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(54) Title: PHOTO-ACTIVATED PROTECTING GROUPS

(57) Abstract: Novel photo-activated protecting groups, photo-activatable groups, and methods for their synthesis and use are described. The photo-activated protecting groups are useful in making photo-activatable forms, i.e., inactive proforms, of compounds that can be activated in situ, for example, for initiating chemical reactions upon photo-activation or providing an inactive proform of a therapeutic agent to a subject and photo-activating the therapeutic agent at a selected area of the subject. Also disclosed are methods for administering a photo-activatable compound to a subject then activating the compound at a selected area of the subject by exposing that area to light.



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Photo-activated Protecting Groups

CROSS-REFERENCE TO PRIORITY APPLICATION

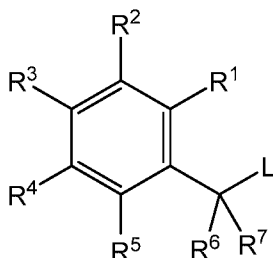
This application claims priority to U.S. Provisional Application No. 61/103,685, filed October 8, 2008, which is incorporated herein by reference in its entirety.

BACKGROUND

The ability to protect various reactive groups of molecules, e.g., hydroxyl or carbonyl groups, can be advantageous in synthetic chemistry. Similarly, the ability to provide inactive forms, i.e., proforms, of drugs that can subsequently be activated when in a selected site in a subject can be advantageous in medicine. In organic chemistry, protecting groups are commonly used that require the addition of further chemicals to remove the protecting group. In medicine, prodrugs are often activated by metabolic processes.

SUMMARY

Novel photo-activated protecting groups and methods for making and using them are disclosed. A class of photo-activated protecting groups comprise compounds of the following formula:

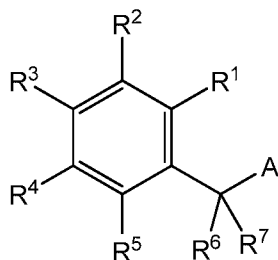


and includes pharmaceutically acceptable salts thereof. In this class of compounds, R¹, R³, and R⁵ are each independently selected from hydrogen, substituted or unsubstituted hydrocarbon, substituted or unsubstituted hetero-hydrocarbon, halogen, an electron withdrawing group, or an electron donating group; R² and R⁴ are each independently selected from hydrogen, substituted or unsubstituted hydrocarbon, substituted or unsubstituted hetero-hydrocarbon, halogen, or an electron donating group; R⁶ and R⁷ are each independently selected from substituted or unsubstituted

aryl or substituted or unsubstituted heteroaryl; and L is a conjugate base of an acid with a pKa equal to or greater than o-chlorobenzoic acid in water.

Also disclosed is a class of photo-activatable compounds of the following formula:

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and includes pharmaceutically acceptable salts thereof. In this class of compounds, R¹, R³, and R⁵ are each independently selected from hydrogen, substituted or unsubstituted hydrocarbon, substituted or unsubstituted hetero-hydrocarbon, halogen, an electron withdrawing group, or an electron donating group; R² and R⁴ are each independently selected from hydrogen, substituted or unsubstituted hydrocarbon, substituted or unsubstituted hetero-hydrocarbon, halogen, or an electron donating group; R⁶ and R⁷ are each independently selected from substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl; and A is a compound containing a hydroxyl-, amino-, or thio-functional group, A being attached through the hydroxyl-, amino-, or thio-functional group, wherein A is released from the photo-activatable compound upon exposure to light.

Methods of delivering a therapeutic agent to a selected area in a subject are described herein. The methods include administering to the subject an effective amount of the compounds or compositions described herein and transmitting light to the selected area of the subject.

Further described herein are methods of synthesizing a polypeptide. The methods comprise providing a photo-activatable compound, wherein A is a first amino acid attached through its amino group, providing a second amino acid with a free carboxyl end group, and transmitting light to release A, wherein a peptide bond is formed between the first amino acid and the second amino acid.

An intramolecular method of forming a glycosyl bond is also described herein. The method comprises providing a photo-activatable compound wherein R⁶ is a substituted or unsubstituted phenyl ring linked to an anomeric oxygen atom of a substituted or unsubstituted saccharide through a linker X, wherein the anomeric oxygen atom is linked to an anomeric carbon atom, and transmitting light to release

A. The bond between the anomeric carbon atom and the anomeric oxygen atom of the saccharide is broken and a glycosyl bond is formed to link the anomeric carbon atom of the saccharide to A.

Also described is a method of forming a glysoyl bond, the method comprising
5 providing a photo-activatable compound, wherein A is a saccharide containing a hydroxyl- or amino-functional group and is attached through the hydroxyl- or amino-functional group; providing a donor with a leaving group attached; and transmitting light to release A, wherein a glycosyl bond is formed to link A to the donor.

An intramolecular method of forming a glycosan is also provided herein, the
10 method comprising providing a photo-activatable compound, wherein A is a saccharide attached through a hydroxyl functional group and the saccharide contains a leaving group attached to its anomeric carbon, and transmitting light to release A, wherein a glycosyl bond is formed to link the hydroxyl functional group to the anomeric carbon.

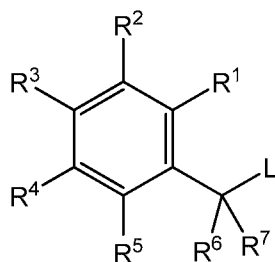
15 Further, a method of site-specifically attaching a biological molecule to a support surface is described herein. The method comprises protecting one or more functional groups of a support surface with a photo-activated protecting group to form a photo-activatable support surface, selecting one or more of the protected functional groups for biological molecule attachment, photomasking the non-selected functional
20 groups, irradiating the photo-activatable support surface to deprotect the one or more selected functional groups, and covalently attaching a biological molecule to one or more selected functional groups.

DETAILED DESCRIPTION

Novel photo-activated protecting groups, photo-activatable groups, and
25 methods for their synthesis and use are disclosed. The photo-activated protecting groups are useful in synthesizing photo-activatable forms, i.e., inactive proforms, of compounds that can be activated *in situ*, for example, for initiating chemical reactions upon photo-activation or providing an inactive proform of a therapeutic agent to a subject and photo-activating the therapeutic agent at a selected area of the subject.

The photo-activated protecting groups described herein are represented by

Compound I:

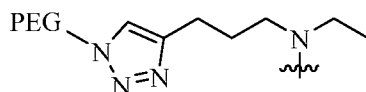


I

or pharmaceutically acceptable salts thereof.

In **Compound I**, R^1 , R^3 , and R^5 are each independently selected from hydrogen, substituted or unsubstituted hydrocarbon, substituted or unsubstituted hetero-hydrocarbon, halogen, an electron withdrawing group, or an electron donating group.

Also in **Compound I**, R^2 and R^4 are each independently selected from hydrogen, substituted or unsubstituted hydrocarbon, substituted or unsubstituted hetero-hydrocarbon, halogen, or an electron donating group. As an example, one of R^2 or R^4 is a dimethylamino group, a methoxy group, PEG, or



Additionally in **Compound I**, R^6 and R^7 are each independently selected from substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl. In one example, R^6 and R^7 are each phenyl groups.

Further in **Compound I**, L is a conjugate base of an acid with a pKa equal to or greater than o-chlorobenzoic acid in water. As an example, L is acetate, benzyl acetate, trifluoroacetate, formate, fluoride, nitrite, or hydrogen carbonate.

As used herein, the term hydrocarbon includes alkanes, alkenes, alkynes, cycloalkanes, cycloalkenes, and cycloalkynes. Hydrocarbons useful with the compounds and methods described herein include C_1 - C_{60} alkanes, C_2 - C_{60} alkenes, C_2 - C_{60} alkynes, C_3 - C_{60} cycloalkanes, C_3 - C_{60} cycloalkenes, and C_7 - C_{60} cycloalkynes. Additional hydrocarbons useful with the compounds and methods described herein include C_1 - C_{40} alkanes, C_2 - C_{40} alkenes, C_2 - C_{40} alkynes, C_3 - C_{40} cycloalkanes, C_3 - C_{40} cycloalkenes, and C_7 - C_{40} cycloalkynes; C_1 - C_{30} alkanes, C_2 - C_{30} alkenes, C_2 - C_{30} alkynes, C_3 - C_{30} cycloalkanes, C_3 - C_{30} cycloalkenes, and C_7 - C_{30} cycloalkynes; C_1 - C_{20}

alkanes, C₂-C₂₀ alkenes, C₂-C₂₀ alkynes, C₃-C₂₀ cycloalkanes, C₃-C₂₀ cycloalkenes, and C₇-C₂₀ cycloalkynes; C₁-C₁₆ alkanes, C₂-C₁₆ alkenes, C₂-C₁₆ alkynes, C₃-C₁₆ cycloalkanes, C₃-C₁₆ cycloalkenes, and C₇-C₁₆ cycloalkynes; C₁-C₁₂ alkanes, C₂-C₁₂ alkenes, C₂-C₁₂ alkynes, C₃-C₁₂ cycloalkanes, C₃-C₁₂ cycloalkenes, and C₇-C₁₂ cycloalkynes; C₁-C₈ alkanes, C₂-C₈ alkenes, C₂-C₈ alkynes, C₃-C₈ cycloalkanes, C₃-C₈ cycloalkenes, and C₇-C₈ cycloalkynes; C₁-C₆ alkanes, C₂-C₆ alkenes, C₂-C₆ alkynes, C₃-C₆ cycloalkanes, C₃-C₆ cycloalkenes, and C₇ cycloalkynes; and C₁-C₄ alkanes, C₂-C₄ alkenes, C₂-C₄ alkynes, C₃-C₄ cycloalkanes, and C₃-C₄ cycloalkenes.

As used herein, the term hetero-hydrocarbon includes heteroalkanes, heteroalkenes, heteroalkynes, heterocycloalkanes, heterocycloalkenes, and heterocycloalkynes. Hetero-hydrocarbons include substitutions along their main chain of atoms such as O, N, or S. Hydrocarbons useful with the compounds and methods described herein include C₁-C₆₀ heteroalkanes, C₂-C₆₀ heteroalkenes, C₂-C₆₀ heteroalkynes, C₃-C₆₀ heterocycloalkanes, C₃-C₆₀ heterocycloalkenes, and C₇-C₆₀ heterocycloalkynes. Additional hetero-hydrocarbons useful with the compounds and methods described herein include C₁-C₄₀ heteroalkanes, C₂-C₄₀ heteroalkenes, C₂-C₄₀ heteroalkynes, C₃-C₄₀ heterocycloalkanes, C₃-C₄₀ heterocycloalkenes, and C₇-C₄₀ heterocycloalkynes; C₁-C₃₀ heteroalkanes, C₂-C₃₀ heteroalkenes, C₂-C₃₀ heteroalkynes, C₃-C₃₀ heterocycloalkanes, C₃-C₃₀ heterocycloalkenes, and C₇-C₃₀ heterocycloalkynes; C₁-C₂₀ heteroalkanes, C₂-C₂₀ heteroalkenes, C₂-C₂₀ heteroalkynes, C₃-C₂₀ heterocycloalkanes, C₃-C₂₀ heterocycloalkenes, and C₇-C₂₀ heterocycloalkynes; C₁-C₁₆ heteroalkanes, C₂-C₁₆ heteroalkenes, C₂-C₁₆ heteroalkynes, C₃-C₁₆ heterocycloalkanes, C₃-C₁₆ heterocycloalkenes, and C₇-C₁₆ heterocycloalkynes; C₁-C₁₂ heteroalkanes, C₂-C₁₂ heteroalkenes, C₂-C₁₂ heteroalkynes, C₃-C₁₂ heterocycloalkanes, C₃-C₁₂ heterocycloalkenes, and C₇-C₁₂ heterocycloalkynes; C₁-C₈ heteroalkanes, C₂-C₈ heteroalkenes, C₂-C₈ heteroalkynes, C₃-C₈ heterocycloalkanes, C₂-C₈ heterocycloalkenes, and C₇-C₈ heterocycloalkynes; C₁-C₆ heteroalkanes, C₂-C₆ heteroalkenes, C₂-C₆ heteroalkynes, C₃-C₆ heterocycloalkanes, C₇ heterocycloalkenes, and C₃-C₆ heterocycloalkynes; and C₁-C₄ alkanes, C₂-C₄ alkenes, C₂-C₄ alkynes, C₃-C₄ cycloalkanes, and C₃-C₄ heterocycloalkenes.

Aryl and heteroaryl molecules are also useful with the compounds and methods described herein. Aryl molecules include, for example, cyclic hydrocarbons

that incorporate one or more planar sets of six carbon atoms that are connected by delocalized electrons numbering the same as if they consisted of alternating single and double covalent bonds. An example of an aryl molecule is benzene. Heteroaryl molecules include substitutions along their main cyclic chain of atoms such as O, N, or S. When heteroatoms are introduced, a set of five atoms, e.g., four carbon and a heteroatom can create an aromatic system. Examples of heteroaryl molecules include, furan, pyrrole, thiophene, imidazole, oxazole, pyridine, and pyrazine. Aryl and heteroaryl molecules can also include additional fused rings, for example, benzofuran, indole, benzothiophene, naphthalene, anthracene, and quinoline.

As used herein, the term electron withdrawing group refers to an atomic group that draws electrons from surrounding atomic groups by a resonance effect or an inductive effect more than a hydrogen atom would if it occupied the same position in the molecule. Electron withdrawing groups useful with the compounds and methods described herein include, for example, halogen (e.g. F, Br, Cl, or I), nitro, cyano, carboxyl, carbonyl, sulfonyl, trifluoromethyl, and trialkylaluminum.

As used herein, the term electron donating group refers to an atomic group that is capable of releasing electrons into surrounding atomic groups by a resonance effect or an inductive effect more than a hydrogen atom would if it occupied the same position in the molecule. Electron donating groups useful with the compounds and methods described herein include, for example, alkoxy, amino, aryl, heteroaryl, hydrocarbon, and hetero-hydrocarbon.

The hydrocarbon, hetero-hydrocarbon, aryl, heteroaryl, electron donating, and electron withdrawing molecules used herein can be substituted or unsubstituted. As used herein, the term substituted includes the addition of a hydrocarbon, hetero-hydrocarbon, aryl, or heteroaryl group (as described herein) to a position attached to the main chain of the hydrocarbon, hetero-hydrocarbon, aryl, or heteroaryl, e.g., the replacement of a hydrogen by one of these molecules. Examples of substitution groups include, but are not limited to, hydroxyl, halogen (e.g., F, Br, Cl, or I), and carboxyl groups. Conversely, as used herein, the term unsubstituted indicates the hydrocarbon, hetero-hydrocarbon, aryl, or heteroaryl group has a full complement of hydrogens, i.e., commensurate with its saturation level, with no substitutions, e.g., linear decane $-(CH_2)_9-CH_3$.

Polyethylene glycol (PEG) can be incorporated into the compounds described herein to improve solubility and uptake when administered to a subject. PEG is commonly used in drug development to improve a drug's aqueous solubility, circulation half-life, and other pharmacokinetic properties. PEG is soluble (in organic solvents and water), nontoxic, nonimmunogenic, and eliminated by a combination of renal and hepatic pathways. A monofunctional PEG has only one reactive hydroxyl group, and is herein referred to as mPEG. PEG molecules useful with the photo-activated protecting groups include substituted and unsubstituted PEG molecules with a molecular weight of greater than about 1,000 Daltons and PEG molecules with a molecular weight of greater than about 10,000 Daltons. PEG molecules with a molecular weight of 10,000 Daltons or greater show a significantly higher accumulation in tumors than within normal tissue, irrespective of tumor size. The photochemical properties of the compounds described herein are not affected by attaching PEG. Incorporation of PEG into the compounds described herein can be achieved with various synthetic methods known to one skilled in the art of organic synthesis.

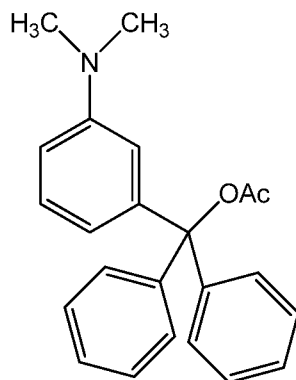
L is a conjugate base of an acid with a pKa equal to or greater than o-chlorobenzoic acid in water. The pKa of o-chlorobenzoic acid in water is 2.94, thus conjugate bases of acids with a pKa of greater than 2.94 are described. Additional L groups useful with **Compound I** include L groups with a pKa equal to or greater than 3, equal to or greater than 3.5, equal to or greater than 4, equal to or greater than 4.5, and equal to or greater than 5. Examples of acids (and their conjugate bases) with a pKa of greater than 2.94 in water include acetic acid (acetate ion; 4.76), formic acid (formate; 3.72), HF (fluoride; 3.16), nitric acid (nitrite; 3.37), and carbonic acid (hydrogen carbonate; 3.6).

In **Compound I**, adjacent R groups on the phenyl ring, i.e., R¹, R², R³, R⁴, and R⁵, can be combined to form substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkane, substituted or unsubstituted cycloalkene, substituted or unsubstituted cycloalkyne substituted or unsubstituted heterocycloalkane, substituted or unsubstituted heterocycloalkene, or substituted or unsubstituted heterocycloalkyne groups. For example, R¹ can be a methanimine group and R² can be an ethylene group that combine to form a C₆

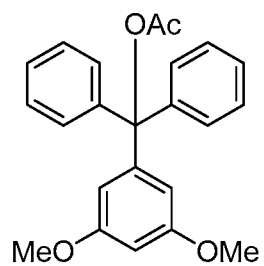
heteroaryl group. Other adjacent R groups include the combinations of R² and R³, R³ and R⁴, and R⁴ and R⁵.

Further examples of **Compound I** include:

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**I-1**

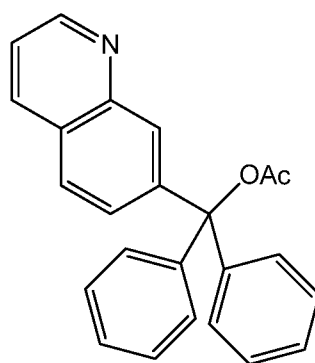
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**I-2**

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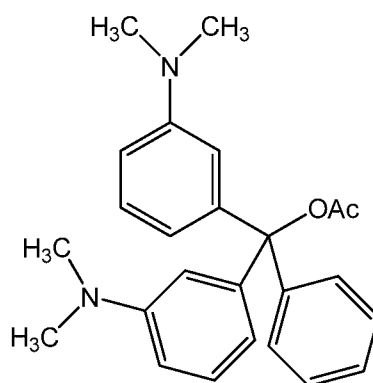
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**I-3**

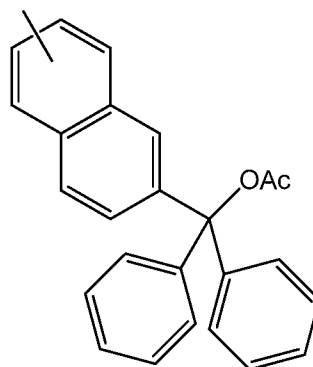
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**I-4**

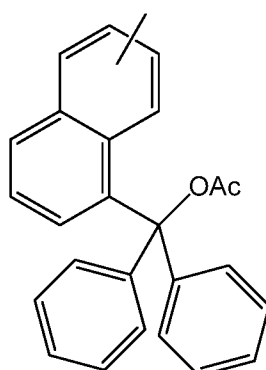
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**I-5**

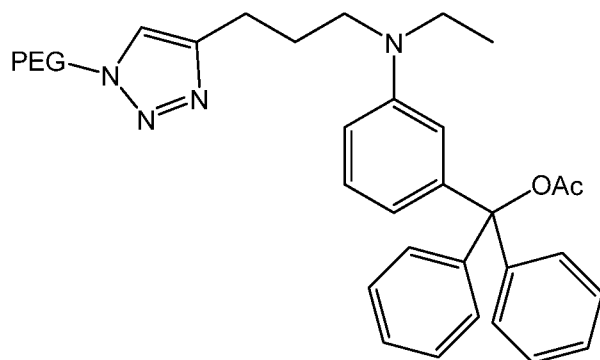
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**I-6**

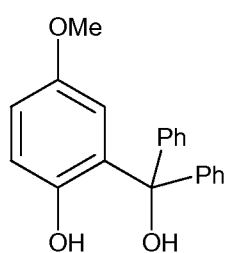
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**I-7**

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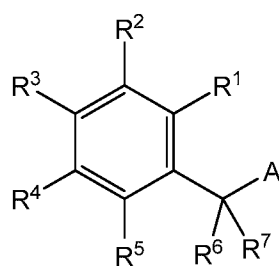
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**I-8**

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Further described are photo-activatable compounds as represented by
Compound II:

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**II**

or pharmaceutically acceptable salts thereof.

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In **Compound II**, R¹, R², R³, R⁴, R⁵, R⁶, and R⁷ are as described above for
Compound I.

Also in **Compound II**, A is a compound containing a hydroxyl-, amino-, or thio-functional group and A is attached to **Compound II** through the hydroxyl-, amino-, or thio-functional group. A can also include a linker containing a hydroxyl-, amino-, or thio-functional group, with the A—linker molecule being attached through the linker containing a hydroxyl-, amino-, or thio-functional group. If A is a therapeutic agent, the A—linker molecule can be a proform of the therapeutic agent. As used herein, the term proform is intended to mean a precursor or derivative form of a therapeutic agent that includes a property, such as, for example, lower toxicity, increased solubility, or improved transfer rate, as compared to the parent therapeutic agent that is capable of being converted into the more active parent form through a metabolic pathway or other activation method. When A is a proform of a therapeutic agent, **Compound II** is in a sense a double-proform as the molecule must first be activated by light then further activated from the proform into the active parent form. Examples of linker molecules include oxygen, substituted or unsubstituted hydrocarbons, and substituted or unsubstituted hetero-hydrocarbons. Examples of A—linker molecules include —O—phosphoramidate mustard and —O—
isophosphoramidate mustard.

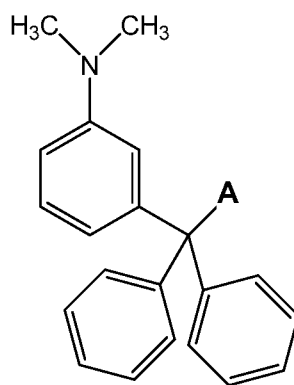
Further examples of A include therapeutic agents that a medical or other practitioner may wish to deliver to a patient in an inactive form that can be activated subsequent to administration. Examples of such therapeutic agents include cancer therapeutic agents. Cancer therapeutic agents include, for example, anthracyclines, bleomycin, calicheamicins, chlorambucil, daunorubicin, dactinomycin, diethylstilbestrol, doxorubicin, dynemicins, esperimicins, etoposide, 5-fluorouracil, floxuridine, FR-900482/FR-66979, melphalan, 6-mercaptopurine, methotrexate, mitomycin, nitrogen mustards, paclitaxel, teniposide, 6-thioguanine, vincristine, vinblastine, and derivatives thereof. Examples of nitrogen mustards include phosphoramidate, isophosphoramidate, cyclophosphamide, ifosfamide, and trofosfamide. Further examples of anti-cancer compounds and therapeutic agents are found in The Merck Manual of Diagnosis and Therapy, 15th Ed., Berkow et al., eds., 1987, Rahway, N.J.; Sladek et al. Metabolism and Action of Anti-Cancer Drugs, 1987, Powis et al. eds., Taylor and Francis, New York, N.Y.; and Pratt et al. The Anticancer Drugs, 2nd Ed., 1994, Oxford University Press, New York, N.Y.

Additional examples of A include amino acids. When A is an amino acid the amino acid can be attached through the amino end or carboxyl end of the amino acid. Further, an amino acid can be attached through a side chain hydroxyl-, amino-, or thio-functional group. Such compounds wherein A is an amino acid can be used, for example, for polypeptide synthesis.

A is released from **Compound II** when **Compound II** is exposed to light. When A includes a linker, the A—linker molecule is released when **Compound II** is exposed to light. As used herein, light refers to ultraviolet, visible, or infrared light. Ultraviolet light can be, for example, UVA or UVB light. Ultraviolet light can be provided, for example, from a commercially available 450 W medium pressure mercury lamp. The sun is also a suitable light source. The intensity of the light provided can impact the release of A. For example, fluorescent lighting may not initiate release of A or may do so at a much slower rate than sunlight or another light source.

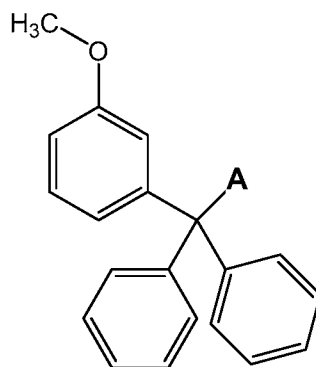
Compound II can be used when activation of compound A is desired to be delayed such as, for example, industrial and smaller scale chemical reactions and controlled/targeted *in situ* activation in medical applications. The use of delayed activating compounds like **Compound II** can provide, for example, for improved mixing prior to the initiation of a reaction or, if other protecting groups were previously used that required various deprotecting agents, the elimination of additional chemicals to initiate a reaction.

Further examples of **Compound II** include:



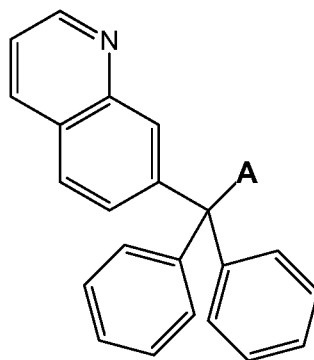
II-1

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II-2

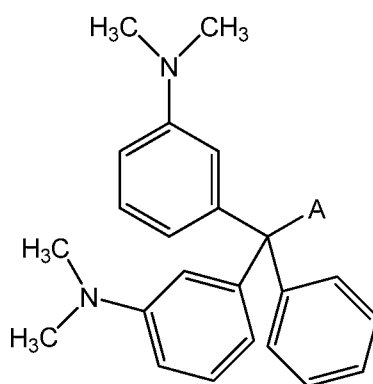
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II-3

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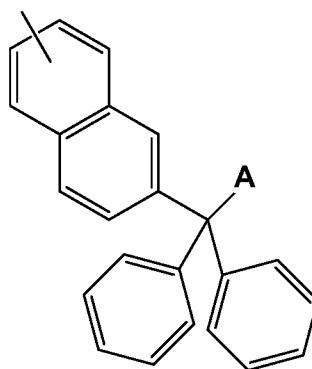
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II-4

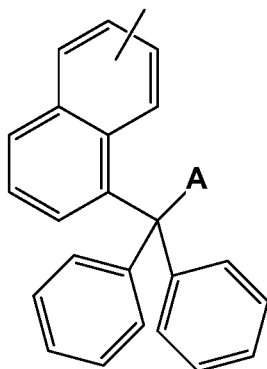
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II-5

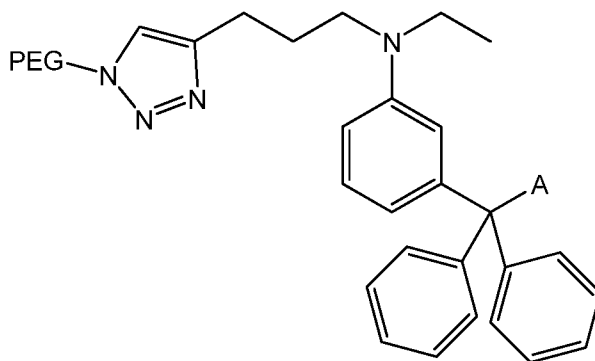
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II-6

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II-7

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The compounds described herein can be prepared in a variety of ways. The compounds can be synthesized using various synthetic methods. At least some of these methods are known in the art of synthetic organic chemistry. The compounds described herein can be prepared from readily available starting materials. Optimum

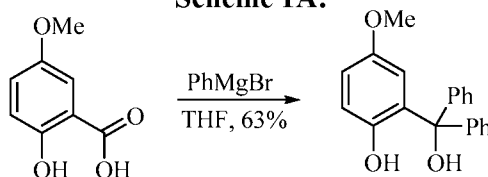
reaction conditions may vary with the particular reactants or solvent used, but such conditions can be determined by one skilled in the art by routine optimization procedures.

Variations on **Compound I** and **Compound II** include the addition,
5 subtraction, or movement of the various constituents as described for each compound. Similarly, when one or more chiral centers are present in a molecule the chirality of the molecule can be changed. Additionally, compound synthesis can involve the protection and deprotection of various chemical groups. The use of protection and deprotection, and the selection of appropriate protecting groups can be determined by
10 one skilled in the art. The chemistry of protecting groups can be found, for example, in Wuts and Greene, Protective Groups in Organic Synthesis, 4th Ed., Wiley & Sons, 2006, which is incorporated herein by reference in its entirety.

Reactions to produce the compounds described herein can be carried out in solvents which can be selected from those in the art of organic synthesis. Solvents
15 can be substantially nonreactive with the starting materials (reactants), the intermediates, or products under the conditions at which the reactions are carried out, i.e., temperature and pressure. Reactions can be carried out in one solvent or a mixture of more than one solvent. Product or intermediate formation can be monitored according to any suitable method known in the art. For example, product
20 formation can be monitored by spectroscopic means, such as nuclear magnetic resonance spectroscopy (e.g., ¹H or ¹³C) infrared spectroscopy, spectrophotometry (e.g., UV-visible), or mass spectrometry, or by chromatography such as high performance liquid chromatography (HPLC) or thin layer chromatography.

A method of making **Compound I** wherein R¹, R³, and R⁴ are hydrogen, R² is
25 methoxy, R⁵ and L are hydroxy, and R⁶ and R⁷ are phenyl is shown in Scheme 1A.

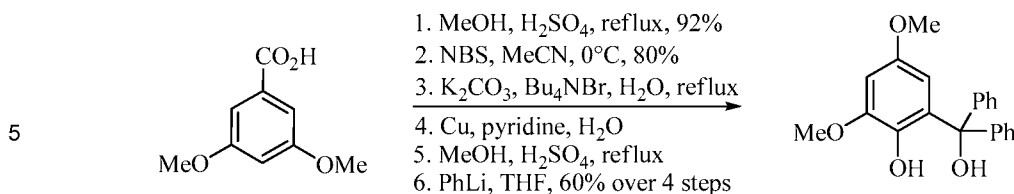
Scheme 1A:



30

A method of making **Compound I** wherein R¹ and R³ are hydrogen, R² and R⁴ are methoxy, R⁵ and L are hydroxy, and R⁶ and R⁷ are phenyl is shown in Scheme 1B.

Scheme 1B:



The methods shown in Schemes 1A and 1B produce the resulting compounds in high yields and are amenable to producing multi-gram quantities of the compounds.

10 A method for making **Compound II** includes the steps of mixing **Compound I** with a compound containing a hydroxyl-, amino-, or thio-functional group (i.e., a neat reaction) and heating the mixture to 120 °C. Reaction in various solvents such as toluene and dimethylformamide (DMF) is also possible. In some examples, **Compound II** can be synthesized in the presence of a catalytic amount of

15 trifluoroacetic acid. In the synthesis of a **Compound II** that includes a linker between A and the compound, the linker can be added to **Compound I** prior to the attachment of A to form **Compound II**. Similarly, the linker can be attached to A, prior to the A—linker molecule being attached to **Compound I** to form **Compound II**.

One or more of the compounds described herein or pharmaceutically

20 acceptable salts thereof can be provided in a pharmaceutical composition. Depending on the intended mode of administration, the pharmaceutical composition can be in the form of solid, semi-solid, or liquid dosage forms, such as, for example, tablets, suppositories, pills, capsules, powders, liquids, or suspensions, preferably in unit dosage form suitable for single administration of a precise dosage. The compositions

25 will include an effective amount of one or more of the compounds described herein or pharmaceutically acceptable salts thereof in combination with a pharmaceutically acceptable carrier and, in addition, may include other medicinal agents, pharmaceutical agents, carriers, or diluents. By pharmaceutically acceptable is meant a material that is not biologically or otherwise undesirable, which can be administered

30 to an individual along with the selected substrate without causing significant undesirable biological effects or interacting in a deleterious manner with any of the other components of the pharmaceutical composition in which it is contained.

As used herein, the term carrier encompasses any excipient, diluent, filler, salt, buffer, stabilizer, solubilizer, lipid, or other similar material for use in pharmaceutical formulations. The choice of a carrier for use in a composition will depend upon the intended route of administration for the composition. The preparation of

5 pharmaceutically acceptable carriers and formulations containing these materials is described in, *e.g.*, Remington's Pharmaceutical Sciences, 21st Edition, ed. University of the Sciences in Philadelphia, Lippincott, Williams & Wilkins, Philadelphia Pa., 2005. Examples of physiologically acceptable carriers include buffers such as phosphate buffers, citrate buffer, and buffers with other organic acids; antioxidants

10 including ascorbic acid; low molecular weight (less than about 10 residues) polypeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, arginine or lysine; monosaccharides, disaccharides, and other carbohydrates including glucose, mannose, or dextrans; chelating agents such as

15 EDTA; sugar alcohols such as mannitol or sorbitol; salt-forming counterions such as sodium; and/or nonionic surfactants such as TWEEN[®] (ICI, Inc.; Bridgewater, New Jersey), polyethylene glycol (PEG), and PLURONICS[™] (BASF; Florham Park, NJ).

Compositions containing one or more of the compounds described herein or pharmaceutically acceptable salts thereof suitable for parenteral injection may

20 comprise physiologically acceptable sterile aqueous or nonaqueous solutions, dispersions, suspensions or emulsions, and sterile powders for reconstitution into sterile injectable solutions or dispersions. Examples of suitable aqueous and nonaqueous carriers, diluents, solvents, or vehicles include water, ethanol, polyols (propyleneglycol, polyethyleneglycol, glycerol, and the like), suitable mixtures

25 thereof, vegetable oils (such as olive oil) and injectable organic esters such as ethyl oleate. Proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersions, and by the use of surfactants.

These compositions may also contain adjuvants such as preserving, wetting,

30 emulsifying, and dispensing agents. Prevention of the action of microorganisms can be ensured by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, and the like. It may also be desirable to include

isotonic agents, for example, sugars, sodium chloride, and the like. Prolonged absorption of the injectable pharmaceutical form can be brought about by the use of agents delaying absorption, for example, aluminum monostearate and gelatin.

Solid dosage forms for oral administration of the compounds described herein or a pharmaceutically acceptable salt thereof include capsules, tablets, pills, powders, and granules. In such solid dosage forms, one or more compounds described herein or pharmaceutically acceptable salts thereof is/are admixed with at least one inert customary excipient (or carrier) such as sodium citrate or dicalcium phosphate or (a) fillers or extenders, as for example, starches, lactose, sucrose, glucose, mannitol, and silicic acid; (b) binders, as for example, carboxymethylcellulose, alginates, gelatin, polyvinylpyrrolidone, sucrose, and acacia; (c) humectants, as for example, glycerol; (d) disintegrating agents, as for example, agar-agar, calcium carbonate, potato or tapioca starch, alginic acid, certain complex silicates, and sodium carbonate; (e) solution retarders, as for example, paraffin; (f) absorption accelerators, as for example, quaternary ammonium compounds; (g) wetting agents, as for example, cetyl alcohol, and glycerol monostearate; (h) adsorbents, as for example, kaolin and bentonite; and (i) lubricants, for example, talc, calcium stearate, magnesium stearate, solid polyethylene glycols, sodium lauryl sulfate, or mixtures thereof. In the case of capsules, tablets, and pills, the dosage forms may also comprise buffering agents.

Solid compositions of a similar type may also be employed as fillers in soft and hard-filled gelatin capsules using such excipients as lactose or milk sugar as well as high molecular weight polyethyleneglycols, and the like.

Solid dosage forms such as tablets, dragees, capsules, pills, and granules can be prepared with coatings and shells, such as enteric coatings and others known in the art. They may contain opacifying agents and optionally or additionally can be of such composition that they release the active compound or compounds in a certain part of the intestinal tract in a delayed manner. Examples of embedding compositions which can be used are polymeric substances and waxes. The active compound(s) can also be in micro-encapsulated form, if appropriate, with one or more of the above-mentioned excipients.

Liquid dosage forms for oral administration of the compounds described herein or pharmaceutically acceptable salts thereof include pharmaceutically

acceptable emulsions, solutions, suspensions, syrups, and elixirs. In addition to the active compounds, the liquid dosage forms may contain inert diluents, such as water or other solvents, solubilizing agents, and emulsifiers, as for example, ethyl alcohol; isopropyl alcohol; ethyl carbonate; ethyl acetate; benzyl alcohol; benzyl benzoate; 5 propyleneglycol; 1,3-butyleneglycol; dimethylformamide; oils, in particular, cottonseed oil, groundnut oil, corn germ oil, olive oil, castor oil, and sesame oil; glycerol; tetrahydrofurfuryl alcohol; polyethyleneglycols; fatty acid esters of sorbitan; or mixtures of these substances, and the like.

Besides such inert diluents, the composition can also include adjuvants, such 10 as wetting, emulsifying, suspending, sweetening, flavoring, or perfuming agents.

Suspensions, in addition to the active compound or compounds, may contain suspending agents, as for example, ethoxylated isostearyl alcohols, polyoxyethylene sorbitol and sorbitan esters, microcrystalline cellulose, aluminum metahydroxide, bentonite, agar-agar and tragacanth, or mixtures of these substances, and the like.

15 Compositions of one or more compounds described herein or pharmaceutically acceptable salts thereof for rectal administrations are optionally suppositories, which can be prepared by mixing the compounds with suitable non-irritating excipients or carriers such as cocoa butter, polyethyleneglycol, or a suppository wax, which are solid at ordinary temperatures but liquid at body 20 temperature and therefore, melt in the rectum or vaginal cavity and release the active component.

Dosage forms for topical administration of the compounds described herein or pharmaceutically acceptable salts thereof include ointments, powders, sprays, and inhalants. The compounds described herein or pharmaceutically acceptable salts 25 thereof are admixed under sterile conditions with a physiologically acceptable carrier and any preservatives, buffers, or propellants as may be required. Ophthalmic formulations, ointments, powders, and solutions are also contemplated as being within the scope of the compositions.

The term pharmaceutically acceptable salts as used herein refers to those salts 30 of the compounds described herein that are, within the scope of sound medical judgment, suitable for use in contact with the tissues of subjects without undue

toxicity, irritation, allergic response, and the like, commensurate with a reasonable benefit/risk ratio, and effective for their intended use, as well as the zwitterionic forms, where possible, of the compounds described herein. The term salts refers to the relatively non-toxic, inorganic and organic acid addition salts of the compounds described herein. These salts can be prepared *in situ* during the isolation and purification of the compounds or by separately reacting the purified compound in its free base form with a suitable organic or inorganic acid and isolating the salt thus formed. Representative salts include the hydrobromide, hydrochloride, sulfate, bisulfate, nitrate, acetate, oxalate, valerate, oleate, palmitate, stearate, laurate, borate, benzoate, lactate, phosphate, tosylate, citrate, maleate, fumarate, succinate, tartrate, naphthylate mesylate, glucoheptonate, lactobionate, methane sulphonate, and laurylsulphonate salts, and the like. These may include cations based on the alkali and alkaline earth metals, such as sodium, lithium, potassium, calcium, magnesium, and the like, as well as non-toxic ammonium, quaternary ammonium, and amine cations including, but not limited to ammonium, tetramethylammonium, tetraethylammonium, methylamine, dimethylamine, trimethylamine, triethylamine, ethylamine, and the like. (See S.M. Berge et al., J. Pharm. Sci. (1977) 66:1-19, which is incorporated herein by reference in its entirety, at least, for compositions taught therein.)

A method of delivering a therapeutic agent to a selected area in a subject is also described. In this method, an effective amount of **Compound II** as described above is administered to a subject, and then light is transmitted to the selected area of the subject. The effective amount of **Compound II** can be delivered systemically to the subject or delivered to a specific area of the subject, i.e., the selected area, its vicinity, or its blood supply. The amount of time between the administration step and the transmission of light to the selected area of the subject will depend upon the rate of transfer of the effective amount of **Compound II** to the selected area. An effective amount of **Compound II** is the amount needed for delivery of an effective amount of the therapeutic agent that will be released from **Compound II** to the selected area in the subject. Thus, for systemic delivery an amount of **Compound II** greater than the amount needed at the selected area of the subject may be provided (unless **Compound II** is such that the entire amount administered to the subject is delivered to the selected area).

The transmission of light to the selected area of a subject can be accomplished using methods and apparatus known to those of skill in the surgical arts. For example, the light can be transmitted through an optical fiber or an optical probe to the selected area. Further, the optical fiber or optical probe can be housed in a needle.

- 5 The optical fiber, optical probe, or needle housing the optical fiber or optical probe can be guided to the selected area using CT scan or MRI, which methods are known to those of skill in the surgical arts.

As an example, in the treatment of a cancer tumor, **Compound II** having a cancer therapeutic agent as A can be administered to a subject having a cancer tumor.

- 10 Once **Compound II** has been transmitted through the subject to the cancer tumor site, the cancer tumor site can be irradiated with light to release the cancer therapeutic agent. Molecules containing with PEG groups with molecular weights greater than 10,000 Daltons are known to collect in cancerous tissues; thus, a **Compound II** containing PEG groups may collect in cancer tissue increasing the transfer efficiency
15 of **Compound II** to a tumor site (thereby lowering the overall amount of **Compound II** that is administered to the subject to deliver an effective amount).

Administration of the compounds described herein or pharmaceutically acceptable salts thereof can be carried out using therapeutically effective amounts of the compounds described herein or pharmaceutically acceptable salts thereof. The
20 effective amount of the compounds described herein or pharmaceutically acceptable salts thereof may be determined by one of ordinary skill in the art, and includes exemplary dosage amounts for a mammal of from about 0.05 to about 100 mg/kg of body weight of active compound per day, which may be administered in a single dose or in the form of individual divided doses, such as from 1 to 4 times per day.

- 25 Alternatively, the dosage amount can be from about 0.05 to about 75 mg/kg of body weight of active compound per day, about 0.5 to about 50 mg/kg of body weight of active compound per day, about 0.5 to about 25 mg/kg of body weight of active compound per day, about 1 to about 20 mg/kg of body weight of active compound per day, about 1 to about 10 mg/kg of body weight of active compound per day, about 20
30 mg/kg of body weight of active compound per day, about 10 mg/kg of body weight of active compound per day, or about 5 mg/kg of body weight of active compound per day. Those of skill in the art will understand that the specific dose level and

frequency of dosage for any particular subject may be varied and will depend upon a variety of factors, including the dispersion rate through the subject, the activity of the specific therapeutic agents being delivered, the metabolic stability and length of action of that compound, the species, age, body weight, general health, sex and diet of the subject, the mode and time of administration, rate of excretion, drug combination, and severity of the particular condition.

In the methods described herein, the subjects treated can be further treated with one or more additional agents. The one or more additional agents and the compounds described herein or pharmaceutically acceptable salts thereof can be administered in any order, including simultaneous administration, as well as temporally spaced order of up to several days apart. The methods may also include more than a single administration of the one or more additional agents and/or the compounds described herein or a pharmaceutically acceptable salt thereof. The administration of the one or more additional agents and the compounds described herein or pharmaceutically acceptable salts thereof may be by the same or different routes and concurrently or sequentially.

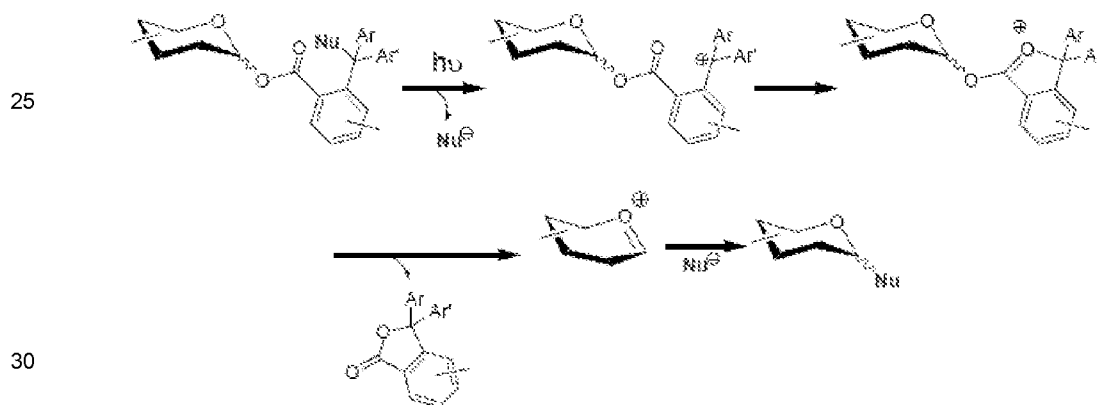
Additionally, a method of synthesizing a polypeptide is described herein. The method involves providing **Compound II** wherein A is a first amino acid attached through its amino end group. Next a second amino acid with a free carboxyl end group is provided. Then light is transmitted to release A (i.e., the first amino acid). Finally, peptide bond formation is initiated to form a peptide linkage between the first amino acid and the second amino acid. The first amino acid can be attached to a support surface, e.g., through its carboxyl end. The support surface can be, for example, a bead, solid-phase resin (such as polydimethylacrylamide), or a microarray.

In the method of synthesizing a polypeptide as described herein, **Compound II** is used instead of known protecting groups typically used in polypeptide synthesis, e.g., t-Boc (di-tert-butyl dicarbonate) or Fmoc (9-fluorenylmethoxycarbonyl). Use of the photo-activated protecting groups described herein in polypeptide synthesis alleviates the necessity of using chemical deprotecting agents, e.g., trifluoroacetic acid for t-Boc removal and piperidine for Fmoc removal, as the photo-activated protecting groups described herein are activated by light (i.e., light becomes the deprotecting agent).

Further provided herein is an intramolecular method of forming a glycosyl bond. The method involves providing **Compound II** wherein R⁶ is a substituted or unsubstituted phenyl ring linked to an anomeric oxygen atom of a substituted or unsubstituted saccharide through a linker X, wherein the anomeric oxygen atom is
 5 linked to an anomeric carbon atom. The linker X is a substituted or unsubstituted carbonyl (e.g., -C(O)- or -C(O)CH₂-) or a substituted or unsubstituted hydrocarbon (e.g., -CH₂- or -CH₂CH₂-). Then light is transmitted to release A. In some examples A is a peptide, a protein, or a substituted or unsubstituted saccharide. Upon exposure to light, the bond between the anomeric carbon atom and the anomeric oxygen atom
 10 of the saccharide is broken. Finally, formation of a glycosyl bond to link the anomeric carbon atom of the saccharide to A is initiated. The saccharide can be a monosaccharide or a polysaccharide. The methods described herein can be used for immobilization of photolithographic on-chip synthesis of carbohydrates for carbohydrate array preparation (e.g., high density microarrays).

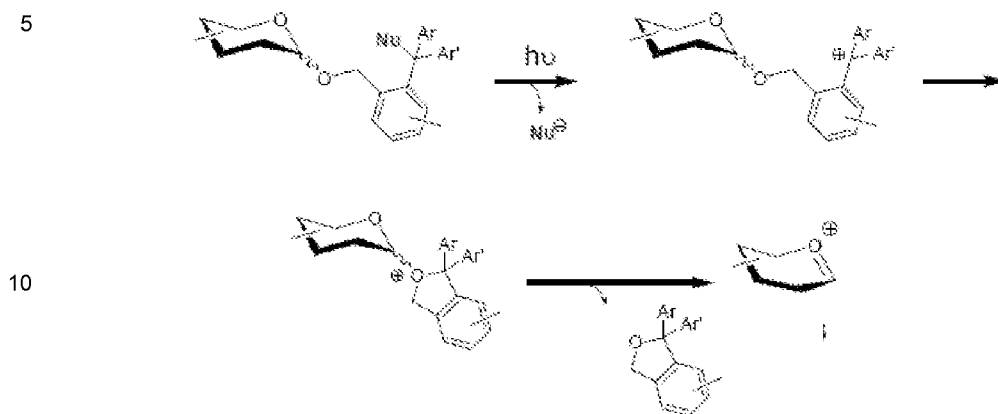
15 Examples of the intramolecular glycosylation reaction are shown in Schemes 2 and 3. In Scheme 2, A is represented as Nu. Irradiation of the glycoside generates the tritylium ion. Intramolecular stabilization of the carbocation by the anomeric ester moiety leads to the oxonium cation intermediate, which releases the lactone and yields the oxocarbenium. In the presence of the nucleophile (Nu⁻) released after the
 20 irradiation, the glycosyl bond is formed. This reaction can proceed under solvent-free conditions.

Scheme 2:



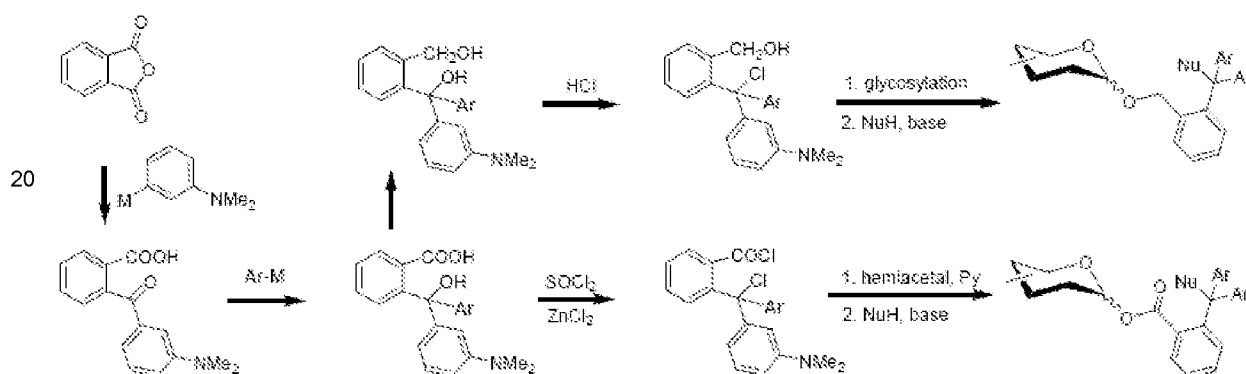
In Scheme 3, the anomeric ether glycoside produces the oxocarbenium similarly to the anomeric ester glycoside of Scheme 2.

Scheme 3:



A method of making **Compound II** used in Schemes 2 and 3 is shown below in Scheme 4. In Scheme 4, M is metal (e.g., lithium).

Scheme 4:

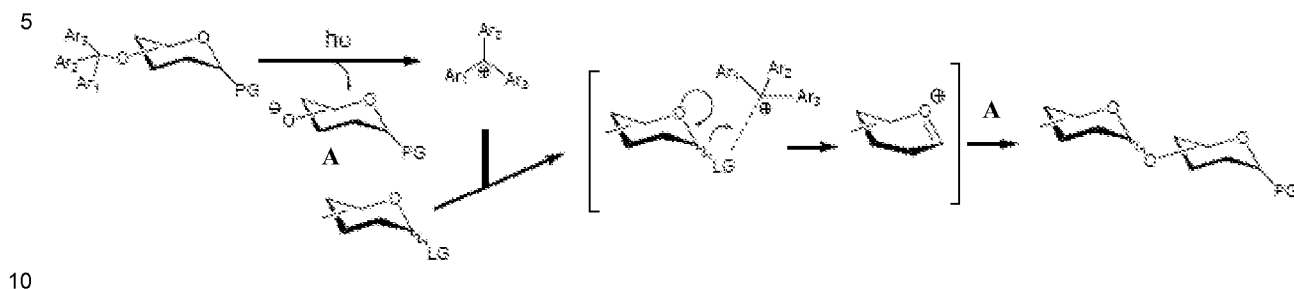


Also described herein is a method of forming a glycosyl bond. The method includes providing **Compound II**, wherein A is a saccharide containing a hydroxyl- or amino-functional group and A is attached through one of its hydroxyl- or amino-functional group (e.g., the C-2, C-3, C-4, or C-5 hydroxyl group). Next, a donor with a leaving group attached is provided. Light is then transmitted to release A. Once A is released a glycosyl bond is formed to link A to the donor. In some examples, the donor is selected from the group consisting of an anomeric enol ether glycoside, a glycosyl fluoride, a 1,2-O-cyanoethylidene donor, a 1,2-thio-orthoester donor, a 1-O-bromoacetyl donor, a 1-thiocyano donor, a dimethylphosphinothioate, a glycosyl

30

phenylcarbonate, and a glycosyl thioformimidate. In some examples, the donor is a saccharide with a leaving group attached to its anomeric carbon. In Scheme 5, the donor is a saccharide with a leaving group attached to its anomeric carbon.

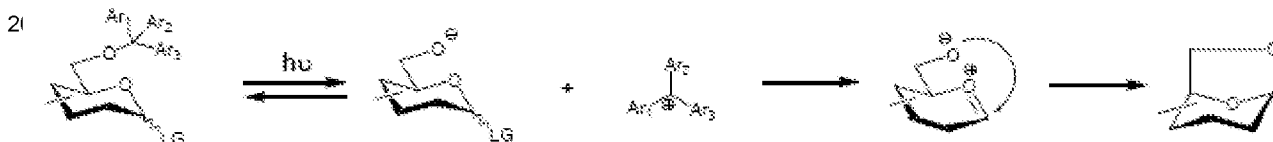
Scheme 5:



Further described herein is an intramolecular method of forming a glycosan. The method includes providing **Compound II**, wherein A is a saccharide attached through a hydroxyl functional group and the saccharide contains a leaving group attached to its anomeric carbon. Light is then transmitted to release A. Once A is released, a glycosyl bond is formed to link the hydroxyl functional group to the anomeric carbon. In some examples, the hydroxyl functional group is a C-6 hydroxyl functional group. The intramolecular method of forming a glycosan is shown in Scheme 6.

15

Scheme 6:



A method of site-specifically attaching a biological molecule to a support surface is also described herein. The method includes protecting one or more functional groups (e.g., amino or carbonyl groups) of a support surface (e.g., a functionalized glass slide) with **Compound I** to form a photo-activatable support surface. One or more of the protected functional groups are then selected for biological molecule attachment. To prevent biological molecule attachment at non-selected sites, photo-masking of the non-selected functional groups is performed. In some examples, the photo-masking is performed by photolithography. The photo-activatable support surface is then irradiated to deprotect the one or more selected functional groups. The photo-masked functional groups remain protected. Finally,

25

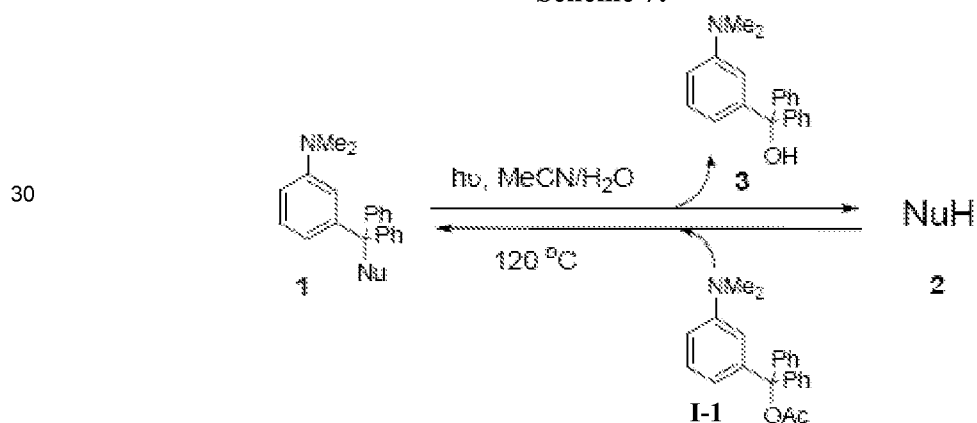
30

the biological molecule is then covalently attached to the one or more selected functional groups. The biological molecule can be, for example, a carbohydrate. The covalent attachment can be performed using chemical methods known to those of skill in the art, including, for example, reductive amination when using carbohydrates
5 containing a terminal carbonyl group. The site-specific method can be continued to attach carbohydrates to each functional group of the surface. The examples below are intended to further illustrate certain aspects of the methods and compounds described herein, and are not intended to limit the scope of the claims.

10 **Example 1: Synthesis and Analysis of Photo-Activatable Protected Molecules**

Several photo-activatable protected molecules were synthesized to determine their protection and deprotection yields. The photo-activated protecting group used for this analysis had the structure **I-1** as shown above. The photo-activatable protected molecules were synthesized by reacting **I-1** with a molecule containing a
15 hydroxyl-, amino-, or thio-functional group at 120°C without additional solvent (toluene and DMF were tried as solvents, but the protection reaction was slower). Scheme 7 describes the synthesis and subsequent photo-activation of the photo-activatable protected molecules in acetonitrile/water without excluding air. The synthesized photo-activatable compounds are stable under laboratory lighting and can
20 be handled without using special precautions. The photo-activation was initiated using a medium pressure mercury-vapor immersion lamp with a 450 W output that was filtered through Pyrex (manufactured by Hanovia Ltd.; Berkshire, UK; available from Ace Glass, Inc. (Lamp No. 7825-34); Vineland, NJ). The presence of water during photo-activation was noticed to accelerate the deprotection reaction. In
25 Scheme 7 and Table 1, NuH represents the compound containing a hydroxyl-, amino-, or thio-functional group (i.e., A).

Scheme 7:

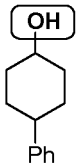
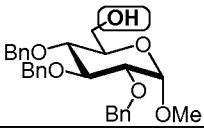
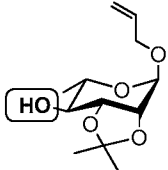


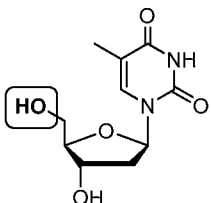
Alternatively, the protection of alcohols according to the reaction in Scheme 7 can also be accomplished by reacting the alcohols with structure **I-1** at room temperature in the presence of a catalytic amount of trifluoroacetic acid.

5 The specific NuH molecules protected and their deprotection and protection yields are shown in Table 1. For the protection reaction, 0.1 mmol of NuH and 0.15-0.3 mmol of structure **I-1** were heated at 120 °C in a sealed tube neat or with 50-100 μ L of toluene. For the deprotection of the compounds, the protected compound was irradiated with a 450 W medium-pressure mercury-vapor immersion lamp equipped
10 with a Pyrex filter sleeve without deaeration. For compounds 2a and 2d, the concentration of the reaction solutions ranged from 0.25 mM to 5 mM. The concentration of the reaction solution for compound 2b was 5mM in acetonitrile/water (9:1). The concentration of the reaction solution for compound 2c was 5mM in methanol. The protecting group was installed on the boxed functional group.

15

Table 1: Protection/Deprotection Yield Results

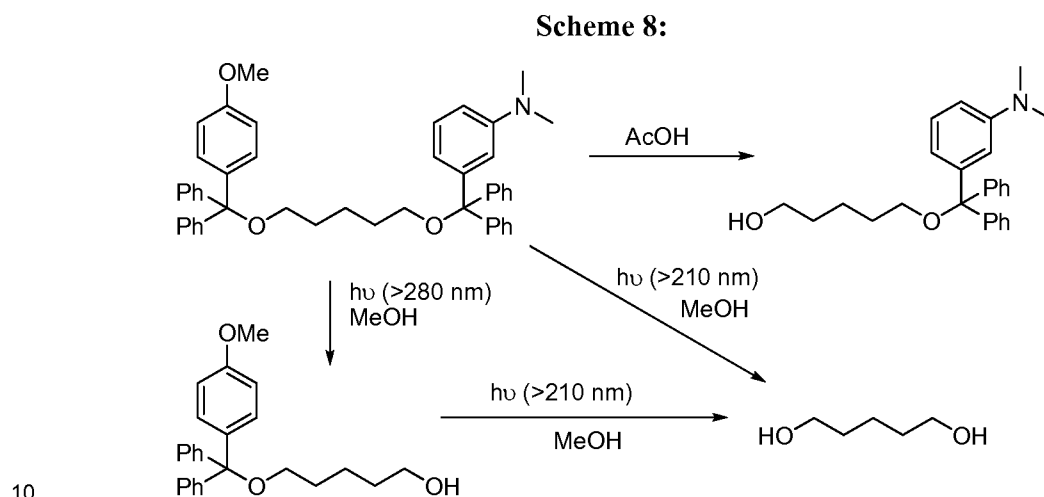
Compound	NuH	Protection Yield (%)	Deprotection Yield (%)	Irradiation Time (min)
2a		92	87	15
2b		93	84	35
2c		83	86	30

2d		79	81	60
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As can be seen from Table 1, protection yields are high and the deprotection yields for those compounds tested were similarly high.

Example 2: Other Photo-Activatable Protected Molecules

- 5 A 1,6-dihydroxyhexane was protected at one end with structure **I-1** and at the other end with a 4-methoxytriphenylmethyl group as shown in Scheme 8 (using the same method described above for Example 1):



- As depicted in Scheme 8, both protecting groups released the ends of the protected molecule upon irradiation. The photo-activatable protecting groups **I-1** was selectively removed by irradiating with a wavelength of 280 nm or greater. Both protecting groups were removed upon irradiation at a wavelength of 210 nm.
- 15

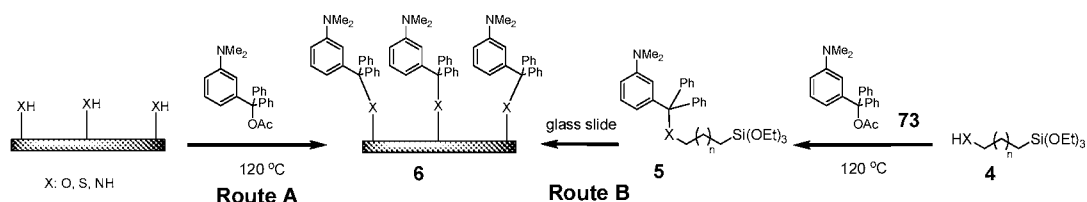
Example 3: Site-specific Attachment of a Carbohydrate to a Support Surface

- The functional groups of functional group-coated slides (e.g., amino, hydroxyl, or thio) are protected with **Compound I** by heating the slide to 120 °C in the presence of **Compound I** (Scheme 9, Route A). Alternatively, **Compound I** can
- 20

be reacted with 3-aminopropyl-triethoxysilane (**4**, $n=1$) to form the protected compound **5**. The obtained protected compound **5** can be bound to untreated glass slides by immersing the glass slides in a dilute solution of **5** (Scheme 9, Route B).

5

Scheme 9:



To determine the efficiency of surface derivatization, a fluorescent ligand stain, e.g., ninhydrin, can be used to monitor the progress in making the photo-activatable support surface. The fluorescent ligand stain can also be used for quantitative measurements to determine the efficiency of photochemical removal of the photo-activatable group. The same general strategy applies to derivatizing aldehyde-coated surfaces.

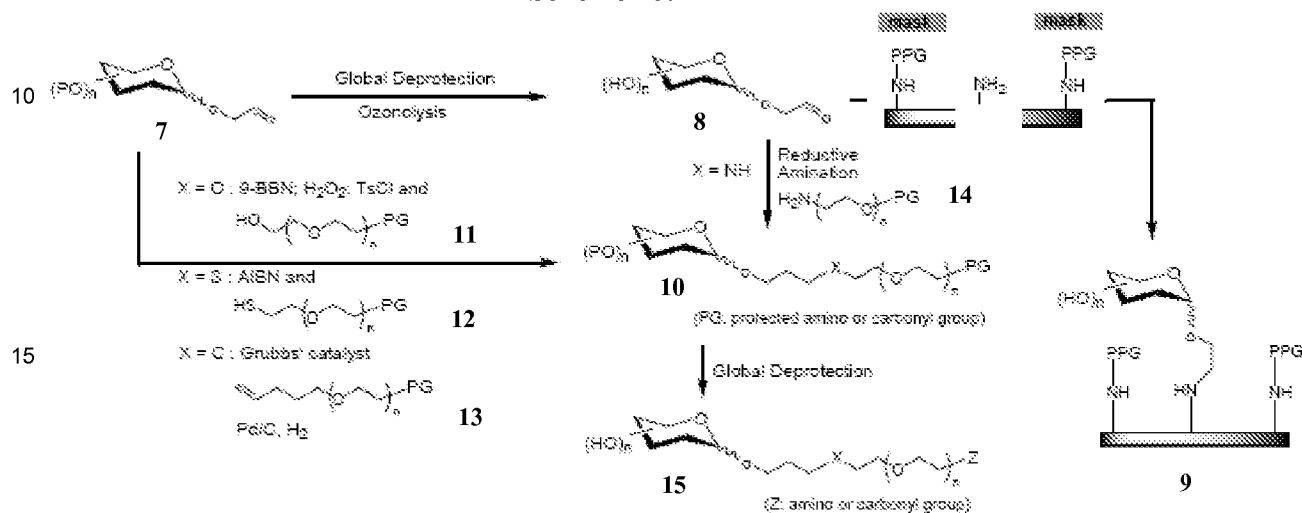
To attach carbohydrates to the surface, anomeric groups of synthetic oligosaccharides are transformed to functionalities useful for immobilization, e.g., amino groups for aldehyde-coated surfaces and carbonyl groups for amine-coated surfaces (see, e.g., Scheme 10). Subsequent highly efficient reductive amination reaction between ligands and substrates furnish attachment. The reductive amination can be carried out either in solution or on the solid phase, by spotting carbohydrate ligands to the spot of corresponding surfaces where functional groups have been photochemically revealed, followed by spotting sodium cyanoborohydride.

In Scheme 10, the anomeric allyl groups are functionalized for surface attachment. Allyl glycoside **7** is converted to **8** via the sequence of global deprotection followed by ozonolysis. Numerous methods are available for removing protecting groups without disturbing the anomeric olefin (C=C). Subsequent reductive amination with patterned amine-coated surfaces leads to spatially specified immobilization to produce **9**. The linker between carbohydrates and surfaces can affect binding events. Glycosides with adjustable linker length (e.g. **10**) are also

conveniently prepared from allyl glycoside **7** and reagents **11-13** via routine reactions.

The reaction to be adopted for derivatization depends on convenience and also compatibility of the new functionality with the global deprotection conditions. The obtained glycoside **15** equipped with necessary anchor (either an amino group or a carbonyl group) is used for immobilization onto the corresponding functionalized surfaces by using reductive amination.

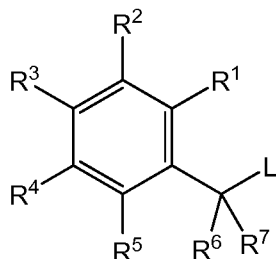
Scheme 10:



The compounds and methods of the appended claims are not limited in scope by the specific compounds and methods described herein, which are intended as illustrations of a few aspects of the claims and any compounds and methods that are functionally equivalent are within the scope of this disclosure. Various modifications of the compounds and methods in addition to those shown and described herein are intended to fall within the scope of the appended claims. Further, while only certain representative compounds, methods, and aspects of these compounds and methods are specifically described, other compounds and methods are intended to fall within the scope of the appended claims. Thus a combination of steps, elements, components, or constituents may be explicitly mentioned herein; however, all other combinations of steps, elements, components, and constituents are included, even though not explicitly stated.

WHAT IS CLAIMED IS:

1. A compound of the following formula:



or a pharmaceutically acceptable salt thereof, wherein:

R^1 , R^3 , and R^5 are each independently selected from hydrogen, substituted or unsubstituted hydrocarbon, substituted or unsubstituted hetero-hydrocarbon, halogen, an electron withdrawing group, or an electron donating group;

R^2 and R^4 are each independently selected from hydrogen, substituted or unsubstituted hydrocarbon, substituted or unsubstituted hetero-hydrocarbon, halogen, or an electron donating group;

R^6 and R^7 are each independently selected from substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl; and

L is a conjugate base of an acid with a pKa equal to or greater than o-chlorobenzoic acid in water.

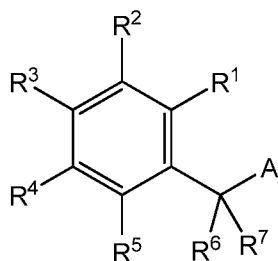
2. The compound of claim 1, wherein R^1 and R^2 are combined to form a substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkane, substituted or unsubstituted cycloalkene, substituted or unsubstituted cycloalkyne, substituted or unsubstituted heterocycloalkane, substituted or unsubstituted heterocycloalkene, or substituted or unsubstituted heterocycloalkyne.

3. The compound of claim 1, wherein R^2 and R^3 are combined to form a substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkane, substituted or unsubstituted cycloalkene, substituted or unsubstituted cycloalkyne, substituted or unsubstituted heterocycloalkane, substituted or unsubstituted heterocycloalkene, or substituted or unsubstituted heterocycloalkyne.

4. The compound of claim 1, wherein R^3 and R^4 are combined to form a substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkane, substituted or unsubstituted cycloalkene, substituted or unsubstituted cycloalkyne, substituted or unsubstituted heterocycloalkane, substituted or unsubstituted heterocycloalkene, or substituted or unsubstituted heterocycloalkyne.
5. The compound of claim 1, wherein R^4 and R^5 are combined to form a substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkane, substituted or unsubstituted cycloalkene, substituted or unsubstituted cycloalkyne, substituted or unsubstituted heterocycloalkane, substituted or unsubstituted heterocycloalkene, or substituted or unsubstituted heterocycloalkyne.
6. The compound of claim 1, wherein R^2 or R^4 is substituted or unsubstituted amino or alkoxy.
7. The compound of claim 1, wherein the pKa of L is equal to or greater than 3.
8. The compound of claim 1, wherein R^2 or R^4 is methoxy, dimethylamino, PEG, or
- CCN(CC)CCCC1=CN=C(N1)PEG
9. The compound of claim 8, wherein the PEG has a molecular weight greater than about 1,000 Daltons.
10. The compound of claim 9, wherein the PEG has a molecular weight greater than about 10,000 Daltons.
11. The compound of any of claims 8-10, wherein the PEG is substituted.
12. The compound of claim 11, wherein the PEG is mPEG.
13. The compound of claim 1, wherein R^3 is hydrogen.
14. The compound of any of claims 1-13, wherein R^6 and R^7 are each phenyl.
15. A composition, comprising a compound of any one of claims 1-14 and a pharmaceutically acceptable carrier.

16. A method of making a photo-activatable compound, comprising combining a compound of claim 1 with a compound containing a hydroxyl-, amino-, or thio-functional group, wherein the compound containing a hydroxyl-, amino-, or thio-functional group is released from the photo-activatable compound upon exposure to light.
17. The method of claim 16, wherein the compound containing a hydroxyl-, amino-, or thio-functional group is a cancer therapeutic agent.
18. The method of claim 17, wherein the cancer therapeutic agent is selected from the group consisting of calicheamicins or derivatives thereof, esperimicins or derivatives thereof, dynemicins or derivatives thereof, FR-900482/FR-66979 or derivatives thereof, nitrogen mustards or derivatives thereof, anthracyclines or derivatives thereof, and paclitaxel or derivatives thereof.
19. The method of claim 16, wherein the light is ultraviolet, visible, or infrared light.
20. The method of claim 18, wherein the ultraviolet light is UVA or UVB.
21. A method of delivering a therapeutic agent to a selected area in a subject, comprising:
- administering to the subject an effective amount of a compound made by of any of claims 16-20; and
 - transmitting light to the selected area of the subject.

22. A photo-activatable compound of the following formula:



or a pharmaceutically acceptable salt thereof, wherein:

R¹, R³, and R⁵ are each independently selected from hydrogen, substituted or unsubstituted hydrocarbon, substituted or unsubstituted hetero-hydrocarbon, halogen, an electron withdrawing group, or an electron donating group;

R² and R⁴ are each independently selected from hydrogen, substituted or unsubstituted hydrocarbon, substituted or unsubstituted hetero-hydrocarbon, halogen, or an electron donating group;

R⁶ and R⁷ are each independently selected from substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl; and

A is a compound containing a hydroxyl-, amino-, or thio-functional group, A being attached through the hydroxyl-, amino-, or thio-functional group,

wherein A is released from the photo-activatable compound upon exposure to light.

23. The compound of claim 22, wherein R¹ and R² are combined to form a substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkane, substituted or unsubstituted cycloalkene, substituted or unsubstituted cycloalkyne, substituted or unsubstituted heterocycloalkane, substituted or unsubstituted heterocycloalkene, or substituted or unsubstituted heterocycloalkyne.

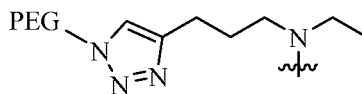
24. The compound of claim 22, wherein R² and R³ are combined to form a substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkane, substituted or unsubstituted cycloalkene, substituted or unsubstituted cycloalkyne, substituted or unsubstituted heterocycloalkane, substituted or unsubstituted heterocycloalkene, or substituted or unsubstituted heterocycloalkyne.

25. The compound of claim 22, wherein R³ and R⁴ are combined to form a substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkane, substituted or unsubstituted cycloalkene, substituted or unsubstituted cycloalkyne, substituted or unsubstituted heterocycloalkane, substituted or unsubstituted heterocycloalkene, or substituted or unsubstituted heterocycloalkyne.

26. The compound of claim 22, wherein R⁴ and R⁵ are combined to form a substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkane, substituted or unsubstituted cycloalkene, substituted or unsubstituted cycloalkyne, substituted or unsubstituted heterocycloalkane, substituted or unsubstituted heterocycloalkene, or substituted or unsubstituted heterocycloalkyne.

27. The compound of claim 22, wherein R² or R⁴ is substituted or unsubstituted amino or alkoxy.

28. The compound of claim 22, wherein R² or R⁴ is methoxy, dimethylamino, PEG, or



29. The compound of claim 28, wherein the PEG has a molecular weight greater than about 1,000 Daltons.

30. The compound of claim 29, wherein the PEG has a molecular weight greater than about 10,000 Daltons.

31. The compound of any of claims 28-30, wherein the PEG is substituted.

32. The compound of claim 31, wherein the PEG is mPEG.

33. The compound of claim 22, wherein R³ is hydrogen.

34. The compound of any of claims 22-33, wherein R⁶ and R⁷ are each phenyl.

35. The compound of claim 22, wherein A includes a linker containing a hydroxyl-, amino-, or thio-functional group, A being attached through the linker.

36. The compound of claim 22, wherein the A including a linker is —O—phosphoramidate mustard or —O—isophosphoramidate mustard.
37. The compound of claim 22, wherein the light is ultraviolet, visible, or infrared light.
38. The compound of claim 37, wherein the ultraviolet light is UVA or UVB.
39. The compound of claim 22, wherein A is a cancer therapeutic agent.
40. The compound of claim 39, wherein the cancer therapeutic agent is selected from the group consisting of calicheamicins or derivatives thereof, esperimicins or derivatives thereof, dynemicins or derivatives thereof, FR-900482/FR-66979 or derivatives thereof, nitrogen mustards or derivatives thereof, anthracyclines or derivatives thereof, and paclitaxel or derivatives thereof.
41. The compound of claim 22, wherein A is an amino acid.
42. The compound of claim 41, wherein the amino acid is attached through its amino end.
43. A composition, comprising a compound of any one of claims 22-42 and a pharmaceutically acceptable carrier.
44. A method of delivering a therapeutic agent to a selected area in a subject, comprising:
administering to the subject an effective amount of the compounds or compositions of any of claims 22-43; and
transmitting light to the selected area of the subject.
45. The method of claim 44, wherein the compounds or compositions are delivered systemically.
46. The method of claim 44 or 45, wherein an optical fiber or optical probe is used to transmit the light.

47. The method of claim 46, wherein the optical fiber or optical probe is housed in a needle and the needle is positioned near a cancer site.
48. The method of claim 47, wherein the optical fiber or optical probe is guided to the selected area using CT scan or MRI.
49. A method of synthesizing a polypeptide, comprising:
providing a compound or composition of any of claims 22-43, wherein A is a first amino acid attached through its amino end group;
providing a second amino acid with a free carboxyl end group; and
transmitting light to release A,
wherein a peptide bond is formed between the first amino acid and the second amino acid.
50. The method of claim 49, wherein the first amino acid is attached to a support surface through its carboxyl end.
51. The method of claim 50, wherein the support surface is a bead.
52. The method of claim 50, wherein the support surface is a microarray.
53. An intramolecular method of forming a glycosyl bond, comprising:
providing a compound or composition of any of claims 22-43, wherein R⁶ is a substituted or unsubstituted phenyl ring linked to an anomeric oxygen atom of a substituted or unsubstituted saccharide through a linker X, wherein the anomeric oxygen atom is linked to an anomeric carbon atom; and
transmitting light to release A,
wherein the bond between the anomeric carbon atom and the anomeric oxygen atom of the saccharide is broken and a glycosyl bond is formed to link the anomeric carbon atom of the saccharide to A.
54. The method of claim 53, wherein the saccharide is a monosaccharide or a polysaccharide.
55. The method of claim 53 or 54, wherein A is a peptide or a protein.

56. The method of claim 53 or 54, wherein A is a substituted or unsubstituted saccharide.
57. The method of any of claims 53-56, wherein X is a substituted or unsubstituted carbonyl or a substituted or unsubstituted hydrocarbon.
58. The method of claim 57, wherein X is -C(O)-, -C(O)CH₂-, -CH₂-, or -CH₂CH₂-.
59. A method of forming a glycosyl bond, comprising:
providing a compound or composition of any of claims 22-43, wherein A is a saccharide containing a hydroxyl- or amino-functional group and A is attached through the hydroxyl- or amino-functional group;
providing a donor with a leaving group attached; and
transmitting light to release A,
wherein a glycosyl bond is formed to link A to the donor.
60. The method of claim 59, wherein the donor is a saccharide with a leaving group attached to its anomeric carbon.
61. An intramolecular method of forming a glycosan, comprising:
providing a compound or composition of any of claims 22-43 wherein A is a saccharide attached through a hydroxyl functional group and the saccharide contains a leaving group attached to its anomeric carbon; and
transmitting light to release A,
wherein a glycosyl bond is formed to link the hydroxyl functional group to the anomeric carbon.
62. The method of claim 61, wherein the hydroxyl functional group is a C-6 hydroxyl functional group.

63. A method of site-specifically attaching a biological molecule to a support surface, comprising:
- protecting one or more functional groups of a support surface with a compound of any of claims 1-14 to form a photo-activatable support surface;
 - selecting one or more of the protected functional groups for biological molecule attachment;
 - photomasking the non-selected functional groups;
 - irradiating the photo-activatable support surface to deprotect the one or more selected functional groups; and
 - covalently attaching a biological molecule containing compound to the one or more selected functional groups.
64. The method of claim 63, wherein the biological molecule is a carbohydrate.
65. The method of claim 63, wherein the functional group is an amino group.
66. The method of claim 63, wherein the functional group is a carbonyl group.
67. The method of claim 63, wherein the photomasking is performed by photolithography.