyl)malonate



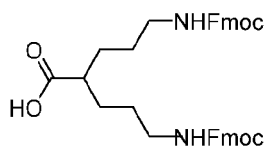
[000177] To a solution of the title compound from Step 1 (2.0 g, 8.4 mmol) and di-*tert*-butyl malonate (726 mg, 3.36 mmol) in THF (20 mL) at 0 °C under nitrogen was added NaH (60%) (403 mg, 10.1 mmol) portion wise. The reaction was warmed up to room temperature and stirred for 4 h. The reaction contents were slowly added to ice-cold water (50 mL) and extracted with ethyl acetate (2x50 mL). The combined organic layers were dried over sodium sulphate, filtered and concentrated under reduced pressure. The crude residue was purified by silica gel column chromatography to afford the title compound (1.2 g, 67% yield). LCMS: 531 [M+H]⁺.

[000178] Step 3: 5-Amino-2-(3-aminopropyl)pentanoic acid



[000179] A mixture of the title compound from Step 2 (5 g, 9.4 mmol) in AcOH (50 mL) and 3N HCl (50 mL) was heated at 80 °C for 48 h. The reaction mixture was cooled to room temperature and concentrated under reduced pressure to afford the title compound (2.5 g Crude). $^1\text{H-NMR}$ (400 MHz, D_2O) δ 2.91 (bs, 4H), 2.41 (bs, 1H), 1.58–1.50 (m, 8H).

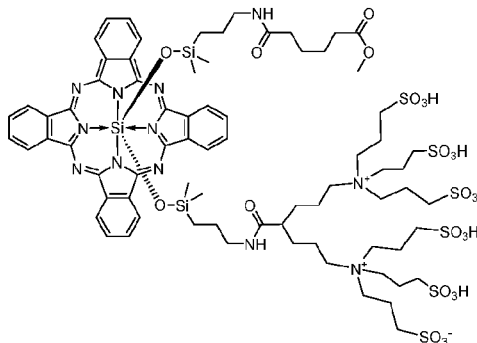
[000180] Step 4: 5-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-2-(3-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)propyl)pentanoic acid.



[000181] To a solution of the title compound from Step 3 (790 mg, 4.5 mmol) in a THF (10 mL) and aqueous saturated NaHCO_3 (10 mL) mixture was added Fmoc-OSu (3.8 g, 11.3 mmol) at room temperature. The reaction mixture was stirred at room temperature for 4 h. The pH was adjusted to between 7 and 8 by using 1N HCl and the reaction was then extracted with ethyl acetate (3x50 mL). The combined organic layers were dried over sodium sulphate, filtered and concentrated under reduced pressure. The residue was purified by silica gel

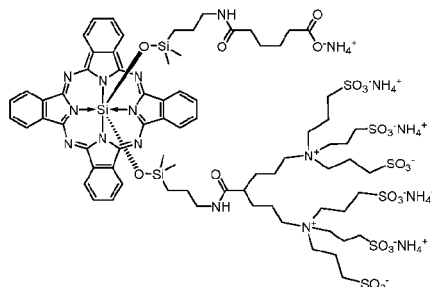
trituration using diethyl ether (2x3 mL) to afford the title compound (65 mg, crude) as a blue solid. LCMS: 1104 [M+H]⁺.

[000186] Step 7: 3,3'-((4-((3-(((19-(((3-(6-Methoxy-6-oxohexanamido)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)carbamoyl)heptane-1,7-diyl)bis(bis(3-sulfopropyl)ammoniumdiyl))bis(propane-1-sulfonate).



[000187] To a solution of the title compound of Step 6 (65 mg, 0.06 mmol) in sulfolane (5 mL) at room temperature under nitrogen was added 1,3-propanesultone (360 mg, 2.9 mmol) and DIPEA (0.77 mL, 4.4 mmol). The reaction was heated at 120 °C for 10 h. The reaction mixture was cooled to room temperature, added drop-wise to THF (20 mL) and stirred for 30 minutes. The supernatant was removed, and the solids were further washed with THF (2x10 mL) and dried under vacuum to afford the title compound (410 mg crude). LCMS: 917 [M-1/2]⁻.

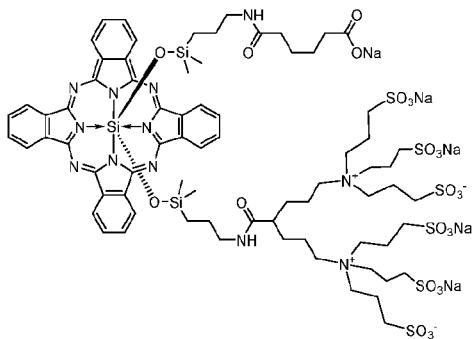
[000188] Step 8: Ammonium 6-((3-(((19-((dimethyl(3-(5-(tris(3-sulfonatopropyl)ammonio)-2-(3-(tris(3-sulfonatopropyl) ammonio)propyl)pentanamido)propyl)silyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-6-oxohexanoate.



[000189] The title compound was prepared in a manner similar to Example 17, Step 6 by replacing the title compound from Example 17, Step 5 for the title compound from Step 5

(410 mg, 0.22 mmol) to afford the title compound (14 mg, 12% over two step) as a blue solid.
LCMS: 910 [M-1/2].

[000190] Step 9: Sodium 6-(((3-(((19-(((dimethyl(3-(5-(tris(3-sulfonatopropyl)ammonio)-2-(3-(tris(3-sulfonatopropyl) ammonio)propyl)pentanamido)propyl)silyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo [7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)amino)-6-oxohexanoate).

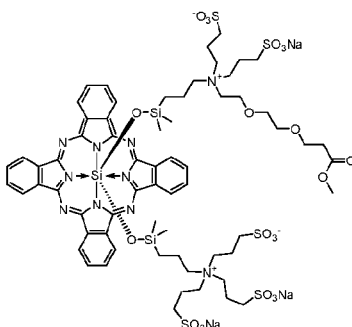


[000191] The title compound of Step 8 (18 mg, 0.009 mmol) was submitted to the ion exchange procedure described in Example 14, Step 1 to afford the title compound (16 mg, 88%). ¹H NMR (400 MHz, D₂O) δ 9.57 (m, 8H), 8.40 (m, 8H), 3.19 (m, 12H), 3.03 (m, 4H), 2.73 (m, 12H), 1.94 (m, 15H), 1.81 (m, 4H), 1.25 (m, 2H), 1.25 (m, 6H), 1.14 (m, 6H), -1.16 (m, 2H), -1.28 (m, 2H) -2.23 (m, 4H), -2.92 (s, 6H), -2.96 (s, 6H). LCMS: 910 [M-1/2].

Example 21

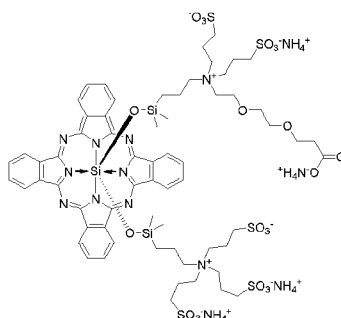
Preparation of sodium 2-(((19-(((dimethyl(3-(tris(3-sulfonatopropyl)ammonio)propyl)silyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)-2-methyl-6,6-bis(3-sulfonatopropyl)-9,12-dioxa-6-aza-2-silapentadecan-6-ium-15-oate

[000192] Step 1: Sodium 3,3',3''-(((3-(dimethyl((19-((2-methyl-15-oxo-6,6-bis(3-sulfonatopropyl)-9,12,16-trioxa-6-aza-2-silaheptadecan-6-ium-2-yl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10] tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)silyl)propyl)ammonio)tris(propane-1-sulfonate).



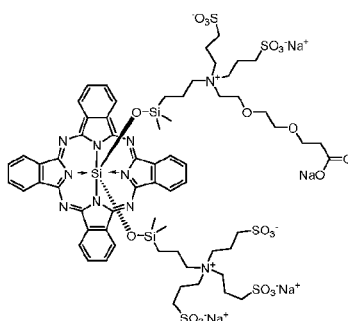
[000193] The title compound was prepared in a manner similar to Example 18, Step 5 by replacing sodium 4-iodobutane-1-sulfonate for sodium 3-iodopropane-1-sulfonate (444 mg, 1.6 mmol) to afford the title compound (500 mg crude). LCMS: 794 [M-1/2]⁻.

[000194] Step 2: Ammonium 2-((19-((dimethyl(3-(tris(3-sulfonatopropyl)ammonio)propyl)silyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)-2-methyl-6,6-bis(3-sulfonatopropyl)-9,12-dioxa-6-aza-2-silapentadecan-6-ium-15-oate.



[000195] The title compound was prepared in a manner similar to Example 17, Step 6 by replacing the title compound from Example 17, Step 5 for the title compound from Step 1 (480 mg, 0.29 mmol) to afford the title compound (30 mg, 22% over two steps) as a blue solid. LCMS: 787 [M-1/2]⁻.

[000196] Step 3: Sodium 2-((19-((dimethyl(3-(tris(3-sulfonatopropyl)ammonio)propyl)silyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)-2-methyl-6,6-bis(3-sulfonatopropyl)-9,12-dioxa-6-aza-2-silapentadecan-6-ium-15-oate.



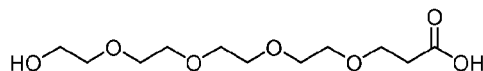
[000197] The title compound of Step 2 (30 mg, 0.02 mmol) was submitted to the ion exchange procedure described in Example 14, Step 1 to afford the title compound (28 mg, 92%). ¹H NMR (400 MHz, D₂O) δ 9.66 (m, 8H), 8.46 (m, 8H), 3.30 (m, 2H), 3.23 (m, 2H), 2.87–2.83 (m, 6H), 2.72 (m, 8H), 2.59–2.36 (m, 12H), 2.03 (m, 2H), 1.92 (m, 2H), 1.73 (t, J =

6.8 Hz, 2H), 1.64 (m, 2H) 1.54 (m, 8H), -1.55 (m, 2H), -1.68 (m, 2H), -2.01 (m, 4H), -2.88 (s, 6H), -2.92 (s, 6H). LCMS: 787 [M-1/2]⁻.

Example 22

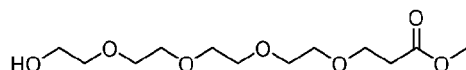
Preparation of sodium 2-((19-((dimethyl(3-(tris(4-sulfonatobutyl)ammonio)propyl)silyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)-2-methyl-6,6-bis(4-sulfonatobutyl)-9,12,15,18-tetraoxa-6-aza-2-silahenicosan-6-ium-21-oate

[000198] Step 1: 1-Hydroxy-3,6,9,12-tetraoxapentadecan-15-oic acid.



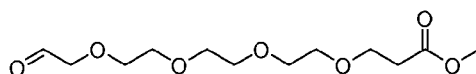
[000199] The title compound was prepared in a manner similar to Example 17, Step 1 by replacing tert-butyl 3-(2-(2-(2-hydroxyethoxy)ethoxy)ethoxy)ethoxy)propanoate for tert-butyl 1-hydroxy-3,6,9,12-tetraoxapentadecan-15-oate (2 g, 6.2 mmol) to afford the crude title compound (1.6 g) that was used in the following step without further purification.

[000200] Step 2: Methyl 1-hydroxy-3,6,9,12-tetraoxapentadecan-15-oate.



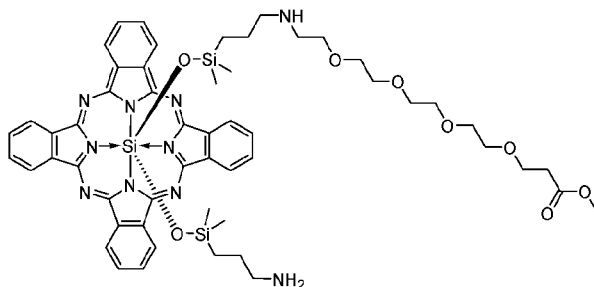
[000201] The title compound was prepared in a manner similar to Example 17, Step 2 by replacing 3-(2-(2-(2-Hydroxyethoxy)ethoxy)ethoxy)ethoxy)propanoic acid for the title compound from Step 1 (1.6 g, 6.0 mmol) to afford the title compound (1.2 g, 71%). ¹H NMR (400 MHz, D₂O) δ 3.69 (t, J = 5.8 Hz, 2H), 3.60-3.52 (m, 17H), 3.53 (m, 2H), 2.57 (t, J = 6.0 Hz, 2H).

[000202] Step 3: Methyl 1-oxo-3,6,9,12-tetraoxapentadecan-15-oate.



[000203] The title compound was prepared in a manner similar to Example 17, Step 3 by replacing methyl 3-(2-(2-(2-hydroxyethoxy)ethoxy)ethoxy)ethoxy)propanoate for the title compound from Step 2 (0.5 g, 1.8 mmol) to afford the title compound (210 mg, 42%) as a liquid.

[000204] Step 4: Methyl 2-((19-(((3-aminopropyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)-2-methyl-9,12,15,18-tetraoxa-6-aza-2-silahenicosan-21-oate.

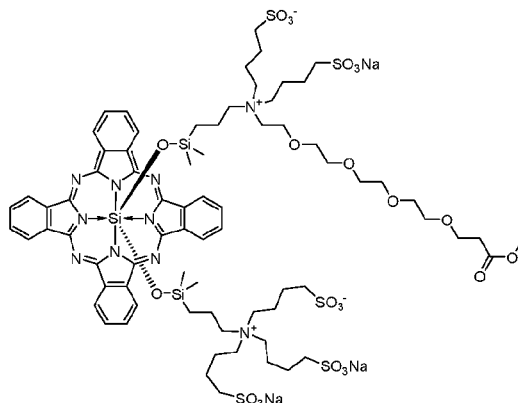


[000205] The title compound was prepared in a manner similar to Example 17, Step 4 by replacing methyl 3-(2-(2-(2-oxoethoxy)ethoxy)ethoxy)ethoxy)propanoate for the title compound

from Step 3 (83 mg, 0.3 mmol) to afford the title compound (30 mg, 19%) as a blue solid.

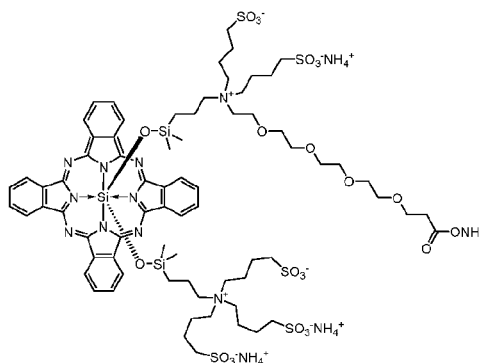
LCMS: 1068 $[M+2H]^+$.

[000206] Step 5: Sodium 4,4',4''-((3-(dimethyl((19-((2-methyl-21-oxo-6,6-bis(4-sulfonatobutyl)-9,12,15,18,22-pentaoxa-6-aza-2-silatricosan-6-ium-2-yl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)silyl)propyl)ammonio)tris(butane-1-sulfonate).



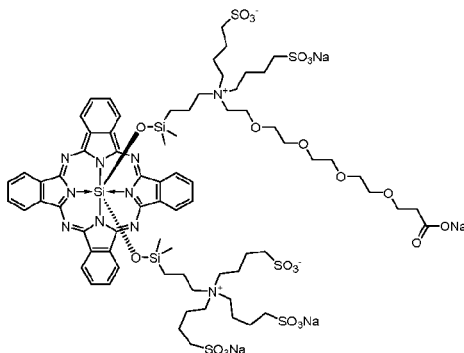
[000207] The title compound was prepared in a manner similar to Example 17, Step 5 by replacing the title compound from Example 17, Step 4 for the title compound from Step 4 (35 mg, 0.03 mmol) to afford the title compound (81 mg crude) as a blue solid. LCMS: 875 $[M/2+2H]^+$.

[000208] Step 6: Ammonium 4,4',4''-((3-(((19-((20-carboxy-2-methyl-6,6-bis(4-sulfonatobutyl)-9,12,15,18-tetraoxa-6-aza-2-silaicosan-6-ium-2-yl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)ammonio)tris(butane-1-sulfonate).



[000209] The title compound was prepared in a manner similar to Example 17, Step 6 by replacing the title compound from Example 17, Step 5 for the title compound from Step 5 (140 mg, 0.08 mmol) to afford the title compound (18 mg, 18% over two step) as a blue solid. LCMS: 866 $[M-1/2]^+$.

[000210] Step 7: Sodium 2-(((19-(((dimethyl(3-(tris(4-sulfonatobutyl)ammonio)propyl)silyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[3]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)-2-methyl-6,6-bis(4-sulfonatobutyl)-9,12,15,18-tetraoxa-6-aza-2-silahenicosan-6-ium-21-oate.



[000211] The title compound of Step 6 (18 mg, 0.01 mmol) was submitted to the ion exchange procedure described in Example 14, Step 1 to afford the title compound (16 mg, 87%). ¹H NMR (400 MHz, D₂O) δ 9.65 (m, 8H), 8.46 (m, 8H), 3.40 (t, *J* = 6.8 Hz, 2H), 3.30 (m, 2H), 3.24 (m, 2H), 3.11 (m, 2H), 2.85 (m, 6H), 2.73 (m, 8H), 2.65 (m, 6H), 2.59 (m, 4H), 2.30 (m, 4H), 2.18 (t, *J* = 6.8 Hz, 4H), 1.92 (m, 2H), 1.58 (m, 8H), 1.44 (m, 2H), 1.31 (m, 4H), 1.15 (m, 8H), -1.50 (m, 2H), -1.64 (m, 2H), -2.06 (m, 4H), -2.91 (s, 6H), -2.93 (s, 6H). LCMS: 866 [M-1/2]⁻.

Example 23

Preparation of sodium 4,4',4''-(((3-(((19-(((15-((2,5-dioxopyrrolidin-1-yl)oxy)-2-methyl-15-oxo-6,6-bis(4-sulfonatobutyl)-9,12-dioxa-6-aza-2-silapentadecan-6-ium-2-yl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)ammonio)tris(butane-1-sulfonate)

[000212] The title compound was prepared in a manner similar to Example 14, Step 2 by replacing the title compound from Example 14, Step 1 for the title compound from Example 18 (2.8 mg, 1.6 μmol) to afford the title compound (0.7 μmol). LCMS: 869.8 [M-2/2]⁻.

Example 24

Preparation of sodium 4,4',4''-(((3-(((19-(((18-((2,5-dioxopyrrolidin-1-yl)oxy)-2-methyl-18-oxo-6,6-bis(4-sulfonatobutyl)-9,12,15-trioxa-6-aza-2-silaoctadecan-6-ium-2-yl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)ammonio)tris(butane-1-sulfonate)

[000213] The title compound was prepared in a manner similar to Example 14, Step 2 by replacing the title compound from Example 14, Step 1 for the title compound from Example 17 (2.5 mg, 1.4 μmol) to afford the title compound (1.3 μmol). LCMS: 891.5 [M-2/2]⁻.

Example 25

Preparation of sodium 3,3',3''-(((3-(((19-(((15-((2,5-dioxopyrrolidin-1-yl)oxy)-2-methyl-15-oxo-6,6-bis(3-sulfonatopropyl)-9,12-dioxo-6-aza-2-silapentadecan-6-ium-2-yl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)ammonio)tris(propane-1-sulfonate)

[000214] The title compound was prepared in a manner similar to Example 14, Step 2 by replacing the title compound from Example 14, Step 1 for the title compound from Example 21 (2.4 mg, 1.4 μ mol) to afford the title compound (0.8 μ mol). LCMS: 834.4 [M-2/2]-.

Example 26

Preparation of sodium 4,4',4''-(((3-(((19-(((dimethyl(3-((6-oxo-6-(perfluorophenoxy)hexyl)bis(4-sulfonatobutyl)ammonio)propyl)silyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)ammonio)tris(butane-1-sulfonate)

[000215] To a solution of the title compound from Example 16, Step 1 (4.5 mg, 0.002 mmol) in DMSO (0.2 mL) under nitrogen was sequentially added EDCI (27 μ L of 0.1 M solution in DMSO, 1.2 eq). After ten minutes, 2,3,4,5,6-pentafluorophenol (27 μ L of 0.1 M solution in DMSO, 1.2 eq) and DMAP (3 μ L of 0.1 M solution in DMSO, 0.1 eq) were sequentially added. The resulting mixture was stirred at room temperature for four days. The reaction was diluted with DMF (0.2 mL) and filtered through a 0.45 μ m syringe filter into vigorously stirred MTBE (3.5 mL) over a ten-minute period. The reaction vial was washed with DMF (0.06 mL). A blue precipitate forms. The suspension was stirred for 2 min and then allowed to settle over a 30-minute period. The clear supernatant was removed and fresh MTBE (3.5 mL) was added. The suspension was stirred for 30 seconds and allowed to settle for 30 min. The clear supernatant was removed to afford the title compound as a solid. LCMS: 881.2 (M-2/2)-.

Example 27

Preparation sodium 4,4',4''-(((3-(((19-(((3-(((6-((2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)ethyl)amino)-6-oxohexyl)bis(4-sulfonatobutyl)ammonio)propyl)dimethylsilyl)oxy)-19H-6,11-(azeno)-17,21-(azeno[1]episoindoloazeno)benzo[7,8][1,3,5,10]tetraaza[2]silacycloundecino[4,3-a:11,1-a']diisoindol-19-yl)oxy)dimethylsilyl)propyl)ammonio)tris(butane-1-sulfonate)

[000216] N,N-Diisopropylethylamine (3 μ L of a 0.1 M solution in DMSO, 5 eq) and 1-(2-aminoethyl)-1H-pyrrole-2,5-dione hydrochloride (1.2 μ L of a 0.1 M solution in DMSO, 2 eq) were sequentially added to the title compound from Example 16, Step 1 (10 μ L of a 5.7 mM solution in DMSO). The resulting solution was kept in the dark for 1h. The reaction mixture was diluted with DMF (20 μ L) and added dropwise to MTBE (0.28 mL) with stirring. The reaction vial was washed with DMF (10 μ L) that was added to the MTBE. A blue precipitate formed. The suspension was allowed to settle over a 30-minute period. The clear supernatant was removed, and fresh MTBE (0.3 mL) was added. The suspension was sonicated for five

seconds and allowed to settle for 15 min. The clear supernatant was removed, and the residue dried under reduced pressure to afford the title compound as a blue solid. LCMS: 859.0 (M-2/2)⁺.

II. Evaluation of Properties

Example 1

Determination of kinetic and thermodynamic solubility

[000217] A working 1 mM stock solution of the test compound in DMSO was prepared from a 10 mM DMSO stock solution. A spectrum scan from 220 nm to 1000 nm of this working solution was performed in a 96-well UV plate to identify the wavelength maxima. If peaks were merged and/or optical density saturation was observed, the spectrum scan was repeated with a diluted stock (i.e. 100 μ M, 50 μ M, 25 μ M, 12.5 μ M). The selected stock solution was serially diluted in DMSO to confirm linearity and generate a seven to eight-point calibration curve. Of note, only linear points were considered in the curve.

[000218] To determine the aqueous solubility of the test compound, 50 μ L of its 10 mM stock solution was added to 950 μ L of pH 7.4 Dulbecco's phosphate-buffered saline (DPBS) without calcium, magnesium and Phenol red. The resulting solution was placed on a RotoSpin™ shaker at 50 rpm for 4 hours at room temperature (25 °C). The solution was then filtered using a 0.45 μ m PVDF filter to remove any insoluble fraction of the compound. A 150 μ L aliquot of the filtrate was taken for quantification using UV spectroscopy (POLARstar Omega BMG Plate Reader). The optical densities of the standard solutions and the test sample were acquired at the same wavelength maxima. The test sample concentration was calculated from its optical density using the linearity/calibration curve.

[000219] To determine the thermodynamic solubility of the test compound, x mg (powder form of the compound) was added to y mL of pH 7.4 Dulbecco's phosphate-buffered saline (without calcium, magnesium and Phenol red) so the final concentration of the solution was 1 mg/mL. The resulting solution was placed on a RotoSpin™ shaker at 50 rpm for 24 hours at room temperature (25 °C). The solution was then filtered using a 0.45 μ m PVDF filter to remove any insoluble fraction of the compound. A 150 μ L aliquot of the filtrate was taken for quantification using UV spectroscopy (POLARstar Omega BMG Plate Reader). The optical densities of the standard solutions and the test sample were acquired at the same wavelength maxima. The test sample concentration was calculated from its optical density using the linearity/calibration curve.

[000220] The solubility of various compounds is shown in Table 3, in which data are designated within the following ranges: A: ≤ 1 $\mu\text{g/mL}$; B: > 1 $\mu\text{g/mL}$ to ≤ 100 $\mu\text{g/mL}$; C: > 100 $\mu\text{g/mL}$.

Table 3

Example No.	Solubility* ($\mu\text{g/mL}$)
3	A
5	C
7	A
8	A
9	A
12	C
13	C
15	B
17	C
18	C
19	C
20	C
21	C
22	C

* Kinetic solubility for all Examples except thermodynamic for 20, 21 and 22.

Example 2

Measurement of UV-Vis Absorption

[000221] The UV-Vis absorption spectra of the compounds in either an organic solvent or aqueous media was recorded in a *Varian Cary® 50 UV-Vis* spectrophotometer. Compounds of the invention show absorption in the 600-800 nm region of the spectra.

[000222] The UV-Vis spectra of Chemical Synthesis Example 1 is shown in Figure 1. The UV-Vis spectra of chemical Synthesis Example 12 is shown in Figure 2.

Example 3

Determination of single oxygen quantum yield

[000223] Photogeneration quantum yields of singlet oxygen (Φ_{Δ}) were obtained by an indirect method, using either diphenylisobenzofuran (DPBF) or anthracene-9,10-bis-methylmalonate (ADMA) as chemical quenchers in either N,N-dimethylformamide or aqueous media, respectively. Typically, a solution of the phthalocyanine and the quencher was irradiated with a red LED lamp (670 nm) at 5 mW/cm^2 . The initial DPBF or ADMA concentrations were kept the same for both the reference and the test samples. The degradation of the DPBF band at 414 nm or ADMA at 401 nm was monitored in a *Varian Cary® 50 UV-Vis* spectrophotometer, every five seconds in the case of DPBF (up to 30 seconds) and every minute in the case of ADMA (up to five minutes). ZnPc ($\Phi_{\Delta} =$

0.67) and AlPcSmix ($\Phi_{\Delta} = 0.42$) were used as references in N,N-dimethylformamide or aqueous media, respectively.

[000224] The relative method shown by Eq. (1) was employed for calculations of the Φ_{Δ} :

$$\Phi_{\Delta} = \Phi_{\Delta\text{ref}} \frac{m \times I_{\text{ref}}}{m_{\text{ref}} \times I} \quad (1)$$

where Φ_{Δ} and $\Phi_{\Delta\text{ref}}$ are the $^1\text{O}_2$ generation quantum yields for the sample and reference, respectively, m and m_{ref} are the DPBF or ADMA photobleaching rates in the presence of the phthalocyanine of the invention and the reference, respectively, and I and I_{ref} are the rates of light absorption by the phthalocyanine derivative and reference, respectively. Concentrations of the test compound and reference were chosen such that their respective absorptions at the irradiation wavelength were the same.

[000225] The singlet oxygen quantum yield of various compounds is shown in Table 4, in which Φ_{Δ} data are designated within the following ranges: A: ≤ 0.5 ; B: > 0.5 .

Table 4

Dye Compound No.	Quencher	Φ_{Δ}
1	DPBF	A
5	ADMA	B
12	ADMA	B
13	ADMA	B
17	ADMA	B
18	ADMA	B
19	ADMA	B

Example 4

Cell Killing of Free Dye PIT

[000226] The PIT killing activity of free dyes were evaluated using the molecules synthesized as Example 12 and Example 13. BxPC3 cells (#CRL-1687, ATCC, Manassas VA) were plated, 5,000 cells per well, in RPMI-1640 media supplemented with 10% FBS and 1 % Penicillin/Streptomycin (complete culture media) in a deep-well 96-well plate. Following overnight incubation at 37 °C, the culture media were removed and the cells were incubated in 100 μL complete media with 1, 0.333, 0.111, 0.03704, 0.01235, 0.00412, 0.00137, or 0 $\mu\text{g/mL}$ Example 12, Example 13, or IRDye 700DX carboxylate (control) for one hour at 4 °C. Following incubation, the cells were illuminated with a 690 nm laser at a light dose of 64 J/cm^2 or protected from light (0 J/cm^2).

[000227] The effect of different treatment regimens on cell death was measured using the CellTox™ Green Cytotoxicity Assay (Cat No: G8742, Promega, Madison, WI). After the light

treatment, all cells were incubated with 1x CellTox™ Green reagent diluted complete culture media. Wells that did not include any cells were also incubated with 1xCellTox Green reagent diluted in complete culture media to serve as background subtraction wells during fluorescent signal detection. The CellTox™ Green fluorescence signal was measured at 24 hours after light treatment using a fluorescence plate reader. The cells were then lysed with diluted lysis solution (Cat No: G1821, Promega, Madison, WI), incubated at 37 °C for 30 minutes, and the CellTox™ Green fluorescence signal was measured again post-lysis. The percentages of dead cells were calculated by taking the ratio between background (1x CellTox™ Green in complete culture media without cells)-subtracted CellTox™ Green signal per well prior to and post lysis and multiplying the ratio by 100.

[000228] As shown in Figure 3, no effect on cell death was observed for any sample exposed to 0 J/cm² during the PIT treatment at any dose of the free dyes, indicating that the dyes were not cytotoxic in the absence of light irradiation. In contrast, dose-dependent cell killing was observed for samples that were irradiated with a 690 nm laser at a light dose 64 J/cm².

Example 5

Generation of Dye Conjugates

[000229] This example describes a method for preparing exemplary conjugates containing a dye described herein linked to exemplary biomolecules. In this example, dye molecules such as those described herein, are conjugated to several types of biomolecules. The provided methods are exemplary and similar methods may be employed to conjugate other antibodies or targeting molecules to any of the provided dyes.

Antibody Conjugates

[000230] In this example, dye molecules such as those described herein, are conjugated to exemplary antibody biomolecules.

1) Cetuximab (CTX) Conjugates

a) CTX-C12 and CTX-C13 Conjugates

[000231] A volume of 1 mL of Cetuximab (2 mg/mL solution) was buffer-exchanged into 100 mM sodium phosphate buffer (pH 8.65) using an Amicon® Ultra-15 centrifugal filter (50 kDa cutoff). The resulting Cetuximab antibody solution (approximately 1 mL) was transferred to a translucent 2 mL plastic vial. Dye Compound Example 14 (NHS ester of Compound 12 sodium salt) (89 µL, 0.6 M DMSO solution) was added with gentle swirling to create the conjugate CTX-C12. This step was carried out at room temperature under green light. The conjugation reaction was

performed to a final molar ratio of 4:1 (dye: Cetuximab). The vial was placed inside an opaque container protected from light. The conjugation reaction was allowed to proceed for 270 min.

[000232] The conjugation reaction was quenched by the addition of 1 M glycine (20 μ L) and mixing for 50 min. The solution was transferred to an Amicon® Ultra-15 centrifugal filter (50 kDa cutoff) and its volume reduced to 0.7 mL. 1X PBS buffer pH 7.1 (10 mL) was added, and the resulting solution was centrifuged to a volume of approximately 1 mL. The 1X PBS buffer exchange was repeated two more times (2x10 mL). The resulting Cetuximab conjugate was stored in the dark at 2-6 °C.

[000233] The conjugate was submitted for SEC-HPLC analysis to determine concentration, dye to antibody ratio (DAR) and purity. A 30 μ L sample was run in a Shodex Protein® 5 μ m KW-803 (8 x 300 mm, 300Å) size-exclusion chromatography column on an Agilent 1100 HPLC instrument. Samples were run in a 1X PBS pH 7.1 mobile phase at a flow rate of 1 mL/min for a total of 20 minutes. Dye to antibody ratio (DAR) was determined by measuring the absorbance of the conjugates at wavelengths of 280nm and 677nm. The percent area of the main peak for the monomer content of the sample was determined, as well as calculation for high molecular weight species (HMW).

[000234] The CTX-C13 conjugate was prepared and analyzed in a manner similar to that of CTX-C12, replacing Compound 14 with the Compound 16 (NHS ester of Compound 13 sodium salt). The results and protein concentration of the conjugates are provided in Table 5a below.

Table 5a

Conjugate	% HMW	Avg. DAR	Concentration (mg/mL)
CTX-C12	1.5	2.8	1.7
CTX-C13	2.3	3.4	2.7

b) Dye Conjugates CTX-C17, CTX-C18, and CTX-C21 Conjugates

[000235] The title compound from Example 24 (NHS ester of Compound 17) (36.5 μ L, 10 mg/mL DMSO solution) was added to the Cetuximab antibody (0.65 mL, 7.7 mg/mL 100mM phosphate, pH 8.65 solution). The reaction container was protected from light and mixed by gentle inversion. No continuous mixing was performed during the two-hour reaction at room temperature. In process SEC analysis indicated a DAR of 2.5. A second portion of dye (4.9 μ L, 10 mg/mL DMSO solution) was added, and the solution was allowed to stand for one hour.

[000236] The conjugation reaction was quenched by addition of 1 M glycine (35 μ L). The container was protected from light and mixed by gentle inversion at the beginning and end of the overnight reaction time at room temperature. The contents of the container were transferred to an

Amicon® Ultra-15 centrifugal filter (30 kDa cutoff), topped off with 1X PBS buffer pH 7.1, and centrifuged at 3,500 rpm for 30 min. The 1X PBS buffer exchange was repeated three more times. The resulting Cetuximab conjugate was transferred to a 15 mL conical tube and stored in the dark at 2-6 °C.

[000237] The conjugate was submitted for SEC-HPLC analysis to determine concentration, dye to antibody ratio (DAR) and purity. A 35 μ L sample was run in a Shodex Protein® 5 μ m KW-803 (8 x 300 mm, 300Å) size-exclusion chromatography column on an Agilent 1100 HPLC instrument. Samples were run in a 1X PBS pH 7.1 mobile phase at a flow rate of 1 mL/min for a total of 20 minutes. Dye to antibody ratio (DAR) was determined by measuring the absorbance of the conjugates at wavelengths of 280nm and 677nm. The percent area of the main peak for the monomer content of the sample was determined, as well as calculation for high molecular weight species (HMW).

[000238] The CTX-C18 and CTX-C21 conjugates were prepared and analyzed in a manner similar to that of CTX-C17, replacing the compound of Example 24 with the compound of Example 23 (NHS ester of Compound 18) or Example 25 (NHS ester of Compound 21), respectively. The results and protein concentration of the conjugates are provided in Table 5b below.

Table 5b

Conjugate	% HMW	Avg. DAR	Concentration (mg/mL)
CTX-C17	1.0	2.7	3.0
CTX-C18	1.3	2.9	2.8
CTX-C21	1.6	3.2	3.3

2) Anti-EphA2 Conjugates

[000239] Approximately 30 mg of mouse anti-human EphA2, clone 1C1 (Absolute Antibody, Catalog Number Ab00430-1.1) was buffer-exchanged into 25 mM phosphate buffer (pH 8.2) using a 30 kDa Amicon® centrifugal filter. Approximately 12 mg of the anti-EphA2 antibody solution (at a concentration of 4.59 mg/mL) were transferred to an appropriately sized container. 14.46 μ L of a stock solution of dye Compound 16 (NHS ester of Compound 13 sodium salt), at a concentration of 10 mg/mL DMSO, was added with gentle swirling, at room temperature under green light for 1 hour, to create the conjugate anti-EphA2-C13. The conjugation reaction was performed to a final molar ratio of approximately 6.5:1 (dye: anti-EphA2).

[000240] The conjugation reaction was quenched by the addition of 89.2 μ L of 1 M glycine, to achieve a final concentration of 20 mM glycine and mixing overnight at room temperature,

protected from light. The solution was buffer-exchanged into 1 x phosphate-buffered saline (1 x PBS) using an Amicon® Ultra-15 centrifugal filter (30 kDa cutoff). The resulting anti-EphA2-C13 conjugate was stored in the dark at 4 °C.

[000241] The conjugate was submitted for SEC-HPLC analysis to determine concentration, dye to antibody ratio (DAR) and purity. A 37 µL sample was run in a Sepax Zenix™-C 300Å size-exclusion chromatography column on an Agilent 1100 HPLC instrument. Samples were run in a 1X PBS pH 7.1 mobile phase at a flow rate of 1 mL/min for a total of 20 minutes. Dye to antibody ratio (DAR) was determined by measuring the absorbance of the conjugates at wavelengths of 280 nm and 677 nm. The results and protein concentration of the conjugates are provided in Table 5c below.

Table 5c

Conjugate	Avg. DAR	Concentration (mg/mL)
anti-EphA2-C13	2.5	1.5

3) Anti-CTLA-4 Conjugates

[000242] Approximately 6 mg of mouse anti-CTLA-4 antibody, with a heavy chain of the amino acid sequence set forth in SEQ ID NO: 1 and a light chain of the amino acid sequence set forth in SEQ ID NO: 2, in 1 x PBS was buffer-exchanged into 25 mM phosphate buffer (pH 8.2) using a 30 kDa Amicon® centrifugal filter, to a final concentration of 2.38 mg/mL. Approximately 2 mg of the anti-EphA2 antibody solution (840 µL) were transferred to two appropriately sized containers. 9.70 or 12.13 µL of a stock solution of dye Compound 16 (NHS ester of Compound 13 sodium salt) (, at a concentration of 10 mg/mL DMSO, for a molar ratio of 4:1 or 5:1 (dye: anti-CTLA-4), respectively) was added with gentle inversion at the start of the reaction time and no further mixing. The reaction continued at room temperature, protected from light for 1 hour, to create the conjugate anti-CTLA-4-C13.

[000243] The conjugation reaction was quenched by the addition of 17 µL of 1 M glycine, to achieve a final concentration of 20 mM glycine and mixing overnight at room temperature, protected from light. The mixture was gently inverted at the beginning and end of the overnight reaction. The solution was buffer exchanged into 1 x PBS using an Amicon® Ultra-15 centrifugal filter (30 kDa cutoff). The resulting anti-CTLA-4-C13 conjugates were stored in the dark at 4 °C.

[000244] The conjugates were submitted for SEC-HPLC analysis to determine concentration, dye to antibody ratio (DAR) and purity. A 33 µL sample was run in a Sepax Zenix™-C 300Å size-exclusion chromatography column on an Agilent 1100 HPLC instrument. Samples were run in a 1X PBS pH 7.1 mobile phase at a flow rate of 1 mL/min for a total of 20 minutes. Dye to antibody ratio

(DAR) was determined by measuring the absorbance of the conjugates at wavelengths of 280 nm and 677 nm. The results and protein concentration of the conjugates are provided in Table 5d below.

Table 5d

Conjugate	Molar Ratio	Avg. DAR	Concentration (mg/mL)
anti-CTLA-4-C13 (MR4)	4	2.6	2.3
anti-CTLA-4-C13 (MR5)	5	2.9	2.0

Antibody Fragment Conjugates

[000245] In this example, dye molecules such as those described herein, were conjugated to an exemplary antibody-binding fragment (Fab). The exemplary Fab contains the constant and variable domains of the heavy and light chains of the anti-EGFR antibody, Cetuximab, the amino acid sequences of which are set forth in SEQ ID NOs: 3 and 4, respectively.

[000246] Approximately 1.16 mL (3.8 mg) of the anti-EGFR Fab in 1 x PBS were transferred to an appropriately sized container and diluted to a concentration of 1.2 mg/mL with 100 mM Sodium Phosphate, pH8.5. 70 μ L of a stock solution of dye Compound 16 (NHS ester of Compound 13 sodium salt), at a concentration of 10 mg/mL DMSO, to achieve a molar ratio of 5:1 (dye: Fab), was added with pipette mixing at the start of the reaction time, but no further mixing. The reaction continued at room temperature, protected from light for 2 hours, to create the conjugate anti-EGFR Fab-C13.

[000247] The conjugation reaction was quenched by the addition of 65.1 μ L of 1 M glycine, to achieve a final concentration of 20 mM glycine. The mixture was mixed by pipetting at the beginning of the reaction, and then incubated for 1 hour at room temperature, without further mixing and protected from light. The solution was injected into a HiLoad® 16/600 Superdex® 200 SEC column on an AKTA Pure 150 instrument to remove excess dye and exchange the buffer into 1 x PBS. The main peak fractions were collected and concentrated to 1.5 mL using a 10 kDa Amicon® filter. A 80 μ L sample was run in a Sepax Zenix™-C 100Å size-exclusion chromatography column on an Agilent 1100 HPLC instrument. Samples were run in a 1X PBS pH 7.1 mobile phase at a flow rate of 1 mL/min for a total of 20 minutes. Dye to antibody ratio (DAR) was determined by measuring the absorbance of the conjugates at wavelengths of 280 nm and 677 nm. % Monomer was determined by measuring the absorbance at 280 nm. The main peak fractions were collected and concentrated to 1.5 mL using a 10 kDa Amicon® filter. The resulting anti-EGFR Fab-C13 conjugates were stored in the dark at 4 °C. The results and protein concentration of the conjugates are provided in Table 5e below.

Table 5e

Conjugate	Avg. DAR	Concentration (mg/mL)	A280 % Monomer
anti-EGFR Fab-C13	1.7	1.9	99.9

Nanobody/VHH Domain Conjugates

[000248] In this example, dye molecules such as those described herein, were conjugated to an exemplary nanobody/VHH domain, 7D12. 7D12 is approximately 14.58 kDa, binds epidermal growth factor receptor (EGFR), and has the amino acid sequence set forth in SEQ ID NO: 5.

[000249] Approximately 1.02 mL (3.8 mg) of the VHH solution were transferred to an appropriately sized container and diluted to a concentration of 1.2 mg/mL with 100 mM Sodium Phosphate, pH8.5. 202.4 μ L of a stock solution of dye Compound 16 (NHS ester of Compound 13 sodium salt), to achieve a molar ratio of 5:1 (dye: VHH), was added with pipette mixing at the start of the reaction time, but no further mixing. The reaction continued at room temperature, protected from light for 2 hours, to create the conjugate anti-EGFR VHH-C13.

[000250] The conjugation reaction was quenched by the addition of 67.7 μ L of 1 M glycine, to achieve a final concentration of 20 mM glycine. The mixture was mixed by pipetting at the beginning of the reaction and then incubated overnight at room temperature, without further mixing and protected from light. The resulting solution was injected into a HiLoad® 16/600 Superdex® 75 SEC column on an AKTA Pure 150 instrument to remove excess dye and exchange the buffer into 1 x PBS. The main peak fractions were collected and concentrated to 1.5 mL using a 3 kDa Amicon® filter. A 80 μ L sample was run in a Sepax Zenix™-C 100Å size-exclusion chromatography column on an Agilent 1100 HPLC instrument. Samples were run in a 1X PBS pH 7.1 mobile phase at a flow rate of 1 mL/min for a total of 20 minutes. Dye to antibody ratio (DAR) was determined by measuring the absorbance of the conjugates at wavelengths of 280 nm and 677 nm. The resulting anti-EGFR VHH-C13 conjugates were stored in the dark at 4 °C. The results and protein concentration of the conjugates are provided in Table 5f below.

Table 5f

Conjugate	Avg. DAR	Concentration (mg/mL)
anti-EGFR VHH-C13	1.0	1.4

Peptide Conjugates

[000251] GE11 is an EGF-competitive peptide that binds to epidermal growth factor receptor (EGFR). In this example, Compound 16 was conjugated to GE11 peptide, modified by adding a

short GGG linker to the C-terminus, followed by a terminal lysine to generate a modified GE11 peptide with the sequence Ac-YHWYGYTPQNVIGGGK (SEQ ID NO: 6), as an exemplary peptide for conjugation.

[000252] To prepare the conjugate, 1 μ L of a 0.1 M solution of N, N-Diisopropylethylamine (DIPEA) in DMSO and 0.9 μ L of a 5.7 mM solution of dye Compound 16 (NHS ester of Compound 13 sodium salt) were sequentially added to 4.8 μ L of a 1 mM solution of the modified GE11 peptide in DMSO in a 0.5 mL Eppendorf tube. The resulting mixture was incubated 6 hours in the dark. Liquid chromatography/mass spectrometry (LCMS) analysis, in negative ion mode, confirmed formation of the peptide conjugate with an $[(M-2)/2]^-$ ion of mass 1729.1 Da. The reaction was diluted with DMF (10 μ L) and added to MTBE (0.25 mL). The reaction tube was washed with DMF (10 μ L) that was added to the MTBE. A light blue precipitate formed. The suspension was allowed to stand for 30 minute and the precipitate was isolated by filtration.

Example 6

Cell Killing Activity of CTX-C12 and CTX-C13 PIT

[000253] To evaluate PIT killing activity of the CTX-C12 and CTX-C13 conjugates in pancreatic carcinoma cells, BxPC3 cells (#CRL-1687, ATCC, Manassas VA) were plated, 5,000 cells per well in RPMI-1640 media supplemented with 10% FBS and 1 % Penicillin/Streptomycin (complete culture media) in a deep-well 96-well plate. Following overnight incubation at 37 °C, the culture media were removed, and the cells were incubated in 100 μ L complete media with 1, 0.333, 0.111, 0.03704, 0.01235, 0.00412, 0.00137, or 0 μ g/mL CTX-C12, CTX-C13, or cetuximab-IRDye 700DX (CTX-IR700) (control) for one hour at 4 °C. Following incubation, the cells were illuminated with a 690 nm laser at a light dose of 64 J/cm² or protected from light (0 J/cm²).

[000254] The effect of different treatment regimens on cell death was measured using the CellTox™ Green Cytotoxicity Assay 24 hours after illumination as described above.

[000255] As shown in Figure 4, no effect on cell death was observed for any sample exposed to 0 J/cm² during the PIT treatment at any dose of the antibody conjugates, indicating that the conjugates were not cytotoxic in the absence of light irradiation. In contrast, dose-dependent cell killing was observed for samples that were irradiated with a 690 nm laser at a light dose of 64 J/cm².

Example 7

Cell Killing Activity of EGFR-Targeted C13 Conjugates

[000256] In this example, PIT killing activity of EGFR-targeted-C13 conjugates, was measured on A431 squamous carcinoma cells. The conjugates evaluated were anti-EGFR antibody

(Cetuximab (CTX)), anti-EGFR Fab, and an anti-EGFR VHH conjugated to C13, as described above. The same antibody, Fab, VHH domain were also conjugated to IR700 as reference molecules.

[000257] A431 cells (#CRL-1555, ATCC Manassas VA) were plated at 5,000 cells per well in deep-well 96-well plates in complete RPMI-1640 media. Following overnight incubation at 37 °C, the culture media were removed, and the cells were incubated in 100 μ L complete media with 20, 5, 1.25, 0.313, 0.078, 0.02, 0.005, or 0 nM CTX-C13, anti-EGFR Fab-C13, anti-EGFR VHH-C13, or the corresponding IR700 conjugates for one hour at 4 °C. Following incubation, the cells were illuminated with a 690 nm laser at a light dose of 64 J/cm² or protected from light (0 J/cm²). The effect of different treatment regimens on cell death was measured using the CellTox™ Green Cytotoxicity Assay 24 hours after illumination as described above. Dose response curves of percent cell death following PIT for the antibody, Fab, and VHH conjugates are shown in Figures 5A, 5B, and 5C, respectively.

[000258] As shown in Figures 5A-5C, dose-dependent A431 cell killing was observed for all the EGFR-Targeted C13 and IR700 conjugates following irradiation with a 690 nm laser at a dose of 64 J/cm².

Example 8

Photoimmunotherapy (PIT) Using CTX-C13 Conjugates

[000259] To evaluate direct photoimmunotherapy (PIT) killing activity of tumor cells by the CTX-C13 conjugates, *in vivo*, immunocompromised NuNu mice were inoculated with 5x10⁶ BxPC3 pancreatic cancer cells engineered to express luciferase (BxPC3-luc) subcutaneously on the right hind flank. On Day 6 after tumor cell inoculation, when allograft tumors grew to a volume of about 150 mm³, the mice were retro-orbitally administered CTX-C13 (100 μ g), generated as described above. On Day 7, the tumors in the right flank of half of the animals were illuminated at 690 nm at a dosage of 200 J/cm². Tumor cell depletion was determined by measuring bioluminescence (BLI) of the tumors, using quantitative luciferase activity, prior to illumination and 4-6 hours, 1 day, 5 days, and 7 days post-illumination. The average BLI of the tumors over time for CTX- C13 and CTX-C13 with illumination (CTX-C13 + PIT) groups is plotted in Figure 6.

[000260] As shown in Figure 6, illumination of the CTX-C13 conjugates (CTX-C13 + PIT group; closed circles) resulted in a reduction in the tumor cell BLI by 4 hours after illumination, followed by gradual tumor regrowth beginning 5 days after illumination in this immunocompromised model. Tumors treated with the CTX-C13 conjugate without illumination

(Figure 6, open circles), did not significantly reduce the tumor BLI. These results demonstrate tumor cell depletion resulting from CTX-C13 photoimmunotherapy.

Example 9

Photoimmunotherapy (PIT) Using Anti-EphA2-C13 Conjugate

[000261] To evaluate photoimmunotherapy (PIT) killing activity of the Anti-EphA2-C13 conjugates, *in vivo*, BALB/c mice were inoculated with 1×10^6 CT26-EphA2 cells subcutaneously on the right hind flank. On Day 8 after tumor cell inoculation, when allograft tumors grew to a volume of about 135 mm^3 , the mice were retro-orbitally administered saline ($100 \text{ }\mu\text{L}$; $n=10$) or anti-EphA2-C13 ($100 \text{ }\mu\text{g}$; $n=20$), generated as described above. On Day 9, the tumors of half of the animals administered anti-EphA2-C13 were illuminated at 690 nm at a dosage of 100 J/cm^2 . The tumors of the remaining mice were not illuminated as controls. The growth of the tumors was observed over time, and tumor volumes were calculated using the formula: tumor volume = (width x length) x height/2. Average tumor volumes for each group are plotted in Figure 7.

[000262] As shown in Figure 7, the average tumor volumes of non-illuminated tumors in animals treated with saline (open squares, solid line), or EphA2-C13 conjugate alone (open circle, solid line) exhibited rapid, continuous tumor growth over the course of the study. Tumors treated with EphA2-C13 with illumination at 100 J/cm^2 (closed circles, solid line) exhibited reduced tumor growth compared to the saline and EphA2-C13 conjugate controls. These results demonstrate that EphA2-C13 PIT inhibits tumor growth *in vivo*.

Sequence Listings

Table 6 provides the sequence listing recited in the specification.

Table 6

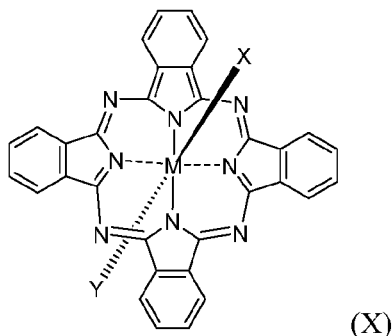
SEQ ID NO.	Description	Sequence
1	CTLA-4 VH	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYTMHWVRQAPGKGLEWVTFI SYDGNNKYYADSVKGRFTISRDNKNTLYLQMNSLRAEDTAIYYCARTGWLG PFDYWGGQGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVT VSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSN TKVDKRVEPKSCDKTHTCPPCPAPPELLGGPSVFLFPPKPKDTLMISRTPEVTCV VVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
2	CTLA-4 VL	EIVLTQSPGTLSPGERATLSCRASQSVGSSYLAWYQQKPGQAPRLLIYGAFS RATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSPWTFGQGTKEI KRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN SQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG EC
3	CTX Fab heavy chain	QVQLKQSGPGLVQPSSLSITCTVSGFSLTNYGVHWVRQSPGKGLEWLGVI WSGGNTDYNTPFTSRLSINKDNSKSQVFFKMNSLQSNDAIYYCARALTYD YEFAYWGQGLTVTVSACSTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPV TVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPS NTKVDKRVEPKSCDKTHT
4	CTX light chain	DILLTQSPVILSVSPGERVSFSCRASQSIGTNIHWYQQRNGSPRLLIKYASESIS GIPSRFSGSGSGTDFTLSINSVESEDIADYYCQQNNNWPTTFGAGTKLELKRT VAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
5	anti-EGFR VHH (7D12) - Cys-Myc-His10	QVKLEESGGGSVQTGGSLRLTCAASGRTSRSYGMGWFRQAPGKEREFVSGI SWRGDSTGYADSVKGRFTISRDNKNTVDLQMNSLKPEDTAIYYCAAAGS AWYGTLYEYDYWGQGTQVTVSSCSGSSEQLISEEDLASHHHHHHHHHH
6	GE11 peptide	Ac-YHWYGYTPQNVIGGGK

[000263] The embodiments described above are intended to be merely exemplary, and those skilled in the art will recognize, or will be able to ascertain using no more than routine experimentation, numerous equivalents of specific compounds, materials and procedures. All such equivalents are considered to be within the scope of the claimed subject matter and are encompassed by the appended claims. Since modifications will be apparent to those of skill in the art, it is intended that the claimed subject matter be limited only by the scope of the appended claims.

CLAIMS

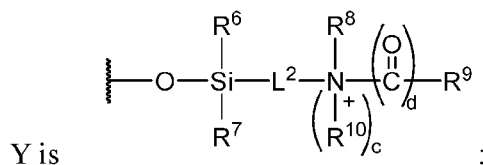
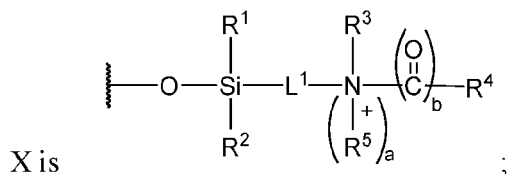
We claim:

1. A phthalocyanine dye having the Formula (X):



or a salt, stereoisomer, or tautomer thereof, wherein,

M is a metal or metalloid;



R¹ and R² are each independently optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, or optionally substituted heteroaralkyl;

R³, R⁴ or R⁵ are selected from substituent group (a) or substituent group (b) wherein,

(a) R³ is hydrogen, -L³-H, -L³-A, or -L³-Z;

R⁴ is -L⁴-H, -(NH)_m-L⁴-A, -(NH)_m-L⁴-Z, -(O)_m-L⁴-A or -(O)_m-L⁴-Z;

R⁵ is -L⁵-H or -L⁵-A; and

(b) R³ is -L³-H, or -L³-A;

R⁴ is -L⁴-H, -(NH)_m-L⁴-A, or -(O)_m-L⁴-A; wherein R³ and R⁴ are connected with a bond to form a heterocyclyl substituted with -L⁴-A; and

R⁵ is -L⁵-H or -L⁵-A;

provided at least one of R³, R⁴ and R⁵ is a group containing A;

A is a reactive group capable of forming a covalent bond with a thiol, hydroxyl, carboxyl or amino group of a second moiety, or a protected form thereof or a reacted form thereof;

R^6 and R^7 are each independently optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted heterocyclyl, optionally substituted heterocyclalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl or optionally substituted heteroaralkyl;

R^8 , R^9 or R^{10} are selected from substituent group (a) or substituent group (b) wherein,

(a) R^8 is hydrogen, $-L^8-H$, $-L^8-A$ or $-L^8-Z$;

R^9 is $-L^9-H$, $-L^9-A$, $-(NH)_n-L^9-Z$ or $-(O)_n-L^9-Z$;

R^{10} is $-L^{10}-A$, $-L^{10}-Z$; and

(b) R^8 and R^9 are connected with a bond to form a heterocyclyl substituted with $-L^9-Z$ and R^{10} is $-L^{10}-H$ or $-L^{10}-Z$;

provided at least one of R^8 , R^9 and R^{10} is a group containing Z;

Z is a water soluble group optionally substituted with A or $L'-A$;

L^1 and L^2 are each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkyl, or optionally substituted heterocyclyl;

L^3 , L^4 , L^5 , L^8 , L^9 and L^{10} are each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkylene, optionally substituted heterocyclene, optionally substituted arylene, optionally substituted aralkylene, optionally substituted heteroaralkylene, or optionally substituted heteroarylene, where the carbon atom of the alkylene, heteroalkylene, alkenylene, heteroalkenylene, cycloalkylene, heterocyclene, arylene, aralkylene, heteroaralkylene, or optionally substituted heteroarylene is further optionally substituted with Z and each nitrogen atom of the heteroalkylene or heteroalkenylene is optionally substituted with one or two $L'-Z$;

L' is each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkylene, optionally substituted heterocyclene, optionally substituted arylene, optionally substituted aralkylene, optionally substituted heteroaralkylene, or optionally substituted heteroarylene;

a is 0 or 1;

b is 0 or 1;

c is 0 or 1;

d is 0 or 1;

m is 0 or 1;

n is 0 or 1;

provided that if b is 1, then a is 0;

if d is 1, then c is 0;

if m is 1, b is 1; and

if n is 1, c is 1;.

2. The compound of claim 1, or a salt, stereoisomer, or tautomer thereof, wherein L^3 , L^4 , L^5 , L^8 , L^9 and L^{10} are each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene or optionally substituted heteroalkenylene, where each nitrogen atom of the heteroalkylene or heteroalkenylene is further optionally substituted with one or two L' -Z and L' is independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene or optionally substituted heteroalkenylene.
3. The compound of claim 1 or 2, or a salt, stereoisomer, or tautomer thereof, wherein L^1 and L^2 , are each independently optionally substituted C_{1-10} alkylene, optionally substituted hetero C_{1-10} alkylene, optionally substituted C_{2-10} alkenylene or hetero C_{2-10} alkenylene.
4. The compound of any one of claims 1 to 3, or a salt, stereoisomer, or tautomer thereof, wherein L^1 and L^2 , are each independently C_{2-4} alkylene, hetero C_{2-4} alkylene, optionally substituted C_{2-4} alkenylene or optionally substituted hetero C_{2-4} alkenylene.
5. The compound of any one of claims 1 to 4, or a salt, stereoisomer, or tautomer thereof, wherein L^1 and L^2 are each optionally substituted C_{2-4} alkylene.
6. The compound of any one of claims 1 to 5, or a salt, stereoisomer, or tautomer or thereof, wherein the reactive group A is each independently selected from:
 - C(O)OR¹¹,
 - NR¹²R¹³,
 - NHC(O)R¹⁴,
 - C(O)R¹⁵,
 - OR¹⁶,
 - SR¹⁶,
 - OS(O)₂R¹⁷,

-OP(OR¹⁸)(NR¹⁹R²⁰),

-N=C=O;

-N=C=S,

-S-C≡N,

-SO₂-F,

-SO₂-Cl,

-SO₂-Br,

-S-SR²¹, or

a 5- or 6- membered dioxo-substituted heterocyclyl;

wherein each R¹¹ is independently hydrogen, alkyl, haloalkyl, alkenyl, heterocyclyl, aryl or heteroaryl, and each R¹¹ is independently optionally substituted with one to five groups each independently selected from halo, -SO₃H and -SO₂F;

each R¹² is independently hydrogen, alkyl or haloalkyl;

each R¹³ is aryl or heteroaryl, and each R¹³ is independently optionally substituted with one to five groups each independently selected from halo, -SO₃H and -SO₂F; or optionally R¹² and R¹³, together with the nitrogen to which they are attached, form a cyclic imide;

each R¹⁴ is independently optionally substituted haloalkyl or optionally substituted aralkyl;

each R¹⁵ is independently aryl optionally substituted with one to five groups each independently halo, heterocyclyl, -SO₃H or -SO₂F;

each R¹⁶ is independently aryl optionally substituted with one to five groups each independently halo or heterocyclyl;

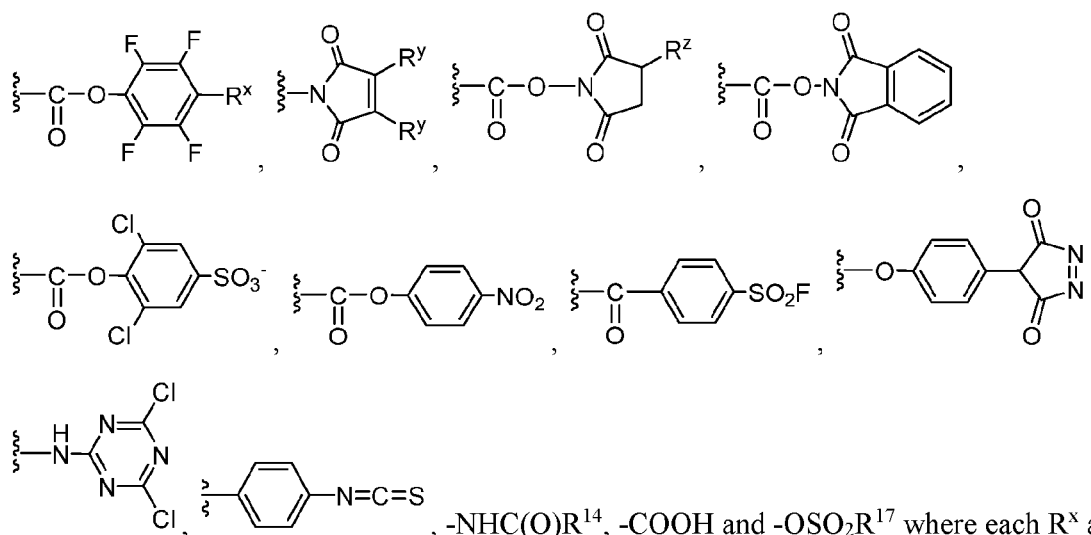
each R¹⁷ is independently optionally substituted alkyl, optionally substituted haloalkyl, optionally substituted alkenyl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, optionally substituted aryl or optionally substituted heteroaryl, wherein the heterocyclyl, aryl or heteroaryl is optionally substituted with one to five groups each independently selected from halo, -SO₃H, -SO₂F, and -C(O)OR^c;

each R^c is independently optionally substituted alkyl, optionally substituted haloalkyl, optionally substituted cycloalkyl or optionally substituted aryl;

R¹⁸, R¹⁹ and R²⁰ are each independently optionally substituted alkyl or optionally substituted haloalkyl; and

R²¹ is heteroaryl.

7. The compound of any one of claims 1-6 wherein the reactive group A is selected from the group consisting of:



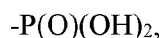
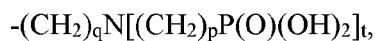
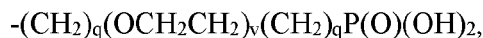
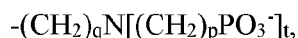
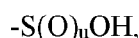
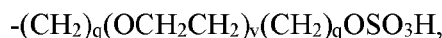
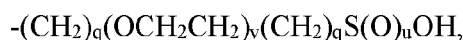
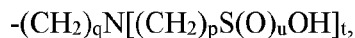
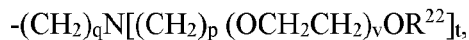
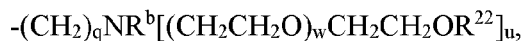
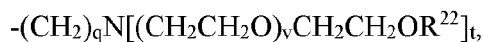
independently hydrogen or halo, and R^z is hydrogen or $-SO_3H$;

R¹⁴ is optionally substituted haloalkyl or optionally substituted aralkyl; and

R¹⁷ is independently optionally substituted alkyl, optionally substituted haloalkyl, optionally substituted alkenyl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, optionally substituted aryl or optionally substituted heteroaryl, wherein the heterocyclyl, aryl or heteroaryl is optionally substituted with one to five groups each independently selected from halo, -SO₃H, -SO₂F and -C(O)OR^c; and

each R^c is independently optionally substituted alkyl, optionally substituted haloalkyl, optionally substituted cycloalkyl or optionally substituted aryl.

8. The compound of any one of claims 1 to 7, or a salt, stereoisomer, or tautomer thereof, wherein the reactive group is independently -C(O)OR¹¹ or -NR¹²R¹³.
9. The compound of any one of claims 1 to 8, or a salt, stereoisomer, or tautomer thereof, wherein the water soluble group Z is
- C(O)OH,
 - (CH₂)_q(OCH₂CH₂)_v(CH₂)_qC(O)OH,
 - (CH₂CH₂O)_v(CH₂)_pC(O)OH,
 - (CH₂)_q(OCH₂CH₂)_vOR²²,
 - (CH₂CH₂O)_v(CH₂)_pOR²²,
 - (CH₂)_q(OCH₂CH₂)_vSR²²,
 - (CH₂CH₂O)_v(CH₂)_pSR²²,
 - O(CH₂)_vN[(CH₂CH₂O)_nCH₂CH₂OR²²]_t,
 - (CH₂)_q(OCH₂CH₂)_vN[(CH₂CH₂O)_wCH₂CH₂OR²²]_t,



glutamate, aspartate, histidine, 1,3-beta-glucan or 1,4-beta-glucan;

each R^{22} is independently alkyl, haloalkyl, cycloalkyl or aryl;

each R^b is independently hydrogen, alkyl optionally substituted with $-\text{CO}_2\text{H}$, heteroalkylene optionally substituted with $-\text{CO}_2\text{H}$, haloalkyl or cycloalkyl;

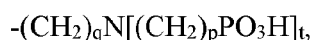
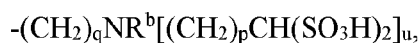
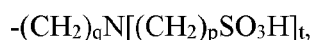
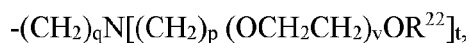
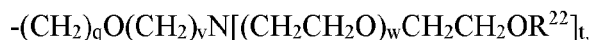
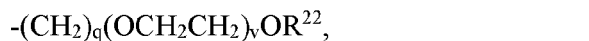
each v , w and p are independently an integer from 1 to 10;

each q is independently an integer from 0 to 10;

t is 2 or 3; and

u is 1 or 2.

10. The compound of any one of claims 1 to 9, or a salt, stereoisomer, or tautomer thereof, wherein the water soluble group Z is selected from



each R^{22} is independently alkyl, haloalkyl, cycloalkyl or aryl;

each R^b is independently hydrogen, alkyl, haloalkyl or cycloalkyl;

each v, w and p are independently an integer from 1 to 10;

each q is independently an integer from 0 to 10;

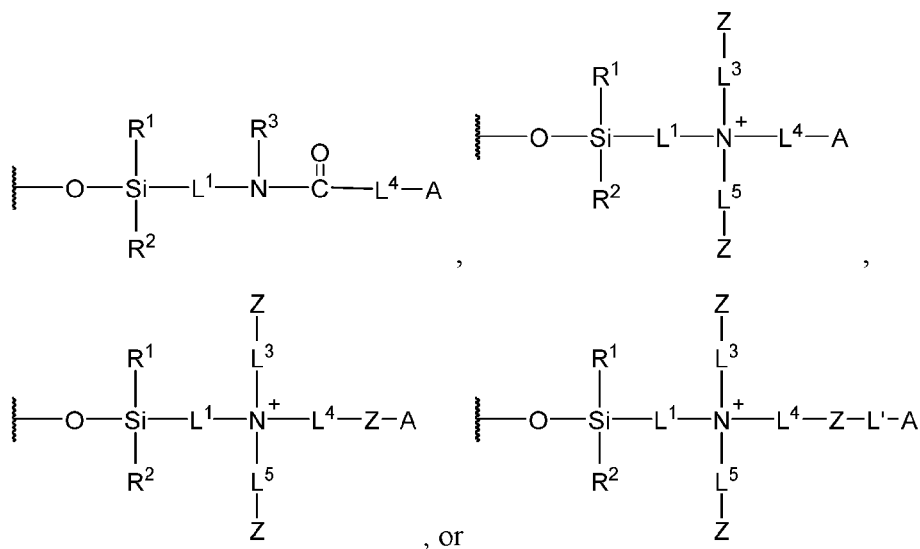
t is 2 or 3; and

u is 1 or 2.

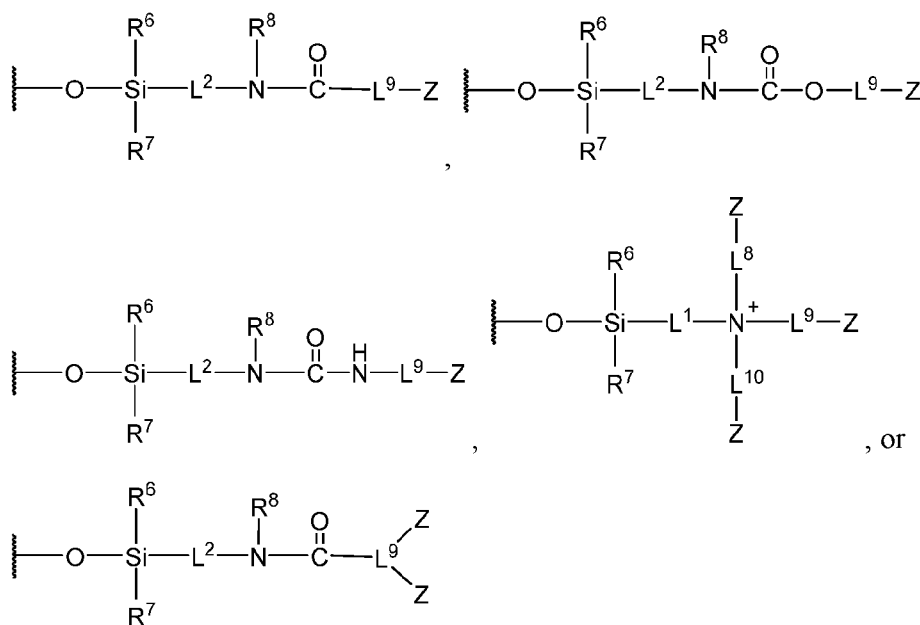
11. The compound of any one of claims 1 to 10, or a salt, stereoisomer, or tautomer thereof, wherein a and c are 0, and b and d are 1.

12. The compound of any one of claims 1 to 10, or a salt, stereoisomer, or tautomer thereof, wherein a and c are 1, and b and d are 0.

13. The compound of any one of claims 1 to 12, or a salt, stereoisomer, or tautomer thereof, wherein X is:

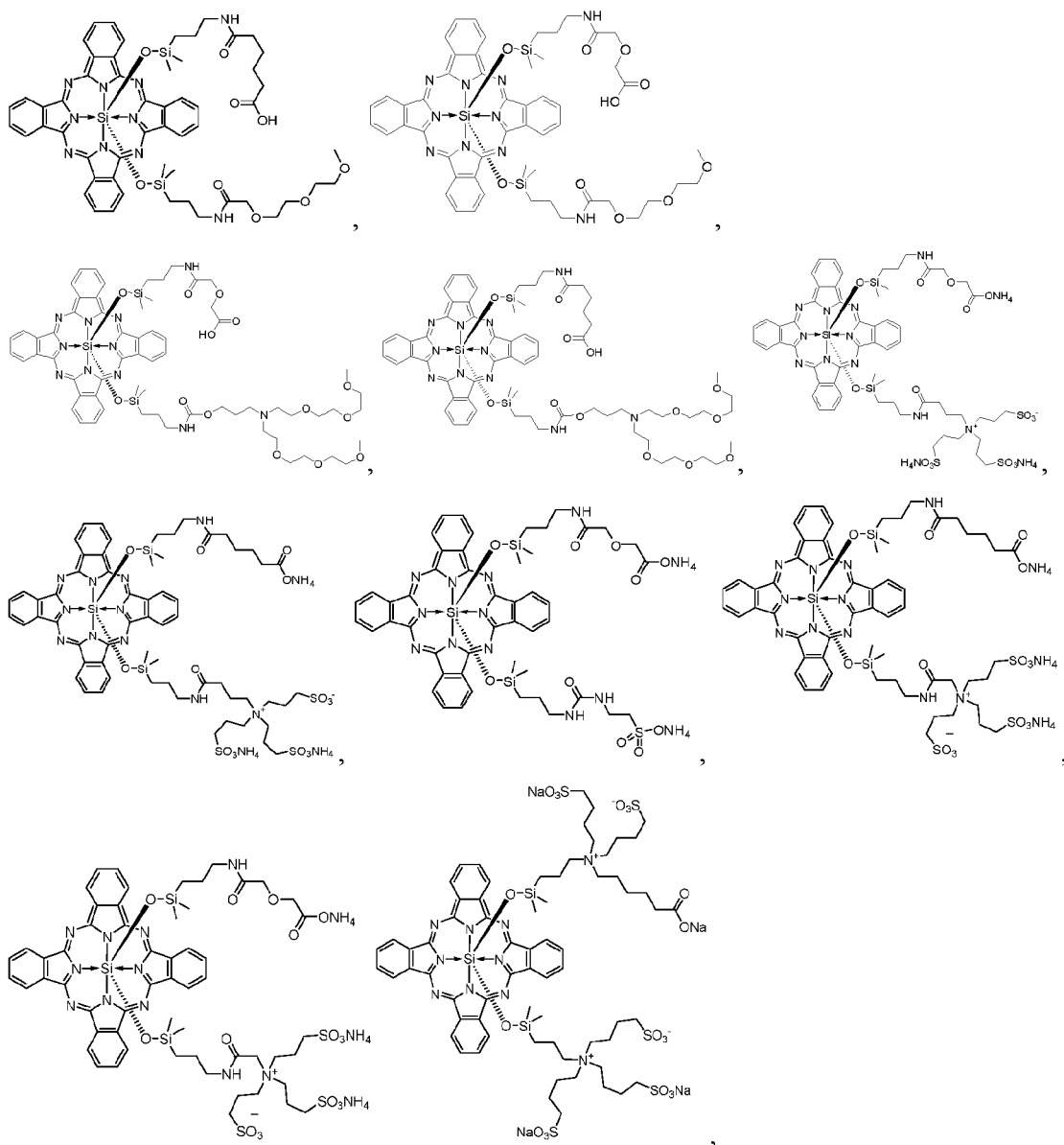


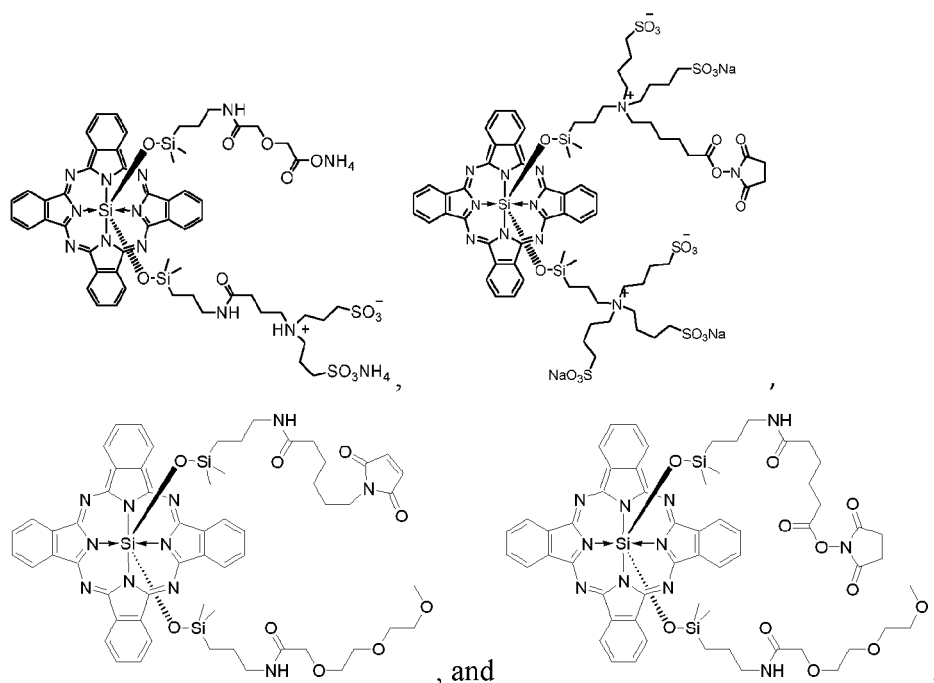
14. The compound of any one of claims 1 to 13, or a salt, stereoisomer, or tautomer thereof, wherein Y is:



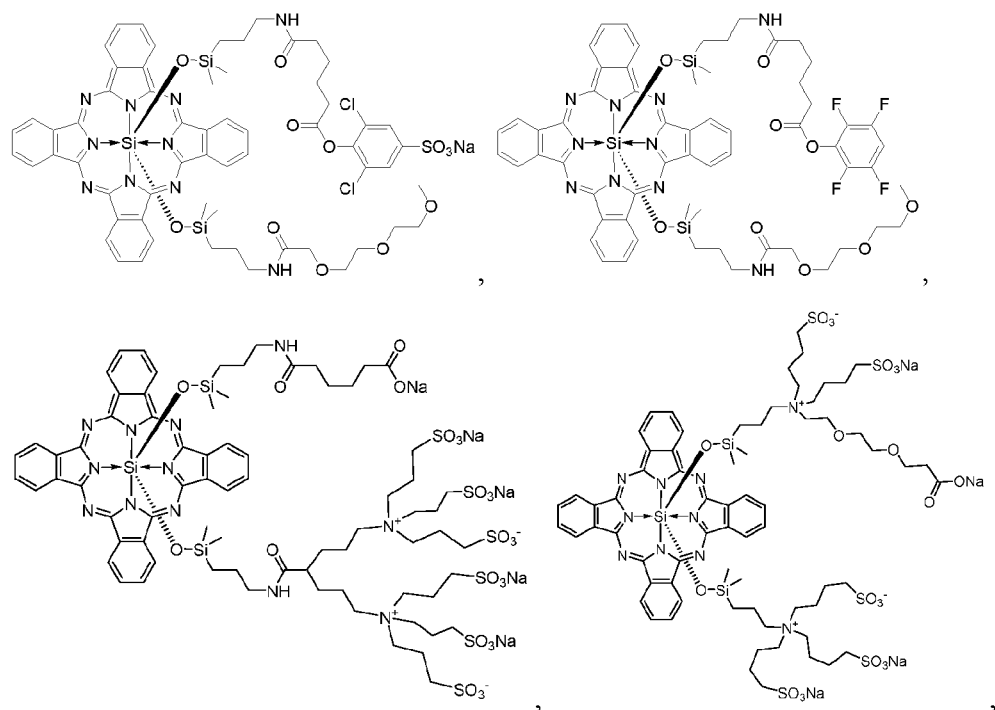
15. The compound of any one of claims 1 to 14, or a salt, stereoisomer, or tautomer thereof, wherein M is Si or Ge.

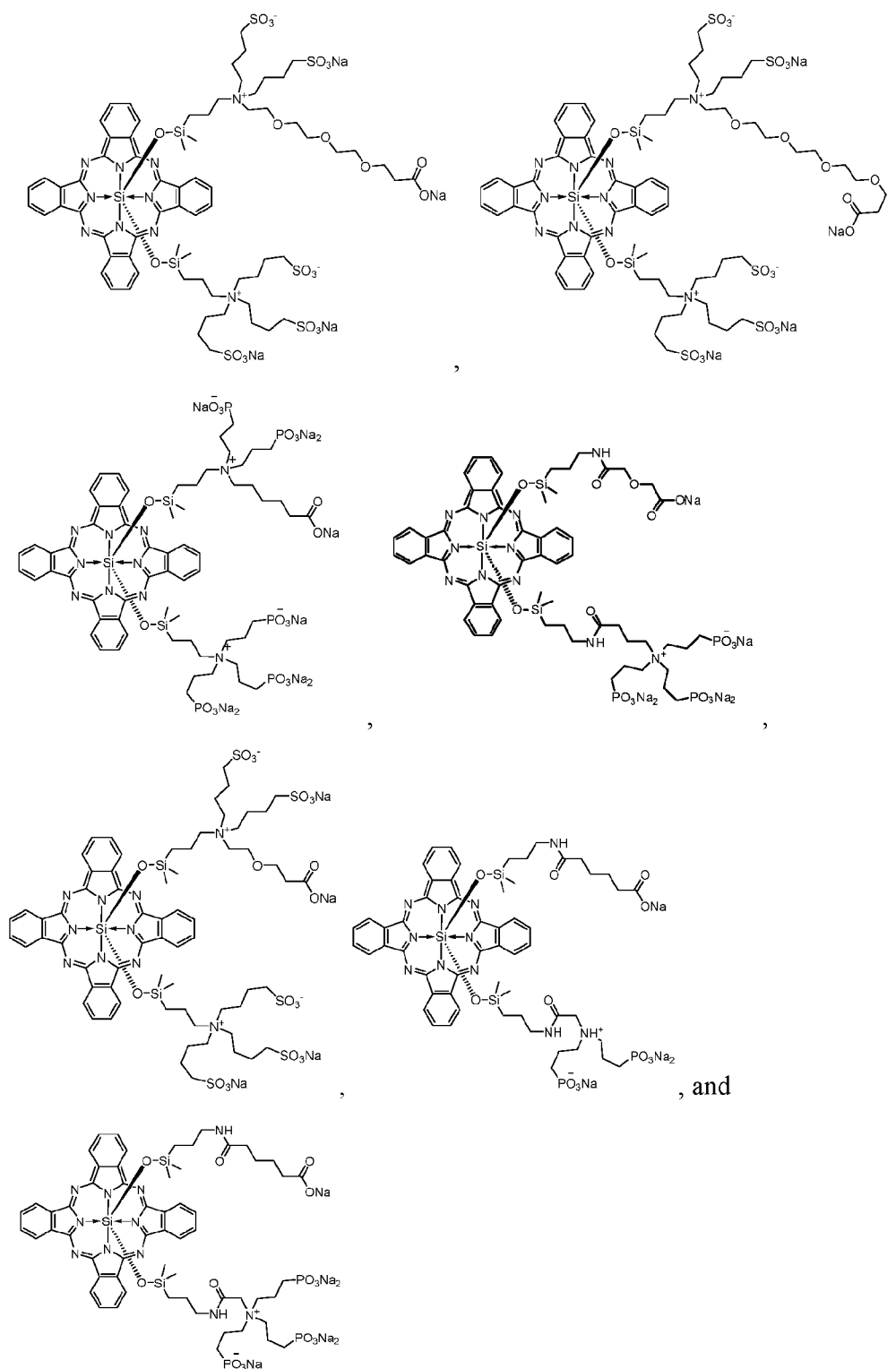
16. The compound of any one of claims 1 to 15, or a salt, stereoisomer, or tautomer thereof, selected from the group consisting of:



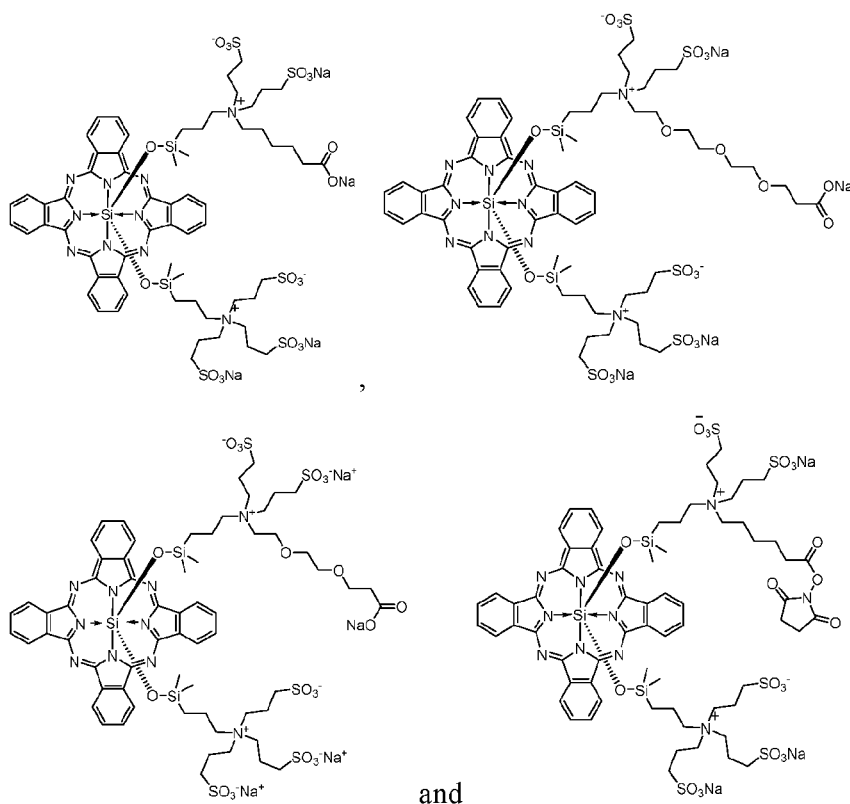


17. The compound of any one of claims 1 to 15, or a salt, stereoisomer, or tautomer thereof, selected from the group consisting of:



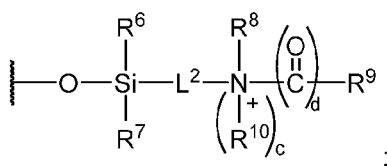


18. The compound of any one of claims 1 to 15, or a salt, stereoisomer, or tautomer thereof, selected from the group consisting of:



19. A compound, or salt, stereoisomer, or tautomer thereof, comprising a silicon atom coordinated by (a) an unsubstituted phthalocyanine, (b) a first axial silicon-containing ligand comprising a conjugatable group; and (c) a second axial silicon-containing ligand comprising a water-solubilizing group, but not a conjugatable group, and wherein the chemical structures of the first and second axial ligands are different.
20. The compound of claim 19, or salt, stereoisomer, or tautomer thereof, wherein the axial silicon-containing ligand having a conjugatable group further comprises a water-solubilizing group.
21. The compound of claims 19 or 20, or salt, stereoisomer, or tautomer thereof, wherein the water-solubilizing group is a group comprising one or more polar and/or ionic substituents.
22. The compound of claim 21, or salt, stereoisomer, or tautomer thereof, wherein the one or more polar and/or ionic substituents on the water-solubilizing group are selected from carboxylate (—CO_2), poly(ethylene glycol), sulfonate ($\text{—SO}_3\text{H}$) group, a sulfonyl ($\text{—SO}_2\text{H}$) group, a sulfate (—SO_4) group, a hydroxyl (—OH) group, a phosphate ($\text{—OPO}_3\text{H}$) group, a phosphonate ($\text{—PO}_3\text{H}$) group, an amine (—NH_2) group and an optionally substituted quaternized nitrogen.

23. The compound of claims 19 or 20, or salt, stereoisomer, or tautomer thereof, wherein the one or more polar and/or ionic substituents on the water-solubilizing group are selected from a trivalent or tetravalent nitrogen-containing group, tris-sulfoalkyl quaternary ammonium, tris-sulfonate quaternary ammonium, bis-sulfoalkyl amine, bis-sulfonate amine, or bis-alkoxypolyethylene glycol amine.
24. The compound of any one of claims 19 to 23, or salt, stereoisomer, or tautomer thereof, wherein the axial silicon-containing ligand having a water-solubilizing group has the structure of



R^6 and R^7 are each independently optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl or optionally substituted heteroaralkyl;

R^8 , R^9 or R^{10} are selected from substituent group (a) or substituent group (b) wherein,

(a) R^8 is hydrogen, $-\text{L}^8\text{-H}$ or $-\text{L}^8\text{-Z}$;

R^9 is $-\text{L}^9\text{-H}$, $-(\text{NH})_n\text{-L}^9\text{-Z}$ or $-(\text{O})_n\text{-L}^9\text{-Z}$;

R^{10} is $-\text{L}^{10}\text{-Z}$; and

(b) R^8 and R^9 are connected with a bond to form a heterocyclyl substituted with $-\text{L}^9\text{-Z}$ and R^{10} is $-\text{L}^{10}\text{-H}$ or $-\text{L}^{10}\text{-Z}$; provided at least one of R^8 , R^9 and R^{10} is a group containing Z; Z is a water-solubilizing group;

L^2 is an optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene or optionally substituted heteroalkenylene;

L^8 , L^9 and L^{10} are each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkylene, optionally substituted heterocyclene, optionally substituted arylene, optionally substituted aralkylene, optionally substituted heteroaralkylene, or optionally substituted heteroarylene, where the carbon atom of the alkylene, heteroalkylene, alkenylene, heteroalkenylene, cycloalkylene, heterocyclene, arylene aralkylene, optionally substituted heteroaralkylene, or optionally substituted

heteroarylene, is further optionally substituted with Z and each nitrogen atom of the heteroalkylene or heteroalkenylene is optionally substituted with one or two L'-Z; L' is each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkylene, optionally substituted heterocyclene, optionally substituted arylene, optionally substituted aralkylene, optionally substituted heteroaralkylene, or optionally substituted heteroarylene;

c is 0 or 1;

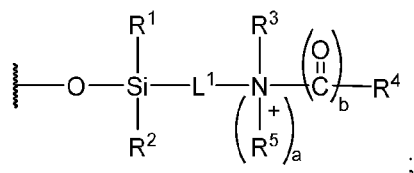
d is 0 or 1;

n is 0 or 1;

if d is 1, then c is 0; and

if n is 1, c is 1.

25. The compound of any one of claims 19 to 24, or salt, stereoisomer, or tautomer thereof, wherein the axial silicon-containing ligand having a conjugatable group has the structure of



R¹ and R² are each independently optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl or optionally substituted heteroaralkyl;

R³, R⁴ or R⁵ are selected from substituent group (a) or substituent group (b) wherein,

(a) R³ is hydrogen, -L³-H, -L³-A, or -L³-Z;

R⁴ is -L⁴-H, -(NH)_m-L⁴-A, -(NH)_m-L⁴-Z, -(O)_m-L⁴-A or -(O)_m-L⁴-Z;

R⁵ is -L⁵-H or -L⁵-A; and

(b) R³ and R⁴ are connected with a bond to form a heterocyclyl substituted with -L⁴-A and R⁵ is -L⁵-H or -L⁵-A;

provided at least one of R³, R⁴ and R⁵ is a group containing A;

A is a conjugatable group capable of forming a covalent bond with a thiol, hydroxyl, carboxyl or amino group of a second moiety, or a protected form thereof or a reacted form thereof;

Z is a water-solubilizing group optionally substituted with A or L'-A;

L¹ is an optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene or optionally substituted heteroalkenylene;

L³, L⁴, and L⁵ are each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkylene, optionally substituted heterocyclene, optionally substituted arylene, optionally substituted aralkylene, optionally substituted heteroaralkylene, or optionally substituted heteroarylene where the carbon atom of the alkylene, heteroalkylene, alkenylene, heteroalkenylene, cycloalkylene, heterocyclene, aralkylene, heteroaralkylene, heteroarylene, or arylene is further optionally substituted with Z and each nitrogen atom of the heteroalkylene or heteroalkenylene is optionally substituted with one or two L'-Z;

L' is each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkylene, optionally substituted heterocyclene, optionally substituted arylene, optionally substituted aralkylene, optionally substituted heteroaralkylene, or optionally substituted heteroarylene;

a is 0 or 1;

b is 0 or 1;

m is 0 or 1;

provided that if b is 1, then a is 0; and

if m is 1, b is 1.

26. The compound of claim 25, or salt, stereoisomer, or tautomer thereof, wherein L³, L⁴, L⁵, L⁸, L⁹ and L¹⁰ are each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene or optionally substituted heteroalkenylene, where each nitrogen atom of the heteroalkylene or heteroalkenylene is further optionally substituted with one or two L'-Z; and L' is independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene or optionally substituted heteroalkenylene.
27. The compound of any one of claims 25 or 26, or salt, stereoisomer, or tautomer thereof, wherein L¹ and L², are each independently optionally substituted C₁₋₁₀alkylene, optionally substituted heteroC₁₋₁₀alkylene, optionally substituted C₂₋₁₀alkenylene or hetero C₂₋₁₀alkenylene.

28. The compound of any one of claims 25 to 27, or salt, stereoisomer, or tautomer thereof, wherein L^1 and L^2 , are each independently C_{2-4} alkylene, hetero C_{2-4} alkylene, optionally substituted C_{2-4} alkenylene or optionally substituted hetero C_{2-4} alkenylene.
29. The compound of any one of claims 25 to 28, or salt, stereoisomer, or tautomer thereof, wherein L^1 and L^2 are each optionally substituted C_{2-4} alkylene.
30. The compound of any one of claims 19 to 29, or salt, stereoisomer, or tautomer thereof, wherein the conjugatable group is each independently
- C(O)OR¹¹,
 - NR¹²R¹³,
 - NHC(O)R¹⁴,
 - C(O)R¹⁵,
 - OR¹⁶,
 - SR¹⁶,
 - OS(O)₂R¹⁷,
 - OP(OR¹⁸)(NR¹⁹R²⁰),
 - N=C=O;
 - N=C=S,
 - S-C≡N,
 - SO₂-F,
 - SO₂-Cl,
 - SO₂-Br,
 - S-SR²¹, or
- a 5- or 6- membered dioxo-substituted heterocyclyl;
- each R¹¹ is independently hydrogen, alkyl, haloalkyl, alkenyl, heterocyclyl, aryl, or heteroaryl, and wherein each R¹¹ is independently optionally substituted with one to five groups each independently selected from halo, -SO₃H and -SO₂F;
- each R¹² is independently hydrogen or alkyl or haloalkyl;
- each R¹³ is aryl, or heteroaryl, and each R¹³ is independently optionally substituted with one to five groups each independently selected from halo, -SO₃H and -SO₂F; or optionally R¹² and R¹³, together with the nitrogen to which they are attached, form a cyclic imide;
- each R¹⁴ is independently optionally substituted haloalkyl, or optionally substituted aralkyl;

each R^{15} is independently aryl optionally substituted with one to five groups each independently halo, heterocyclyl, $-\text{SO}_3\text{H}$ or $-\text{SO}_2\text{F}$;

each R^{16} is independently aryl optionally substituted with one to five groups each independently halo or heterocyclyl;

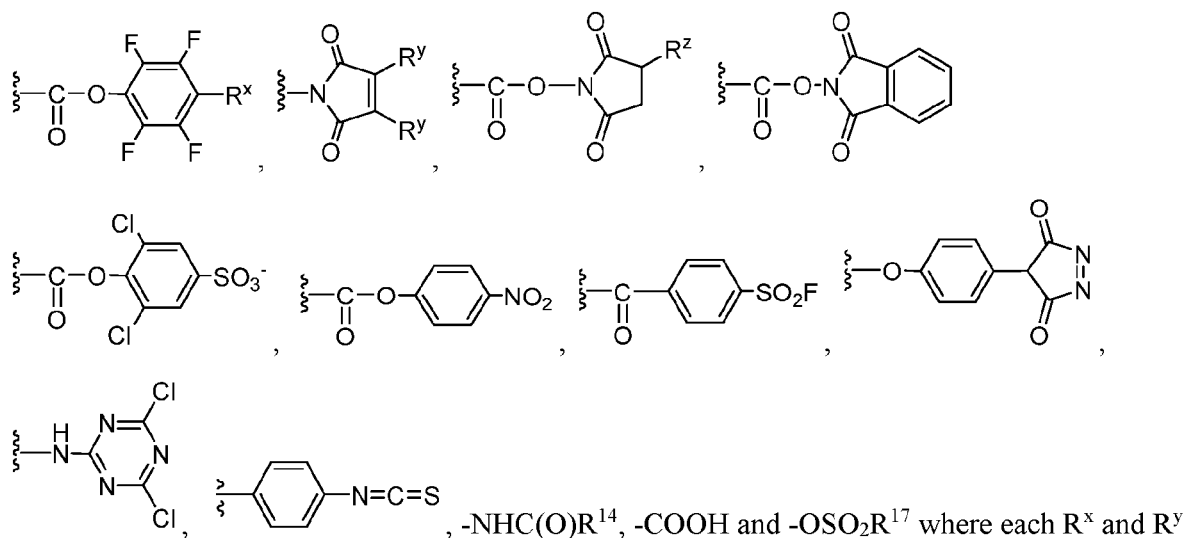
each R^{17} is independently optionally substituted alkyl, optionally substituted haloalkyl, optionally substituted alkenyl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, optionally substituted aryl or optionally substituted heteroaryl, wherein the heterocyclyl, aryl or heteroaryl is optionally substituted with one to five groups each independently selected from halo, $-\text{SO}_3\text{H}$, $-\text{SO}_2\text{F}$ and $-\text{C}(\text{O})\text{OR}^c$;

each R^c is independently optionally substituted alkyl, optionally substituted haloalkyl, optionally substituted cycloalkyl or optionally substituted aryl;

R^{18} , R^{19} and R^{20} are each independently optionally substituted alkyl or optionally substituted haloalkyl; and

R^{21} is heteroaryl.

31. The compound of any one of claims 19 to 30, or salt, stereoisomer, or tautomer thereof, wherein the conjugatable group is selected from the group consisting of:



R^{14} is optionally substituted haloalkyl or optionally substituted aralkyl;

each R^{17} is independently optionally substituted alkyl, optionally substituted haloalkyl, optionally substituted alkenyl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, optionally substituted aryl or optionally substituted heteroaryl, wherein the heterocyclyl, aryl or heteroaryl is optionally substituted with one to five groups each independently selected from halo, $-\text{SO}_3\text{H}$, $-\text{SO}_2\text{F}$ and $-\text{C}(\text{O})\text{OR}^c$; and

each R^c is independently optionally substituted alkyl, optionally substituted haloalkyl, optionally substituted cycloalkyl or optionally substituted aryl.

32. The compound of any one of claims 30 to 31, or salt, stereoisomer, or tautomer thereof, wherein the conjugatable group is each independently -C(O)OR¹¹ or -NR¹²R¹³.

33. The compound of any one of claims 19 to 32, or salt, stereoisomer, or tautomer thereof, wherein the water-solubilizing group is

-C(O)OH,
 -(CH₂)_q(OCH₂CH₂)_v(CH₂)_qC(O)OH,
 -(CH₂CH₂O)_v(CH₂)_pC(O)OH,
 -(CH₂)_q(OCH₂CH₂)_vOR²²,
 -(CH₂CH₂O)_v(CH₂)_pOR²²,
 -(CH₂)_q(OCH₂CH₂)_vSR²²,
 -(CH₂CH₂O)_v(CH₂)_pSR²²,
 -O(CH₂)_vN[(CH₂CH₂O)_mCH₂CH₂OR²²]_t,
 -(CH₂)_q(OCH₂CH₂)_vN[(CH₂CH₂O)_wCH₂CH₂OR²²]_t,
 -(CH₂CH₂O)_m(CH₂)_pN[(CH₂CH₂O)_wCH₂CH₂OR²²]_t,
 -NH₂,
 -(CH₂)_qN[(CH₂CH₂O)_vCH₂CH₂OR²²]_t,
 -(CH₂)_qNR^b[(CH₂CH₂O)_wCH₂CH₂OR²²]_u,
 -(CH₂)_qN[(CH₂)_p(OCH₂CH₂)_vOR²²]_t,
 -(CH₂)_qN[(CH₂)_pSO₃H]_t,
 -(CH₂)_qNR^b[(CH₂)_pSO₃H]_u,
 -(CH₂)_qNR^b(CH₂)_pCH(SO₃H)₂,
 -(CH₂)_qN[(CH₂)_pS(O)_uOH]_t,
 -(CH₂)_qN[(CH₂)_pOSO₃H]_t,
 -(CH₂)_q(OCH₂CH₂)_v(CH₂)_qSO₃H,
 -(CH₂)_q(OCH₂CH₂)_v(CH₂)_qS(O)_uOH,
 -(CH₂)_q(OCH₂CH₂)_v(CH₂)_qOSO₃H,
 -SO₃H,
 -CH(SO₃H)₂,
 -OSO₃H,
 -S(O)_uOH,

$-\text{P}(\text{O})(\text{OH})_2$,
 $-\text{CH}(\text{P}(\text{O})(\text{OH})_2)_2$,
 $-(\text{CH}_2)_q\text{N}[(\text{CH}_2)_p\text{P}(\text{O})(\text{OH})_2]_t$,
 $-(\text{CH}_2)_q(\text{OCH}_2\text{CH}_2)_v(\text{CH}_2)_q\text{P}(\text{O})(\text{OH})_2$,
 $-(\text{CH}_2)_q\text{N}[(\text{CH}_2)_p\text{OP}(\text{O})(\text{OH})_2]_t$,
 $-\text{OP}(\text{O})(\text{OH})_2$,
 $-(\text{CH}_2)_q(\text{OCH}_2\text{CH}_2)_v(\text{CH}_2)_q\text{P}(\text{O})(\text{OH})_2$,
 $-(\text{CH}_2)_q\text{N}[(\text{CH}_2)_p\text{P}(\text{O})(\text{OH})_2]_t$,
 $-\text{P}(\text{O})(\text{OH})_2$, glutamate, aspartate, histidine, 1,3-beta-glucan or 1,4-beta-glucan;
 each R^{22} is independently alkyl, haloalkyl, cycloalkyl or aryl;
 each R^b is independently hydrogen, alkyl, haloalkyl or cycloalkyl;
 each v , w and p are independently an integer from 1 to 10;
 each q is independently an integer from 0 to 10;
 t is 2 or 3; and
 u is 1 or 2.

34. The compound of any one of claims 19 to 33, or salt, stereoisomer, or tautomer thereof, wherein the water-solubilizing Z group is selected from:

$-(\text{CH}_2)_q(\text{OCH}_2\text{CH}_2)_v\text{OR}^{22}$,
 $-(\text{CH}_2)_q\text{O}(\text{CH}_2)_v\text{N}[(\text{CH}_2\text{CH}_2\text{O})_w\text{CH}_2\text{CH}_2\text{OR}^{22}]_t$,
 $-(\text{CH}_2)_q\text{N}[(\text{CH}_2)_p(\text{OCH}_2\text{CH}_2)_v\text{OR}^{22}]_t$,
 $-(\text{CH}_2)_q\text{N}[(\text{CH}_2)_p\text{SO}_3\text{H}]_t$,
 $-(\text{CH}_2)_q\text{NR}^b[(\text{CH}_2)_p\text{SO}_3\text{H}]_u$,
 $-(\text{CH}_2)_q\text{NR}^b[(\text{CH}_2)_p\text{CH}(\text{SO}_3\text{H})_2]_u$,
 $-\text{SO}_3\text{H}$,
 $-\text{CH}(\text{SO}_3\text{H})_2$,
 $-\text{P}(\text{O})(\text{OH})_2$,
 $-(\text{CH}_2)_q\text{N}[(\text{CH}_2)_p\text{P}(\text{O})(\text{OH})_2]_t$,
 $-(\text{CH}_2)_q\text{NR}^b[(\text{CH}_2)_p\text{P}(\text{O})(\text{OH})_2]_u$ and
 $-(\text{CH}_2)_q\text{NR}^b(\text{CH}_2)_p\text{CH}(\text{P}(\text{O})(\text{OH})_2)_2$;

wherein,

each R^{22} is independently alkyl, haloalkyl, cycloalkyl or aryl;
 each R^b is independently hydrogen, alkyl, haloalkyl or cycloalkyl;
 each v , w and p are independently an integer from 1 to 10;

each q is independently an integer from 0 to 10;

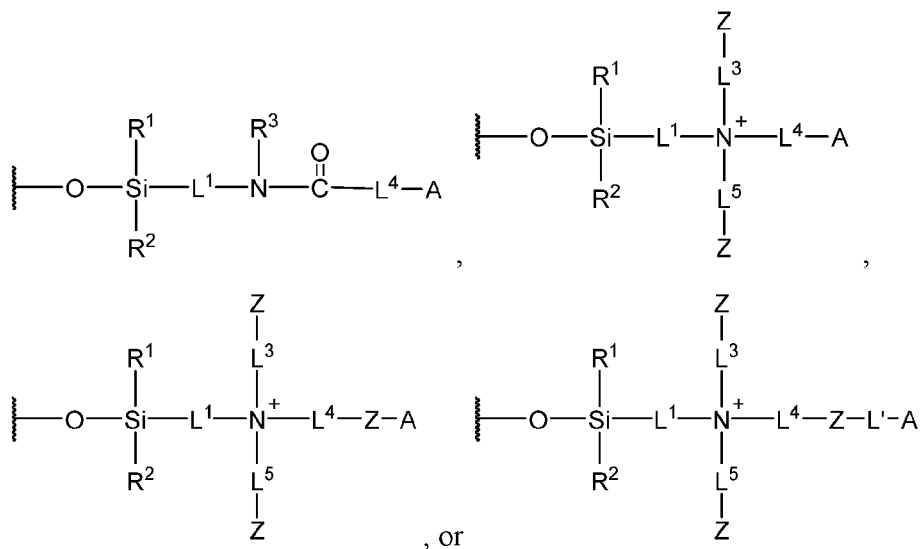
t is 2 or 3; and

u is 1 or 2.

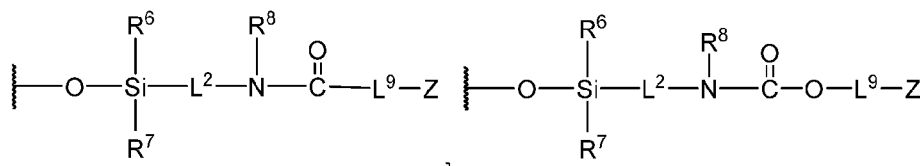
35. The compound of any one of claims 25 to 34, or salt, stereoisomer, or tautomer thereof, wherein a and c are 0, and b and d are 1.

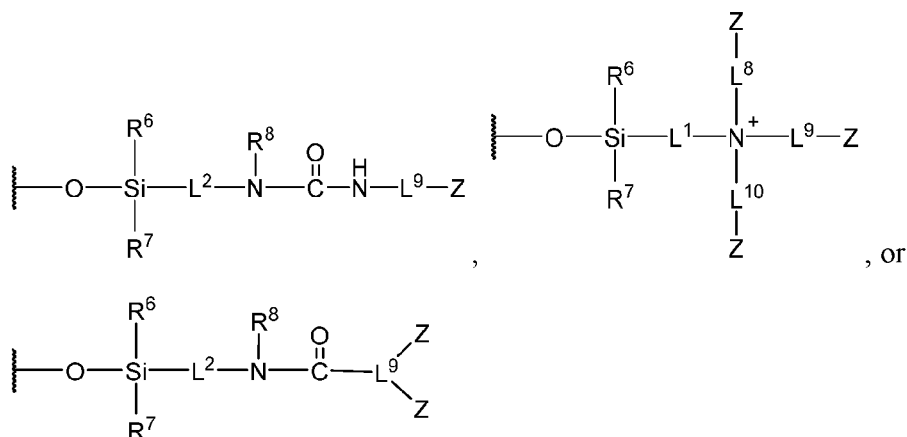
36. The compound of any one of claims 25 to 34, or salt, stereoisomer, or tautomer thereof, wherein a and c are 1, and b and d are 0.

37. The compound of any one of claims 25 to 36, or salt, stereoisomer, or tautomer thereof, wherein X is:

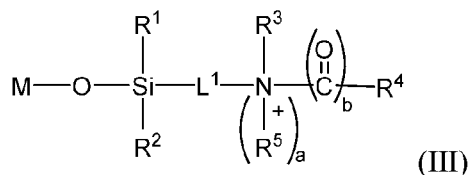


38. The compound of any one of claims 25 to 37, or salt, stereoisomer, or tautomer thereof, wherein Y is:





39. A compound of Formula (III), or a salt, stereoisomer, or tautomer thereof, having the structure:



wherein M is a metal or metalloid selected from Si, Ge, Sn, Al, or Zn, optionally further ligated on the metal or metalloid;

R¹ and R² are each independently optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl or optionally substituted heteroaralkyl;

R³, R⁴ or R⁵ are selected from substituent group (a) or substituent group (b) wherein,

(a) R³ is hydrogen, -L³-H, -L³-A, or -L³-Z;

R⁴ is -L⁴-H, -(NH)_m-L⁴-A, -(NH)_m-L⁴-Z, -(O)_m-L⁴-A or -(O)_m-L⁴-Z;

R⁵ is -L⁵-H or -L⁵-A; and

(b) R³ is -L³-H, or -L³-A;

R⁴ is -L⁴-H, -(NH)_m-L⁴-A, or -(O)_m-L⁴-A; wherein R³ and R⁴ are connected with a bond to form a heterocyclyl substituted with -L⁴-A; and

R⁵ is -L⁵-H or -L⁵-A;

provided at least one of R³, R⁴ and R⁵ is a group containing A;

A is a reactive group capable of forming a covalent bond with a thiol, hydroxyl, carboxyl or amino group of a second moiety, or a protected form thereof or a reacted form thereof;

L¹ is optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene or optionally substituted heteroalkenylene;

Z is a water soluble group optionally substituted with A or L'-A;

L³, L⁴, and L⁵ are each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkylene, optionally substituted heterocyclene, optionally substituted arylene, optionally substituted aralkylene, optionally substituted heteroaralkylene, or optionally substituted heteroarylene where the carbon atom of the alkylene, heteroalkylene, alkenylene, heteroalkenylene, cycloalkylene, heterocyclene, arylene, aralkylene, heteroaralkylene, or heteroarylene is further optionally substituted with Z and each nitrogen atom of the heteroalkylene or heteroalkenylene is optionally substituted with one or two L'-Z;

L' is each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkylene, optionally substituted heterocyclene, optionally substituted arylene, optionally substituted aralkylene, optionally substituted heteroaralkylene, or optionally substituted heteroarylene;

a is 0 or 1;

b is 0 or 1;

m is 0 or 1;

provided that if b is 1, then a is 0; and

if m is 1, b is 1.

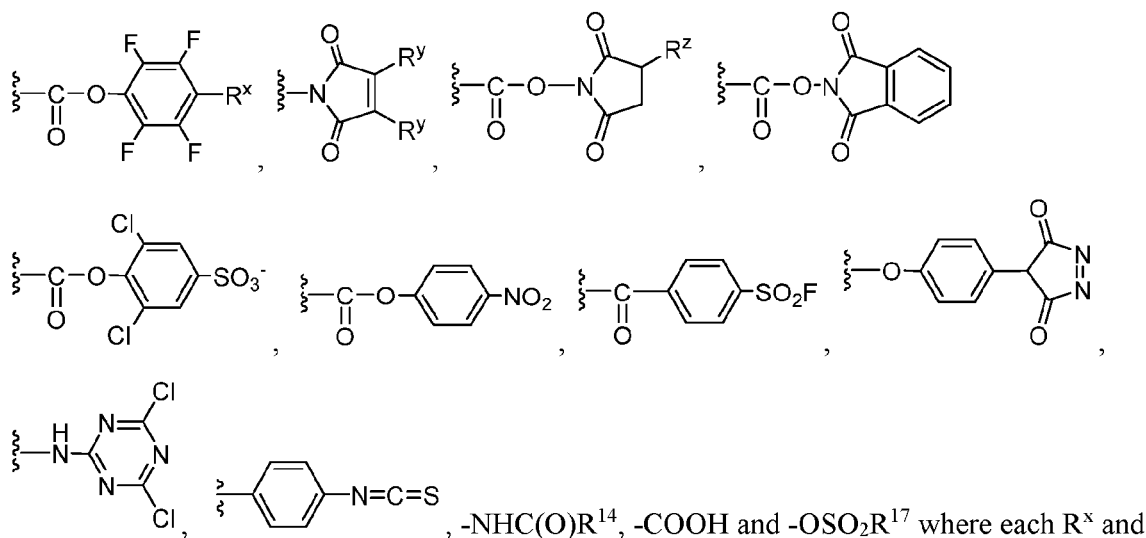
40. The compound of claim 39, or a salt, stereoisomer, or tautomer thereof, wherein L³, L⁴, L⁵, are each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene or optionally substituted heteroalkenylene, where each nitrogen atom of the heteroalkylene or heteroalkenylene is further optionally substituted with one or two L'-Z; and
L' is independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene or optionally substituted heteroalkenylene.

41. The compound of claim 39 or 40, or a salt, stereoisomer, or tautomer thereof, wherein L¹ and L², are each independently optionally substituted C₁₋₁₀alkylene, optionally substituted heteroC₁₋₁₀alkylene, optionally substituted C₂₋₁₀alkenylene or hetero C₂₋₁₀alkenylene.

42. The compound of any one of claims 39 to 41, or a salt, stereoisomer, or tautomer thereof, wherein L^1 and L^2 , are each independently C_{2-4} alkylene, hetero C_{2-4} alkylene, optionally substituted C_{2-4} alkenylene or optionally substituted hetero C_{2-4} alkenylene.
43. The compound of any one of claims 39 to 42, or a salt, stereoisomer, or tautomer thereof, wherein L^1 and L^2 are each optionally substituted C_{2-4} alkylene.
44. The compound of any one of claims 39 to 43, or a salt, stereoisomer, or tautomer thereof, wherein the reactive group A is each independently selected from:
- C(O)OR¹¹,
 - NR¹²R¹³,
 - NHC(O)R¹⁴,
 - C(O)R¹⁵,
 - OR¹⁶,
 - SR¹⁶,
 - OS(O)₂R¹⁷,
 - OP(OR¹⁸)(NR¹⁹R²⁰),
 - N=C=O;
 - N=C=S,
 - S-C≡N,
 - SO₂-F,
 - SO₂-Cl,
 - SO₂-Br,
 - S-SR²¹; or
- 5- or 6- membered dioxo-substituted heterocyclyl;
- each R¹¹ is independently hydrogen, alkyl, haloalkyl, alkenyl, heterocyclyl, aryl or heteroaryl, wherein each R¹¹ is independently optionally substituted with one to five groups each independently selected from halo, -SO₃⁻ and -SO₂F;
- each R¹² is independently hydrogen, alkyl or haloalkyl;
- each R¹³ is aryl or heteroaryl, each R¹³ independently optionally substituted with one to five groups each independently selected from halo, -SO₃⁻ and -SO₂F; or optionally R¹² and R¹³, together with the nitrogen to which they are attached, form a cyclic imide;
- each R¹⁴ is independently optionally substituted haloalkyl or optionally substituted aralkyl;

each R^{15} is independently aryl optionally substituted with one to five groups each independently halo, heterocyclyl, $-\text{SO}_3^-$ or $-\text{SO}_2\text{F}$;
 each R^{16} is independently aryl optionally substituted with one to five groups each independently halo or heterocyclyl;
 each R^{17} is independently optionally substituted alkyl, optionally substituted haloalkyl, optionally substituted alkenyl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, optionally substituted aryl or optionally substituted heteroaryl, wherein the heterocyclyl, aryl or heteroaryl is optionally substituted with one to five groups each independently selected from halo, $-\text{SO}_3^-$, $-\text{SO}_2\text{F}$ and $-\text{C}(\text{O})\text{OR}^c$;
 each R^c is independently optionally substituted alkyl, optionally substituted haloalkyl, optionally substituted cycloalkyl or optionally substituted aryl;
 R^{18} , R^{19} and R^{20} are each independently optionally substituted alkyl or optionally substituted haloalkyl; and
 R^{21} is heteroaryl.

45. The compound of any one of claims 39-44, or a salt, stereoisomer, or tautomer thereof, wherein the reactive group A is selected from the group consisting of:



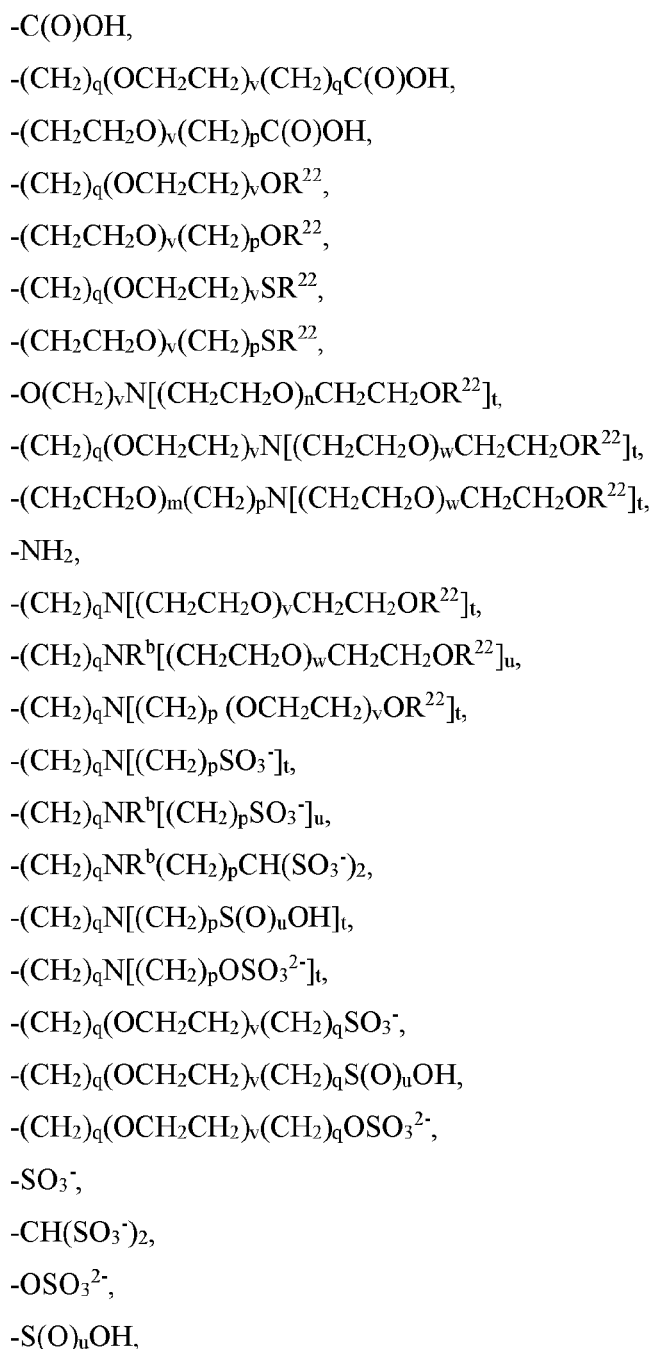
R^{14} is optionally substituted haloalkyl or optionally substituted aralkyl; and

R^{17} is independently optionally substituted alkyl, optionally substituted haloalkyl, optionally substituted alkenyl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, optionally substituted aryl or optionally substituted heteroaryl, wherein the heterocyclyl, aryl or heteroaryl is optionally substituted with one to five groups each independently selected from halo, $-\text{SO}_3^-$, $-\text{SO}_2\text{F}$ and $-\text{C}(\text{O})\text{OR}^c$; and

each R^c is independently optionally substituted alkyl, optionally substituted haloalkyl, optionally substituted cycloalkyl or optionally substituted aryl.

46. The compound of any one of claims 39 to 45, or a salt, stereoisomer, or tautomer thereof, wherein the reactive group is each independently $-C(O)OR^{11}$ or $-NR^{12}R^{13}$.

47. The compound of any one of claims 39 to 46, or a salt, stereoisomer, or tautomer thereof, wherein the water soluble group Z is



$-\text{PO}_3^{2-}$,
 $-\text{CH}(\text{PO}_3^{2-})_2$,
 $-(\text{CH}_2)_q\text{N}[(\text{CH}_2)_p\text{PO}_3^-]_t$,
 $-(\text{CH}_2)_q(\text{OCH}_2\text{CH}_2)_v(\text{CH}_2)_q\text{PO}_3^-$,
 $-(\text{CH}_2)_q\text{N}[(\text{CH}_2)_p\text{OPO}_3^-]_t$,
 $-\text{OPO}_3^-$,
 $-(\text{CH}_2)_q(\text{OCH}_2\text{CH}_2)_v(\text{CH}_2)_q\text{P}(\text{O})(\text{OH})_2$,
 $-(\text{CH}_2)_q\text{N}[(\text{CH}_2)_p\text{P}(\text{O})(\text{OH})_2]_t$,
 $-\text{P}(\text{O})(\text{OH})_2$,

glutamate,

aspartate,

histidine,

1,3-beta-glucan, or

1,4-beta-glucan;

each R^{22} is independently alkyl, haloalkyl, cycloalkyl or aryl;

each R^b is independently hydrogen, alkyl optionally substituted with $-\text{CO}_2\text{H}$, heteroalkylene optionally substituted with $-\text{CO}_2\text{H}$, haloalkyl or cycloalkyl;

each v , w and p are independently an integer from 1 to 10;

each q is independently an integer from 0 to 10;

t is 2 or 3; and

u is 1 or 2.

48. The compound of any one of claims 39 to 47, or a salt, stereoisomer, or tautomer thereof,

wherein the water soluble group Z is

$-(\text{CH}_2)_q(\text{OCH}_2\text{CH}_2)_v\text{OR}^{22}$,
 $-(\text{CH}_2)_q\text{O}(\text{CH}_2)_v\text{N}[(\text{CH}_2\text{CH}_2\text{O})_w\text{CH}_2\text{CH}_2\text{OR}^{22}]_t$,
 $-(\text{CH}_2)_q\text{N}[(\text{CH}_2)_p(\text{OCH}_2\text{CH}_2)_v\text{OR}^{22}]_t$,
 $-(\text{CH}_2)_q\text{N}[(\text{CH}_2)_p\text{SO}_3^-]_t$,
 $-(\text{CH}_2)_q\text{NR}^b[(\text{CH}_2)_p\text{SO}_3^-]_u$,
 $-(\text{CH}_2)_q\text{NR}^b[(\text{CH}_2)_p\text{CH}(\text{SO}_3^-)_2]_u$,
 $-\text{SO}_3^-$,
 $-\text{CH}(\text{SO}_3^-)_2$,
 $-\text{PO}_3^{2-}$,
 $-(\text{CH}_2)_q\text{N}[(\text{CH}_2)_p\text{PO}_3^-]_t$,



each R^{22} is independently alkyl, haloalkyl, cycloalkyl or aryl;

each R^b is independently hydrogen, alkyl optionally substituted with $-\text{CO}_2\text{H}$, heteroalkylene optionally substituted with $-\text{CO}_2\text{H}$, haloalkyl or cycloalkyl;

each v , w and p are independently an integer from 1 to 10;

each q is independently an integer from 0 to 10;

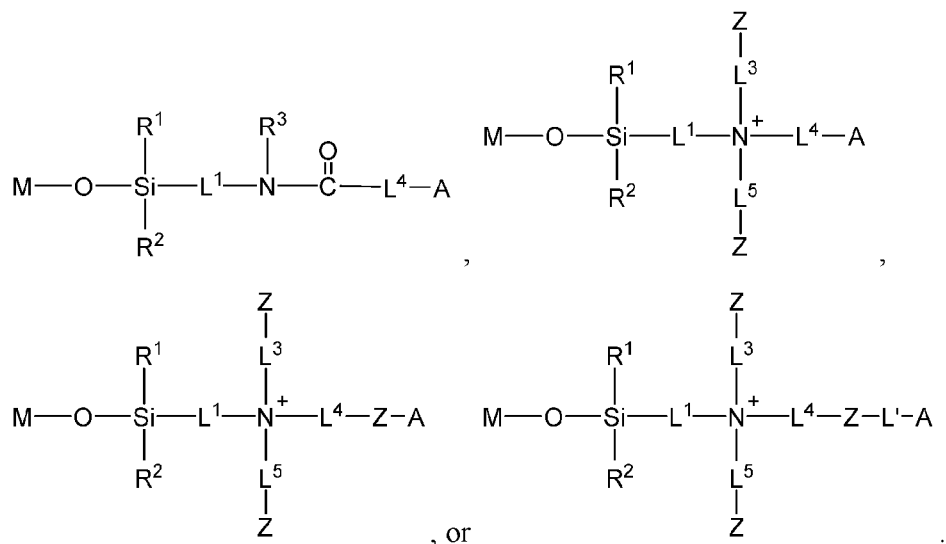
t is 2 or 3; and

u is 1 or 2.

49. The compound of any one of claims 39 to 48, or a salt, stereoisomer, or tautomer thereof, wherein a is 0, and b is 1.

50. The compound of any one of claims 39 to 48, or a salt, stereoisomer, or tautomer thereof, wherein a is 1, and b is 0.

51. The compound of any one of claims 39 to 50, or a salt, stereoisomer, or tautomer thereof, wherein the compound of Formula (III) has the structure:



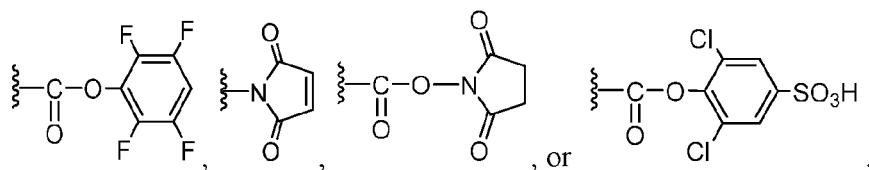
52. The compound of any one of claims 39 to 51, or a salt, stereoisomer, or tautomer thereof, wherein L^1 is selected from $-(\text{CH}_2)_2-$, $-(\text{CH}_2)_3-$, or $-(\text{CH}_2)_4-$.

53. The compound of any one of claims 39 to 52, or a salt, stereoisomer, or tautomer thereof, wherein L^1 is $-(\text{CH}_2)_3-$.

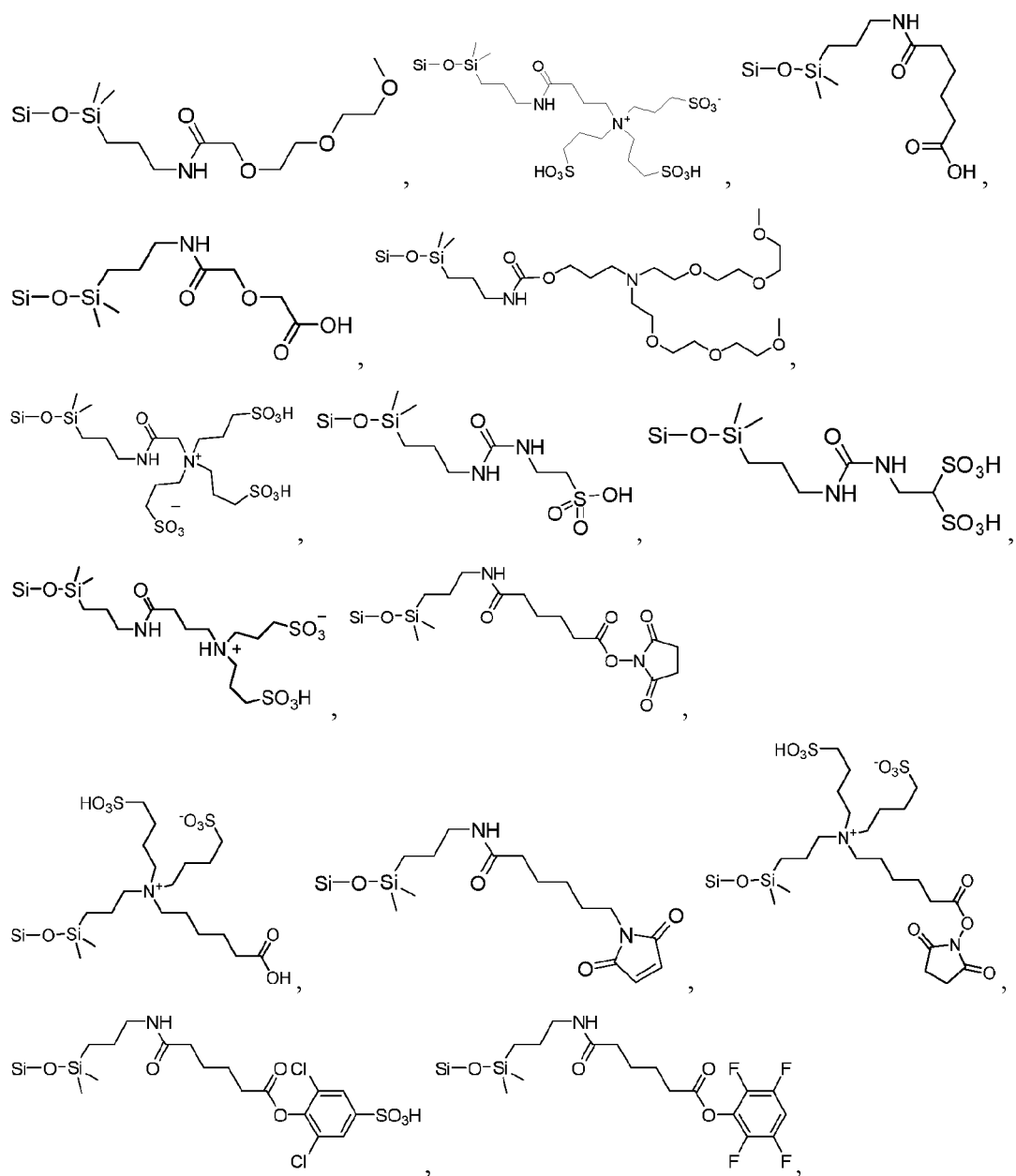
54. The compound of any one of claims 39 to 53, or a salt, stereoisomer, or tautomer thereof, wherein L^4 is selected from $-(CH_2)-$, $-(CH_2)_2-$, $-(CH_2)_3-$, $-(CH_2)_4-$, or $-(CH_2)_5-$.
55. The compound of any one of claims 39 to 54, or a salt, stereoisomer, or tautomer thereof, wherein L^4 is $-(CH_2)-$ or $-(CH_2)_2-$.
56. The compound of any one of claims 39 to 54, or a salt, stereoisomer, or tautomer thereof, wherein L^4 is $-(CH_2)_3-$.
57. The compound of any one of claims 39 to 54, or a salt, stereoisomer, or tautomer thereof, wherein L^4 is $-(CH_2)_4-$.
58. The compound of any one of claims 39 to 54, or a salt, stereoisomer, or tautomer thereof, wherein L^4 is $-(CH_2)_5-$.
59. The compound of any one of claims 39 to 58, or a salt, stereoisomer, or tautomer thereof, wherein L^5 is selected from $-(CH_2)_3-$, $-(CH_2)_4-$ or $-(CH_2)_5-$.
60. The compound of any one of claims 39 to 58, or a salt, stereoisomer, or tautomer thereof, wherein L^5 is $-(CH_2)_3-$.
61. The compound of any one of claims 39 to 58, or a salt, stereoisomer, or tautomer thereof, wherein L^5 is $-(CH_2)_4-$.
62. The compound of any one of claims 39 to 58, or a salt, stereoisomer, or tautomer thereof, wherein L^5 is $-(CH_2)_5-$.
63. The compound of any one of claims 39 to 62, or a salt, stereoisomer, or tautomer thereof, wherein R^3 , R^4 or R^5 are selected from substituent group (a).
64. The compound of any one of claims 39 to 63, or a salt, stereoisomer, or tautomer thereof, wherein R^3 is hydrogen.
65. The compound of any one of claims 39 to 64, or a salt, stereoisomer, or tautomer thereof, wherein R^3 is hydrogen, a is 0, and b is 1.
66. The compound of any one of claims 39 to 63, or a salt, stereoisomer, or tautomer thereof, wherein R^3 is $-L^3-Z$.
67. The compound of any one of claims 39 to 66, or a salt, stereoisomer, or tautomer thereof, wherein R^4 is $-(NH)_m-L^4-Z$.
68. The compound of any one of claims 39 to 66, or a salt, stereoisomer, or tautomer thereof, wherein R^4 is $-(O)_m-L^4-Z$.
69. The compound of any one of claims 67 or 68, or a salt, stereoisomer, or tautomer thereof, wherein m is 0.
70. The compound of claim 69, or a salt, stereoisomer, or tautomer thereof, wherein L^4 is alkylene, and the carbon atom of the alkylene is further substituted with a second Z.

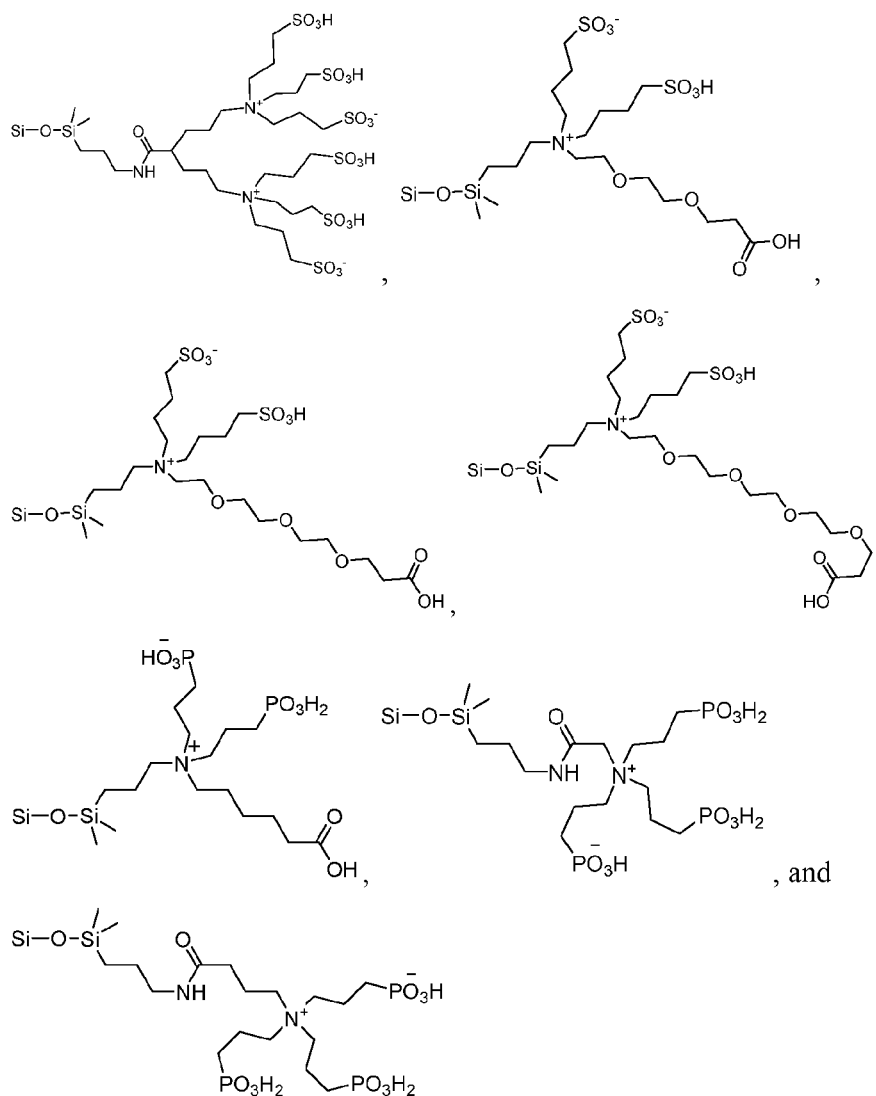
71. The compound of claim 70, or a salt, stereoisomer, or tautomer thereof, wherein the L⁴ alkylene is a C₂₋₅ alkylene.
72. The compound of claim 70, or a salt, stereoisomer, or tautomer thereof, wherein said second Z is $-(\text{CH}_2)_q\text{N}[(\text{CH}_2)_p\text{SO}_3^-]_t$.
73. The compound of claim 72, or a salt, stereoisomer, or tautomer thereof, wherein t is 3, q is 2-6, and p is 2-4.
74. The compound of any one of claims 39 to 68, or a salt, stereoisomer, or tautomer thereof, wherein R⁵ is -L⁵-A.
75. The compound of any one of claims 39 to 68, or a salt, stereoisomer, or tautomer thereof, wherein R³, R⁴ or R⁵ are selected from substituent group (b).
76. The compound of claim 69, or a salt, stereoisomer, or tautomer thereof, wherein L⁴ is C₂₋₅ alkylene, and Z is $-(\text{CH}_2)_q\text{N}[(\text{CH}_2)_p\text{SO}_3^-]_t$, wherein q is 0.
77. The compound of claim 69, or a salt, stereoisomer, or tautomer thereof, wherein p is 2-5, and t is 3.
78. The compound of claim 69, or a salt, stereoisomer, or tautomer thereof, wherein p is 3.
79. The compound of claim 69, or a salt, stereoisomer, or tautomer thereof, wherein p is 4.
80. The compound of claim 69, or a salt, stereoisomer, or tautomer thereof, wherein L⁴ is C₂₋₅ alkylene, and Z is $-(\text{CH}_2)_q\text{N}[(\text{CH}_2)_p\text{PO}_3^-]_t$, wherein q is 0.
81. The compound of claim 80, or a salt, stereoisomer, or tautomer thereof, wherein p is 2-5, and t is 3.
82. The compound of claim 81, or a salt, stereoisomer, or tautomer thereof, wherein p is 3.
83. The compound of claim 81, or a salt, stereoisomer, or tautomer thereof, wherein p is 4.
84. The compound of claim 69, or a salt, stereoisomer, or tautomer thereof, wherein L⁴ is C₂₋₅ alkylene, and Z is $-(\text{CH}_2)_q\text{NR}^b(\text{CH}_2)_p\text{CH}(\text{SO}_3^-)_2$, wherein q is 0.
85. The compound of claim 84, or a salt, stereoisomer, or tautomer thereof, wherein R^b is alkyl optionally substituted with -CO₂H, or heteroalkylene optionally substituted with -CO₂H.
86. The compound of claim 84, or a salt, stereoisomer, or tautomer thereof, wherein R^b is hydrogen.
87. The compound of any one of claims 84-86, or a salt, stereoisomer, or tautomer thereof, wherein p is 2-5.
88. The compound of claim 69, or a salt, stereoisomer, or tautomer thereof, wherein L⁴ is C₂₋₅ alkylene, and Z is $-(\text{CH}_2)_q\text{NR}^b[(\text{CH}_2)_p\text{PO}_3^-]_2$, wherein q is 0.
89. The compound of claim 84, or a salt, stereoisomer, or tautomer thereof, wherein R^b is alkyl optionally substituted with -CO₂H, or heteroalkylene optionally substituted with -CO₂H.

90. The compound of claim 84, or a salt, stereoisomer, or tautomer thereof, wherein R^b is hydrogen.
91. The compound of any one of claims 84-86, or a salt, stereoisomer, or tautomer thereof, wherein p is 2-5.
92. The compound of claim 69, or a salt, stereoisomer, or tautomer thereof, wherein L^4 is C_{1-5} alkylene or heteroalkylene, and Z is $-C(O)OH$, or $-(CH_2)_q(OCH_2CH_2)_vOR^{22}$,
93. The compound of claim 92, or a salt, stereoisomer, or tautomer thereof, wherein q is 1-3 and v is 1-3.
94. The compound of claim 67 or 68, or a salt, stereoisomer, or tautomer thereof, wherein m is 1.
95. The compound of claim 94, or a salt, stereoisomer, or tautomer thereof, wherein L^4 is C_{1-5} alkylene, and Z is $-SO_3^-$, or $-CH(SO_3^-)_2$.
96. The compound of claim 94, or a salt, stereoisomer, or tautomer thereof, wherein L^4 is C_{2-5} alkylene, and Z is $-(CH_2)_qN[(CH_2CH_2O)_vCH_2CH_2OR^{22}]_2$ wherein q is 0, and v is 1-3.
97. The compound of any one of claims 39 to 66, or a salt, stereoisomer, or tautomer thereof, wherein R^4 is $-(NH)_m-L^4-A$.
98. The compound of any one of claims 39 to 66, or a salt, stereoisomer, or tautomer thereof, wherein R^4 is $-(O)_m-L^4-A$.
99. The compound of claim 97 or 98, or a salt, stereoisomer, or tautomer thereof, wherein m is 0.
100. The compound of claim 99, or a salt, stereoisomer, or tautomer thereof, wherein L^4 is C_{1-5} alkylene or heteroalkylene.
101. The compound of claim 100, or a salt, stereoisomer, or tautomer thereof, wherein A is selected from the group consisting of:

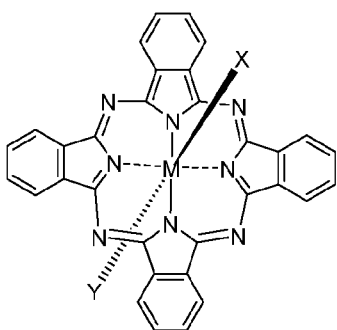


102. The compound of any one of claims 39 to 101, or a salt, stereoisomer, or tautomer thereof, wherein M is Si or Ge.
103. The compound of any one of claims 39-101, or a salt, stereoisomer, or tautomer thereof, selected from the group consisting of:





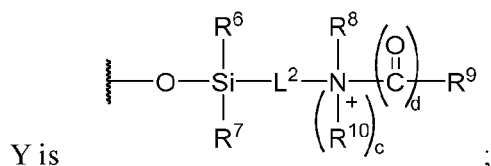
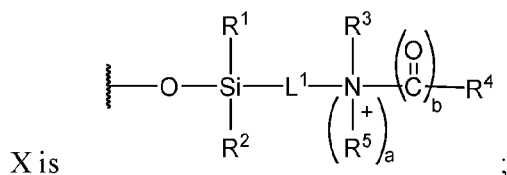
104. A conjugate comprising a silicon phthalocyanine dye covalently linked to a targeting molecule, wherein the silicon phthalocyanine dye comprises a silicon atom coordinated by (a) an unsubstituted phthalocyanine, (b) a first axial silicon-containing ligand comprising a conjugatable group; and (c) a second axial silicon-containing ligand comprising a water-solubilizing group, but not a conjugatable group; and wherein the chemical structures of the first and second axial ligands are different.
105. The conjugate of claim 104, wherein the axial silicon-containing ligand having a conjugatable group further comprises a water-solubilizing group.
106. The conjugate of claim 104, wherein the silicon phthalocyanine dye has the Formula (X):



(X)

or a salt, stereoisomer, tautomer or conjugate thereof, wherein,

M is Si;



R¹ and R² are each independently optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl or optionally substituted heteroaralkyl;

R³, R⁴ or R⁵ are selected from substituent group (a) or substituent group (b) wherein,

(a) R³ is hydrogen, -L³-H, -L³-A, or -L³-Z;

R⁴ is -L⁴-H, -(NH)_m-L⁴-A, -(NH)_m-L⁴-Z, -(O)_m-L⁴-A or -(O)_m-L⁴-Z;

R⁵ is -L⁵-H or -L⁵-A; and

(b) R³ is -L³-H, or -L³-A;

R⁴ is -L⁴-H, -(NH)_m-L⁴-A, or -(O)_m-L⁴-A; wherein R³ and R⁴ are connected with a bond to form a heterocyclyl substituted with -L⁴-A; and

R⁵ is -L⁵-H or -L⁵-A;

provided at least one of R³, R⁴ and R⁵ is a group containing A;

A is a reactive group capable of forming a covalent bond with a thiol, hydroxyl, carboxyl or amino group of the targeting molecule, or a protected form thereof or a reacted form thereof;

R^6 and R^7 are each independently optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted heterocyclyl, optionally substituted heterocyclalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl or optionally substituted heteroaralkyl;

R^8 , R^9 or R^{10} are selected from substituent group (a) or substituent group (b) wherein,

(a) R^8 is hydrogen, $-L^8-H$ or $-L^8-Z$;

R^9 is $-L^9-H$, $-(NH)_n-L^9-Z$ or $-(O)_n-L^9-Z$;

R^{10} is $-L^{10}-Z$; and

(b) R^8 and R^9 are connected with a bond to form a heterocyclyl substituted with $-L^9-Z$ and R^{10} is $-L^{10}-H$ or $-L^{10}-Z$;

provided at least one of R^8 , R^9 and R^{10} is a group containing Z;

Z is a water soluble group optionally substituted with A or $L'-A$;

L^1 and L^2 are each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkyl, or optionally substituted heterocyclyl;

L^3 , L^4 , L^5 , L^8 , L^9 and L^{10} are each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkylene, optionally substituted heterocyclene, optionally substituted arylene, optionally substituted aralkylene, optionally substituted heteroaralkylene or optionally substituted heteroarylene where the carbon atom of the alkylene, heteroalkylene, alkenylene, heteroalkenylene, cycloalkylene, heterocyclene or arylene is further optionally substituted with Z and each nitrogen atom of the heteroalkylene or heteroalkenylene is optionally substituted with one or two $L'-Z$;

L' is each independently optionally substituted alkylene, optionally substituted heteroalkylene, optionally substituted alkenylene, optionally substituted heteroalkenylene, optionally substituted cycloalkylene, optionally substituted heterocyclene, optionally substituted arylene or optionally substituted heteroarylene;

a is 0 or 1;

b is 0 or 1;

c is 0 or 1;

d is 0 or 1;

m is 0 or 1;

n is 0 or 1;

provided that if b is 1, then a is 0;

if d is 1, then c is 0;

if m is 1, b is 1; and

if n is 1, c is 1.

107. The conjugate according to any one of claims 104-106, wherein the targeting molecule comprises a polypeptide that binds to the surface of a cell.
108. The conjugate according to any one of claims 104-107, wherein the targeting molecule is an antibody.
109. The conjugate according to any one of claims 104-107, wherein the targeting molecule is an antigen-binding antibody fragment.
110. The conjugate according to claim 109, wherein the targeting molecule is an antigen-binding antibody fragment selected from the group consisting of a Fab, a single VH domain, and a multiple VH domain.
111. The conjugate according to claim 109, wherein the targeting molecule is an antigen-binding antibody fragment comprising a single chain variable fragment (scFv), a multivalent scFv, a bispecific scFv, or an scFv-CH3 dimer.
112. The conjugate according to any one of claims 104-111, wherein the antibody or an antigen-binding antibody fragment binds to EGFR, HER2, CD25, PD-1, PD-L1, CTLA-4, MUC1, PSMA, CEA or FAP.
113. The conjugate according to any one of claims 108-112, wherein the antibody or an antigen-binding antibody fragment comprises 3F8, 8H9, AB122, ab75705, Abagovomab, Abciximab, Abituzumab, Abrezekimab, Abrilumab, Actoxumab, Adalimumab, Adecatumumab, ADG116, ADU-1604, Aducanumab, Afasevikumab, Afelimomab, Afutuzumab, AGEN1181, AGEN1884, AGX-115, AK104, AK105, Alacizumab pegol, Alemtuzumab, Alirocumab, Altumomab pentetate, Amatuximab, AMG 404, AMP-224, AMP-514, Anatumomab mafenatox, Andecaliximab, Anetumab ravtansine, Anifrolumab, Anrukinzumab, anti-CD133, Apolizumab, Aprutumab ixadotin, Arcitumomab, arcitumomab Fab fragment, Ascrinvacumab, Aselizumab, Atezolizumab, Atidortoxumab, Atinumab, Atlizumab (Tocilizumab), ATOR-1015, Atorolimumab, Avelumab, Azintuxizumab vedotin, B72.3, Bapineuzumab, Basiliximab, Bavituximab, BCD-100, BCD-135, BCD-145, BCD-217, Bectumomab, Begelomab, Belantamab mafodotin, Belimumab, Bemarituzumab, Benralizumab, Berlimatoxumab, Bermekimab, Bersanlimab, Bertilimumab, Besilesomab, Bevacizumab, Bezlotoxumab, BGB-A333, BI 754091, Biciromab, Bimagrumab, Bimekizumab, Birtamimab, Bivatuzumab, Bivatuzumab mertansine, BL-8040, Bleselumab, Blinatumomab, Blontuvetmab, Blosozumab, BMS-

936559, BMS-986218, Bococizumab, Brazikumab, Brentuximab vedotin, Briakinumab, Brodalumab, Brolucizumab, Brontictuzumab, Burosumab, Cabiralizumab, Camidanlumab tesirine, Camrelizumab, Canakinumab, Cantuzumab mertansine, Cantuzumab ravtansine, Caplacizumab, Capromab, Capromab pendetide, Carlumab, Carotuximab, Catumaxomab, cBR96-doxorubicin immunoconjugate, CBT-502, CC-90002, CDC-022, Cedelizumab, Cemiplimab, Cergutuzumab amunaleukin, Certolizumab pegol, Cetrelimab, Cetuximab, Cibisatamab, Cirmtuzumab, Citatuzumab bogatox, Cixutumumab, Clazakizumab, Clenoliximab, Clivatuzumab tetraxetan, CMAB302, Codrituzumab, Cofetuzumab pelidotin, Coltuximab ravtansine, Conatumumab, Concizumab, Cosfroviximab, Cosibelimab, CP-870,893, CR6261, Crenezumab, Crizanlizumab, Crotedumab, CS1001, CS1003, Cusatuzumab, CX-188, Dacetuzumab, Daclizumab, Dalotuzumab, Dapirolizumab pegol, Daratumumab, Dectrekumab, Demcizumab, Denintuzumab mafodotin, Denosumab, Depatuxizumab mafodotin, Derlotuximab biotin, Detumomab, Dezamizumab, Dinutuximab, Diridavumab, Domagrozumab, Dorlimomab aritox, Dostarlimab, Drozitumab, DS-8201, Duligotumab, Duligotuzumab, Dupilumab, Durvalumab, Dusigitumab, Duvortuxizumab, Echromeximab, Eculizumab, Edobacomab, Edrecolomab, Efalizumab, Eftilagimod alpha, Efungumab, Eldelumab, Elezanumab, Elgemitumab, Elotuzumab, Elsilimomab, Emactuzumab, Emapalumab, Emibetuzumab, Emicizumab, Enapotamab vedotin, Enavatuzumab, Enfortumab vedotin, Enlimomab pegol, Enoblituzumab, Enokizumab, Enoticumab, Ensituximab, Eptumomab cituxetan, Epratuzumab, Eptinezumab, Erenumab, Erlizumab, Ertumaxomab, Etaracizumab, Etigilimab, Etrolizumab, Evinacumab, Evolocumab, Exbivirumab, F520, Fanolesomab, Faralimomab, Faricimab, Farletuzumab, Fasinumab, FAZ053, FBTA05, Felvizumab, Fezakinumab, Fibatuzumab, Ficlatuzumab, Figitumumab, Firivumab, Flanvotumab, Fletikumab, Flotetuzumab, Fontolizumab, Foralumab, Foravirumab, Fremanezumab, Fresolimumab, Frovocimab, Frunevetmab, Fulranumab, Futuximab, Galcanezumab, Galiximab, Gancotamab, Ganitumab, Gantenerumab, Gatipotuzumab, Gavilimomab, GB221, Gedivumab, Gemtuzumab ozogamicin, genolimzumab, Gevokizumab, Gilvetmab, Gimsilumab, Girentuximab, Glembatumumab vedotin, GLS-010, Golimumab, Gomiliximab, Gosuranemab, Guselkumab, HD201, Hervycta, HLX02, HLX10, HLX20, HLX22, HX008, HX009, Ianalumab, Ibalizumab, IBI308, Ibritumomab tiuxetan, Icrucumab, Idarucizumab, Ieramylimab, Ifabotuzumab, Igovomab, Iladatuzumab vedotin, IMAB362, Imalumab, Imaprelimab, Imciromab, Imgatuzumab, INBRX-105, Inclacumab, Indatuximab ravtansine, Indusatumab vedotin, Inebilizumab, Infliximab, Inolimomab,

Inotuzumab ozogamicin, Intetumumab, Iomab-B, IPH2101, Ipilimumab, Iratumumab, Isatuximab, Iscalimab, Istiratumab, Itolizumab, Ixekizumab, JTX-4014, Keliximab, KN035, KN046, Labetuzumab, Lacnotuzumab, Ladiratuzumab vedotin, Lambrolizumab (Pembrolizumab), Lampalizumab, Lanadelumab, Landogrozumab, Laprituximab emtansine, Larcaviximab, LDP, Lebrikizumab, Lemalesomab, Lendalizumab, Lenvervimab, Lenzilumab, Lerdelimumab, Leronlimab, Lesofavumab, Letolizumab, Lexatumumab, Libivirumab, Lifestuzumab vedotin, Ligelizumab, Lilotomab satetraxetan, Lintuzumab, Lirilumab, Lodelcizumab, Lokivetmab, Loncastuximab tesirine, Lorvotuzumab mertansine, Losatuxizumab vedotin, Lucatumumab, Lulizumab pegol, Lumiliximab, Lumretuzumab, Lupartumab, Lupartumab amadotin, Lutikizumab, LY3300054, LY3415244, LZM009, mAb114, Mapatumumab, Margetuximab, Marstacimab, Maslimomab, Matuzumab, Mavrilimumab, MCLA-145, MED16469, MEDI6383, Mepolizumab, Metelimumab, MGA012, MGD013, MGD019, Milatuzumab, Minretumomab, Mirikizumab, Mirvetuximab soravtansine, Mitumomab, MK-1308, MK-4166, MNRP1685A, Modotuximab, Mogamulizumab, Monalizumab, Morolimumab, Mosunetuzumab, Motavizumab, Moxetumomab pasudotox, MOXR0916, MSB2311, Muromonab-CD3, Nacolomab tafenatox, Namilumab, Naptumomab estafenatox, Naratuximab emtansine, Narnatumab, Natalizumab, Navicixizumab, Navivumab, Naxitamab, Nebacumab, Necitumumab, Nemolizumab, NEOD001, Nerelimomab, Nesvacumab, Netakimab, Nimotuzumab, Nirsevimab, Nivolumab, NM-01, Nofetumomab merpentan, Obiltoxaximab, Obinutuzumab, OC125 monoclonal antibody, Ocaratuzumab, Ocrelizumab, Odulimomab, Ofatumumab, Olaratumab, Oleclumab, Olendalizumab, Olokizumab, Omalizumab, Omburtamab, OMS721, Onartuzumab, Ontuxizumab, Onvatilimab, Opicinumab, Oportuzumab monatox, Oregovomab, Orticumab, Otelixizumab, Otilimab, Otlertuzumab, Oxelumab, Ozanezumab, Ozoralizumab, Pagibaximab, Palivizumab, Pamrevlumab, Panitumumab, Pankomab, Panobacumab, Parsatuzumab, Pascolizumab, Pasotuxizumab, Pateclizumab, Patritumab, PDR001, Pembrolizumab, Pentumomab, Perakizumab, Pertuzumab, Pexelizumab, PF-05280014, PF-06801591, Pidilizumab, Pinatuzumab vedotin, Pintumomab, Placulumab, Plozalizumab, Pogalizumab, Polatuzumab vedotin, Ponezumab, Porgaviximab, Prasinezumab, Prezalizumab, Prezalumab, Priliximab, Pritoxaximab, Pritumumab, PRO 140, Quilizumab, Racotumomab, Radretumab, Rafivirumab, Ralpancizumab, Ramucirumab, Ranevetmab, Ranibizumab, Ravagalimab, Ravulizumab, Raxibacumab, Refanezumab, Regavirumab, REGN2810, REGN3504, REGN4659, REGN-EB3, Relatlimab, Remtolumab, Reslizumab, rHIgM12B7, Rilotumumab, Rinucumab,

Risankizumab, Rituximab, Rituximab, Rivabazumab pegol, Rmab, RO7121661, Robatumumab, Roledumab, Romilkimab, Romosozumab, Rontalizumab, Rosmantuzumab, Rovalpituzumab tesirine, Rovelizumab, Rozanolixizumab, Ruplizumab, SA237, Sacituzumab, Sacituzumab govitecan, Samalizumab, Samrotamab vedotin, Sarilumab, Satralizumab, Satumomab pendetide, SB3, SCT-I10A, SEA-CD40, Secukinumab, Selicrelumab, Seribantumab, Setoxaximab, Setrusumab, Sevirumab, SG001, SGN-CD19A, SHP647, SHR-1316, SIBP-01, Sibrotuzumab, Sifalimumab, Siltuximab, Simtuzumab, Sintilimab, Siplizumab, Sirtratumab vedotin, Sirukumab, Sofituzumab vedotin, Solanezumab, Solitomab, Sonepcizumab, Sontuzumab, Spartalizumab, Stamulumab, STI-3031, Sulesomab, Suptavumab, Sutimlimab, Suvizumab, Suvratoxumab, Sym021, Tabalumab, Tacatuzumab tetraxetan, Tadocizumab, Talacotuzumab, Talizumab, Tamtuvatmab, Tanezumab, Taplitumomab paptox, Tarextumab, Tavolimab, Tefibazumab, Telimomab aritox, Telisotuzumab, Telisotuzumab vedotin, Tenatumomab, Teneliximab, Teplizumab, Tepoditamab, Teprotumumab, Tesidolumab, Tetulomab, Tezepelumab, TG-1501, TGN1412, Tibulizumab, Ticilimumab, Tigatuzumab, Tildrakizumab, Timigutuzumab, Timolumab, Tiragolumab, Tiragotumab, Tislelizumab, Tisotumab vedotin, TNX-650, Tocilizumab, Tocilizumab, Tomuzotuximab, Toralizumab, Toripalimab, Tosatoxumab, Tositumomab, Tositumomab, Tovetumab, Tralokinumab, Trastuzumab, Trastuzumab deruxtecan, Trastuzumab-anns, trastuzumab-dkst, Trastuzumab emtansine, TRBS07, Tregalizumab, Tremelimumab, Trevogrumab, TRX385, TRX518, TSR-042, Tucotuzumab celmoleukin, Tuvirumab, TX05, Ublituximab, Ulocuplumab, Urelumab, Urtoxazumab, Ustekinumab, Utomilumab, Vadastuximab talirine, Vanalizumab, Vandortuzumab vedotin, Vantictumab, Vanucizumab, Vapaliximab, Varisacumab, Varlilumab, Vatelizumab, Vedolizumab, Veltuzumab, Vepalimomab, Vesencumab, Visilizumab, Vobarilizumab, Volociximab, Vonlerolizumab, Vopratelimab, Vorsetuzumab mafodotin, Votumumab, Vunakizumab, Xentuzumab, XmAb20717, XmAb22841, XMAB-5574, Zalutumumab, Zanolimumab, Zatuximab, Zenocutuzumab, Ziralimumab, ZKAB001, Zolbetuximab, Zolimomab aritox, or an antigen-binding fragment thereof.

114. The conjugate according to any one of claims 104-111, wherein the targeting molecule comprises Alacizumab pegol, Cetuximab, Depatuxizumab mafodotin, Futuximab, Icrucumab, Imgatuzumab, Laprituximab emtansine, Matuzumab, Modotuximab, Necitumumab, Nimotuzumab, Panitumumab, Ramucirumab, Tomuzotuximab, Zalutumumab, or an antigen-binding fragment thereof.

115. The conjugate according to any one of claims 104-111, wherein the targeting molecule comprises Basiliximab (SIMULECT), Camidanlumab tesirine, daclizumab (Zinbryta; Zenapax), Inolimomab, RA8, STI-003, Xenopax or an antigen-binding fragment thereof.
116. The conjugate according to any of claims 104-111, wherein the targeting molecule comprises an anti-PD-L1 antibody selected from the group consisting of atezolizumab (MPDL3280A, Tecentriq), avelumab (Bavencio), durvalumab (MEDI4736, Imfinzi), LDP, NM-01, STI-3031, KN035, LY3300054, M7824 (MSB0011359C), BMS-936559, MSB2311, BCD-135, BGB-A333, CBT-502, cosibelimab (CK-301), CS1001, FAZ053, MDX-1105, SHR-1316, TG-1501, ZKAB001, INBRX-105, MCLA-145, KN046, LY3415244, REGN3504, HLX20, and antigen-binding fragments of any thereof.
117. The conjugate according to any one of claims 104-111, wherein the targeting molecule comprises an anti-PD-1 antibody selected from the group consisting of pembrolizumab (MK-3475, Keytruda), nivolumab (Opdivo), cemiplimab (Libtayo), toripalimab (JS001), HX008, SG001, GLS-010, dostarlimab (TSR-042), tislelizumab (BGB-A317), cetrelimab (JNJ-63723283), pidilizumab (CT-011), genolimzumab (APL-501, GB226), BCD-100, cemiplimab (REGN2810), F520, sintilimab (IBI308), GLS-010, CS1003, LZM009, camrelizumab (SHR-1210), SCT-I10A, MGA012, AK105, PF-06801591, AMP-224, AB122, AMG 404, BI 754091, HLX10, JTX-4014, MEDI0680, Sym021, MGD019, MGD013, AK104, XmAb20717, RO7121661, CX-188, spartalizumab and, antigen-binding fragments of any thereof.
118. The conjugate according to any one of claims 104-111, wherein the targeting molecule comprises ipilimumab (Yervoy®), tremelimumab (ticilimumab), AGEN1181, AGEN1884, ADU-1064, BCD-145, BCD-217, or an antigen-binding fragment of any thereof.
119. The conjugate according to any one of claims 104-111, wherein the targeting molecule comprises CDC-022 (HERtiCAD), CMAB302 (Cipterbin), DS-8201, Gancotamab, GB221, HD201, Hervycta, HLX02, HLX22, Margetuximab, Pertuzumab (Perjeta), PF-05280014 (Trazimera), SB3, SIBP-01, Timigutuzumab, Trastuzumab (Herceptin), trastuzumab deruxtecan (ENHERTU), Trastuzumab emtansine (Kadcyla), trastuzumab-anns (Kanjinti), trastuzumab-dkst (Ogivri), TX05, or an antigen-binding fragment thereof.

120. The conjugate according to any one of claims 104-111, wherein the antibody or an antigen-binding antibody fragment comprises cetuximab, basiliximab, declizimab, trastuzumab, panitumimab, or antigen-binding fragment thereof.
121. The conjugate according to any one of claims 104-111, wherein the targeting molecule is a peptide or small molecule that binds to EGFR, HER2, CD25, PD-1, PD-L1, or CTLA-4.
122. The conjugate according to any one of claims 104-111, wherein the targeting molecule binds to CD25 but does not substantially block IL-2 signaling.
123. The conjugate according to any one of claims 104-120, wherein the conjugate has a dye to targeting molecule ratio of about 5:1, 4:1, 3:1, 2:1 or 1:1.
124. The conjugate according to any one of claims 104-118, wherein the conjugate has a dye to targeting molecule ratio between about 1:1 to 5:1, 1.5:1 to 4:1, 1.5:1 to 3.5:1, 1.5:1 to 3:1 or about 2:1 to 3:1.
125. The conjugate according to any one of claims 104-123, wherein the phthalocyanine dye has a maximum absorption at a wavelength between about 600 nm to 800 nm, about 620 nm to 720 nm, about 640 to 700 nm, about 640 to 680 nm or about 660 to 680 nm.
126. The conjugate according to any one of claims 104-123, wherein the phthalocyanine dye has a maximum absorption at a wavelength no more than 680 nm.
127. The conjugate according to any one of claims 104-123, wherein the phthalocyanine dye is selected from Compound 1, 5, 12, 13, 14, 16, 17, 18 or 19 of Table 1.
128. A pharmaceutical composition comprising a conjugate according to any of claims 104-125 and a pharmaceutically acceptable excipient.
129. A method of treating a subject having a disease or condition comprising:
- a) administering to a subject the conjugate according to any one of claims 104-124 or the pharmaceutical composition of claim 128,
 - b) after administering the conjugate, illuminating a target region of the subject at a wavelength of at or about 600 nm to at or about 850 nm at a dose of or of about 10 J/cm² to a dose of or of about 200 J/cm² or at a dose from at or about 10 J/cm fiber length to at or about 100 J/cm fiber length, thereby treating the disease or condition in the subject.
130. The method of claim 129, wherein the wavelength is at least about 600 nm, 610 nm, 620 nm, 630, nm, 640 nm, 650 nm, 660 nm, 670 nm, 680 nm, 690 nm or 700 nm.
131. The method of claim 126, wherein the wavelength is between 660 nm and 680 nm.
132. The method of claim 129, wherein the wavelength is at or about 670 ± 50 nm, or at or about 670 ± 40 nm or at or about 670 ± 20 nm, or at or about 670 ± 10 nm.

133. The method of claim 129, wherein the wavelength is less than 690 nm or less than 680 nm.
134. The method according to any one of claims 129-132, wherein the target region is a tumor cell, a mass of tumor cells, a solid tumor, in the vicinity of a solid tumor, a metastasis, a metastized tumor cell, in the vicinity of a metastasis or a pre-cancerous lesion.
135. The method according to any one of claims 129-134, wherein the illumination is performed at least 5 minutes after administration of the conjugate.
136. The method according to any one of claims 129-134, wherein the illumination is performed at about 1 hour, 5 hours, 10 hours, 15 hours, 20 hours, 21 hours, 22 hours, 23 hours, 24 hours, 25 hours, 26 hours, 27 hours, 28 hours, 29 hours, or 30 hours after administration of the conjugate.
137. The method according to any one of claims 129-134, wherein the illumination is performed 24 +/- 4 h after administration of the conjugate.
138. The method according to any one of claims 129-137, wherein the disease or condition is a cancer.
139. The method of claim 138, wherein the cancer is selected from the group consisting of colon cancer, colorectal cancer, pancreatic cancer, breast cancer, skin cancer, lung cancer, non-small cell lung carcinoma, renal cell carcinoma, thyroid cancer, prostate cancer, head and neck cancer, esophageal, gastrointestinal cancer, stomach (gastric) cancer, cancer of the small intestine, colon cancer, spindle cell neoplasm, hepatic carcinoma, liver cancer, cholangiocarcinoma, cancer of peripheral nerve, brain cancer, cancer of skeletal muscle, cancer of smooth muscle, bone cancer, cancer of adipose tissue, cervical cancer, uterine cancer, cancer of genitals, lymphoma, and multiple myeloma.
140. The method according to any one of claims 129-139, wherein the steps of administering the conjugate and illuminating are repeated.
141. A method of imaging a cell or tissue having a target molecule, the method comprising:
- a) administering to a subject the conjugate according to any one of claims 104-125 or the pharmaceutical composition of claim 128; and
 - b) illuminating a target region of the subject at a wavelength of at or about 600 nm to at or about 850 nm, thereby providing an image of the presence of the target molecule associated with the cell or tissue.
142. A system for treating a subject having a disease or condition comprising:

- a conjugate according to any one of claims 104-125 or a pharmaceutical composition of claim 128;
- a laser capable of emitting light at a wavelength of 670 ± 20 nm;
- an optic fiber operably connected to the laser for transmitting the light to a target region of the subject; and
- a light diffusing device comprising a non-circular core fiber.
143. The system of claim 141, wherein the non-circular core fiber has a "top hat" core irradiance distribution.
144. The system of claim 141, wherein the light diffusing device is a cylindrical diffuser or a frontal diffuser.
145. The system of any of claims 141-143, wherein the non-circular core fiber comprises a hexagonal core fiber.

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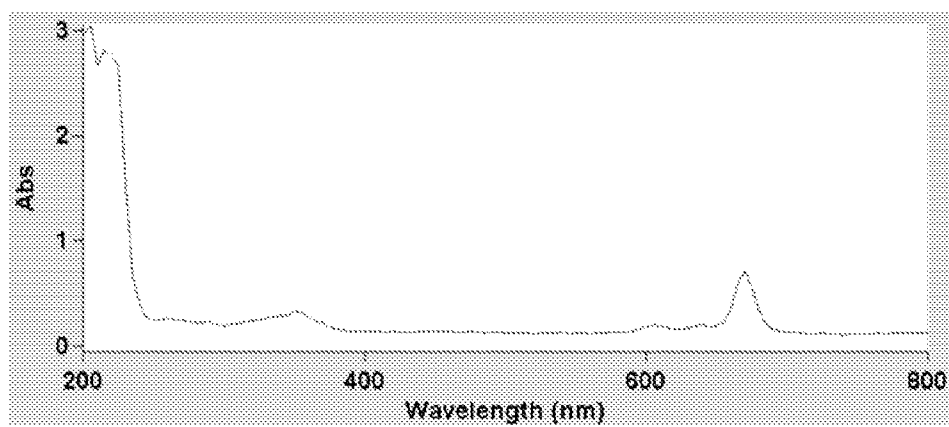


FIG. 1

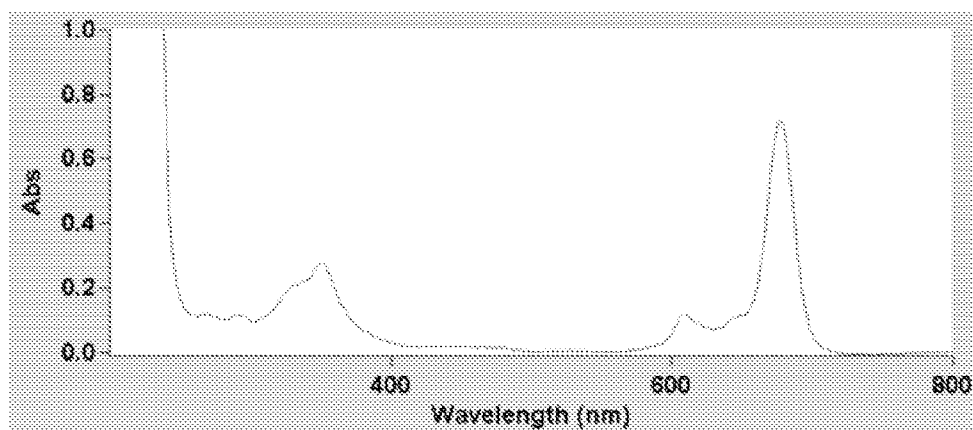
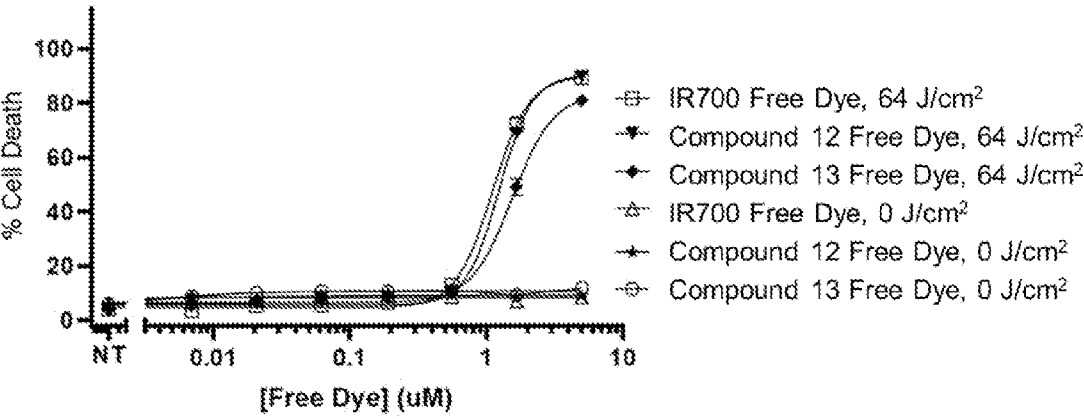


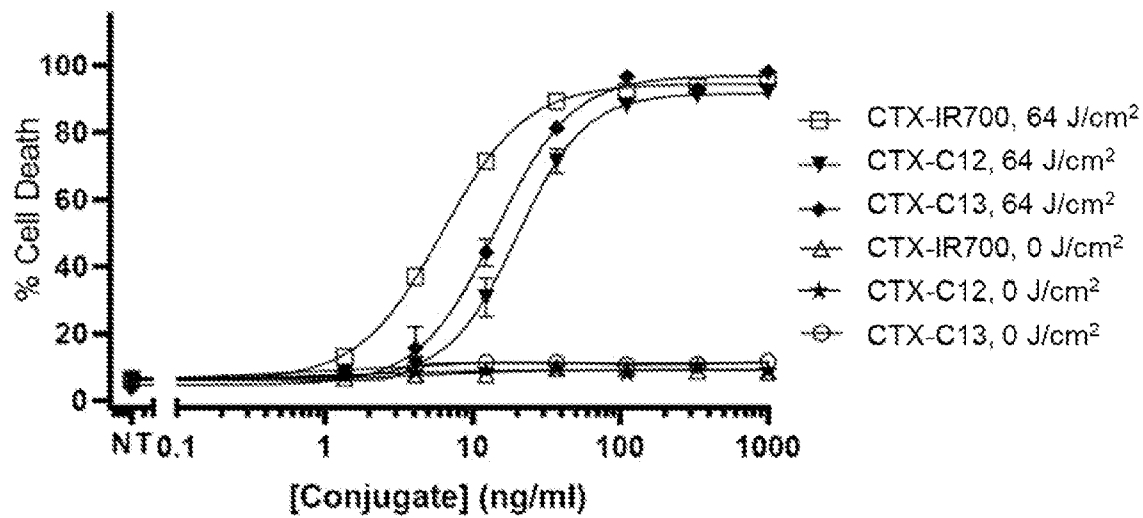
FIG. 2



	IR700 Free Dye, 64 J/cm ²	Compound 12, 64 J/cm ²	Compound 13, 64 J/cm ²
EC50	1.108	1.241	1.552

FIG. 3

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	CTX-IR700, 64 J/cm ²	CTX-C12, 64 J/cm ²	CTX-C13, 64 J/cm ²
EC50	6.263	20.17	14.41
R ²	0.9987	0.9967	0.9950

FIG. 4

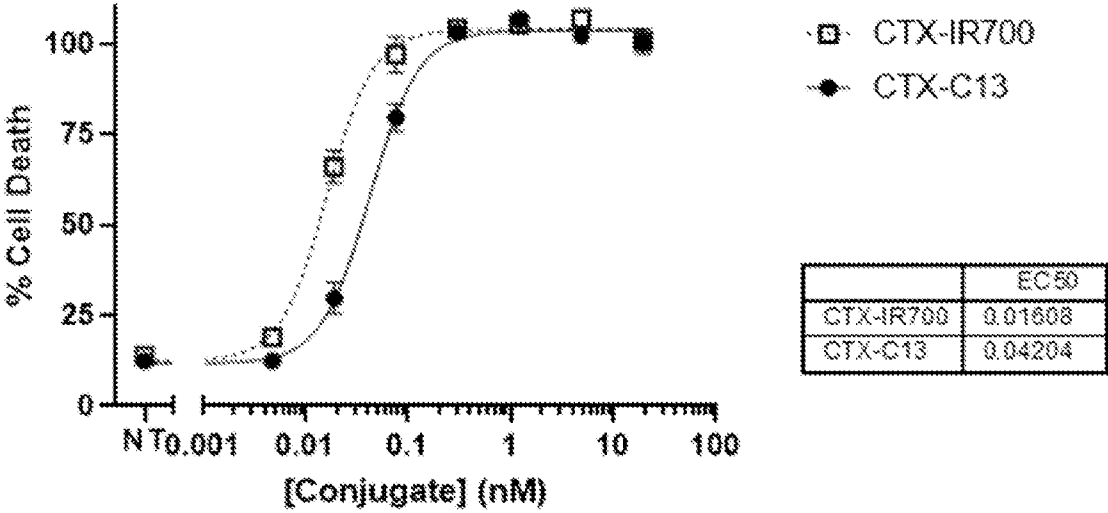


FIG. 5A

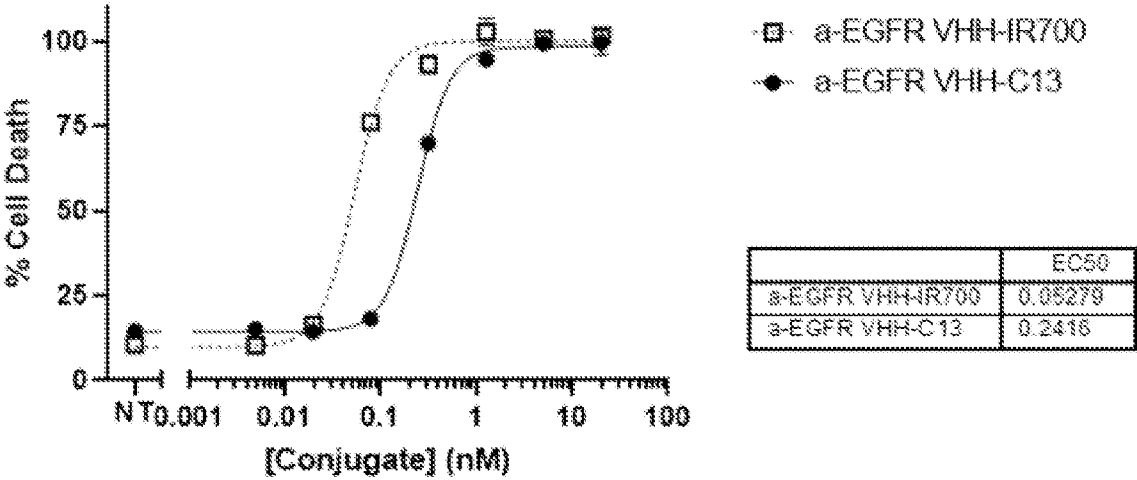


FIG. 5B

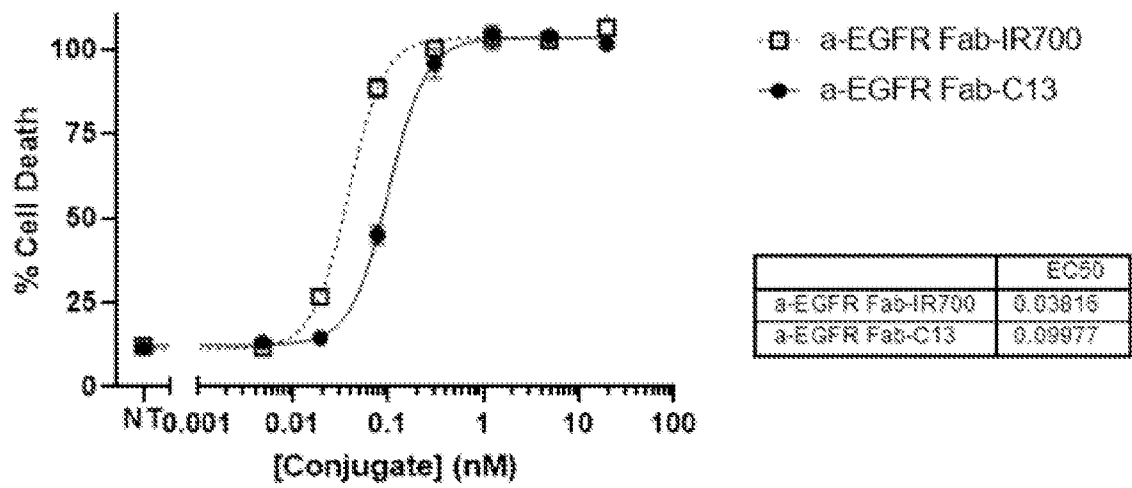


FIG. 5C

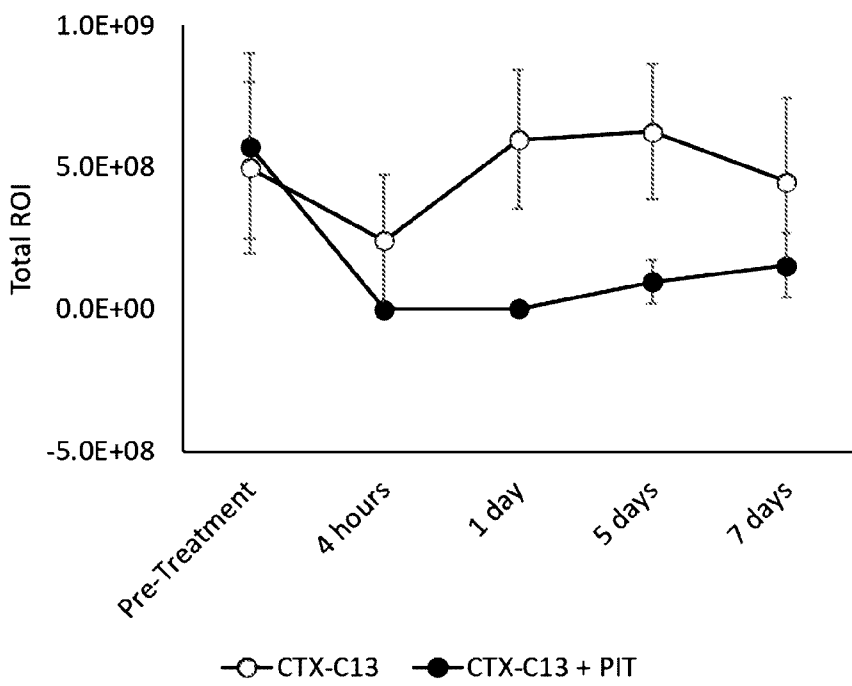


FIG. 6

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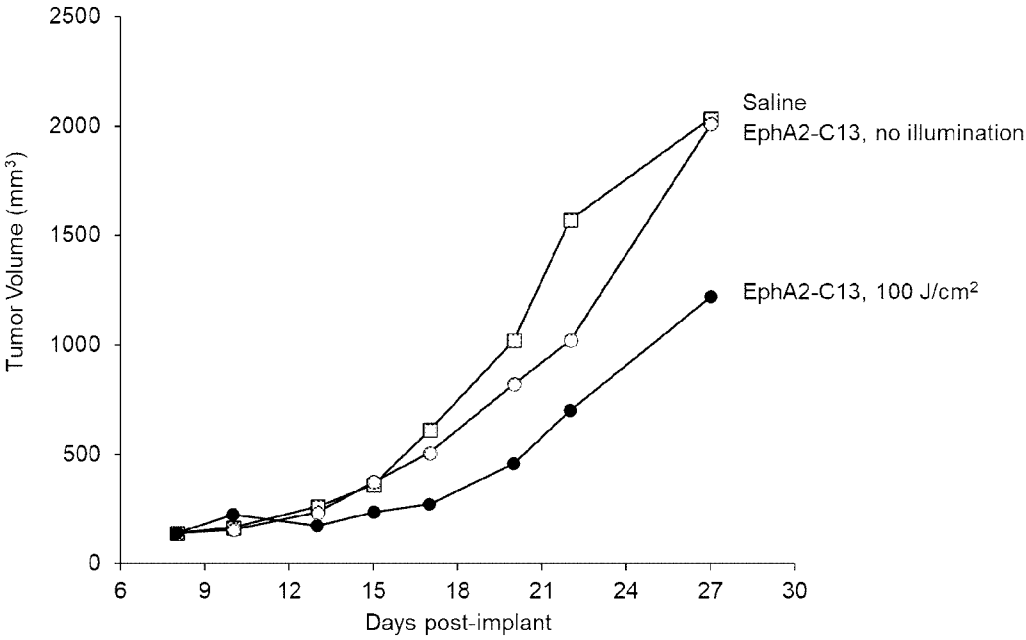


FIG. 7