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(54) Title: COMPOUNDS WITH CLEAVABLE CROSSLINKING INDUCING GROUPS AND POYLMER NETWORKS DERIVED THEREOF

(57) Abstract: The invention relates to a synthetic compound comprising (a.) one or more crosslinkable groups and one or more cleavable groups, (b.) wherein at least one crosslinkable group forms a covalent bond with a C-H group by a C,H insertion reaction upon an external stimulation, (c.) wherein at least one crosslinkable group is covalently bound to at least one cleavable group, and (d.) wherein a covalent bond of the cleavable group is cleavable upon an external stimulation. The invention further relates to an oligomer composite comprising the synthetic compound, a method for producing said oligomer composite and a method for cleaving said oligomer composite.

COMPOUNDS WITH CLEAVABLE CROSSLINKING INDUCING GROUPS AND POYLMER NETWORKS DERIVED THEREOF

DESCRIPTION

The invention is in the field of chemistry, in particular in the field of synthetic crosslinkable compounds and oligomeric networks.

The invention relates to a synthetic compound comprising (a.) one or more crosslinkable groups and one or more cleavable groups, (b.) wherein at least one crosslinkable group forms a covalent bond with a C-H group by a C,H insertion reaction upon an external stimulation, (c.) wherein at least one crosslinkable group is covalently bound to at least one cleavable group, and (d.) wherein a covalent bond of the cleavable group is cleavable upon an external stimulation.

The invention further relates to an oligomer composite comprising the synthetic compound, a method for producing said oligomer composite and a method for cleaving said oligomer composite.

BACKGRUND OF THE INVENTION

Artificial networks, such as polymer networks, in which all polymer chains of the network are covalently linked, have the advantage over non-crosslinked polymers that they are solvent-resistant, have a higher mechanical stability and are non-deformable (such as duroplasts) or be deformed in a reversible manner(such as elastomers or rubbers), swellable and non-meltable. Polymer networks can be obtained either by cross-linking *in-situ* polymerization or by polymer-analogue linking of polymer chains via reactive groups in the side chains of the polymers. To achieve sufficient reactivity and speed of the crosslinking process, usually crosslinking of the polymer chains in solution or melt is necessary to form a network.

If such polymer networks are formed, the resulting structures can usually not be cleaved, dissolved and re-formed in a reversible manner. In this respect, the materials of such polymer networks are only recyclable to a very limited extent and can for example not be reused after damage. Further, particles or biological cells bound to such polymer networks can often only be released under harsh conditions. In many of these release processes, the cells are damaged. Furthermore, it is also difficult to vary or change the crosslinking properties of these polymer networks, e.g. to modify the mechanical properties of the network, to remodel the network or to release biological molecules or cells from the polymer network, while retaining the general properties of the polymer network.

Polymer networks are usually produced by *in-situ* polymerization using a mixture of mono- and bifunctional monomers. Polymer chains are built up and crosslinked in one process, thereby forming a covalent polymer network. However, the structure of the synthesis product cannot be further adjusted, and its characteristics cannot be changed after the *in situ* polymerization process in a controlled manner. If cleavable groups such as thiol groups are incorporated into the polymer network during *in-situ* polymerization, the polymer networks can subsequently be

cleaved and dissolved using specific stimuli. However, if such polymer networks are cleaved and dissolved, usually the entire polymer network structure is destroyed, and reutilization and recycling of the polymer network is not possible.

A further disadvantage of such covalent polymer networks produced by *in situ* polymerization is that this type of polymerization and network formation is subject to several process-related restrictions with regard to general processing and applicability, as a monomeric liquid is polymerized. However, monomers are generally categorized as hazardous substances and the processing of these substances is restricted to chemical laboratories.

If single polymers chains are crosslinked after synthesis by using low-molecular agents to form a polymeric network, sufficient mobility of the polymer chains must be ensured for the cross-linking process to be effective. For this purpose, the polymers must be transferred either into a melt or into a solution, rendering such crosslinking for example for the formation of thin layers difficult, especially on non-planar surfaces to be coated.

Several approaches for the formation of crosslinked polymer networks by the above-mentioned methods are disclosed in the prior art. WO/2013/163655A1 and CN112778548 disclose the synthesis of crosslinkable polyesters comprising thiol-groups and/or ester groups, which can subsequently be crosslinked, e.g., by thermal or oxidative treatment, thereby forming disulfide-linkages or by addition of catalysts such as metal or organic base catalysts for crosslinking of the ester groups by a transesterification reaction. The disulfide linkages or crosslinked ester groups of the polymer network formed can be cleaved such as by the addition of dithiotreithol (DTT) or under mechanical or high temperature conditions.

EP1970400A1, WO/2022/080408A1, US20120232027, EP3808786A1, US 8367051 and WO/2010/128007A1 disclose hydrophilic polymers, hydrogels, microbeads and polymer networks crosslinked by disulfide bonds synthesized by *in situ* polymerization or by subsequent crosslinking after polymer synthesis. These disulfide bonds can for example be cleaved in biological environment. EP2111872A2 discloses a polymeric prodrug, wherein a therapeutic agent is covalently bound to a polymer backbone by a crosslinker, which is cleavable by biological stimuli. US20060003900 discloses the use of boronic acids as crosslinking agents for the formation of a crosslinked gelling agent for increasing the viscosity of a fluid.

However, these approaches are limited to crosslinking of very specific functional groups such as thiol and/or ester groups and subsequent cleavage of these groups by specific agents and stimuli and are thus not universally applicable for different polymer networks. Further, these polymer networks and their properties, such as mechanical properties or the release of a cell or therapeutic agent are not adjustable in a controlled manner as the entire polymer network structure is either crosslinked or cleaved.

Polymers comprising crosslinkable groups, which enable crosslinking via C-H insertion reactions (CHic reaction) allow polymer network formation with a variety of polymers comprising C-H groups. These crosslinkable groups are usually photochemically or thermally activated. Materials obtained by the CHic process are suitable for coatings, as the surface layer thickness is easily scalable, and the reaction allows the production of objects of arbitrary size and shape.

WO/2019/106047A1, WO/2023/277333A1, US11591461B2, WO/2001/092403, WO/2013/090396A1, WO2003040095 and Straub et al. ("CHicable" and "Clickable" Copolymers for Network Formation and Surface Modification", Langmuir 2021), Kost et al., ("Thermally Induced Cross-Linking of Polymers via C,H Insertion Cross-Linking (CHic) under Mild Conditions" J. Am. Chem. Soc. 2021) and Jung et al. ("Facile, scalable, and universal modification strategy of polyolefin utilizing noncatalytic C-H insertion capability of azide: Sulfonyl azide end-functionalized polystyrene to modify polyethylene", European Polymer Journal 2021) disclose the synthesis of various polymers and polymer networks using C-H insertion reactions. However, none of these documents discloses polymer networks that are cleavable in a controlled manner and thus adjustable in their properties and recyclable after network formation.

Thus, no polymers with cleavable and crosslinking groups are known in the prior art which can be used to form polymer networks from the glass state of such polymer.

Despite these technologies known in the prior art, there is the urgent need for improved or alternative means for the formation of covalent polymer networks, which are cleavable and adjustable in their properties in a time and spatially controlled manner and which are recyclable after cleavage. There is further the need for means for the formation of covalent polymer networks, which can be easily and safely be used for the formation of covalent polymer networks.

SUMMARY OF THE INVENTION

In light of the prior art the technical problem underlying the present invention is the provision of improved or alternative means for the formation of covalent oligomer or polymer networks that overcome the disadvantages of the prior art.

Another object of the present invention was the provision of improved or alternative means for the formation of covalent oligomer or polymer networks, which are responsive to one or more stimuli with regards to crosslinking thereby forming a covalent network and which are cleavable in a stimuli-responsive manner.

Another object of the present invention was the provision of improved or alternative means for the formation of covalent oligomer or polymer networks that can be crosslinked and cleaved and thus modulated in their chemical and mechanical properties in a timely and spatially controlled manner using a suitable external stimulus.

Another object of the present invention was the provision of improved or alternative means for the formation of covalent oligomer or polymer networks that are recyclable or reusable after cleavage.

Another object of the present invention was the provision of improved or alternative means that can be used for the formation of oligomer or polymer networks with different types of oligomers and polymers.

Another object of the present invention was the provision of improved or alternative means that allow the efficient formation of oligomer or polymer networks and that can be easily and safely

applied for the formation of oligomer or polymer networks without requiring specialized equipment or preprocessing of the polymer to be covalently crosslinked.

Another object of the present invention was the provision of improved or alternative means for the formation of covalent oligomer or polymer networks, which release biological molecules, cells and therapeutic agents in a controlled manner in response to one or more external stimuli.

These problems are solved by the features of the independent claims. Preferred embodiments of the present invention are provided by the dependent claims.

In one aspect the invention relates to a synthetic compound comprising

a. one or more crosslinkable groups and one or more cleavable groups,

b. wherein at least one crosslinkable group forms a covalent bond with a C-H group by a C,H insertion reaction upon an external stimulation,

c. wherein at least one crosslinkable group is covalently bound to at least one cleavable group, and

d. wherein a covalent bond of the cleavable group is cleavable upon an external stimulation.

The synthetic compounds of the present invention advantageously allow the effective and controlled formation of oligomer or polymer composites (also termed covalent oligomer or polymer networks), which are adjustable in their chemical and mechanical properties by temporally and spatially controlled formation of covalent bonds (crosslinking) and cleavage of covalent bonds in response to external stimuli such as thermal, light, mechanic, oxidative or biological stimuli.

The synthetic compounds of the present invention comprise (i) at least one functional group that allows covalent bond formation and thus crosslinking of the synthetic compound with a second synthetic compound or an oligomer or polymer via a C-H insertion reaction (Chic reaction) to form a covalent network and (ii) at least one functional group that is covalently linked to the CH-insertion group and cleavable by external stimuli. The synthetic compounds of the present invention thus comprise a “cleavable CH-insertion group” as exemplarily shown in Figure 1.

Synthetic compounds comprising such “cleavable CH-insertion groups” that crosslink via C-H insertion reactions (CHic reaction), allow effective and fast covalent network formation of the synthetic compound with a second synthetic compound, or oligomers and polymers in the solid state and glass state, thus not requiring specific reaction conditions or preprocessing of the synthetic compound, oligomers and polymers such as melting and dissolution.

The “cleavable CH-insertion groups” are advantageously activated by photochemical, thermal or mechanic stimuli, thus allowing simple and controllable crosslinking and covalent network formation by simple means. Further, the CHic reaction allows crosslinking of a variety of different oligomers polymers comprising C-H groups, such as thermoplastic polymers, and can thus be used for a variety of applications including without limitation surface coatings with controllable layer thickness, the formation of hydrogel networks and particles, the formation of porous materials, fibers and non-woven materials.

A further advantage of the CHic process is the possibility of covalently binding the polymer network to any surface comprising C-H groups in order to obtain a surface-bound network. In this way, for example, a hydrogel network covalently bound to a surface can be obtained. In addition, surface structuring (topographies) can be achieved easily, e.g. using photolithographic processes.

Advantageously, the crosslinking-inducing CH-insertion groups of the synthetic compounds of the present invention can also covalently immobilize functional molecules such as therapeutic agents, proteins, nucleic acids or dyes, or contribute to covalent bonding to organic surfaces

Due to the covalent linkage of the CH-insertion group to a cleavable group (thereby forming a "cleavable CH-insertion group"), crosslinkages formed within a covalent oligomer or polymer network can advantageously be cleaved in a timely and spatially controlled manner by using specific stimuli such as a change in pH, temperature, light exposure or oxidative state (Figure 2).

The incorporation of such "cleavable CH-insertion group" within the synthetic compounds of the present invention allows the chemical, mechanical and physical properties of the covalent network formed to be subsequently and reversibly adjusted in its structural properties in different ways, i.e., by increasing the degree of crosslinking and amount of covalent bonds within the network or by decreasing the degree of crosslinking by cleavage of covalent bonds within the network. By increasing or decreasing the degree of crosslinking, for example the mesh size, elasticity and swellability of the oligomer or polymer network can be adjusted. Further, the oligomer or polymer network formed can be subsequently modified in terms of topography or local properties, such as by photostructuring of specific network areas.

Further, functional molecules such as therapeutic agents may be easily covalently bound to the oligomer or polymer network by the "cleavable CH-insertion groups" and released from the network by applying a specific stimulus thereby cleaving the cleavable group.

Changing the cross-linking density of the network formed by the synthetic compounds of the present invention advantageously also allows cells, particles and/or molecules such as therapeutic agents to be captured and and released from the network in a timely and spatially controlled manner. For example, by increasing the crosslinking density of the network and thereby reducing the mesh size of the network cells, particles or molecules can be captured within the network. By decreasing the degree of crosslinking by controlled cleavage of "cleavable CH-insertion groups" of the network and thereby increasing the mesh size of the network the cells, particles or molecules captured are released from the network. By controlling the degree of cross-linking of the network in this way, cells, particles and molecules can be gently encapsulated and released from the network.

The synthetic compounds of the present invention and oligomer or polymer networks formed by these compounds thus advantageously can be used in a wide range of applications, including without limitation applications in the field of life sciences, pharmaceuticals and medical technology, the automotive industry, building engineering, mechanical engineering, tool engineering, microelectronics and optics.

Further, the covalent oligomer or polymer networks formed by the synthetic compounds of the present invention can advantageously be efficiently and simply converted into reprocessable and recyclable polymers by controlled cleavage of the “cleavable CH-insertion groups”. This allows for example reprocessing of the cleavage products by mixing with the synthetic compounds of the present invention and forming another oligomer or polymer network by crosslinking with the “cleavable CH-insertion group” of the synthetic compounds of the present invention. Further, by cleaving and dissolving the oligomer and polymer networks, the cleaved compounds of the network such as oligomers polymers can be fed back into standard recycling processes and reused.

To the knowledge of the inventors, no synthetic compounds with such “cleavable CH-insertion groups” combining C-H insertion crosslinkable groups directly with easily cleavable functional groups are known from the prior art. Further no such synthetic compounds are known from the prior art, which allow the formation of covalent oligomer or polymer networks and composites from the glass state of a polymer and which are adjustable in their structural, chemical, mechanical and physical properties in a timely and spatially controlled manner by simple means such as by thermal, light or mechanical external stimuli.

In one embodiment the external stimulation for forming a covalent bond of the one or more crosslinkable groups with a C-H group by a C, H insertion reaction is a thermal, a light and/or a mechanic stimulation.

Functional groups that allow covalent bond formation and thus crosslinking of the synthetic compound with a second synthetic compound or an oligomer or polymer via a C-H insertion reaction (CHic reaction) are particularly advantageous as such groups can in a simple and controlled manner be activated by external stimuli such as a thermal, light and/or mechanic stimulation. Such activation by thermal, a light and/or a mechanic stimulation can be carried out easily, without special equipment and at low costs such as by irradiation of the polymer network with a light source of a particular wavelength or heating of the network.

Furthermore, the crosslinking degree of the covalent network formed can be easily and precisely controlled by the type and amount of C-H insertion groups incorporated in the synthetic compound of the present invention and the external stimuli applied, e.g., the wavelength of the light source, the irradiation time and the area of the network irradiated.

In one embodiment the one or more crosslinkable groups are selected from the group consisting of an aromatic ketone such as benzophenone and anthraquinone, an azide such as sulfonyl azide, and a diazo ester group.

In one embodiment the diazo ester group is an alpha-diazo etser group.

In one embodiment the at least one crosslinkable group forms a covalent bond with a C-H group of a second synthetic compound according to the present invention, an oligomer and/or a polymer. In one embodiment the at least one crosslinkable group forms a covalent bond with a C-H group of the oligomer backbone or polymer backbone of a second synthetic compound according to the present invention.

In one embodiment the external stimulation for cleaving a covalent bond of the one or more cleavable groups is a change in temperature, pH value, light exposure, oxidative state and/or the presence of competing exchange reactants.

In one embodiment the external stimulation for cleaving a covalent bond of the one or more cleavable groups is a change in temperature, pH value, light exposure and/or the presence of competing exchange reactants, reductive reactants and/or oxidative reactants. In one embodiment the external stimulation for cleaving a covalent bond of the one or more cleavable groups is a change in temperature, pH value, light exposure and/or the presence of competing exchange reagents, reductive reagents and/or oxidative reagents.

In one embodiment the one or more cleavable groups are selected from the group consisting of a disulfide group, a broronic ester, an oxime, a hydrazine and a Diels-Alder pair.

Functional groups that can be cleaved by external stimuli such as in temperature, pH value, light exposure, oxidative state and/or the presence of competing exchange reactants are particularly advantageous, as cleavage by these stimuli can be easily and precisely controlled and carried out without special equipment or occurs in biological environment, thereby providing biologically responsive oligomer and polymer networks, such as networks releasing a therapeutic agent, protein, nucleic acid or antibody within a tissue of a subject upon a biological stimulus such as in inflamed or tumor tissue having a decreased pH value compared to other tissues.

The cleavage of the covalent network formed can thus easily and precisely controlled by the type and amount of cleavage groups incorporated in the synthetic compound of the present invention and the external stimuli applied, e.g., the pH value, the temperature applied, wavelength of the light applied or irradiation time.

In one embodiment the synthetic compound additionally comprises one or more functional groups selected from the group consisting of carboxyl, amine, alkyne, azide, sulfonate and maleimide.

In one embodiment the synthetic compound comprises at least two crosslinkable groups, wherein the at least two crosslinkable groups can be the same or different.

In one embodiment the synthetic compound comprises at least two cleavable groups, wherein the at least two cleavable groups can be the same or different.

In one embodiment the synthetic compound comprises at least two crosslinkable groups and at least two cleavable groups, wherein the at least two crosslinkable groups can be the same or different and the at least two cleavable groups can be the same or different.

The incorporation of two or more different crosslinkable groups and/or cleavable groups within the synthetic compounds of the present invention and the networks formed by these compounds advantageously allows to precisely adjust the crosslinking degree of the network by activation or cleavage of one or more of the crosslinkable and/or cleavable groups within the network, thereby allowing a versatile and precise adjustment of the structural, chemical, mechanical and physical properties of the network.

In one embodiment the synthetic compound additionally comprises an oligomer backbone and at least one crosslinkable group is covalently bound to the oligomer backbone by at least one cleavable group.

In one embodiment the synthetic compound additionally comprises a polymer backbone and at least one crosslinkable group is covalently bound to the polymer backbone by at least one cleavable group.

In one embodiment the synthetic compound additionally comprises an oligomer backbone or a polymer backbone and at least one crosslinkable group is covalently bound to the oligomer backbone or polymer backbone by at least one cleavable group.

In one embodiment the invention relates to an oligomer compound comprising

a. an oligomer backbone, one or more crosslinkable groups and one or more cleavable groups,

b. wherein at least one crosslinkable group forms a covalent bond with a C-H group by a C,H insertion reaction upon an external stimulation,

c. wherein at least one crosslinkable group is covalently bound to the oligomer backbone by at least one cleavable group, and

d. wherein a covalent bond of the cleavable group is cleavable upon an external stimulation.

In one embodiment the invention relates to an oligomer compound comprising

a. a polymer backbone, one or more crosslinkable groups and one or more cleavable groups,

b. wherein at least one crosslinkable group forms a covalent bond with a C-H group by a C,H insertion reaction upon an external stimulation,

c. wherein at least one crosslinkable group is covalently bound to the polymer backbone by at least one cleavable group, and

d. wherein a covalent bond of the cleavable group is cleavable upon an external stimulation.

In one embodiment the invention relates to an oligomer compound comprising

a. an oligomer backbone or a polymer backbone, one or more crosslinkable groups and one or more cleavable groups,

b. wherein at least one crosslinkable group forms a covalent bond with a C-H group by a C,H insertion reaction upon an external stimulation,

c. wherein at least one crosslinkable group is covalently bound to the oligomer backbone or polymer backbone by at least one cleavable group, and

d. wherein a covalent bond of the cleavable group is cleavable upon an external stimulation.

Synthetic compounds additionally comprising an oligomer backbone or polymer backbone with “cleavable C,H insertion groups” covalently bound to the backbone are particularly advantageous

for the formation of covalent oligomer or polymer networks (also termed composites such as oligomer or polymer composites) as such compounds can directly form an oligomer or polymer network by activating the C,H insertion groups of the synthetic compounds without the need for other types of oligomers or polymers. By activation of the C,H insertion group of one synthetic compound crosslinking occurs with the oligomer backbone or polymer backbone of a second molecule of the synthetic compound thereby forming a covalent network or composite structure. The synthetic compounds of the present invention comprising additionally an oligomer backbone or polymer backbone thus serve as precursor molecules for the formation of covalent oligomer or polymer networks and composites according to the present invention. Thereby, such covalent network or composite can advantageously be formed in the glass state as well as in the swollen state of the synthetic compound by activation of the C,H insertion group by external stimuli such as thermal, light or mechanical stimulation requiring no addition of further reagents.

Advantageously, the synthetic compounds of the present invention comprising additionally an oligomer backbone or polymer backbone thus allow the formation of oligomer or polymer networks or composites that comprise solely the synthetic compounds of the present invention, but also allow the formation of such networks and composites that comprise other types of oligomers or polymers by crosslinking these oligomers or polymers by the synthetic compounds of the present invention.

In one embodiment the oligomer or polymer networks or composites of the present invention comprise in essence one or more covalently linked synthetic compounds of the present invention. Herein, in essence comprising one or more synthetic compounds of the present invention refers to the composite comprising 90 mol%, preferably 95 mol%, more preferably 99 mol% covalently linked synthetic compounds of the present invention of the total oligomers or polymers covalently linked in the network or composite.

Further, the synthetic compounds of the present invention comprising an oligomer backbone or polymer backbone can advantageously be efficiently synthesized by oligomerizing or polymerizing monomers comprising a crosslink-inducing group covalently linked to a cleavable group. After oligomerization or polymerization the compounds of the present invention can be easily and safely used for the formation of a covalent oligomer or polymer network or composite according to the present invention.

In one embodiment the oligomer backbone is a homooligomer or a cooligomer. In one embodiment the oligomer backbone is a homooligomer backbone or a cooligomer backbone.

In one embodiment the oligomer backbone is an unbranched oligomer backbone. In one embodiment the oligomer backbone is an unbranched oligomer.

In one embodiment the polymer backbone is a homopolymer or a copolymer. In one embodiment the polymer backbone is a homopolymer backbone or a copolymer backbone. In one embodiment the polymer backbone is an unbranched polymer backbone. In one embodiment the polymer backbone is an unbranched polymer.

In one embodiment the oligomer backbone has a degree of polymerization of 2 to 50, preferably 2 to 20, more preferably 2 to 20. In one embodiment the oligomer backbone has a degree of

polymerization of 2 to 50, such as 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34,35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or50..

In one embodiment the polymer backbone has a degree of polymerization of 20 to 1000, preferably 50 to 700, more preferably 100 to 500. In one embodiment the polymer backbone has a degree of polymerization of 20 to 1000, such 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, 250, 300, 350, 300, 350, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950 or 1000.

In one embodiment the polymer backbone has a degree of polymerization of at least 20, preferably at least 50, more preferably at least 100.

In one embodiment the synthetic compound comprises two or more crosslinkable groups covalently linked by a cleavable group, wherein the two or more crosslinkable groups may be the same or different.

In one aspect the invention relates to a composite comprising at least one synthetic compound according to the invention, wherein at least one crosslinkable group of the synthetic compound is covalently bound to an oligomer and/or polymer.

In one aspect the invention relates to an oligomer composite comprising at least one synthetic compound according to the invention, wherein at least one crosslinkable group of the synthetic compound is covalently bound to an oligomer and/or polymer. In one aspect the invention relates to a polymer composite comprising at least one synthetic compound according to the invention, wherein at least one crosslinkable group of the synthetic compound is covalently bound to an oligomer and/or polymer. In one aspect the invention relates to an oligomer or polymer composite comprising at least one synthetic compound according to the invention, wherein at least one crosslinkable group of the synthetic compound is covalently bound to an oligomer and/or polymer.

Herein the terms “composite”, “network”, “covalent network” and “covalent composite” may be used interchangeably. In one embodiment the invention thus relates to an oligomer network or polymer network comprising at least one synthetic compound according to the invention, wherein at least one crosslinkable group of the synthetic compound is covalently bound to an oligomer and/or polymer. In one embodiment the invention relates to a covalent oligomer or polymer composite comprising at least one synthetic compound according to the invention, wherein at least one crosslinkable group of the synthetic compound is covalently bound to an oligomer and/or polymer. In one embodiment the invention relates to a covalent oligomer or polymer network comprising at least one synthetic compound according to the invention, wherein at least one crosslinkable group of the synthetic compound is covalently bound to an oligomer and/or polymer.

In one embodiment the invention relates to a composite comprising at least one synthetic compound according to the invention, wherein at least one crosslinkable group of the synthetic compound is covalently bound to an oligomer and/or polymer, wherein the oligomer and/or polymer is a second synthetic compound according to the present invention comprising an oligomer backbone or a polymer backbone and/or a different oligomer or polymer. In one

embodiment the invention relates to an oligomer composite comprising at least one synthetic compound according to the invention, wherein at least one crosslinkable group of the synthetic compound is covalently bound to an oligomer, wherein the oligomer is a second synthetic compound according to the present invention comprising an oligomer backbone and/or a different oligomer. In one embodiment the invention relates to a polymer composite comprising at least one synthetic compound according to the invention, wherein at least one crosslinkable group of the synthetic compound is covalently bound to a polymer, wherein the polymer is a second synthetic compound according to the present invention comprising a polymer backbone and/or a different polymer.

In one embodiment the oligomer composite comprises at least one oligomer compound according to the present invention, wherein at least one crosslinkable group of the oligomer compound is covalently bound to an oligomer.

In one embodiment the oligomer composite comprises at least one oligomer compound according to the present invention, wherein at least one crosslinkable group of the oligomer compound is covalently bound to an oligomer, wherein the oligomer is a second oligomer compound according to the invention and/or a different oligomer.

In one embodiment the oligomer and/or polymer is selected from the group consisting of a thermoplastic oligomer or polymer, and a natural oligomer or polymer such as cellulose, lignin, alginate, collagen, gelatin, silk fibroin and starch. In one embodiment the oligomer is selected from the group consisting of a thermoplastic oligomer and natural oligomer such as cellulose, lignin, alginate, collagen, gelatin, silk fibroin and starch. In one embodiment the polymer is selected from the group consisting of a thermoplastic polymer and natural polymer such as cellulose, lignin, alginate, collagen, gelatin, silk fibroin and starch.

In one embodiment the oligomer and/or polymer is selected from the group consisting of a thermoplastic oligomer or polymer such as polyethylene (PE), polycarbonate (PC), polystyrene (PS), polyvinylchloride (PVC), polyamide (PA), Poly Acrylonitrile butadiene styrene (ABS), polypropylene (PP) and polyethylene terephthalate (PET), and natural oligomer or polymer such as cellulose, lignin, alginate, collagen, gelatin, silk fibroin and starch. In one embodiment the oligomer is selected from the group consisting of a thermoplastic oligomer such as polyethylene (PE), polycarbonate (PC), polystyrene (PS), polyvinylchloride (PVC), polyamide (PA), Poly Acrylonitrile butadiene styrene (ABS), polypropylene (PP) and polyethylene terephthalate (PET), and natural oligomer such as cellulose, lignin, alginate, collagen, gelatin, silk fibroin and starch. In one embodiment the polymer is selected from the group consisting of a polymer such as polyethylene (PE), polycarbonate (PC), polystyrene (PS), polyvinylchloride (PVC), polyamide (PA), Poly Acrylonitrile butadiene styrene (ABS), polypropylene (PP) and polyethylene terephthalate (PET), and natural polymer such as cellulose, lignin, alginate, collagen, gelatin, silk fibroin and starch.

In one embodiment the oligomer and/or polymer is selected from the group consisting of a second synthetic compound according to the invention comprising an oligomer backbone or polymer backbone, a thermoplastic oligomer or polymer, and a natural oligomer or polymer such as cellulose, lignin, alginate, collagen, gelatin, silk fibroin and starch. In one embodiment the

oligomer is selected from the group consisting of a synthetic compound according to the present invention comprising an oligomer backbone, a thermoplastic oligomer and natural oligomer such as cellulose, lignin, alginate, collagen, gelatin, silk fibroin and starch. In one embodiment the polymer is selected from the group consisting of a second synthetic compound according to the invention comprising a polymer backbone, a thermoplastic polymer, and a natural polymer such as cellulose, lignin, alginate, collagen, gelatin, silk fibroin and starch.

In one embodiment the oligomer and/or polymer is selected from the group consisting of a synthetic compound according to the present invention comprising an oligomer backbone or a polymer backbone, a thermoplastic oligomer or polymer such as polyethylene (PE), polycarbonate (PC), polystyrene (PS), polyvinylchloride (PVC), polyamide (PA), Poly acrylonitrile butadiene styrene (ABS), polypropylene (PP) and polyethylene terephthalate (PET), and natural oligomer or polymer such as cellulose, lignin, alginate, collagen, gelatin, silk fibroin and starch.In one embodiment the oligomer is selected from the group consisting of a synthetic compound according to the present invention comprising an oligomer backbone, a thermoplastic oligomer such as polyethylene (PE), polycarbonate (PC), polystyrene (PS), polyvinylchloride (PVC), polyamide (PA), Poly acrylonitrile butadiene styrene (ABS), polypropylene (PP) and polyethylene terephthalate (PET), and natural oligomer such as cellulose, lignin, alginate, collagen, gelatin, silk fibroin and starch. In one embodiment the polymer is selected from the group consisting of a synthetic compound according to the present invention comprising a polymer backbone, a thermoplastic polymer such as polyethylene (PE), polycarbonate (PC), polystyrene (PS), polyvinylchloride (PVC), polyamide (PA), Poly acrylonitrile butadiene styrene (ABS), polypropylene (PP) and polyethylene terephthalate (PET), and natural polymer such as cellulose, lignin, alginate, collagen, gelatin, silk fibroin and starch.

In one embodiment the different oligomer or polymer is selected from the group consisting of a thermoplastic oligomer or polymer and a natural oligomer or polymer such as cellulose, lignin, alginate, collagen, gelatin, silk fibroin and starch. In one embodiment the different oligomer is selected from the group consisting of a thermoplastic oligomer and a natural oligomer such as cellulose, lignin, alginate, collagen, gelatin, silk fibroin and starch. In one embodiment the different polymer is selected from the group consisting of a thermoplastic polymer and a natural polymer such as cellulose, lignin, alginate, collagen, gelatin, silk fibroin and starch.

In one embodiment the different oligomer or polymer is selected from the group consisting of a thermoplastic oligomer or polymer such as polyethylene (PE), polycarbonate (PC), polystyrene (PS), polyvinylchloride (PVC), polyamide (PA), Polyacrylonitrile butadiene styrene (ABS), polypropylene (PP) and polyethylene terephthalate (PET), and natural oligomer or polymer such as cellulose, lignin, alginate, collagen, gelatin, silk fibroin and starch. In one embodiment the different oligomer is selected from the group consisting of a thermoplastic oligomer such as polyethylene (PE), polycarbonate (PC), polystyrene (PS), polyvinylchloride (PVC), polyamide (PA), Polyacrylonitrile butadiene styrene (ABS), polypropylene (PP) and polyethylene terephthalate (PET), and natural oligomer such as cellulose, lignin, alginate, collagen, gelatin, silk fibroin and starch. In one embodiment the different polymer is selected from the group consisting of a thermoplastic polymer such as polyethylene (PE), polycarbonate (PC), polystyrene (PS), polyvinylchloride (PVC), polyamide (PA), Polyacrylonitrile butadiene styrene (ABS),

polypropylene (PP) and polyethylene terephthalate (PET), and natural polymer such as cellulose, lignin, alginate, collagen, gelatin, silk fibroin and starch.

In one embodiment the composite additionally comprises one or more affinity molecules. In one embodiment the oligomer composite additionally comprises one or more affinity molecules. In one embodiment the oligomer or polymer composite additionally comprises one or more affinity molecules.

In one embodiment the composite additionally comprises one or more affinity molecules, wherein the affinity molecules are covalently bound to the oligomer composite and preferably selected from the group consisting of an antibody or a fragment thereof, a peptide, a protein, a nucleic acid and a receptor-like molecule. In one embodiment the oligomer composite additionally comprises one or more affinity molecules, wherein the affinity molecules are covalently bound to the oligomer composite and preferably selected from the group consisting of an antibody or a fragment thereof, a peptide, a protein, a nucleic acid and a receptor-like molecule. In one embodiment the oligomer or polymer composite additionally comprises one or more affinity molecules, wherein the affinity molecules are covalently bound to the oligomer composite and preferably selected from the group consisting of an antibody or a fragment thereof, a peptide, a protein, a nucleic acid and a receptor-like molecule.

In one embodiment the invention relates to a composite comprising a synthetic compound according to the invention and a two or more oligomers and/or polymers,

a. wherein the synthetic compound according to the invention comprises two crosslinkable groups covalently linked by a cleavable group, wherein the two crosslinkable groups are the same or different, and
b. wherein each of the crosslinkable groups forms a covalent bond with a C-H group of one of the two oligomers and/or polymers upon an external stimulation.

In one embodiment the invention relates to an oligomer or polymer composite comprising a synthetic compound according to the invention and a two or more oligomers and/or polymers,

a. wherein the synthetic compound according to the invention comprises two crosslinkable groups covalently linked by a cleavable group, wherein the two crosslinkable groups are the same or different, and

wherein each of the crosslinkable groups forms a covalent bond with a C-H group of one of the two oligomers and/or polymers upon an external stimulation. In one aspect the invention relates to a method of producing a composite according to the present invention, comprising

a. providing a synthetic compound according to the invention, the synthetic compound comprising one or more crosslinkable groups and one or more cleavable groups,
b. providing at least one oligomer and/or polymer, and
c. initiating a C,H insertion reaction of at least one crosslinkable group of the synthetic compound with the at least one oligomer, wherein a covalent bond between the synthetic compound and the at least one oligomer and/or polymer is formed.

In one aspect the invention relates to a method of producing an oligomer or polymer composite according to the present invention, comprising

a. providing a synthetic compound according to the invention, the synthetic compound comprising one or more crosslinkable groups and one or more cleavable groups,

b. providing at least one oligomer and/or polymer, and

c. initiating a C,H insertion reaction of at least one crosslinkable group of the synthetic compound with the at least one oligomer, wherein a covalent bond between the synthetic compound and the at least one oligomer and/or polymer is formed.

In one embodiment (a.) the synthetic compound and (b.) the at least one oligomer and/or polymer are mixed prior to (c.) initiating a C,H insertion reaction.

In one embodiment (a.) the synthetic compound and (b.) the at least one oligomer are mixed prior to (c.) initiating a C,H insertion reaction.

In one embodiment the invention relates to a method of producing a composite according to the present invention, comprising

a. providing a synthetic compound according to the invention, the synthetic compound comprising one or more crosslinkable groups and one or more cleavable groups,

b. providing at least one oligomer and/or polymer, wherein the at least one oligomer and/or polymer is selected from the group consisting of a second synthetic compound according to the invention comprising an oligomer backbone or a polymer backbone and/or a different oligomer or polymer, and

c. initiating a C,H insertion reaction of at least one crosslinkable group of the synthetic compound with the at least one oligomer, wherein a covalent bond between the synthetic compound and the at least one oligomer and/or polymer is formed.

In one embodiment the invention relates to a method of producing an oligomer or polymer composite according to the present invention, comprising

a. providing a synthetic compound according to the invention, the synthetic compound comprising one or more crosslinkable groups and one or more cleavable groups,

b. providing at least one oligomer and/or polymer, wherein the at least one oligomer and/or polymer is selected from the group consisting of a second synthetic compound according to the invention comprising an oligomer backbone or a polymer backbone and/or a different oligomer or polymer, and

c. initiating a C,H insertion reaction of at least one crosslinkable group of the synthetic compound with the at least one oligomer, wherein a covalent bond between the synthetic compound and the at least one oligomer and/or polymer is formed.

In one embodiment (a.) the synthetic compound and (b.) the at least one oligomer and/or polymer are mixed prior to (c.) initiating a C,H insertion reaction.

In one embodiment (a.) the synthetic compound and (b.) the at least one oligomer are mixed prior to (c.) initiating a C,H insertion reaction.

In one embodiment the invention relates to a method of producing an oligomer composite according to the present invention, comprising

a. providing an oligomer compound according to the invention, the oligomer compound comprising one or more crosslinkable groups and one or more cleavable groups,

b. providing at least one oligomer, and

c. initiating a C,H insertion reaction of at least one crosslinkable group of the oligomer compound with the at least one oligomer, wherein a covalent bond between the oligomer compound and the at least one oligomer is formed.

In one embodiment the invention relates to a method of producing an oligomer composite according to the present invention, comprising

a. providing an oligomer compound according to the invention, the oligomer compound comprising one or more crosslinkable groups and one or more cleavable groups,

b. providing at least one oligomer, wherein the at least one oligomer is selected from the group consisting of a second oligomer compound according to the invention and/or a different oligomer, and

c. initiating a C,H insertion reaction of at least one crosslinkable group of the oligomer compound with the at least one oligomer, wherein a covalent bond between the oligomer compound and the at least one oligomer is formed.

In one embodiment (a.) the oligomer compound and (b.) the at least one oligomer are mixed prior to (c.) initiating a C,H insertion reaction.

In one embodiment the C,H insertion reaction is initiated by thermal, light and/or mechanic stimulation.

In one aspect the invention relates to a method of cleaving a composite according to the invention, the method comprising

a. providing a composite according to the present invention,

b. initiating a cleavage of at least one covalent bond of a cleavable group of the composite by a change in temperature, pH value, light exposure, oxidative state and/or the presence of competing exchange reactants.

In one aspect the invention relates to a method of cleaving an oligomer or polymer composite according to the invention, the method comprising

a. providing an oligomer or polymer composite according to the present invention,

b. initiating a cleavage of at least one covalent bond of a cleavable group of the oligomer or polymer composite by a change in temperature, pH value, light exposure, oxidative state and/or the presence of competing exchange reactants.

In one aspect the invention relates to an oligomer or polymer compound comprising

e. an oligomer backbone or polymer backbone, one or more crosslinkable groups and one or more cleavable groups,

f. wherein at least one crosslinkable group forms a covalent bond with a C-H group by a C,H insertion reaction upon an external stimulation,

g. wherein at least one crosslinkable group is covalently bound to the oligomer backbone or polymer backbone by at least one cleavable group, and

h. wherein a covalent bond of the cleavable group is cleavable upon an external stimulation.

In one aspect the invention relates to an oligomer compound comprising

a. an oligomer backbone, one or more crosslinkable groups and one or more cleavable groups,

b. wherein at least one crosslinkable group forms a covalent bond with a C-H group by a C,H insertion reaction upon an external stimulation,

c. wherein at least one crosslinkable group is covalently bound to the oligomer backbone by at least one cleavable group, and

d. wherein a covalent bond of the cleavable group is cleavable upon an external stimulation.

In one aspect the invention relates to a polymer compound comprising

a. a polymer backbone, one or more crosslinkable groups and one or more cleavable groups,

b. wherein at least one crosslinkable group forms a covalent bond with a C-H group by a C,H insertion reaction upon an external stimulation,

c. wherein at least one crosslinkable group is covalently bound to the polymer backbone by at least one cleavable group, and

d. wherein a covalent bond of the cleavable group is cleavable upon an external stimulation.

Further embodiments of the invention:

In one embodiment the invention relates to a copolymerized monomer component comprising a copolymeric unbranched structure having at least one C,H-insertion Crosslinker that can be same or different and at least one cleavable group, wherein the cleavable group connects the C,H-insertion crosslinker with the unbranched (linear) backbone of the copolymeric structure.

In one embodiment the cleavable group is selected from the group comprising disulfide groups, boronic acids, Diels Alder pairs, oximes, imines and hydrazones.

In one embodiment the cleavable group is cleavable by adjusting temperature, pH value, light exposure and/or oxidative state, or by presenting competitive exchange reactants.

In one embodiment the copolymeric component comprises at least two C,H-insertion crosslinker and at least two cleavable groups, wherein the at least two cleavable groups connect the at least

two C,H-insertion crosslinker with the backbone of the copolymeric component, wherein the cleavable groups can be the same or different and wherein the C,H-insertion crosslinker can be the same or different.

In one embodiment the C,H-insertion crosslinker acts as a molecule that induces network formation and is selected from the group comprising (1) aromatic ketones, for example, benzophenone and anthraquinones, which upon activation form ketyl biradicals, (2) azides, for example, sulfonyl azides, which form nitrenes, and (3) diazo groups, which form carbenes.

In one embodiment the C,H-insertion crosslinker is thermo reactive and/or photoreactive and/or mechano-reactive.

In one embodiment the copolymeric component comprises additionally functional groups, preferred selected from the groups comprising carboxyl groups, amine groups, alkynes, azides and maleimide groups.

In one embodiment the cleavable group can be at least partially inactivated by light.

In one embodiment the invention relates to a polymer material or polymer composite or polymer network comprising at least one co-polymeric component according to at least one of the preceding embodiment, wherein the co-polymeric component is bound to at least one polymer chain of the polymer material or polymer composite or polymer network via the C,H-insertion crosslinker to crosslink the material or composite or network at least partially.

In one embodiment the at least partially crosslinked polymer material or polymer composite or polymer network can be at least partially broken up by cleaving the cleavable group.

In one embodiment at least some of the polymer chains are thermoplastic polymers or non-crosslinked plastics including naturally occurring polymers such as cellulose.

In one embodiment the polymer material or polymer composite or polymer network further comprises covalently bound affinity molecules, preferably bio-affinity molecules such as antibodies, peptides, nucleotides or receptor-like molecules.

In one embodiment the invention relates to a polymer material or polymer composite or polymer network that can be structured, preferably micro-structured by at least some of the cleavable groups.

In one embodiment the invention relates to a method of producing a polymer material or polymer composite or polymer network comprising

a. providing at least one copolymeric component according to the invention,

b. providing at least two polymer chains, and

c. initiation of C,H-insertion reactions to connect the copolymeric component with the polymer chains via the C,H-insertion crosslinker.

In one embodiment the CH insertion is initiated via light and/or temperature and/or mechanical stimulation.

In one embodiment the invention relates to a method of cleaving a polymer material or polymer composite or polymer network, comprising

a. Providing a polymer material or polymer composite or polymer network according to the invention, and

b. Cleaving of the cleavable groups at least partially.

In one embodiment cleaving of the cleavable groups is activated by light, temperature, pH value and/or oxidative state, or by presenting competitive ex-change reactants.

All features described in the present specification may be employed to define any other embodiment or aspect of the invention. For example, features used to describe the method may be used to describe the synthetic compounds and oligomer composite or oligomer network, and vice versa.

DETAILED DESCRIPTION

The invention relates broadly to a synthetic compound comprising one or more crosslinkable C,H insertion groups and one or more cleavable groups, wherein at least one crosslinkable group is covalently bound to at least one cleavable group. The invention further relates to covalent oligomer composites formed by these compounds and methods for producing and cleaving these composites. The compounds, composites and methods may comprise multiple further features and steps, each of which may be used to define the invention, without necessary limitation to all other features or method steps disclosed herein.

The synthetic compound comprises one or more crosslinkable groups forming a covalent bond with a C-H group by a C,H insertion reaction upon an external stimulation. A skilled person is aware of such crosslinkable groups and external stimuli in the context of C,H insertion reactions. Suitable non-limiting examples for such groups and external stimuli are disclosed herein.

The synthetic compound further comprises one or more cleavable groups, wherein a covalent bond of the cleavable group is cleavable upon an external stimulation. A skilled person is aware of such cleavable groups and external stimuli. Suitable non-limiting examples for such groups and external stimuli are disclosed herein.

General terms:

All words and terms used herein shall have the same meaning commonly given to them by the person skilled in the art unless the context indicates a different meaning. All terms used in the singular shall include the plural of that term and vice versa.

The use of the word "a" or "an" when used in conjunction with the term "comprising" in the claims and/or the specification may mean "one," but it is also consistent with the meaning of "one or more", "at least one", and "one or more than one". The term "or" in the claims is used to mean "and/or" unless explicitly indicated to refer to alternatives only or the alternatives are mutually exclusive. However, the disclosure supports a definition of only alternatives and "and/or".

Synthetic compounds and oligomer composites:

The term “synthetic compound” refers to a chemically synthesized or modified molecule that is artificially created by chemical synthesis or chemical modification of a naturally occurring substance, such as by incorporation of an additional functional group into the naturally occurring molecule. In one embodiment the term preferably refers to small molecules, oligomers or polymers comprising at least one crosslinkable group and at least one cleavable group covalently linked to the crosslinkable group.

The term “crosslinking” refers to the formation of covalent bonds between two or more molecules, resulting in a three-dimensional network or composite structure also termed “oligomer composite” or “polymer composite”. In a preferred embodiment crosslinking refers to the formation of covalent bonds between two or more molecules such as between a synthetic compound according to the present invention an oligomer or two synthetic compounds of the present invention. Crosslinking and in particular the degree of crosslinking alters the structural, chemical, mechanical and physical properties of the molecules and the network or composite formed. For example, a network formed may have a particular mesh size or pore size. In one embodiment the mesh size or pore size of the network or composite may be increased by reducing the degree of crosslinking. In one embodiment the mesh size or pore size of the network or composite may be reduced by increasing the degree of crosslinking. Further, the crosslinked network or composite such as an oligomer or polymer network or composite according to the present invention may without limitation have an altered swellability, hydrophobicity, mechanical strength, translucency, chemical resistance to specific chemical agents such as acids, oxidative agents and/or bases and/or flexibility compared to a non-crossliked molecule such as a synthetic compound according to the present invention, an oligomer or a polymer.

The “degree of crosslinking” in the context of the present invention refers to the extent to which the molecules of a network or composite such as oligomer or polymer chains are interconnected through covalent crosslinking bonds. The degree of crosslinking quantifies the density or concentration of such bonds (crosslinks) within network or composite. A higher degree of crosslinking indicates a greater number of crosslinks per unit volume or weight of the overall network or composite. A person skilled in the art is aware of methods for determining the degree of crosslinking of an oligomer or polymer network or composite. Such methods may include measurement of the degree of crosslinking by swelling tests. The crosslinked sample such as the network or composite is placed into a good solvent at a specific temperature, and either the change in mass or the change in volume is measured. The higher the number of crosslinks, the less swelling is attainable. Based on the degree of swelling, the Flory Interaction Parameter (which relates the solvent interaction with the sample), and the density of the solvent, the theoretical degree of crosslinking can be calculated according to Flory's Network Theory.

The term “crosslinkable group” also termed “crosslinkable functional group” or “crosslinking group” according to the present invention refers to a functional group of a chemical compound or molecule such as the synthetic compound of the present invention, which may form a covalent bond with another molecule or with the molecule it is comprised in, thereby forming a covalent network or composite. In one embodiment a crosslinkable group according to the present invention forms a covalent bond upon activation, preferably thermal, light or mechanic stimulation. In one embodiment a crosslinkable group according to the present invention forms a covalent bond with another molecule or within the molecule it is comprised in by a C,H insertion reaction

upon external stimulation, preferably upon thermal, light or mechanic stimulation. Such crosslinkable group that forms a covalent bond with another molecule or within the molecule it is comprised in by a C,H insertion reaction upon external stimulation is termed “C,H insertion group”. Examples of such “crosslinkable groups” by a C,H insertion reaction include without limitation an aromatic ketone such as benzophenone and anthraquinone, an azide such as sulfonyl azide and a diazo ester group.

The term C,H insertion reaction, also known as a carbon-hydrogen insertion reaction, refers to a chemical reaction in which a carbon atom (C) of a reagent such as of a crosslinkable group of the synthetic compound according to the present invention is inserted into a carbon-hydrogen (C-H) bond of a molecule such as of an oligomer or a polymer, thereby breaking the C-H bond and forming a new carbon-carbon (C-C) bond between the reagent and the organic molecule. This type of reaction advantageously allows for the direct functionalization of C-H bonds, which are typically considered inert and challenging to activate and is applicable to a wide range of organic compounds comprising C-H bonds. Examples for the synthesis of molecules by C,H insertion reaction are disclosed in Straub et al. ("CHicable" and "Clickable" Copolymers for Network Formation and Surface Modification”, Langmuir 2021), Kost et al., (“Thermally Induced Cross-Linking of Polymers via C,H Insertion Cross-Linking (CHic) under Mild Conditions” J. Am. Chem. Soc. 2021) and Jung et al. (“Facile, scalable, and universal modification strategy of polyolefin utilizing noncatalytic C-H insertion capability of azide: Sulfonyl azide end-functionalized polystyrene to modify polyethylene”, European Polymer Journal 2021).

C,H insertion reactions typically require reagents that possess specific functional groups capable of facilitating the insertion of a carbon atom into a C-H bond upon activation such as by external stimuli, for example thermal, light or mechanical stimuli. Functional groups that form a covalent bond by a C,H insertion reaction upon external stimulation include without limitation a diazo group (-C=N=N), an azide such as azide ($-N_3$) a sulfonyl azide ($-SO_2N_3$), an aromatic ketone such as benzophenone and anthraquinone and an iodonium ylide.

A diazo ester group, such as an alpha-diazo ester group can for example be activated for an C,H insertion reaction by external thermal, mechanical and/or light stimulation. Activation by a thermal stimulus also termed thermal stimulation comprises applying an increased temperature resulting in decomposition of the diazo ester group thereby forming a carbene group which reacts with the C-H group of a molecule such as an oligomer or a polymer. In one embodiment thermal stimulation of an diazo ester group comprises applying a temperature of 50 to 200 °C, preferably 60 to 180, more preferably 60 to 150 °C, such as 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195 or 200 °C. . In one embodiment thermal stimulation of an diazo ester group comprises applying a temperature of 50 to 200 °C, preferably 60 to 180, more preferably 60 to 150 °C in the presence of nitrogen. In one embodiment activation by a light stimulus, also termed photochemical activation comprises irradiation or exposure of the diazo group to light of a specific wavelength or a range of wavelengths, preferably irradiation or exposure to light, preferably to light of a wavelength equal or below 500 nm, more preferably equal or below 430 nm, even more preferably equal or below 380 nm, such as equal or below 500, 450, 430, 400, 380, 350, 300, 260, 250, 240, 230, 220, 210 or 200 nm. Similar to thermal activation photochemical activation of

a diazo group results in decomposition of the diazo group and formation a carbene group reacting with the C-H group of a molecule.

An azide such as azide (-N_3) and sulfonyl azide (-SO_2N_3) can for example be activated for an C,H insertion reaction by external thermal, mechanical and/or light stimulation. Thermal stimulation comprises applying an increased temperature to the azide resulting in decomposition of the azide and formation of a nitrene such as a sulfonyl nitrene, which reacts with the C-H group of a molecule such as an oligomer or a polymer. In one embodiment thermal stimulation of an diazo ester group comprises applying a temperature of at least 100 °C, more preferably at least 110 °C, even more preferably at least 120 °C, such as 100, 110, 120, 130, 140, 150, 160, 170, 180, 190 or 200 °C. In one embodiment hotochemical activation comprises irradiation or exposure of the azide group to light of a specific wavelength or a range of wavelengths, preferably to UV-light, preferably irradiation or exposure to light of a wavelength equal or below 380 nm, more preferably equal or below 300 nm, even more preferably equal or below 260 nm, such as equal or below 260, 250, 240, 230, 220, 210 or 200 nm. Similar to thermal activation photochemical activation of an azide results in decomposition of the azide and formation a nitrene such as a sulfonyl nitrene reacting with the C-H group of a molecule.

The term “aromatic ketone” refers to a compound or functional group characterized by the presence of a carbonyl group (C=O) covalently linked to an aromatic ring. The structure of an aromatic ketone can be represented as Ar-CO-R, where "Ar" denotes an aromatic group, such as a phenyl or substituted phenyl group, and "R" is an alkyl, aryl, or hydrogen group. Aromatic ketones include without limitation benzophenone, anthraquinone, acetophenone, 4-methoxyacetophenone, 4-chloroacetophenone and phenylacetone.

An aromatic ketone such as benzophenone and anthraquinone can for example be activated for an C,H insertion reaction by external light stimulation and/or mechanical stimulation. In one embodiment photochemical activation comprises irradiation or exposure of the aromatic ketone to light of a specific wavelength or a range of wavelengths, preferably to UV-light, preferably to light of a wavelength equal or below 380 nm, more preferably equal or below 300 nm, even more preferably equal or below 260 nm, such as equal or below 260, 250, 240, 230, 220, 210 or200 nm. Photochemical activation of an aromatic ketone thereby results in activation of the carbonyl group thereby generate a triplet excited state reacting with the C-H group of a molecule.

The term “external activation” or “external stimulation” refers to the application of external conditions providing energy for a chemical reaction sources and optionally the addition a catalyst to a chemical compound or a mixture of chemical compounds to induce chemical reactions such as the formation of a covalent bond by the crosslinkable group of the synthetic compounds of the present invention or cleavage of the cleavable group of the synthetic compounds of the present invention and oligomer or polymer networks and composited formed. In the context of C,H insertion reactions, external stimulation involves without limitation applying external stimuli such as light (photochemical), heat (thermal), mechanical force (mechanochemical) and/or electric fields to generate highly reactive intermediates that can insert into C-H bonds of molecules thereby forming a covalent bond.

“Light stimulation” also termed “light activation” or “photochemical activation” refers to the process of using light energy, typically ultraviolet (UV) or visible light, to induce chemical reactions by

exciting the molecules involved, such as the synthetic compounds of the present invention comprising a crosslinkable group. In the context of C,H insertion reactions, photochemical activation involves using the irradiation or exposure to light to generate highly reactive intermediates such as carbenes or nitrenes, which can then insert into C-H bonds of molecules, such as oligomers or polymers. Methods and means for photochemical activation are well known to a person skilled in the art.

"Thermal stimulation" also termed "thermal activation" refers to the process of using heat to induce chemical reactions by providing the energy needed to overcome the activation barriers of those reactions. In the context of C,H insertion reactions, thermal activation involves heating the reactants to generate highly reactive intermediates such as carbenes and nitrenes. These intermediates can then insert into C-H bonds of molecules, modifying their structure and leading to the formation of new chemical products. Methods and means for thermal activation are well known to a person skilled in the art.

"Mechanical stimulation" also termed "mechanical activation" or "mechanochemical activation" involves the use of mechanical force to induce chemical reactions. Mechanochemical activation of a reactant comprising a crosslinkable group, which forms a covalent bond with a C-H group by a C,H insertion reaction, comprises for example grinding or ball milling of the reactant and the molecule to react with, such as the synthetic compound of the present invention and an oligomer or polymer, thereby generating localized high temperatures and pressures resulting in reactive intermediates of the reactant. Mechanochemical activation may further comprise application of shearing forces to the reactant comprising the aromatic ketone and the molecule to react with, thereby leading to bond breakage and formation of reactive intermediates. Mechanochemical activation may further comprise ultrasonication of the reactant comprising the corsslinkable group and the molecule to react with, thereby generating localized high temperatures and pressures, resulting in reactive intermediates of the reactant and formation of a covalent bond with the molecule to react with. Methods for mechanochemical activation are well known to a person skilled in the art.

The term "cleavable group" also termed "cleavable functional group" refers to a functional group of a chemical compound or molecule such as the synthetic compound of the present invention, in which a covalent bond can be selectively broken (also termed "cleaved") under specific conditions, without cleaving the remaining parts of the chemical compound or molecule. A cleavable group can be for example cleaved by external stimuli such as chemical, enzymatic, or physical external stimuli including without limitation changes in the pH value, changes in temperature, exposure to specific enzymes such as esterases, light (photocleavage), heat, or the presence of specific chemical reagents such as agents changing the oxidative state (such as oxidative or reductive agents) and or competing exchange reactants. Such cleavable groups include without limitation an ester cleavable for example by esterases, a disulfide bond cleavable for example by thiol/disulfide exchange such as by DTT as competing exchange reactant, acetal and ketal cleavable for example by hydrolysis under acidic conditions, nitrobenzyl cleavable for example by exposure to light of a specific wavelength, boronic acid/ester, oxime and hydrazine cleavable by changes in the pH values, sugars as competing exchange reactants and a Diels-Alder pair cleavable for example by a Retro-Diels-Alder-reaction upon changes in temperature

such as heating. A person skilled in the art is aware of cleavable functional groups and external stimuli for cleaving such groups.

A Diels-Alder reaction involves the [4+2] cycloaddition of a diene and a dienophile to form a cyclohexene ring system. This reaction can be reversed under thermal conditions (Retro-Diels-Alder reaction), where the adduct breaks back into the original diene and dienophile components. One example for Diels-Alder-Pairs is a furan-maleimide Diels-Alder-pair forming a furan-maleimide-adduct, which can be cleaved in a Retro-Diels-Alder reaction upon heating,

Specific functional groups are cleavable in the presence of competing exchange reactants also termed “competing exchange reagent”. These functional groups are designed to undergo selective cleavage or exchange reactions while being stable when the competing exchange reactant is not present. Examples of such cleavable groups and competing exchange reactants include without limitation disulfide bonds that are cleavable in the presence of DTT as competing exchange reactant, boronic esters that are cleavable in the presence of a diol as competing exchange reactant, imines and hydrazones that are cleavable in the presence of amines or hydrazines as competing exchange reactants and thioesters that are cleavable in the presence of thiols or nucleophilic compounds as competing exchange reactants.

The term “cleavable C,H insertion group” in the context of the present invention refers to C,H insertion group linked to a cleavable group by a covalent bond. The term thus refers to a functional group comprising a crosslinkable group that forms a covalent bond with another molecule or within the molecule it is comprised in by a C,H insertion reaction upon external stimulation, which is covalently linked to a cleavable group.

The term "amine" refers to a group of the formula -NRR', where R and R' can be, independently, hydrogen or an alkyl, alkenyl, alkynyl, aryl, aralkyl, cycloalkyl, halogenated alkyl, or hetero cycloalkyl group described above. The term primary amine refers to a group of the formula -NH2. The term secondary amine refers to a group of the formula -NRH, wherein R can be an alkyl, alkenyl, alkynyl, aryl, aralkyl, cycloalkyl, halogenated alkyl, or hetero cycloalkyl group described above. The term secondary amine refers to a group of the formula -NRR', wherein R and R’ can be, independently an alkyl, alkenyl, alkynyl, aryl, aralkyl, cycloalkyl, halogenated alkyl, or hetero cycloalkyl group described above. Alkyne

The term “oligomer” or “oligomer “compound” refers to a molecule comprising at least two identical or similar substructures (also termed “subunits”) linked to each other, preferably by a covalent bond. A substructure or subunit of an oligomer is termed monomer. An oligomer comprising at least 50 subunits, such as 50, 55, 60, 70, 75, 80, 85, 90, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, 350, 300, 350, 400, 450 or 500, is termed a “polymer” or “polymer compound”.

The degree of polymerization (DP) of an oligomer or polymer refers to the number of subunits comprised in an oligomer or polymer. The DP is a critical parameter that determines the molecular weight and, consequently, the physical and mechanical properties of the oligomer or polymer. A higher DP usually correlates with a greater tensile strength, durability, and thermal stability of the oligomer or polymer. The DP can for example be determined by size exclusion

chromatography (SEC), nuclear magnetic resonance spectroscopy (NMR), osmometry, viscometry and mass spectrometry.

Size Exclusion Chromatography (SEC), is a technique used to determine the molecular weight distribution of polymers. By comparing the elution volume of the polymer with that of known standards, the average molecular weight and the DP can be calculated. NMR spectroscopy can provide detailed information about the chemical structure of the polymer. By analyzing the end groups of the polymer chain, it is possible to determine the DP. This method is especially useful for polymers with well-defined end groups. Osmometry measures the osmotic pressure of a polymer solution to determine the number average molecular weight (Mn). From Mn and the known molecular weight of the repeating unit, the DP can be calculated. Viscometry measures the viscosity of a polymer solution. The intrinsic viscosity of the solution is related to the molecular weight of the polymer. Using Mark-Houwink parameters, the molecular weight, and hence the DP, can be estimated. Mass spectrometry can be used to determine the molecular weight of polymers. Techniques such as MALDI-TOF (Matrix-Assisted Laser Desorption/Ionization Time-of-Flight) allow for the precise determination of the molecular weight distribution and the calculation of the DP. These methods are well known in the prior art and a person skilled in the art is capable of determining the DP of an oligomer or polymer without undue burden by using these methods.

Oligomers such as polymers are usually synthesized by an oligomerization or polymerization reaction, wherein numerous monomers are linked together covalently. The type of synthesis method depends on the type monomers to be covalently linked to each other. Polymerization methods can be classified into chain-growth polymerization including without limitation free-radical polymerization, anionic polymerization, cationic polymerization, coordination polymerization, and step-growth polymerization including without limitation polycondensation, polyaddition and ring-opening polymerization. These methods are well known in the art and a person skilled in the art is capable of choosing a suitable method for synthesizing an oligomer or polymer.

The “oligomer backbone” or “polymer backbone” is the primary, continuous chain of atoms that forms the central framework of an oligomer or polymer. This backbone is composed of the repeating units derived from the monomers, linked together by covalent bonds. The backbone can be linear or branched, and can contain various types of atoms, such as carbon, nitrogen, oxygen, or silicon, depending on the specific monomers used in the polymerization process. Modifications to the backbone, such as the inclusion of side chains or functional groups, can further tailor the properties of the oligomer or polymer for specific applications. A „side chain“, also termed “pendant group”, is a functional group or substituent covalently attached to the oligomer or polymer backbone. A side chain is not part of the primary continuous chain of atoms that forms the backbone of the oligomer or polymer. In one embodiment the synthetic compound of the present invention comprises and oligomer or polymer backbone, wherein at least one crosslinkable group is covalently bound to the oligomer backbone or polymer backbone by a cleavable group. The crosslinkable group and cleavable group covalently linked to each other thus represent a side chain of the synthetic compound.

The terms “homooligomer” and “homopolymer” refer to oligomers or polymers consisting of one type of monomer repeated throughout the oligomer or polymer. The term “cooligomer” and “copolymer” refers to oligomers or polymers comprising at least two different monomers.

Within a cooligomer or copolymer the monomers may be “randomly” or “statistically “distributed, termed “statistical cooligomer” or “statistical copolymers”, distributed in an alternating pattern, termed “alternating cooligomer” or “alternating copolymer”, distributed as a gradient, termed “gradient cooligomer” or “gradient copolymer”, or as 2 or more blocks, such as 2, 3, 4, 5, 6, 7, 8, 9, or 10 block, each comprising a single type of monomer, termed “block oligomer” or “block copolymer”. In one embodiment the oligomer backbone of the synthetic compound of the present invention is a statistical, alternating, gradient or block oligomer. In one embodiment the oligomer backbone of the synthetic compound of the present invention is a statistical, alternating, gradient or block copolymer.

Oligomers and polymers can further be broadly classified into two natural and synthetic oligomers or polymers. Natural oligomers and polymers are of natural origin such as from plants, microorganisms, and animals. They include without limitation carbohydrates and proteins. Examples for natural polymers include without limitation cellulose, lignin, alginate, collagen, gelatin, silk fibroin, starch, hyaluronic acid, chitosan. Synthetic oligomers or polymers are chemically synthesized or modified oligomers or polymers that are artificially created by chemical synthesis or chemical modification of a natural oligomers or polymers, such as by incorporation of an additional functional group. Examples for synthetic polymers include without limitation polyethylene (PE), polypropylene (PP), polystyrene (PS), polyvinyl chloride (PVC), polytetrafluoroethylene (PFTE), polycarbonate (PC), acrylnitrile butadiene styrene (ABS), polycaprolactone (PCL), poly (lactic-co-glycolic acid) (PLGA), polyetheretherketone (PEEK), polyhydroxyalkanoate (PHA) and poly(ethylene glycol) (PEG).

A “thermoplastic oligomer” or “thermoplastic polymer” is a class of oligomers or polymers that become soft and moldable upon heating and solidify upon cooling. This change in physical properties is reversible. The process of melting and solidifying can be repeated multiple times without significantly altering the polymer's chemical structure or properties, making thermoplastic polymers recyclable and versatile for various applications. Thermoplastic oligomers or polymers can be repeatedly heated to their melting point, shaped into desired forms, and then cooled to solidify. Further, thermoplastic oligomers or polymers can be processed using various techniques such as injection molding, extrusion, blow molding, and thermoforming, allowing for the production of a wide range of products including packaging material, automotive parts, consumer goods, medical devices, and construction materials. Examples for thermoplastic oligomers and polymers include without limitation polyethylene (PE), polycarbonate (PC), polystyrene (PS), polyvinylchloride (PVC), polyamide (PA), acrylnitrile butadiene styrene (ABS), polypropylene (PP) and polyethylene terephthalate (PET). Thermoplastic oligomers or polymers may for example be characterized by determining thermal properties such as the melting temperature (Tm) and the glass transition temperature (Tg) and thermal conductivity of the oligomer or polymer, mechanical properties such as tensile strength and modulus, the impact resistance and the hardness, and rheological properties such as the viscosity and the melt flow index (MFI). A person skilled in the art is well aware of these methods and capable to determine the thermoplastic properties of an oligomer or polymer by these methods.

A “covalent bond” is a chemical bond in which electrons are shared between atoms to form electron pairs between atoms; Within a covalent bond two atoms share one or more pairs of electrons in order to achieve a more stable electron configuration, often resulting in each atom attaining a complete outer electron shell. Covalent bonds can form between atoms of the same element or atoms of different elements. A covalent bond may be a single, a double or a triple covalent bond.

“Functional groups” in chemistry refer to specific arrangements of atoms within molecules that impart characteristic chemical properties to those molecules. These groups can undergo predictable reactions regardless of the surrounding molecular structure. Functional groups also play a crucial role in determining the solubility, reactivity, and other chemical and biological properties of organic molecules.

Affinity molecules and therapeutic agents:

The term “therapeutic agent”, "active ingredient" or “API” herein refers to a pharmaceutically active molecule as well as a pro-drug transformed to the pharmaceutically active molecule in the organism, and a pharmaceutically acceptable and/or therapeutically active salt thereof. The term further refers to pharmaceutically acceptable and therapeutically active hydrates, esters, amides, metabolites, enantiomers, polymorphs, analogs, etc. that induce a desired pharmacological or physiological effect or induce a desired pharmacological or physiological effect upon transformation to a pharmaceutically active molecule in the organism. Terms like “therapeutic agent”, "active agent", "active pharmaceutical ingredient", “drug substance”, may be used synonymously for "active ingredient".

The term “affinity molecule” or “binding agent” refers to a molecule that specifically binds to another molecule such as a protein, peptide, nucleic acid or small molecule with high affinity. This interaction is typically highly selective and involves molecular recognition processes such as hydrogen bonding, ionic interactions, Van der Waals forces, and hydrophobic interactions. In embodiments, an “affinity molecule” or “binding agent” that may be selected from, without limitation, an antibody, protein, peptide, nucleic acid, or other small molecule that specifically binds to a biological structure such as a surface marker or receptor and a receptor-like molecule.

A "receptor-like molecule" refers to a molecule that mimics the function or structure of a biological receptor. Receptors are proteins on the surface of cells or within cells that bind to specific ligands (such as hormones, neurotransmitters, or other signaling molecules) and initiate a biological response. Receptor-like molecules are designed to interact similarly with ligands or other molecules. Types of receptor-like molecules include without limitation genetically engineered proteins such as chimeric receptors, peptides, small molecules, molecular imprinted polymers (PIPs), aptamers and nanobodies.

As used herein, an "antibody" generally refers to a protein consisting of one or more polypeptides substantially encoded by immunoglobulin genes or fragments of immunoglobulin genes. Where the term “antibody” is used, the term “antibody fragment” may also be considered to be referred to. The recognized immunoglobulin genes include the kappa, lambda, alpha, gamma, delta, epsilon and mu constant region genes, as well as the myriad immunoglobulin variable region

genes. Light chains are classified as either kappa or lambda. Heavy chains are classified as gamma, mu, alpha, delta, or epsilon, which in turn define the immunoglobulin classes, IgG, IgM, IgA, IgD, and IgE, respectively. The basic immunoglobulin (antibody) structural unit is known to comprise a tetramer or dimer. Each tetramer is composed of two identical pairs of polypeptide chains, each pair having one "light" (L) (about 25 kD) and one "heavy" (H) chain (about 50-70 kD). The N-terminus of each chain defines a variable region of about 100 to 110 or more amino acids, primarily responsible for antigen recognition. The terms "variable light chain" and "variable heavy chain" refer to these variable regions of the light and heavy chains, respectively. Optionally, the antibody or the immunological portion of the antibody, can be chemically conjugated to, or expressed as, a fusion protein with other proteins. "Single-chain Fv" or "scFv" antibody fragments comprise the VH and VL domains of an antibody, wherein these domains are present in a single polypeptide chain and in either orientation (e.g., VL-VH or VH-VL). Generally, the scFv polypeptide further comprises a polypeptide linker between the VH and VL domains which enables the scFv to form the desired structure for antigen binding. "Single-chain Fv" or "scFv" antibody fragments comprise the VH and VL domains of an antibody, wherein these domains are present in a single polypeptide chain and in either orientation {e.g., VL- VH or VH-VL). Generally, the scFv polypeptide further comprises a polypeptide linker between the VH and VL domains which enables the scFv to form the desired structure for antigen binding.

The terms “peptide” and “protein” refer to a chain of amino acids covalently linked by peptide bonds. Peptides are typically consisting of 2 to 50 amino acids, whereas proteins comprise 50 or more amino acids. They play various roles in biological systems, including as hormones, neurotransmitters, and signaling molecules. Peptides and proteins are defined by their specific sequence of amino acids, which determines their three-dimensional structure and biological activity. Peptides and proteins can be classified into natural peptides and proteins, that occur naturally in organism such as hormones or neurotransmitters and antimicrobial peptides, and synthetic peptides and proteins that are artificially synthesized or modified. Common method for synthesizing peptides and proteins includes solid-phase peptide synthesis (SPPS) and recombinant DNA technology for producing peptides and proteins in biological systems such as bacteria and yeast.

Herein, “nucleic acid” may preferably refer to DNA (deoxyribonucleic acid), gDNA (genomic deoxyribonucleic acid), RNA (ribonucleic acid), gRNA (genomic ribonucleic acid), mRNA (messenger ribonucleic acid) and cDNA (complementary deoxyribonucleic acid synthesized from RNA template), or any combination thereof, further also encompassing L-DNA and L-RNA forming so-called mirror-images of the naturally occurring conformation of DNA. As used herein, “nucleic acid” shall mean any nucleic acid molecule, including, without limitation, DNA, RNA, and hybrids or modified variants thereof, including L-DNA and L-RNA.

“Small molecules,” with a molecular weight of less than 900 g/mol constitute a diverse group of organic compounds that play essential roles in various biological processes and pharmacological applications. Unlike larger molecules such as proteins and nucleic acids, small molecules can regulate biological functions by binding to specific targets, including receptors and enzymes. These compounds can exert their effects by modulating signaling pathways, inhibiting enzymatic activity, or disrupting protein-protein interactions. Non-limiting examples of small molecules are metabolites (e.g., sugars), signaling molecules (e.g., hormones, neurotransmitters, cytokines),

natural products (e.g., alkaloids, glycosides, terpenes, antibiotics), drugs, toxins, poisons, lipids (e.g., triglycerides, phospholipids, cholesterol), carbohydrates (e.g., glucose, starch, cellulose), amino acids, nucleotides (e.g., adenine, guanine, thymine, cytosine), heterocyclic compounds (e.g., alkaloids, purines, pyrimidines), and/or aromatic compounds (e.g., benzene, toluene, naphthalene).

FIGURES

The invention is demonstrated by way of the example through the figures disclosed herein. The figures provided represent particular, non-limiting embodiments and are not intended to limit the scope of the invention.

Brief description of the figures

Figure 1: Schematic representation of a synthetic compound according to the present invention.

Figure 2: Schematic representation of the production of covalently bonded oligomer composite, which can be structured by external influences and can also be fully cleaved again.

Detailed description of the figures

Figure 1: Schematic representation of a synthetic compound according to the present invention. for the generation of a covalent oligomer composite by means of C,H insertion via pendant crosslink-inducing groups, whereby these groups are connected to the an oligomer backbone via a cleavable bond and can be separated by external influences if required.

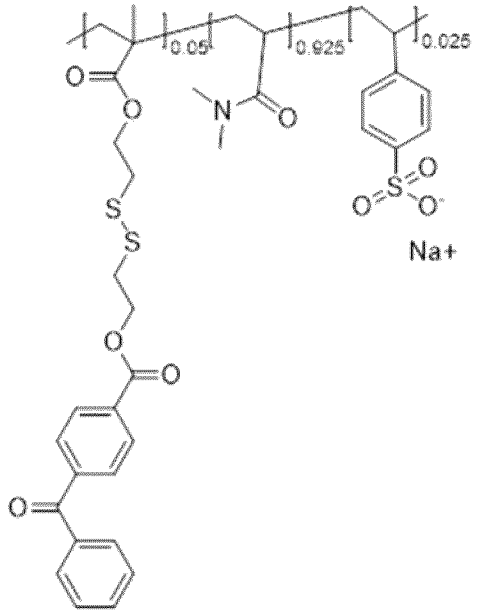
Figure 2: Schematic representation of the production of covalently bonded oligomer composite, which can be structured by external influences and can also be fully cleaved again. Synthetic compounds with cleavable crosslinking-inducing groups are brought into contact with the same or other oligomers, whereby covalent networks are formed by light or temperature-activated C,H insertion by means of crosslinking-inducing groups. The crosslink-inducing groups can be the same or different and can be activated simultaneously or by different stimuli and at different timepoint. The composite formed can be partially or completely cleaved by external stimuli such as via redox-, pH- or temperature-sensitive cleavage. The cleavable groups can be the same or different and the cleavage can take place simultaneously or by different stimuli at different timepoints. Incomplete formation and cleavage of the covalent composite can be alternating while maintaining a network structure of the composite.

EXAMPLES

The invention is demonstrated through the examples disclosed herein. The examples provided represent particular embodiments and are not intended to limit the scope of the invention. The examples are to be considered as providing a non-limiting illustration and technical support for carrying out the invention.

Example 1

Polymer synthesis – Example compound 1:



Sodium styrene sulfonate (SSNa) (0.20 g, 1 mmol), 2-((2-(methacryloyloxy)ethyl)disulfaneyl)ethyl 4-benzoylbenzoate (MADSBB) (0.86 g, 2.0 mmol) and N,N-dimethylacrylamide (DMAA) (3.67 g, 37 mmol) were dissolved in dimethylformamide (DMF) (35 ml). Azobisisobutyronitrile (AIBN) (0.016 g, 0.1) was added and rinsed with DMF (5 ml). The reaction mixture was degassed by performing freezing-and-thawing three times. Polymerization was carried out at 60 °C for 48 hours. The mixture was cooled and precipitated in diethyl ether (400 ml). The supernatant was decanted, and the residue was dissolved in $CHCl_3$. This step was repeated two more times. After the last precipitation, the product was filtered off and dried under high vacuum (HV) overnight. The compound was obtained as a colorless solid.

Yield: 75 %.

The numbers in the structure above refer to the relative amount (mol-%) of the respective monomers in the example compound.

As indicated in the structure above example compound 1 comprises 5 mol-% of a crosslinkable group. The same procedure was carried out to obtain a compound with 2.5 mol% and 7.5 mol% crosslinkable group.

Cleavage:

A solution of example compound 1 in ethanol (30 mg/ml) was applied to silanised wafers by spin-coating (0.07 ml, 2500 rpm, 30 s). Crosslinking was then carried out at 365 nm for 4 J. The wafers were extracted overnight in CHCl3. Coating thicknesses in the range of 180 - 210 nm were obtained.

Wafers coated in this way were treated with an aqueous solution of dithiothreitole (DTT) (232 mg/150 ml, pH ~ 8) for different time intervals (1 - 60 min). The wafers were then washed with deionized (DI) water, dried and the cleavage was monitored by measuring the coating thickness. After 20 minutes, a cleavage of approx. 50 % was measured. In experiments with 2.5 %

crosslinking-inducing groups and 7.5 % crosslinking-inducing groups, the time to reach 50 % cleavage was 7.5 and 40 min respectively.

Furthermore, the cleavage rate could be influenced by the following parameters: By varying the pH of the cleavage solution, adjusted by a phosphate buffer, the cleavage rate could be influenced: In pure DI water (pH = 5.5), no cleavage was observed. When using tap water (pH = 7), the cleavage rate after one hour of treatment was approx. 30 %. When using a solution with pH 10, immediate cleavage (<1 min) was observed.

Further observations:

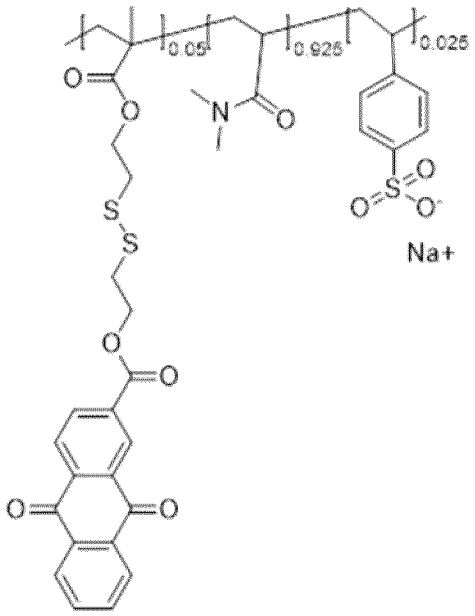
Furthermore, the cleavage rate is influenced by using other cleavage reagents such as DTBA or GSH.

Thus, adjusting the compound properties by varying for example the cross-linking-inducing group content and the cleavage reaction conditions allows the system, in particular the oligomer composite formed by using the compound, to be customized for specific applications.

By illumination with UV light of different wavelengths (<260 nm), specific areas of the composite comprising the compounds can be deactivated by cleavage (photolysis) of the disulfide bridge. This allows simple and fast photostructuring. For this purpose, silicone wafers were coated according to the procedure described above. The illumination was carried out using photomasks: Positive (illumination: 265 nm, 1 J), negative (illumination: 365 nm, 4 J). By subsequent treatment with an aqueous DTT solution (232 mg/150 ml, pH ~ 8, 15 min) only areas exposed to 365 nm were cleaved.

Example 2

Polymer synthesis – Example compound 2:



SSNa (0.12 g, 0.6 mmol), 2-((2-(methacryloyloxy)ethyl)disulfaneyl)ethyl 9,10-dioxo-9,10-dihydroanthracene-2-carboxylate (MADSAQ) (0.54 g, 1.2 mmol) and DMAA (2.20 g, 22 mmol) were dissolved in DMF (15 ml). V70 (0.018 g, 0.06) was added and rinsed with DMF (5 ml). The

reaction mixture was degassed by by performing freezing-and-thawing three times. Polymerization was carried out at 35 °C for 20 h. The mixture was cooled and precipitated in diethyl ether (200 ml). The supernatant was decanted off and the residue was dissolved in CHCl3. This step was repeated two more times. After the last precipitation, the product was filtered off and dried under HV overnight. The compound was obtained as a colourless solid.

The numbers in the structure above refer to the relative amount (mol-%) of the respective monomers in the example compound.

As indicated in the structure above example compound 2 comprises 5 mol-% of a crosslinkable group.

Cleavage and further observations:

Example compound 2 was applied to silanised wafers in a similar way as described in example 1 by rotary coating (0.07 ml, 2500 rpm, 30 s) and crosslinked with 4 J using 365 nm illumination. The investigations of the cleavage were performed as described in example 1, showing a cleavage of 50 % after approx. 40 min and of 100 % after approx. 60 min.

Example compound 2 also exhibited the property of being processable by 2-photon lithography. For this purpose, a solution of the compound in ethanol was applied to a silanised glass wafer by drop-casting. After this layer had dried, a second layer of a magnetic hydrophobic polymer was applied. The multilayer system was cross-linked with power of 30 - 50 mW in a 2-photon lithograph, whereby a covalent linkage of both polymer layers was achieved and a oligomer composite according to the present invention formed. By treatment with DTT solution (23.2 mg/15 ml, pH ~ 8, 15 min) this linkage could be cleaved again, and the magnetic polymer could be separated from the compound.

Furthermore, by creating multilayer systems with any other oligomers or polymers, specific structures and oligomer composites can be created that comprise dissolvable and non-dissolvable domains. For example, functional magnetic, non-water-swellable polymers can be covalently linked to the compounds of the present invention such as example compound 2. After using the layered composite in any application, one or more layers can be released by cleaving the cleavable groups, such as the disulphide links of example compound 2.

Example 3

An aqueous solution of example compound 1 or example compound 2 (100 mg/ml) was microfluidically processed into particles. The aqueous disperse flow was operated at 1.3 µl/min and the oil flow as a continuous phase at 6.5 µl/min. By combining both streams in a T-junction and subsequent illumination with 365 nm for approx. 15 min (approx. 8 J), particles with low polydispersity were obtained. These particles were treated with a solution of DTT (23.2 mg/15 ml, pH ~ 8, 10 mM). Complete cleavage was observed after 8 minutes.

By varying the DTT concentration (23.2 mg/30 ml, pH ~ 8, 5 mM) and 23.2 mg/7.5 ml, pH ~ 8, 20 mM), the cleavage rate was shortened to approx. 25 min for 5 mM and 4 min for 20 mM, respectively.

CLAIMS

1. A synthetic compound comprising
    a. one or more crosslinkable groups and one or more cleavable groups,
    b. wherein at least one crosslinkable group forms a covalent bond with a C-H group by a C,H insertion reaction upon an external stimulation,
    c. wherein at least one crosslinkable group is covalently bound to at least one cleavable group, and
    d. wherein a covalent bond of the cleavable group is cleavable upon an external stimulation.
2. The synthetic compound according claim 1, wherein the external stimulation for forming a covalent bond of the one or more crosslinkable groups with a C-H group by a C, H insertion reaction is a thermal, a light and/or a mechanic stimulation.
3. The synthetic compound according to any one of the preceding claims, wherein the one or more crosslinkable groups are selected from the group consisting of an aromatic ketone such as benzophenone and anthraquinone, an azide such as sulfonyl azide, and a diazo ester group.
4. The synthetic compound according to any one of the preceding claims, wherein the external stimulation for cleaving a covalent bond of the one or more cleavable groups is a change in temperature, pH value, light exposure, oxidative state and/or the presence of competing exchange reactants.
5. The synthetic compound according to any one of the preceding claims, wherein the one or more cleavable groups are selected from the group consisting of a disulfide group, a broronic ester an oxime, a hydrazine and a Diels-Alder pair.
6. The synthetic compound according to any one of the preceding claims, wherein the synthetic compound additionally comprises one or more functional groups selected from the group consisting of a carboxyl group, an amine group, an alkyne, an azide, a sulfonate group and a maleimide group.
7. The synthetic compound according to any one of the preceding claims comprising at least two crosslinkable groups, wherein the at least two crosslinkable groups can be the same or different.
8. The synthetic compound according to any one of the preceding claims, wherein the synthetic compound additionally comprises an oligomer backbone or polymer backbone and wherein at least one crosslinkable group is covalently bound to the oligomer backbone or polymer backbone by at least one cleavable group.
9. The synthetic compounds according to any one of claims 1 to 7, wherein the synthetic compound comprises two or more crosslinkable groups covalently linked by a cleavable group, wherein the two or more crosslinkable groups are the same or different.

10. A composite comprising at least one synthetic compound according to any one of the preceding claims, wherein at least one crosslinkable group of the synthetic compound is covalently bound to an oligomer and/or polymer.

11. The composite according to claim 10, wherein the oligomer and/or polymer is selected from the group consisting of a second synthetic compound comprising an oligomer backbone or polymer backbone according to claim 8, a thermoplastic oligomer or polymer, and a natural oligomer or polymer such as cellulose, lignin, alginate, collagen, gelatin, silk fibroin and starch. ….

12. The composite according to any one of claims 10 and 11 comprising additionally one or more affinity molecules, wherein the affinity molecules are covalently bound to the composite and preferably selected from the group consisting of an antibody or a fragment thereof, a peptide, a protein, a nucleic acid and a receptor-like molecule.

13. A method of producing a composite according to any one of claims 10 to 12, comprising

    a. providing a synthetic compound according to any one of claims 1 to 9, the synthetic compound comprising one or more crosslinkable groups and one or more cleavable groups,

    b. providing at least one oligomer and/or polymer, and

    c. initiating a C,H insertion reaction of at least one crosslinkable group of the synthetic compound with the at least one oligomer and/or polymer, wherein a covalent bond between the synthetic compound and the at least one oligomer and/or polymer is formed.

14. The method according to claim 13, wherein the C,H insertion reaction is initiated by thermal, light and/or mechanic stimulation.

15. A method of cleaving a composite according to any one of claims 10 to 13, the method comprising

    a. providing a composite according to any one of claims 10 to 13,

    b. initiating a cleavage of at least one covalent bond of a cleavable group of the composite by a change in temperature, pH value, light exposure, oxidative state and/or the presence of competing exchange reactants.

Fig.1

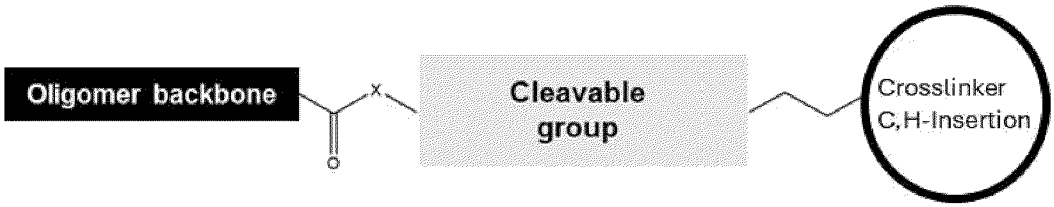
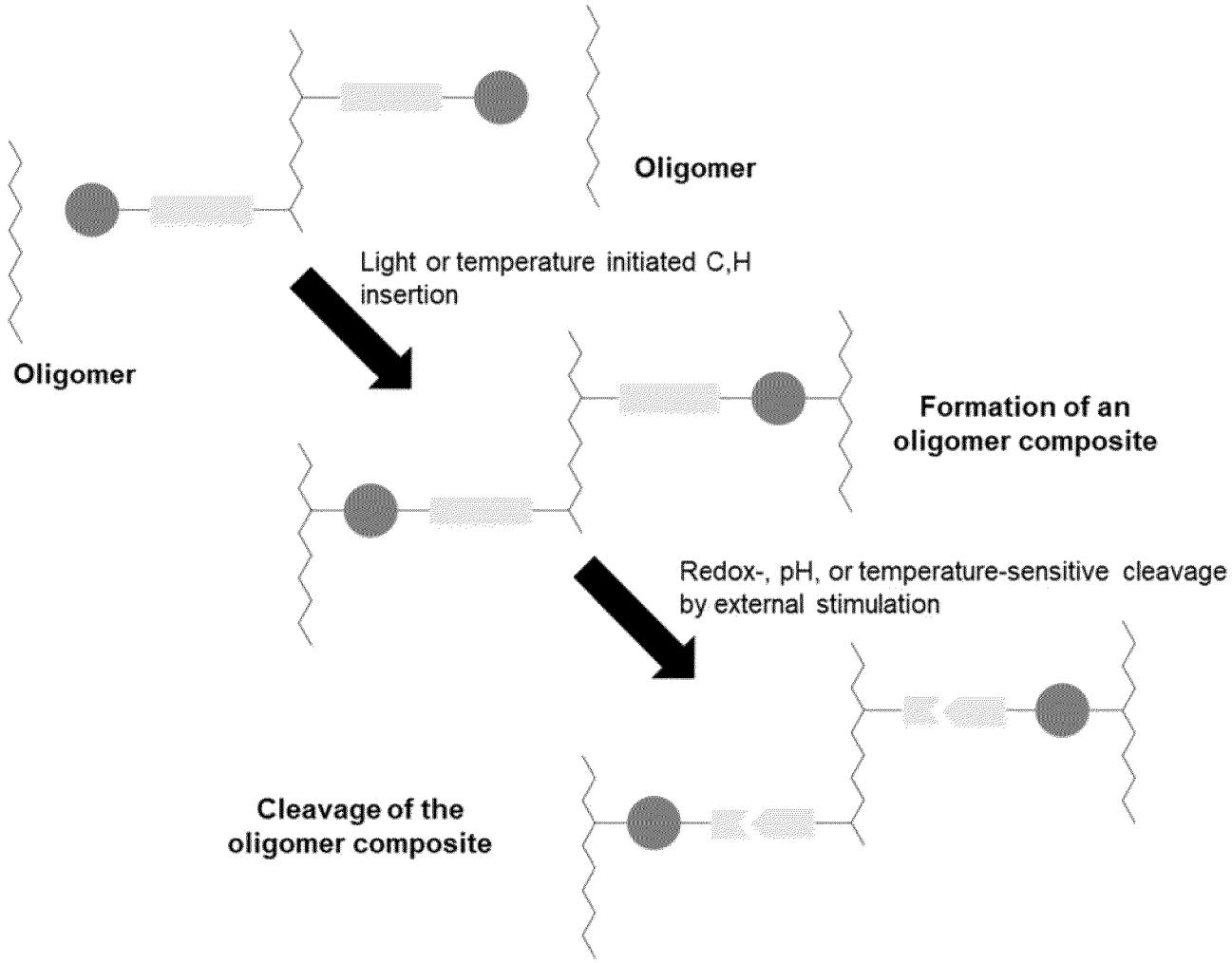

Oligomer backbone
X
O
Cleavable group
Crosslinker C,H-Insertion

Fig.2


Oligomer
Light or temperature initiated C,H insertion
Oligomer
Formation of an oligomer composite
Redox-, pH, or temperature-sensitive cleavage by external stimulation
Cleavage of the oligomer composite

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2024/078873

A. CLASSIFICATION OF SUBJECT MATTER
INV. C08F220/56
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C08F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BI LITING ET AL: "A Cleavable Crosslinking Strategy for Commodity Polymer Functionalization and Generation of Reprocessable Thermosets", ANGEWANDTE CHEMIE, vol. 62, no. 30, 16 June 2023 (2023-06-16) , XP093115496, Hoboken, USA ISSN: 1433-7851, DOI: 10.1002/anie.202304708 Retrieved from the Internet: URL:https://onlinelibrary.wiley.com/doi/epdf/10.1002/anie.202304708>	1,2,4,9, 13-15
A	Schemes 1-2, 4; page 1 - page 5; figure 1	3,5-8, 10-12

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[x] Further documents are listed in the continuation of Box C.

[ ] See patent family annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
31 January 2025	11/02/2025

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Giani, Elena

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INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2024/078873

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	STRAUB ALEXANDER J. ET AL: ""CHicable" and "Clickable" Copolymers for Network Formation and Surface Modification", LANGMUIR, vol. 37, no. 21, 1 June 2021 (2021-06-01), pages 6510-6520, XP093244735, US ISSN: 0743-7463, DOI: 10.1021/acs.langmuir.1c00669 abstract Scheme 1; page 6511 - page 6512; figure 1 page 6515 - page 6512 -----	1-15
A	PHILIP F KOTRADE ET AL: "Malonic Acid Diazoesters for C-H Insertion Crosslinking (CHic) Reactions: A Versatile Method for the Generation of Tailor-Made Surfaces", ANGEWANDTE CHEMIE, WILEY - V C H VERLAG GMBH & CO. KGAA, DE, vol. 129, no. 46, 11 October 2017 (2017-10-11), pages 14597-14602, XP071374396, ISSN: 0044-8249, DOI: 10.1002/ANGE.201704486 abstract Schemes 1-2; page 14597 - page 14598 -----	1-15

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