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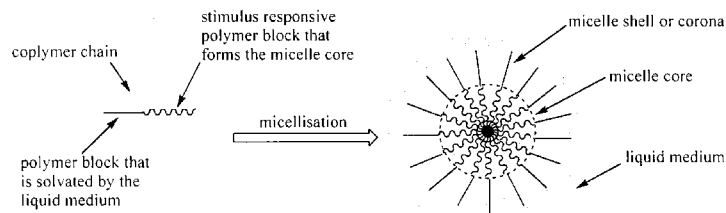


Figure 1

(57) Abstract: The present invention relates to a method of performing a chemical reaction, the method comprising: providing a liquid medium comprising micelles of assembled copolymer chains, the copolymer chains having a stimulus responsive polymer block that forms the core of the micelles, and a polymer block that is solvated by the liquid medium, wherein the micelles contain within their core one or more reactants; reacting the one or more reactants to form a product within the core of the micelles; and subjecting the stimulus responsive polymer block to a stimulus such that it undergoes a transition and causes the micellar assembled copolymer chains to disassemble and release the product into the liquid medium.

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REACTOR AND METHOD FOR PERFORMING A CHEMICAL REACTION

Field of the Invention

- 5 The present invention relates in general to synthetic chemistry, and in particular to a reactor and method for performing a chemical reaction.

Background of the Invention

- 10 Synthetic chemistry has and will continue to play a pivotal role in the developed world. Considerable research effort to date has been directed toward developing reactors and methods for performing chemical reactions in order to produce new products and also to reproduce naturally occurring products. A common approach to performing many chemical reactions involves reacting of one or more reactants in a bulk liquid medium that
15 functions as a solvent for the one or more reactants and/or the resulting product.

- Despite many advances in the art, ongoing challenges faced by synthetic chemists include improving yields, increasing the speed of reactions, improving the purity of products, reducing the number of synthetic steps, and performing reactions that have not previously
20 been possible.

- Performing chemical reactions within the core of micelles has been found to offer advantages over conventional bulk liquid reactions due to the compartmentalisation of reactants or reactants and catalysts within the core of the micelles. However, such micelle
25 based reactions can be complicated by difficulties in isolating with sufficient purity the desired product from the micelle rich reaction mixture.

- An opportunity therefore remains to address or ameliorate one or more disadvantages or shortcomings associated with existing reactors and methods for performing chemical
30 reactions, or to at least provide a useful alternative to conventional reactors and methods for performing chemical reactions.

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Summary of the Invention

The present invention therefore provides a reactor for performing a chemical reaction, the
5 reactor comprising:

10 a liquid medium comprising micelles of assembled copolymer chains, the copolymer chains having a stimulus responsive polymer block that forms the core of the micelles, and a polymer block that is solvated by the liquid medium,

wherein the micelles contain within their core one or more reactants that are capable of reacting to form a product within the core,

15 and wherein the stimulus responsive polymer block is capable of undergoing a stimulus induced transition that causes the micellar assembled copolymer chains to disassemble and release the product into the liquid medium.

The present invention also provides a liquid medium comprising:

20 micelles of assembled copolymer chains, the copolymer chains having a stimulus responsive polymer block that forms the core of the micelles, and a polymer block that is solvated by the liquid medium,

25 wherein the micelles contain within their core one or more reactants that will react to form a product within the core,

and wherein the stimulus responsive polymer block is capable of undergoing a stimulus induced transition that causes the micellar assembled copolymer chains to disassemble and release the product into the liquid medium.

30

The present further provides a method of performing a chemical reaction, the method

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comprising:

5 providing a liquid medium comprising micelles of assembled copolymer chains, the copolymer chains having a stimulus responsive polymer block that forms the core of the micelles, and a polymer block that is solvated by the liquid medium, wherein the micelles contain within their core one or more reactants;

10 reacting the one or more reactants to form a product within the core of the micelles; and

10 subjecting the stimulus responsive polymer block to a stimulus such that it undergoes a transition and causes the micellar assembled copolymer chains to disassemble and release the product into the liquid medium.

15 The present still further provides a method of producing a product from a chemical reaction, the method comprising:

20 providing a liquid medium comprising micelles of assembled copolymer chains, the copolymer chains having a stimulus responsive polymer block that forms the core of the micelles, and a polymer block that is solvated by the liquid medium, wherein the micelles contain within their core one or more reactants;

25 reacting the one or more reactants to form the product within the core of the micelles; and

25 subjecting the stimulus responsive polymer block to a stimulus such that it undergoes a transition and causes the micellar assembled copolymer chains to disassemble and release the product into the liquid medium.

30 The present also provides use of a liquid medium comprising micelles for producing a product from a chemical reaction, the micelles being formed from assembled copolymer

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chains, the copolymer chains having a stimulus responsive polymer block that forms the core of the micelles and a polymer block that is solvated by the liquid medium, wherein the micelles are capable of containing within their core one or more reactants that will react to form the product within the core of the micelles, and wherein the stimulus responsive
5 polymer block is capable of undergoing a stimulus induced transition that causes the micellar assembled copolymer chains to disassemble and release the so formed product into the liquid medium.

In accordance with the methods of the invention, the so formed product released into the
10 liquid medium will generally be isolated. Accordingly, in one embodiment the methods further comprise isolating the so formed product from the liquid medium.

Unlike conventional micelles, micelles used in accordance with the invention are formed of an assembly of copolymer chains, the copolymer chains having a stimulus responsive
15 polymer block that forms the core of the micelles, and a polymer block that is solvated by the liquid medium. Despite the unique nature of the micelles used in accordance with the invention, those skilled in the art will nevertheless appreciate that (a) the polymer block that is solvated by the liquid medium represents the "shell" or "corona" of the micelles, and (b) the stimulus responsive polymer block that forms the core of the micelles is poorly
20 solvated by the liquid medium. Those skilled in the art will also appreciate that stimulus responsive polymers (also referred to as "smart" polymers) are polymers that undergo a physical change or transition in response to stimuli such as a change in temperature, pH, ionic strength and/or wavelength of light.

25 Contained within the core of the micelles are one or more reactants that, upon undergoing a suitable reaction, form a product within the core of the micelles. Prior to the one or more reactants being contained within the micelles, the micelles are conveniently referred to herein as being "capable" of containing within their core one or more reactants. Upon being contained within the core of the micelles, but prior to such a reaction occurring, the
30 reactants are also conveniently referred to herein as being "capable" of reacting to form the product. In other words, the one or more reactants are of a type that will react in

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accordance with the invention to form the product.

By subjecting the stimulus responsive polymer blocks that form the core of the micelles to an appropriate stimulus after the product has been formed, it has been found that the stimulus responsive polymer blocks can undergo a transition that causes the micellar assembled copolymer chains to disassemble (i.e. causes the micelles to "break up") and release the product into the liquid medium. Prior to subjecting the stimulus responsive polymer blocks that form the core of the micelles to an appropriate stimulus, the stimulus responsive polymer blocks are conveniently referred to herein as being "capable" of undergoing a stimulus induced transition that causes the micellar assembled copolymer chains to disassemble and release the product.

Accordingly, the stimulus responsive polymer block of the copolymer chains used in accordance with the invention not only provides an environment within which to perform a chemical reaction (i.e. the micelle core), but also provides a means for effectively and efficiently releasing the so formed product from the micelles. The manner in which this "release" occurs in practice will vary depending upon the nature of the physical change exhibited by a given stimulus responsive polymer in response to a given stimulus.

For example, one form of physical change may be where in response to a stimulus the stimulus responsive polymer block undergoes a transition from being hydrophobic in character to being hydrophilic in character. In that case, where the liquid medium is an aqueous liquid, the polymer block that is solvated by the aqueous liquid medium will of course be hydrophilic in character and form the shell or corona of the micelles, and the stimulus responsive polymer block (prior to the stimulus) will be hydrophobic in character and form the core of the micelles. After the one or more reactants within the core of the micelles have undergone reaction to form a product, the stimulus responsive polymer blocks may be subjected to an appropriate stimulus such that they undergo a transition from being hydrophobic in character to being hydrophilic in character. The micellar assembled copolymer chains can then be solvated by the aqueous liquid medium and as a result cause the micelles to disassemble and release the product into the aqueous liquid

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medium. By virtue of the copolymer chains being solvated by the aqueous liquid medium, the product may be more efficiently and effectively isolated from the reaction mixture.

The copolymer chains used in accordance with the invention may be selected such that
5 upon the micelle being disassembled to release the product, the disassembled copolymer chains are capable of reassembling to form micelles containing within their core one or more reactants that can again form a product within the core. In particular, the stimulus responsive polymer block of the copolymer chains may be selected to undergo a reversible transition such that the disassembled copolymer chains, upon being subjected to an
10 appropriate stimulus, reform micelles used in accordance with the invention so as to take part in a continuous chemical reaction process.

The present invention can advantageously be performed using organic apolar or aqueous polar liquid mediums. Where the liquid medium is an organic apolar liquid medium, the
15 micelles used in accordance with the invention may also be referred to by those skilled in the art as "reverse" micelles (i.e. where the core of the micelle exhibits hydrophilic character and the shell or corona of the micelle is solvated by the organic apolar liquid medium).

20 The present invention advantageously provides a means of performing a chemical reaction in an aqueous polar liquid medium that would conventionally be performed in an organic apolar liquid medium. In particular, the hydrophobic character afforded by the core of the micelles provides a discreet organic environment within the aqueous liquid medium where the chemical reaction can take place. The stimulus polymer blocks that form the micelle
25 cores can then be subjected to an appropriate stimulus that causes the micelles to disassemble and release the product into the aqueous liquid medium.

The use of an aqueous medium as a bulk reaction solvent to perform synthetic organic chemistry is particularly attractive for many reasons. For example, water is a cheap, safe
30 and environmentally benign solvent compared with conventional organic solvents typically used for organic reactions. Water also has unique physical and chemical properties that

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may provide means to realise reactivity or selectivity of chemical reactions that can not otherwise be attained using organic solvents.

5 A variety of chemical reactions can advantageously be performed in accordance with the invention. Such reactions include addition, elimination, substitution, pericyclic, rearrangement, polymerisation and redox reactions. In one embodiment, the chemical reaction performed in accordance with the invention is a polymerisation reaction such as a free radical or condensation polymerisation reaction.

10 Further aspects of the invention are discussed in more detail below.

Brief Description of the Drawings

15 Preferred embodiments of the invention will hereinafter be illustrated by way of example only with reference to the accompanying drawings in which:

Figure 1 illustrates a two dimensional schematic of copolymer chains used in accordance with the invention undergoing micellisation to form a micelle; and

20 Figure 2 illustrates transmission electron micrographs (TEMs) of near uniform particle size distributions of polymer particles prepared in accordance with the invention.

Detailed Description of the Invention

25 According to one aspect of the invention, there is provided a reactor for performing a chemical reaction. The reactor comprises a liquid medium as described herein. By "reactor" is meant a vessel, apparatus or other suitable device for containing the liquid medium and performing a selected chemical reaction.

30 Those skilled in the art will appreciate that the nature of the reactor will at least in part be determined by the type of chemical reaction being performed. For example, the reactor

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will need to be selected such that it is suitable for the conditions under which the chemical reaction is performed (e.g. pressure, temperature etc), and also compatible with the liquid medium, reactants and other reagents contained therein.

- 5 The reactor may be designed to perform the chemical reaction in batch, semicontinuous or continuous mode.

A person skilled in the art will be able to select a suitable reactor having regard to the chemical reaction being performed and the mode in which the reaction is to be performed.

- 10 For example, the reactor may be a glass or metal vessel.

In one embodiment, the reactor comprises a vessel for containing the liquid medium.

- The liquid medium used in accordance with the invention comprises micelles of assembled
15 copolymer chains. Provided that the micelles can be formed, there is no particular limitation on the type of liquid medium that may be used.

- Suitable liquid mediums include those commonly employed in conventional chemical reactions. For example, the liquid medium may be selected from acetic acid, acetone,
20 acetonitrile, benzene, 1-butanol, 2-butanol, 2-butanone, *t*-butyl alcohol, carbon tetrachloride, chlorobenzene, chloroform, cyclohexane, 1,2-dichloroethane, diethyl ether, diethylene glycol, diglyme (diethylene glycol dimethyl ether), 1,2-dimethoxy-ethane (glyme, DME), dimethylether, dimethyl-formamide (DMF), dimethyl sulfoxide (DMSO), dioxane, ethanol, ethyl acetate, ethylene glycol, glycerin, heptane,
25 Hexamethylphosphoramide (HMPA), Hexamethylphosphorous triamide (HMPT), hexane, methanol, methyl *t*-butyl ether (MTBE), methylene chloride, *N*-methyl-2-pyrrolidinone (NMP), nitromethane, pentane, Petroleum ether (ligroine), 1-propanol, 2-propanol, pyridine, tetrahydrofuran (THF), toluene, triethyl amine, water, heavy water, *o*-xylene, *m*-xylene, *p*-xylene, and combinations thereof.

30

In one embodiment of the invention, the liquid medium used is an aqueous liquid medium.

By "aqueous liquid medium" is meant a liquid medium that comprises at least 50 wt. % of water, heavy water (D₂O), or mixture thereof. An aqueous liquid medium may therefore comprise one or more other miscible co-solvents.

- 5 As discussed above, there are a number of advantages that may be derived from using an aqueous liquid medium, and in particular an aqueous liquid medium that predominantly comprises water, for example at least about 70 wt. %, or at least about 80 wt. %, or at least about 90 wt. %, or at least about 95 wt. % of water and/or heavy water. In some embodiments of the invention it may be desirable that the liquid medium consists
10 essentially of water and/or heavy water.

For avoidance of any doubt, reference herein to the liquid medium *per se* is not intended to exclude the presence of other components in that medium. The liquid medium will of course comprises the micelles, and may also comprise one or more additives that may, for
15 example, regulate pH. A liquid medium that consists essentially of water may therefore comprise one or more soluble or insoluble non-liquid additives. Thus, the "consists essentially" language is intended to be a reference to the liquid components of the medium only, and not to non-liquid components that may be present and are soluble or insoluble in the medium.

20

Those skilled in the art will appreciate that a liquid medium used in accordance with the invention may be described in terms of its polarity (i.e. its polar or apolar character), or alternatively in terms of its hydrophilic or hydrophobic character. Terms such as polar, apolar, hydrophilic, and hydrophobic are generally used in the art to convey favourable or
25 unfavourable interactions between one substance relative to another (e.g. attractive or repulsive interactions) and not to define absolute qualities of a particular substance.

For example, polar or hydrophilic materials are more likely to be wetted or solvated by an aqueous medium (attractive interaction), whereas apolar or hydrophobic materials are less
30 likely to be wetted or solvated by an aqueous medium (repulsive interaction). Unless otherwise stated, in the context of the present invention these terms are intended to be a

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reference to the polarity of the liquid medium relative to the polarity of the micelles, and in particular the regions or blocks of the copolymer chains that form the micelles. Thus, where the liquid medium is an aqueous liquid medium, the copolymer chains that form the micelles will present (a) a polymer block that is hydrophilic in character and therefore be
5 solvated by the aqueous liquid medium, and (b) a stimulus responsive polymer block that is hydrophobic in character and therefore forms the core of the micelles.

An important feature of the present invention is that the liquid medium comprises micelles. The term "micelle" is well known in the art to define an assembly or aggregate of
10 amphipathic molecules dispersed within a liquid medium. A conventional micelle in an aqueous liquid medium is made up of assembled molecules having a section or region that exhibits hydrophilic character and is solvated by the surrounding aqueous liquid medium, sequestering a hydrophobic section or region of the molecules so as to form the centre or core of the micelle. This type of micelle is commonly referred to as a "normal phase
15 micelle" or an "oil-in water micelle". "Inverse" or "reverse" micelles may also be formed where the liquid medium is hydrophobic in character (e.g. an apolar organic solvent) and the hydrophobic section or region of the assembled molecules is solvated by the hydrophobic liquid medium, sequestering the hydrophilic section or region of the molecules so as to form the micelle centre or core. Inverse or reverse micelles are also
20 commonly referred to as "water-in-oil micelles".

Micelles are typically spherical or spheroidal in shape, but can also include cylindrical and bilayer shapes. The shape and size of a given micelle is typically determined by the nature of the amphipathic molecule from which it is formed and liquid medium properties such as
25 amphipathic molecule concentration, temperature, pH and ionic strength. The process of forming micelles is commonly referred to as micellisation. The assembled amphipathic molecules may also be referred to as "micellar" assembled amphipathic molecules.

The micelles used in accordance with the invention are micelles of assembled copolymer
30 chains. In other words, the micelles are formed from or formed of copolymer chains. The copolymer chains comprise a stimulus responsive polymer block that forms the core of the

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micelles, and a polymer block that is solvated by the liquid medium. Those skilled in the art will therefore appreciate that the copolymer chains exhibit amphipathic character. The micelles used in accordance with the invention may be further described with reference to Figure 1. Thus, the copolymer chains may be described as an A-B diblock copolymer with
5 one block represented by a stimulus responsive polymer, and the other block represented by a polymer that is capable of being solvated by the liquid medium. Micellisation of the copolymer chains gives rise to a micelle where the stimulus responsive polymer block forms the core of the micelle, and the polymer block that is solvated by the liquid medium forms the micelle shell or corona.

10

Although the copolymer chain illustrated in Figure 1 is described above in terms of being an A-B diblock copolymer, the copolymer chains used in accordance with the invention are not limited to such a structure. In particular, provided that the copolymer chains are capable of forming a micelle and comprise (a) a stimulus responsive polymer block that
15 forms the micelle core, and (b) a polymer block that is solvated by the liquid medium, there is no particular limitation regarding the composition or structure of the copolymer.

For example, the copolymer chains may have an A-B-A triblock copolymer structure where the A blocks, which may be the same or different, represent polymer that is capable
20 of being solvated by the liquid medium, and the B block represents a stimulus responsive polymer that forms the micelle core.

The copolymer chains may be linear or branched.

25 The copolymer chains may comprise one or more stimulus responsive polymer blocks, and one or more polymer blocks that are solvated by the liquid medium.

By the copolymer chains comprising a "polymer block(s)" in the context of a "stimulus responsive polymer block" and a "polymer block that is solvated by the liquid medium" is
30 meant that the polymer chains have a section or region that is (a) stimulus responsive, and

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(b) solvated by the liquid medium. Each polymer block may be independently linear or branched. Each polymer block may be independently a homo- or co-polymer.

The copolymer chains used in accordance with the invention will generally have an overall
5 number average molecular weight ranging from about 600 to about 130,000.

In connection with this, the number average molecular weight of the polymer block that is solvated by the liquid medium will generally range from about 100 to about 50,000, and the number average molecular weight of the stimulus responsive polymer block that forms
10 the core of the micelles will generally range from about 500 to about 80,000.

As will be discussed in more detail below, the stimulus responsive polymer block of the copolymer chains not only forms the core of the micelles but also provides a means to promote disassembly of the micelle structure. The stimulus responsive polymer block
15 provides this means for disassembly by undergoing a transition upon being subjected to an appropriate stimulus.

Stimulus responsive polymers suitable for use in accordance with the invention are, as hereinbefore described, polymers that undergo a physical transition or change in response
20 to stimuli such as a change in temperature, pH, ion concentration and/or wavelength of light.

The physical change exhibited by a stimulus responsive polymer in response to a given stimulus can vary depending upon the type of polymer employed. Nevertheless, in
25 accordance with the invention the physical change must cause the micellar assembled copolymer chains to disassemble.

In one embodiment of the invention, the stimulus responsive polymer is of a type that upon being subjected to a stimulus undergoes a transition from being hydrophobic in character
30 to being hydrophilic in character or vice versa.

The physical change exhibited by the polymer may be, and preferably is, reversible.

Representative stimulus responsive polymers include temperature responsive polymers, pH responsive polymers, light responsive polymers, and specific ion responsive polymers.

5

The stimulus responsive polymer may be in the form of a homopolymer or a copolymer.

The stimulus responsive polymer may be a natural polymer or a synthetic polymer.

- 10 Poly(N-isopropyl acrylamide) (P(NIPAAm)) is a well known temperature responsive polymer and exhibits a lower critical solution temperature (LCST) of about 36°C in an aqueous liquid medium. It can reversibly assume (i) an expanded random coil structure below the LCST that is hydrophilic in character and readily wet or solvated by an aqueous liquid medium, and (ii) a collapsed globular structure above the LCST that is hydrophobic
- 15 in character and not readily wet or solvated by an aqueous liquid medium.

Examples of suitable temperature responsive polymers include P(NIPAAm) homopolymer and copolymers of N-isopropyl acrylamide (NIPAAm) with one or more other ethylenically unsaturated monomers as herein described.

20

- When NIPAAm is copolymerised with one or more hydrophilic comonomers such as acrylamide, the LCST of the copolymer can be raised relative to that of P(NIPAAm). The opposite may occur when it is copolymerised with one or more hydrophobic comonomers, such as N-t-butyl acrylamide. Copolymers of NIPAAm with hydrophilic monomers such
- 25 as acrylamide have a higher LCST and generally a broader temperature range of precipitation (relative to P(NIPAAm)), while copolymers of NIPAAm with hydrophobic monomers such as N-t-butyl acrylamide have a lower LCST (relative to P(NIPAAm)) and are generally more likely to retain the sharp transition characteristic of P(NIPAAm).

- 30 Examples of pH responsive polymers are generally derived from pH responsive vinyl monomers such as acrylic acid, methacrylic acid, and other alkyl-substituted acrylic acids,

maleic anhydride, maleic acid, 2-acryamido-2-methyl-1-propanesulfonic acid, N-vinyl formamide, N-vinyl acetamide, aminoethyl methacrylate, phosphoryl ethyl acrylate or methacrylate. pH responsive polymers may also be prepared as polypeptides from amino acids (e.g. polylysine or polyglutamic acid) all derived from naturally occurring polymers
5 such as proteins (e.g. lysozyme, albumin, casein), or polysaccharides (e.g. alginic acid, hyaluronic acid, carrageenan, chitosan, carboxymethyl, cellulose) or nucleic acids such as DNA. pH responsive polymers usually comprise pendant pH sensitive functional groups such as $-OPO(OH)_2$, $-COOH$ or $-NH_2$.

10 By copolymerising a monomer that gives rise to a temperature responsive polymer such as NIPAAm with a small amount (less than about 10 mole %) of a comonomer that gives rise to a pH responsive polymer such as acrylic acid, the resulting copolymer can display both temperature and pH responsiveness. The LCST of such a copolymer can remain unaffected, sometimes even lowered a few degrees, at a pH where the copolymer is not
15 ionised, but the LCST can be dramatically raised if the pH sensitive groups become ionised. When pH sensitive groups are present at a high concentration, the LCST response of the temperature responsive effect may be for all practical purposes eliminated.

Block copolymers derived from pH and temperature responsive monomers can be prepared
20 such that they retain both pH and temperature transitions independently. For example, a block copolymer having a pH responsive block (polyacrylic acid) and a temperature responsive block (P(NIPAAm)) can retain independent pH and temperature responsiveness.

25 Examples of light responsive polymers include those that contain chromophoric groups pendant to or along the main chain of the polymer and, when exposed to an appropriate wavelength of light, can be isomerised from a trans to a cis form, which can be dipolar and more hydrophilic and promote reversible polymer conformational changes. Other light sensitive groups can also be converted by light stimulation from a relatively non-polar
30 hydrophobic, non-ionised state to a hydrophilic ionic state.

In the case of pendant light-sensitive groups such as a light-sensitive dye (e.g. aromatic azo compounds or stilbene derivatives), they may be conjugated to a reactive monomer (an exception is a dye such as chlorophyllin, which already comprises a vinyl group) and then homopolymerised or copolymerised with one or more other monomers, including
5 temperature responsive or pH responsive monomers. The light sensitive group may also be conjugated to an end of a polymer chain, including a stimulus responsive polymer chain. Techniques for conjugating such light sensitive groups to monomers or polymer chains are known.

10 Generally, the light responsive polymers will be prepared from vinyl monomers that contain light-sensitive pendant groups. Such monomers may be homopolymerised or copolymerised with one or more other ethylenically unsaturated monomers as herein described.

15 The light-sensitive groups may be dye molecules that isomerise or become ionised when they absorb certain wavelength of light, converting them from hydrophobic to hydrophilic confirmations or vice versa, or they may be dye molecules which give off heat when they absorb certain wavelength of light. In the former case, the isomerisation alone can cause chain expansion or collapse, while in the later case the polymer can precipitate if it is also
20 temperature responsive.

Examples of chromophoric groups that may give rise to the light responsive properties include aromatic diazo dyes. When a dye of this type is exposed to 350-410nm UV light, the trans form of the dye, which is hydrophobic in character, can be isomerised to its cis
25 form, which is dipolar and more hydrophilic in character, this in turn can cause polymer conformational changes. Exposure of the dye to visible light at about 750nm can reverse this phenomenon.

Examples of specific ion responsive polymers include polysaccharides such as carrageenan
30 that change their confirmation, for example, from a random to an ordered confirmation, as a function of exposure to ions such as K^+ or Ca^{2+} . Other examples of specific ion

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responsive polymers include polymers with pendant ion chelating groups such histidine or EDTA.

As indicated above, the stimulus responsive polymers may be responsive to multiple
5 stimuli. For example, if a light responsive polymer is also temperature responsive, a UV
or visible light stimulated conversion of a chromophor conjugated along the polymer
backbone to a more hydrophobic or hydrophilic confirmation can also stimulate the
dissolution/wetting or precipitation of the copolymer, depending upon the polymer
composition and temperature. Alternatively, if the chromophor absorbs light and converts
10 it to thermal energy rather than stimulating isomerisation, then the localised heating can
also stimulate a phase change in a temperature responsive polymer such as P(NIPAAm)
when the system temperature is near the phase separation temperature. The incorporation
of multiple sensitivities through the copolymerisation of appropriate monomers can lend
greater versatility to the stimulus responsive polymers used in accordance with the
15 invention.

In one embodiment, the stimulus responsive polymer used in accordance with the
invention comprises a temperature responsive polymer that in response to a change in
temperature undergoes a transition, preferably a reversible transition, from being
20 hydrophobic in character to being hydrophilic in character or vice versa.

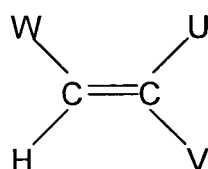
Provided that the copolymer chains assemble to form micelles in the liquid medium, there
is no particular limitation regarding the nature or composition of the polymer block that is
solvated by the liquid medium. This polymer block will generally not be a stimulus
25 responsive polymer block.

The polymer block of the copolymer chains that is solvated by the liquid medium will
generally be a polymer that has been formed by the polymerisation of one or more
ethylenically unsaturated monomers. Suitable ethylenically unsaturated monomers include
30 those that can be polymerised by a radical polymerisation process. If desired, the
monomers should also be capable of being polymerised with other monomers. The factors

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which determine copolymerisability of various monomers are well documented in the art. For example, see: Greenlee, R.Z., in Polymer Handbook 3rd Edition (Brandup, J., and Immergut, E.H. Eds) Wiley: New York, 1989 p II/53.

- 5 Suitable ethylenically unsaturated monomers that may be used in accordance with the invention include those of formula (I):



(I)

- 10 where U and W are independently selected from $-\text{CO}_2\text{H}$, $-\text{CO}_2\text{R}^1$, $-\text{COR}^1$, $-\text{CSR}^1$, $-\text{CSOR}^1$, $-\text{COSR}^1$, $-\text{CONH}_2$, $-\text{CONHR}^1$, $-\text{CONR}^1_2$, hydrogen, halogen and optionally substituted C_1 - C_4 alkyl or U and W form together a lactone, anhydride or imide ring that may itself be optionally substituted, where the optional substituents are independently selected from hydroxy, $-\text{CO}_2\text{H}$, $-\text{CO}_2\text{R}^1$, $-\text{COR}^1$, $-\text{CSR}^1$, $-\text{CSOR}^1$,
15 $-\text{COSR}^1$, $-\text{CN}$, $-\text{CONH}_2$, $-\text{CONHR}^1$, $-\text{CONR}^1_2$, $-\text{OR}^1$, $-\text{SR}^1$, $-\text{O}_2\text{CR}^1$, $-\text{SCOR}^1$, and $-\text{OCSR}^1$;

- V is selected from hydrogen, R^1 , $-\text{CO}_2\text{H}$, $-\text{CO}_2\text{R}^1$, $-\text{COR}^1$, $-\text{CSR}^1$, $-\text{CSOR}^1$, $-\text{COSR}^1$, $-\text{CONH}_2$, $-\text{CONHR}^1$, $-\text{CONR}^1_2$, $-\text{OR}^1$, $-\text{SR}^1$, $-\text{O}_2\text{CR}^1$, $-\text{SCOR}^1$, and $-\text{OCSR}^1$;
20

- where the or each R^1 is independently selected from optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted arylalkyl, optionally substituted heteroarylalkyl, optionally substituted alkylaryl, optionally substituted alkylheteroaryl, and an optionally substituted polymer chain.
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The or each R¹ may also be independently selected from optionally substituted C₁-C₂₂ alkyl, optionally substituted C₂-C₂₂ alkenyl, optionally substituted C₂-C₂₂ alkynyl, optionally substituted C₆-C₁₈ aryl, optionally substituted C₃-C₁₈ heteroaryl, optionally substituted C₃-C₁₈ carbocyclyl, optionally substituted C₂-C₁₈ heterocyclyl, optionally substituted C₇-C₂₄ arylalkyl, optionally substituted C₄-C₁₈ heteroarylalkyl, optionally substituted C₇-C₂₄ alkylaryl, optionally substituted C₄-C₁₈ alkylheteroaryl, and an optionally substituted polymer chain.

R¹ may also be selected from optionally substituted C₁-C₁₈ alkyl, optionally substituted C₂-C₁₈ alkenyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aralkyl, optionally substituted heteroarylalkyl, optionally substituted alkaryl, optionally substituted alkylheteroaryl and a polymer chain.

In one embodiment, R¹ may be independently selected from optionally substituted C₁-C₆ alkyl.

Examples of optional substituents for R¹ include those selected from alkyleneoxidyl (epoxy), hydroxy, alkoxy, acyl, acyloxy, formyl, alkylcarbonyl, carboxy, sulfonic acid, alkoxy- or aryloxy-carbonyl, isocyanato, cyano, silyl, halo, amino, including salts and derivatives thereof. Examples polymer chains include those selected from polyalkylene oxide, polyarylene ether and polyalkylene ether.

Examples of monomers of formula (I) include maleic anhydride, N-alkylmaleimide, N-arylmaleimide, dialkyl fumarate and cyclopolymerisable monomers, acrylate and methacrylate esters, acrylic and methacrylic acid, styrene, acrylamide, methacrylamide, and methacrylonitrile, mixtures of these monomers, and mixtures of these monomers with other monomers.

Other examples of monomers of formula (I) include: methyl methacrylate, ethyl methacrylate, propyl methacrylate (all isomers), butyl methacrylate (all isomers), 2-

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ethylhexyl methacrylate, isobornyl methacrylate, methacrylic acid, benzyl methacrylate, phenyl methacrylate, methacrylonitrile, alpha-methylstyrene, methyl acrylate, ethyl acrylate, propyl acrylate (all isomers), butyl acrylate (all isomers), 2-ethylhexyl acrylate, isobornyl acrylate, acrylic acid, benzyl acrylate, phenyl acrylate, acrylonitrile, styrene,

5 functional methacrylates, acrylates and styrenes selected from glycidyl methacrylate, 2-hydroxyethyl methacrylate, hydroxypropyl methacrylate (all isomers), hydroxybutyl methacrylate (all isomers), N,N-dimethylaminoethyl methacrylate, N,N-diethylaminoethyl methacrylate, triethyleneglycol methacrylate, itaconic anhydride, itaconic acid, glycidyl acrylate, 2-hydroxyethyl acrylate, hydroxypropyl acrylate (all isomers), hydroxybutyl

10 acrylate (all isomers), N,N-dimethylaminoethyl acrylate, N,N-diethylaminoethyl acrylate, triethyleneglycol acrylate, methacrylamide, N-methylacrylamide, N,N-dimethylacrylamide, N-tert-butylmethacrylamide, N-n-butylmethacrylamide, N-methylolmethacrylamide, N-ethylolmethacrylamide, N-tert-butylacrylamide, N-n-butylacrylamide, N-methylolacrylamide, N-ethylolacrylamide, vinyl benzoic acid (all

15 isomers), diethylamino styrene (all isomers), alpha-methylvinyl benzoic acid (all isomers), diethylamino alpha-methylstyrene (all isomers), p-vinylbenzene sulfonic acid, p-vinylbenzene sulfonic sodium salt, trimethoxysilylpropyl methacrylate, triethoxysilylpropyl methacrylate, tributoxysilylpropyl methacrylate, dimethoxymethylsilylpropyl methacrylate, diethoxymethylsilylpropyl methacrylate,

20 dibutoxymethylsilylpropyl methacrylate, diisopropoxymethylsilylpropyl methacrylate, dimethoxysilylpropyl methacrylate, diethoxysilylpropyl methacrylate, dibutoxysilylpropyl methacrylate, diisopropoxysilylpropyl methacrylate, trimethoxysilylpropyl acrylate, triethoxysilylpropyl acrylate, tributoxysilylpropylacrylate, dimethoxymethylsilylpropyl acrylate, diethoxymethylsilylpropyl acrylate, dibutoxymethylsilylpropyl acrylate,

25 diisopropoxymethylsilylpropyl acrylate, dimethoxysilylpropyl acrylate, diethoxysilylpropyl acrylate, dibutoxysilylpropyl acrylate, diisopropoxysilylpropyl acrylate, vinyl acetate, vinyl butyrate, vinyl benzoate, vinyl chloride, vinyl fluoride, vinyl bromide, maleic anhydride, N-phenylmaleimide, N-butylmaleimide, N-vinylpyrrolidone, N-vinylcarbazole, butadiene, ethylene and chloroprene. This list is not exhaustive.

30

The composition of the copolymer chains used in accordance with the invention will

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generally be selected having regard to the type of chemical reaction that is to be performed and the type of liquid medium in which the reaction is to be performed.

In selecting a suitable polymer block of the copolymer chain that is to be solvated by the liquid medium, consideration will of course need to be primarily given to the nature of the liquid medium to be used. Thus, where the liquid medium is hydrophobic in character, the polymer block that is to be solvated by the liquid medium should also be relatively hydrophobic in character. Conversely, where the liquid medium is hydrophilic in character, the polymer block that is to be solvated by the liquid medium should be relatively hydrophilic in character. Those skilled in the art will be able to select a suitable polymer block based on the type of liquid medium to be used.

As a guide only, examples of ethylenically unsaturated monomers that may be used to prepare a hydrophobic polymer include, but are not limited to, styrene, alpha-methyl styrene, butyl acrylate, butyl methacrylate, amyl methacrylate, hexyl methacrylate, lauryl methacrylate, stearyl methacrylate, ethyl hexyl methacrylate, crotyl methacrylate, cinnamyl methacrylate, oleyl methacrylate, ricinoleyl methacrylate, vinyl butyrate, vinyl tert-butyrate, vinyl stearate and vinyl laurate.

As a guide only, examples of ethylenically unsaturated monomers that may be used to prepare hydrophilic polymer include, but are not limited to, acrylic acid, methacrylic acid, hydroxyethyl methacrylate, hydroxypropyl methacrylate, acrylamide and methacrylamide, hydroxyethyl acrylate, N-methylacrylamide, N,N-dimethylacrylamide or dimethylaminoethyl methacrylate, or copolymers thereof.

In one embodiment, the polymer block that is solvated by the liquid medium comprises the polymerised residue of one or more monomers selected from acrylic acid, methacrylic acid, hydroxyethyl methacrylate, hydroxypropyl methacrylate, acrylamide and methacrylamide, hydroxyethyl acrylate, N-methylacrylamide, N,N-dimethylacrylamide and dimethylaminoethyl methacrylate.

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In a further embodiment, the polymer block that is solvated by the liquid medium comprises the polymerised residue of one or more monomers selected from styrene, alpha-methyl styrene, butyl acrylate, butyl methacrylate, amyl methacrylate, hexyl methacrylate, lauryl methacrylate, stearyl methacrylate, ethyl hexyl methacrylate, crotyl methacrylate, 5 cinnamyl methacrylate, oleyl methacrylate, ricinoleyl methacrylate, vinyl butyrate, vinyl tert-butyrate, vinyl stearate and vinyl laurate.

Where the chemical reaction to be performed is of a type that is to take place in a hydrophobic environment, the stimulus responsive polymer block of the copolymer chains 10 will be selected to afford at that point a suitably hydrophobic micelle core. In that case, it will be appreciated that the liquid medium will be relatively hydrophilic in character (e.g. an aqueous liquid medium), and the polymer block of the copolymer chains that is solvated by the liquid medium will be selected such that it is suitably hydrophilic in character.

15 Similarly, where the chemical reaction to be performed is of a type that is to take place in a hydrophilic environment, the stimulus responsive polymer block of the copolymer chains will be selected to afford at that point a suitably hydrophilic micelle core. In that case, it will be appreciated that the liquid medium will be relatively hydrophobic in character (e.g. an apolar organic liquid medium), and the polymer block of the copolymer chains that is 20 solvated by the liquid medium will be selected such that it is suitably hydrophobic in character.

As a more specific example of selecting an appropriate liquid medium and copolymer chains for use in accordance with the invention, the chemical reaction to be performed 25 may, for example, be one that would conventionally be conducted in a hydrophobic environment (e.g. an apolar organic solvent) at about 65°C. In that case, a chemical reaction in accordance with the invention may be performed using an aqueous liquid medium and copolymer chains having (a) a temperature responsive polymer block that is, for example, hydrophobic in character above about 36°C and hydrophilic in character 30 below about 36°C, and (b) a polymer block that is solvated by the aqueous liquid medium. Accordingly, at temperatures above about 36°C the copolymer chains present amphipathic

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character and can assemble into micelles containing within their core the one or more reactants. The chemical reaction may then be performed at 65°C within the core of the micelles. Upon lowering the temperature of the reaction mixture to below about 36°C, the temperature responsive polymer blocks will undergo a transition and become relatively hydrophilic in character. The micellar assembled copolymer chains may then be solvated by the aqueous liquid medium and disassemble to release the product of the reaction into the liquid medium.

The copolymer chains used in accordance with the invention may be prepared by any suitable method known to those skilled in the art. For example, the copolymer chains may be prepared by polymerising ethylenically unsaturated monomers (such as those herein described) by radical, coordination or ionic polymerisation techniques well known to those skilled in the art.

The polymerisation technique employed to prepare the copolymer chains may be living or non-living.

Living polymerisation is generally considered in the art to be a form of chain polymerisation in which irreversible chain termination is substantially absent. An important feature of living polymerisation is that polymer chains will continue to grow while monomer and the reaction conditions to support polymerisation are provided. Polymer chains prepared by living polymerisation can advantageously exhibit a well defined molecular architecture, a predetermined molecular weight and narrow molecular weight distribution or low polydispersity.

Examples of living polymerisation include ionic polymerisation and controlled radical polymerisation (CRP). Examples of CRP include, but are not limited to, iniferter polymerisation, stable free radical mediated polymerisation (SFRP), atom transfer radical polymerisation (ATRP), and reversible addition fragmentation chain transfer (RAFT) polymerisation.

In one embodiment of the invention, the copolymer chains are prepared using living polymerisation techniques. Equipment, conditions, and reagents for performing living polymerisation to prepare copolymers well known to those skilled in the art and will be discussed in more detail below.

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A diverse array of chemical reactions may be performed in accordance with the invention. General chemical reaction types include, but are not limited to, addition reactions, elimination reactions, substitution reactions, pericyclic reactions, polymerisation reactions, rearrangement reactions, coupling reactions and redox reactions.

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Examples of suitable chemical reactions also include those outlined in "Comprehensive Organic Transformations – a guide to functional group preparations" by Richard C. Larock, 1989VCH Publishers, Inc., ISBN 0-89573-710-8, the entire contents of which are incorporated herein by way of cross reference.

15

Examples of more specific chemical reactions include, but are not limited to, Acetoacetic Ester Condensation, Acetoacetic Ester Syntheses, Acyloin Condensation, Adkins-Peterson Reaction, Akabori Amino Acid Reactions, Aldol-Condensation, Algar-Flynn-Oyamada(AFO)Reaction, Allan-Robinson Reaction, Allylic Rearrangement, Amadori
20 Rearrangement, Andrussov Oxidation, Arens-van Dorp Synthesis, Isler Modification, Arndt-Eistert Synthesis, Auwers Synthesis, Aza-Claisen Rearrangement, Azide Alkyne Huisgen Cycloaddition Reaction, Baeyer-Drewson Indigo Synthesis, Baeyer-Villiger Rearrangement, Bakeland(Bakelite)Process, Baker-Venkataraman Transformation, Bally-Scholl Synthesis, Bamberger Rearrangement, Bamberger Triazine Synthesis, Bamford-Stevens Reaction, Barbier Reaction, Barbier-Wieland Degradation, Bardhan-Sengupta
25 Phenanthrene Synthesis, Bart Reaction (Scheller Modification), Barton Deoxygenation (Barton-McCombie Reaction), Barton Olefin Synthesis (Barton-Kellogg Reaction), Barton Reaction, Baudisch Reaction, Baylis-Hillman Reaction, Bechamp Reaction, Beckmann Rearrangement, Benary Reaction, Benkeser Reduction, Benzidine Rearrangement,
30 Semidine Rearrangement, Benzilic Acid Rearrangement, Benzoin Condensation, Bergman Reaction, Bergmann Azlactone Peptide Synthesis, Bergmann Degradation, Bergmann-

Zevars Carbobenzoxy Method, Bernthsen Acridine Synthesis, Betti Reaction, Biginelli Pyrimidine Synthesis, Birch Reduction, Bischler-Möhlau Indole Synthesis, Bischler-Napieralski Reaction, Bischler-Triazine Synthesis, Blaise Ketone Synthesis, Blaise Reaction, Blanc (Chloromethylation) Reaction, Blanc Reaction (Blanc Rule), Bodroux-Chichibabin Aldehyde Synthesis, Bodroux Reaction, Bogert-Cook Synthesis, Bohn-Schmidt Reaction, Boord Olefin Synthesis, Borsche-Drechsel Cyclization, Bosch-Meiser Urea Process, Bouveault Aldehyde Synthesis, Bouveault-Blanc Reduction, Boyland-Sims Oxidation, Bradsher Cyclization(Bradsher Cycloaddition), Bradsher Reaction, Brook Rearrangement, Bucherer-Bergs Reaction, Bucherer Carbazole Synthesis, Bucherer Reaction, Buchner-Curtius-Schlotterbeck Reaction, Buchner Method of Ring Enlargement, Buchwald-Hartwig Cross Coupling Reaction, Camps Quinoline Synthesis, Cannizzaro Reaction, Carroll Rearrangement, Castro-Stephens Coupling(Castro Reaction,Stephens-Castro Coupling), Chapman Rearrangement, Chichibabin Pyridine Synthesis, Chichibabin Reaction, Chugaev Method, Chugaev Reaction (Tshugaeff Olefin Synthesis), Ciamician-Dennstedt Rearrangement, Claisen Condensation, Claisen Rearrangement, Claisen-Schmidt Condensation, Clemmensen Reaction, Combes Quinoline Synthesis, Conrad-Limpach Synthesis, Cope Elimination Reaction, Cope Rearrangement, Corey-Bakshi-Shibata Reduction(CBS), Corey-House Synthesis, Corey-Kim Oxidation, Corey-Winter Olefin Synthesis, Cornforth Rearrangement, Craig Method, Criegee Reaction, Creighton Process, Criegee Reaction, Cu(I)-catalysed [3+2] "CLICK" Chemistry Reaction, Curtius Rearrangement (Curtius Reaction), Dakin Reaction, Dakin-West Reaction, Darapsky Degradation, Darzens Condensation (Darzens-Claisen Reaction; Glycidic Ester Condensation), Darzens Procedure, Darzens Synthesis of Tetralin Derivatives, Darzens-Nenitzescu Synthesis of Ketones, Delepine Reactions, Demjanov Rearrangement, Dess-Martin Oxidation, de Mayo Reaction, D-Homo Rearrangement of Steroids, Dieckmann Reaction, Diels Alder Reaction, Diels Reese Reaction, Dienol Benzene Rearrangement, Dienone-Phenol Rearrangement, Dimroth Rearrangement, Doebner Reaction, Doebner-Miller Synthesis (Beyer Method for Quinolines), Doering-LaFlamme Carbon Chain Extension, Dotz Reaction, Duff Reaction, Dutt-Wormall Reaction, Eastwood Reaction (Eastwood Deoxygenation), Eder Reaction, Edman Degradation, Ehrlich-Sachs Reaction, Einhorn-Brunner Reaction, Elbs Persulfate Oxidation, Elbs Reaction, Eltekoff Reaction,

Emde Degradation, Emmert Reaction, Ene Reaction (Alder-Ene Reaction), Erlenmeyer-Plochl Azlactone and Amino Acid Synthesis, Eschenmoser Fragmentation, Eschweiler-Clarke Reaction, Etard Reaction, Favorskii-Babayan Synthesis, Favorskii Rearrangement, Feist-Benary Synthesis, Fenton Reaction, Ferrario Reaction, Fickelstein Reaction, Fischer-Hepp Rearrangement, Fischer Indole Synthesis, Fischer Oxazole Synthesis, Fischer Peptide Synthesis, Fischer Phenylhydrazine Reaction, Fischer Phenylhydrazone and Oxazone Reaction, Fischer-Speier Esterification Method, Flood Reaction, Forster-Decker Method, Forster Reaction, Franchimont Reaction, Frankland-Duppa Reaction, Frankland Synthesis, Freund Reaction, Friedel-Crafts Reaction, Friedlaender Synthesis, Fries Rearrangement, Fritsch-Buttenberg-Wischell Rearrangement, Fujimoto-Belleau Reaction, Gabriel-Coleman Rearrangement (Gabriel Isoquinoline Synthesis), Gabriel Ethylenimine Method, Gabriel Synthesis, Gallagher-Hollander Degradation, Gastaldi Synthesis, Gattermann Aldehyde Synthesis, Gattermann-Koch Reaction, Gattermann-Skita Synthesis, Gibbs Phthalic Anhydride Process, Glaser Coupling, Gogte Synthesis, Goldschmidt Process, Gomberg-Bachmann-Hey Reaction, Gomberg-Free Radical Reaction, Gould-Jacobs Reaction, Graebe-Ullmann Synthesis, Grob Fragmentation, Griess Diazo Reaction, Witt and Knoevenagel Diazotization Methods, Grignard Degradation, Grignard Reaction, Grundmann Aldehyde Synthesis, Gryszkiewicz-Trochimowski and McCombie Method, Guareschi-Thorpe Condensation, Guerbet Reaction, Gutknecht Pyrazine Synthesis, Haller-Bauer Reaction, Hammick Picolinic Acid Decarboxylation (Hammick Reaction), Hantzsch Pyridine Synthesis, Hantzsch Pyrrole Synthesis, Harries Ozonide Reaction, Haworth Methylation, Haworth Phenanthrene Synthesis, Hayashi Rearrangement, Helferich Method, Heck Reaction, Hell-Vollard-Zelinsky Halogenation, Henkel Reaction, HERON Rearrangement (Heteroatom Rearrangements on Nitrogen), Henry Reaction (Kamlet Reaction), Herz Reaction, Herzig-Meyer Alkamide Group Determination, Heumann Indigo Synthesis, Hilbert-Johnson Reaction, Hinsberg Oxindole and Oxiquinoline Synthesis, Hinsberg Reaction, Hinsberg Sulfone Synthesis, Hinsberg Synthesis of Thiophene Derivatives, Hoch-Campbell Ethylenimine Synthesis, Hofmann Degradation (Exhaustive Methylation), Hofmann Isonitrile Synthesis (Carbylamine Reaction), Hofmann-Löffler Reaction (Löffler-Freytag Reaction), Hofmann-Martius Rearrangement, Hofmann Reaction (Hofmann Rearrangement), Hofmann-Sand Reactions, Hooker Reaction,

Houben-Fischer Synthesis, Houben-Hoesch Reaction, Hunsdiecker Reaction(Borodine Reaction), Hydroboration Reaction, Ivanov(Ivanoff) Reagent, Jacobsen Epoxidation, Jacobsen Rearrangement, Janovsky Reaction, Japp-Klingemann Reaction, Jones Oxidation, Jourdan-Ullmann-Goldberg Synthesis, Julia Olefination (Julia-Lythgoe
5 Olefination), Kabachnik-Fields Reaction, Kendall-Mattox Reaction, Kiliani-Fischer Synthesis, Kishner Cyclopropane Synthesis, Knoevenagel Condensation, Knoop-Oesterlin Amino Acid Synthesis, Knorr Pyrazole Synthesis, Knorr Pyrrole Synthesis, Knorr Quinoline Synthesis, Koch-Haaf Carboxylations, Kochi Reaction, Koenigs-Knorr Synthesis, Kolbe Electrolytic Synthesis, Kolbe-Schmitt Reaction, Kostanecki Acylation,
10 Krafft Degradation, Krapcho Decarboxylation, Krohnke Aldehyde Synthesis (Krohnke Oxidation), Krohnke Pyridine Synthesis, Kucherov Reaction, Kuhn-Winterstein Reaction, Ladenburg Rearrangement, Lebedev Process, Lehmstedt-Tanasescu Reaction, Letts Nitrile Synthesis, Leuckert Amide Synthesis, Leuckart(Leukart) Reaction, Leuckert Thiophenol Reaction, Leuckart-Wallach Reaction, Levinstein Process, Lieben Iodoform Reaction
15 (Haloform Reaction), Lobry de Bruyn-van Ekenstein Transformation, Lossen Rearrangement, McFadyen-Stevens Reaction, McLafferty Rearrangement, Madelung Synthesis, Malaprade Reaction (Periodic Acid Oxidation), Malonic Ester Synthesis, Mannich Reaction, McMurry Reaction, Merckwald Asymmetric Synthesis, Marschalk Reaction, Martinet Dioxindole Synthesis, ter Meer Reaction, Meerwein Arylation,
20 Meerwein-Ponndorf-Verley Reduction, Meisenheimer Rearrangements, Menshutkin Reaction, Mentzer Pyrone Synthesis, Merrifield Solid-Phase Peptide Synthesis (SPPS), Meyer and Hartmann Reaction, Meyer Reaction, Meyer-Schuster Rearrangement; Rupe Reaction, Meyer Synthesis (Victor Meyer Synthesis), Meyers Aldehyde Synthesis, Michael Reaction, Michaelis-Arbuzov Reaction, Miescher Degradation, Mignonac
25 Reaction, Milas Hydroxylation of Olefins, Mislow-Evans Rearrangement, Mitsunobu Reaction, Moore Myers Cyclization, Mukaiyama Aldol Reaction, Mukaiyama-Michael Reaction, Nagata Hydrocyanation, Nametkin Rearrangement, Nazarov Cyclization Reaction, Neber Rearrangement, Nef Reaction, Nencki Reaction, Negishi Cross Coupling, Nenitzescu Indole Synthesis, Nenitzescu Reductive Acylation, Nicholas Reaction,
30 Niementowski Quinazoline Reaction, Niementowski Quinoline Synthesis, Nierenstein Reaction, Nitroxide Coupling Reaction, Norrish Type Cleavage, Noyori Hydrogenation,

- Nozaki-Hiyama Coupling Reaction (Nozaki-Hiyama-Kishi Reaction), Olefin Metathesis, Oppenauer Oxidation, Ostromyslenskii(Ostromisslenskii)Reaction, Overman Rearrangement, Paal-Knorr Pyrrole Synthesis, Parham Cyclization, Paolini Reaction, Passerini Reaction, Paterno-Büchi Reaction, Pauson-Khand Reaction, Payne
- 5 Rearrangement, Pechmann Condensation, Pechmann Pyrazole Synthesis, Pellizzari Reaction, Pelouze Synthesis, Perkin Alicyclic Synthesis, Perkin Reaction, Perkin Rearrangement (Coumarin—Benzofuran Ring Contraction), Perkow Reaction, Peterson Reaction (Olefination), Petrenko-Kritschenko Piperidone Synthesis, Pfau-Plattner Azulene Synthesis, Pfitzinger Reaction, Pfitzner-Moffatt Oxidation (Moffatt Oxidation), Pictet-
- 10 Gams Isoquinoline Synthesis, Pictet-Hubert Reaction, Pictet-Spengler Isoquinoline Synthesis, Piloty Alloxazine Synthesis, Piloty-Robinson Pyrrole Synthesis, Pinacol Coupling Reaction, Pinacol Rearrangement, Pinner Amidine Synthesis, Pinner Method for Ortho Esters, Pinner Triazine Synthesis, Piria Reaction, Polonovski Reaction, Pomeranz-Fritsch Reaction (Schlittler-Müller Modification), Ponzio Reaction, Prévost Reaction,
- 15 Prilezhaev (Prileschajew) Reaction, Prins Reaction, Pschorr Reaction (Pschorr Synthesis), Pummerer Reaction, Purdie (Irvine-Purdie) Methylation, Quelet Reaction, Ramberg-Bäcklund Reaction, Rap-Stoermer Condensation Salol Reaction, Raschig Phenol Process, Reed Reaction, Reformatsky (Reformatskii) Reaction, Reilly-Hickinbottom Rearrangement, Reimer-Tiemann Reaction, Reissert Indole Synthesis, Reissert Reaction,
- 20 Reppe Chemistry, Retro-Diels-Alder Reaction, Retropinacol Rearrangement, Reverdin Reaction, Riehm Quinoline Synthesis, Riemschneider Thiocarbamate Synthesis, Riley Oxidations (Selenium Dioxide Oxidation), Ritter Reaction, Robinson Annellation Reaction, Robinson-Schöpf Reaction, Rosenmund von Braun Synthesis, Rosenmund Reaction(Arsonic Acids), Rosenmund Reduction, Rothmund Reaction, Rowe
- 25 Rearrangement, Rubottom Oxidation, Ruff-Fenton Degradation, Ruzicka Large Ring Synthesis, Saegusa Oxidation, Sakurai Reaction (Hosomi-Sakurai Reaction), Salol Reaction, Sandmeyer Diphenylurea Isatin Synthesis, Sandmeyer Isonitrosoacetanilide Isatin Synthesis, Sandmeyer Reaction, Sarett Oxidation, Schiemann Reaction, Schiff Reaction, Schmidlin Ketene Synthesis, Schmidt Reaction, Scholl Reaction, Schorigin
- 30 (Shorygin) Reaction; Wanklyn Reaction, Schöllkopf Bis-Lactim Amino Acid Synthesis, Schotten Baumann Reaction, Semmler-Wolff Reaction (Wolff-Semmler Aromatization,

- Woff Aromatization), Serini Reaction, Sharpless Dihydroxylation, Sharpless Epoxidation, Sharpless Oxyamination, Simmons-Smith Reaction, Simonini Reaction, Simonis Chromone Cyclization, Skraup Reaction, Smiles Rearrangement, Sommelet Reaction, Sommelet Rearrangement, Sonogashira Coupling Reaction, Sonn-Muller Method,
- 5 Sorenson Formol Titration, Staedel-Rugheimer Pyrazine Synthesis, Staudinger Reaction, Stephen Aldehyde Synthesis, Stevens Rearrangement, Stieglitz Rearrangement, Stille Coupling, Stobbe Condensation, Stollé Synthesis, Stork Enamine Alkylation and Acylation, Strecker Amino Acid Synthesis, Strecker Degradation, Strecker Sulfite Alkylation, Suarez Reaction(Suarez Fragmentation), Sugasawa Reaction, Suzuki Coupling,
- 10 Swarts Reaction, Swern Oxidation, Tafel Rearrangement, Tebbe Olefination(Methylenation), Thiele Reaction(Thiele-Winter Acetoxylation), Thorpe Reaction, Tiemann Rearrangement, Tiffeneau Reaction (Ring Enlargement), Tishchenko Reaction (Tischischenko-Claisen Reaction), Tollens Reagent, Traube Purine Synthesis, Trost Allylation (Tsuji-Trost Reaction), Trost Desymmetrization, Truce-Smiles
- 15 Rearrangement, Tscherniac-Einhorn Reaction, Twitchell Process, Tyrer Sulfonation Process, Ugi Reaction, Ullmann Reaction, Urech Cyanohydrin Method, Urech Hydantoin Synthesis, Van Slyke Determination, Varrentrapp Reaction, Vilsmeier-Haack Reaction, Voight Amination, Volhard-Erdmann Cyclization, von Braun Amide Degradation, von Braun Degradations, von Richter Reaction(Rearrangement), von Richter (Cinnoline)
- 20 Synthesis, Vorbrüggen Glycosylation, Wacker Oxidation, Wagner-Jauregg Reaction, Wagner-Meerwein Rearrangement, Walden Inversion, Wallach Rearrangement, Weerman Degradation, Weiss Reaction, Wenker Ring Closure, Wessely-Moser Rearrangement, Westphalen-Lettré Rearrangement, Wharton Reaction, Whiting Reaction, Wichterle Reaction, Widman-Stoermer Synthesis, Willgerodt-Kindler Reaction, Williamson
- 25 Synthesis, Wittig Reaction, [1,2] Wittig Rearrangement, [2,3] Wittig Rearrangement, Wohl-Aue Reaction, Wohl Degradation, Wohl-Ziegler Reaction, Wohler Synthesis, Wolff-Kishner Reduction, Wolff Rearrangement, Wolffenstein-Boters Reaction, Woodward cis-Hydroxylation, Wurtz-Fittig Reaction, Wurtz Reaction, Zeisel Determination, Zerevitinov (Zerewitinoff) Determination, Ziegler Method (Thorpe-Ziegler Method), Zimmermann
- 30 Reaction, Zincke Disulfide Cleavage, Zinke Nitration, and Zinke-Suhl Reaction.

In one embodiment of the invention, the chemical reaction is a polymerisation reaction. The chemical reaction may be, for example, a radical, ionic, coordination, step-growth or condensation polymerisation. The radical polymerisation reaction may be a living polymerisation reaction.

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The micelles used in accordance with the invention contain within their core one or more reactants that are capable of reacting to form a product within the core. By the core containing the one or more reactants is meant that the reactants are located within the core region of a micelle defined by the collective of stimulus responsive polymer blocks that
10 form the core. Depending upon the relative polarity of the micelle core and the one or more reactants, the one or more reactants may be uniformly distributed or solvated throughout the core, or the one or more reactants may form a discreet region or regions within the core. There is no particular limitation on how the one or more reactants are to be distributed within the core, provided that they can react to form a product within the
15 core.

The type of reactants used in accordance with the invention will of course depend on the type of chemical reaction that is to be performed. Those skilled in the art will appreciate the type and amount of reactants that are to be used to perform a given chemical reaction.
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Compounds that may serve as the one or more reactants used in accordance with the invention may fall into the following broad groups:

I. Aliphatic (straight-chain or branched; optionally substituted)

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1. Hydrocarbons (petroleum and coal-derived)

(a) paraffins or alkanes (saturated) (C_nH_{2n+2}),

(b) olefins (unsaturated),

(1) Alkenes (one double bond) (C_nH_{2n}),

(2) Polyenes (two or more double bonds) (C_nH_{2n+1}),

30

(c) acetylenes or alkynes (triple bond),

2. Alcohols (ROH)

- 30 -

3. Ethers (ROR)
4. Aldehydes (RCHO)
5. Ketones: (RCOR)
6. Carboxylic acids (RCOOH)
- 5 7. Carbohydrates ($C_nH_{2n}O_n$)
 - (a) Sugars: e.g., glucose, fructose, sucrose, gums,
 - (b) Starches: e.g., wheat, corn, potato,
8. Amines (RNH₂, RNHR, RNR₂)
9. Amides (R(CO)NH₂, R(CO)NHR, R(CO)NR₂)
- 10 II. Cyclic (closed ring; optionally substituted)
 1. Alicyclic hydrocarbons:
 - (a) cycloparaffins (naphthenes) (saturated),
 - (b) cycloolefins (unsaturated),
 - (c) cycloacetylenes (triple bond),
 - 15 2. Aromatic hydrocarbons (arenes): unsaturated compounds; single and multiple fused rings, for example,
 - (a) benzene group (1 ring)
 - (b) naphthalene group (2 rings)
 - (c) anthracene group (3 rings)
 - 20 (d) polycyclic group (steroids, sterols)
 3. Heterocyclic: unsaturated and saturated; containing at least one other element besides carbon, for example:
 - (a) pyrroles
 - (b) furans
 - 25 (c) thiazoles
 - (d) porphyrins
 - (e) morpholines
- III. Combinations of aliphatic and cyclic structures (optionally substituted)
 1. terpene hydrocarbons
 - 30 2. amino acids
 3. proteins and nucleic acids

IV. Organometallic compounds (optionally substituted).

In one embodiment, the one or more reactants include one or more monomers that may be polymerised into polymer. Such monomers include, but not limited to, ethylenically
5 unsaturated monomers suitable for use in radical polymerisation, and dicarboxylic acids (and ester derivatives thereof), diols, diamines, diacyl chlorides, amino acids, lactones and hydroxy-acid monomers suitable for use in condensation polymerisation.

In one embodiment of the invention, the one or more reactants include one or more
10 ethylenically unsaturated monomers suitable for free radical or ionic polymerisation. Examples of such monomers include those described herein (such as those defined by general formula (I)).

Where the one or more reactants are ethylenically unsaturated monomers that are to be
15 polymerised by a radical polymerisation technique, the polymerisation will usually require initiation from a source of free radicals. The one or more reactants may therefore also include a source of such free radicals.

A source of initiating radicals can be provided by any suitable means of generating free
20 radicals, such as the thermally induced homolytic scission of suitable compound(s) (thermal initiators such as peroxides, peroxyesters, or azo compounds), the spontaneous generation from monomers (e.g. styrene), redox initiating systems, photochemical initiating systems or high energy radiation such as electron beam, X- or gamma-radiation. The initiating system is chosen such that under the reaction conditions there is no
25 substantial adverse interaction of the initiator or the initiating radicals with the micelles under the conditions of the reaction. The initiator selected should also have the requisite solubility in the core of the micelles.

Thermal initiators are generally chosen to have an appropriate half life at the temperature
30 of polymerisation. These initiators can include one or more of the following compounds:

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2,2'-azobis(isobutyronitrile), 2,2'-azobis(2-cyanobutane), dimethyl 2,2'-azobis(isobutyrate), 4,4'-azobis(4-cyanovaleric acid), 1,1'-azobis(cyclohexanecarbonitrile), 2-(t-butylazo)-2-cyanopropane, 2,2'-azobis{2-methyl-N-[1,1-bis(hydroxymethyl)-2-hydroxyethyl]propionamide}, 2,2'-azobis[2-methyl-N-(2-hydroxyethyl)propionamide], 2,2'-azobis(N,N'-dimethyleneisobutyramidine) dihydrochloride, 2,2'-azobis(2-amidinopropane) dihydrochloride, 2,2'-azobis(N,N'-dimethyleneisobutyramidine), 2,2'-azobis{2-methyl-N-[1,1-bis(hydroxymethyl)-2-hydroxyethyl]propionamide}, 2,2'-azobis{2-methyl-N-[1,1-bis(hydroxymethyl)-2-ethyl]propionamide}, 2,2'-azobis[2-methyl-N-(2-hydroxyethyl)propionamide], 2,2'-azobis(isobutyramide) dihydrate, 2,2'-azobis(2,2,4-trimethylpentane), 2,2'-azobis(2-methylpropane), t-butyl peroxyacetate, t-butyl peroxybenzoate, t-butyl peroxyneodecanoate, t-butyl peroxyisobutyrate, t-amyl peroxy pivalate, t-butyl peroxy pivalate, diisopropyl peroxydicarbonate, dicyclohexyl peroxydicarbonate, dicumyl peroxide, dibenzoyl peroxide, dilauroyl peroxide, potassium peroxydisulfate, ammonium peroxydisulfate, di-t-butyl hyponitrite, dicumyl hyponitrite. This list is not exhaustive.

Photochemical initiator systems are generally chosen to have an appropriate quantum yield for radical production under the conditions of the polymerisation. Examples include benzoin derivatives, benzophenone, acyl phosphine oxides, and photo-redox systems.

Redox initiator systems are generally chosen to have an appropriate rate of radical production under the conditions of the polymerisation; these initiating systems can include, but are not limited to, combinations of the following oxidants and reductants:

oxidants: potassium, peroxydisulfate, hydrogen peroxide, t-butyl hydroperoxide.

reductants: iron (II), titanium (III), potassium thiosulfite, potassium bisulfite.

Other suitable initiating systems are described in commonly available texts. See, for

example, Moad and Solomon "the Chemistry of Free Radical Polymerisation", Pergamon, London, 1995, pp 53-95.

Initiators that are more readily solvated in hydrophilic media include, but are not limited
5 to, 4,4'-azobis(cyanovaleric acid), 2,2'-azobis{2-methyl-N-[1,1-bis(hydroxymethyl)-2-hydroxyethyl]propionamide}, 2,2'-azobis[2-methyl-N-(2-hydroxyethyl)propionamide], 2,2'-azobis(N,N'-dimethyleneisobutyramidine), 2,2'-azobis(N,N'-dimethyleneisobutyramidine) dihydrochloride, 2,2'-azobis(2-amidinopropane) dihydrochloride, 2,2'-azobis{2-methyl-N-[1,1-bis(hydroxymethyl)-2-ethyl]propionamide},
10 2,2'-azobis[2-methyl-N-(2-hydroxyethyl)propionamide], 2,2'-azobis(isobutyramide) dihydrate, and derivatives thereof.

Initiators that are more readily solvated in hydrophilic media include azo compounds exemplified by the well known material 2,2'-azobisisobutyronitrile. Other suitable
15 initiator compounds include the acyl peroxide class such as acetyl and benzoyl peroxide as well as alkyl peroxides such as cumyl and t-butyl peroxides. Hydroperoxides such as t-butyl and cumyl hydroperoxides are also widely used.

Where the chemical reaction to be performed in accordance with the invention is a
20 polymerisation reaction, it may be desirable that the resulting polymer product is crosslinked as part of the chemical reaction process or provided with means to be crosslinked after the polymerisation reactions has been performed.

By the polymer being "crosslinked" is meant a reaction involving sites or groups on
25 polymer chains or an interaction between polymer chains that results in the formation of at least a small region in the polymer chains from which at least four chains emanate.

Those skilled in the art will appreciate that the crosslinking of polymer chains may be achieved in numerous ways. For example, crosslinking may be achieved using multi-
30 ethylenically unsaturated monomers. In that case, crosslinking is typically derived through a free radical reaction mechanism.

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Alternatively, crosslinking may be achieved using ethylenically unsaturated monomers which also contain a reactive functional group that is not susceptible to taking part in free radical reactions (i.e. "functionalised" unsaturated monomers). In that case, such monomers may be incorporated into the polymer backbone through polymerisation of the
5 unsaturated group, and the resulting pendant functional group provides means through which crosslinking may occur. By utilising monomers that provide complementary pairs of reactive functional groups (i.e. groups that will react with each other), the pairs of reactive functional groups can react through non-radical reaction mechanisms to provide crosslinks.

10 A variation on using complementary pairs of reactive functional groups is where the monomers are provided with non-complementary reactive functional groups. In that case, the functional groups will not react with each other but instead provide sites which can subsequently be reacted with a crosslinking agent to form the crosslinks. It will be appreciated that such crosslinking agents will be used in an amount to react with
15 substantially all of the non-complementary reactive functional groups. Formation of the crosslinks under these circumstances will generally occur after polymerisation of the monomers.

A combination of these crosslinking techniques may be used.

The terms "multi-ethylenically unsaturated monomers" and "functionalised unsaturated
20 monomers" mentioned above can conveniently and collectively also be referred to herein as "crosslinking ethylenically unsaturated monomers" or "crosslinking monomers". By the general term "crosslinking ethylenically unsaturated monomers" or "crosslinking monomers" it is meant an ethylenically unsaturated monomer through which a crosslink is or will be derived.

25 It will be appreciated that not all unsaturated monomers that contain a functional group can be used for the purpose of functioning as a crosslinking monomer. For example, acrylic acid should not be considered as a crosslinking monomer unless it is used to provide a site through which a crosslink is to be derived.

Examples of suitable multi-ethylenically unsaturated monomers that may be used to promote crosslinking include ethylene glycol di(meth)acrylate, triethylene glycol di(meth)acrylate, tetraethylene glycol di(meth)acrylate, 1,3-butylene glycol di(meth)acrylate, trimethylolpropane tri(meth)acrylate, 1,4-butanediol di(meth)acrylate, 5 neopentyl glycol di(meth)acrylate, 1,6-hexanediol di(meth)acrylate, pentaerythritol di(meth)acrylate, pentaerythritol tri(meth)acrylate, pentaerythritol tetra(meth)acrylate, glycerol di(meth)acrylate, glycerol allyloxy di(meth)acrylate, 1,1,1-tris(hydroxymethyl)ethane di(meth)acrylate, 1,1,1-tris(hydroxymethyl)ethane tri(meth)acrylate, 1,1,1-tris(hydroxymethyl)propane di(meth)acrylate, 1,1,1- 10 tris(hydroxymethyl)propane tri(meth)acrylate, triallyl cyanurate, triallyl isocyanurate, triallyl trimellitate, diallyl phthalate, diallyl terephthalate, divinyl benzene, methylol (meth)acrylamide, triallylamine, oleyl maleate, glyceryl propoxy triacrylate, allyl methacrylate, methacrylic anhydride and methylenebis (meth) acrylamide.

Examples of suitable ethylenically unsaturated monomers which contain a reactive 15 functional group that is not susceptible to taking part in free radical reactions include acetoacetoxyethyl methacrylate, glycidyl methacrylate, *N*-methylolacrylamide, (isobutoxymethyl)acrylamide, hydroxyethyl acrylate, *t*-butyl-carbodiimidoethyl methacrylate, acrylic acid, γ -methacryloxypropyltriisopropoxysilane, 2-isocynoethyl methacrylate and diacetone acrylamide.

20 Examples of suitable pairs of monomers mentioned directly above that provide complementary reactive functional groups include *N*-methylolacrylamide and itself, (isobutoxymethyl)acrylamide and itself, γ -methacryloxypropyltriisopropoxysilane and itself, 2-isocynoethyl methacrylate and hydroxyethyl acrylate, and *t*-butyl-carbodiimidoethyl methacrylate and acrylic acid.

25 Examples of suitable crosslinking agents that can react with the reactive functional groups of one or more of the functionalised unsaturated monomers mentioned above include hexamethylene diamine, melamine, trimethylolpropane tris(2-methyl-1-aziridine propionate) and adipic bishydrazide. Examples of pairs of crosslinking agents and functionalised unsaturated monomers that provide complementary reactive groups include

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hexamethylene diamine and acetoacetoxyethyl methacrylate, hexamethylene diamine and glycidyl methacrylate, melamine and hydroxyethyl acrylate, trimethylolpropane tris(2-methyl-1-aziridine propionate) and acrylic acid, adipic bishydrazide and diacetone acrylamide.

5

Depending upon the manner in which crosslinking is achieved, the one or more reactants within the core of the micelles may comprise a mixture of non-crosslinking and crosslinking monomers.

- 10 Where the one or more ethylenically unsaturated monomers are to be polymerised by a living polymerisation technique, it will generally be necessary to include as the one or more reactants a living polymerisation agent. By "living polymerisation agent" is meant a compound that can participate in and control or mediate the living polymerisation of one or more ethylenically unsaturated monomers so as to form a living polymer chain (i.e. a
- 15 polymer chain that has been formed according to a living polymerisation technique).

Living polymerisation agents that may be included as the one or more reactants in accordance with the invention include, but are not limited to, those which promote a living polymerisation technique selected from ionic polymerisation and CRP. Examples of CRP

20 include, but are not limited to, iniferter polymerisation, SFRP, ATRP, and RAFT polymerisation.

In one embodiment of the invention, the living polymerisation agent promotes ionic polymerisation, or in other words the living polymerisation agent is an ionic

25 polymerisation agent.

Living ionic polymerisation is a form of addition polymerisation whereby the kinetic-chain carriers are ions or ion pairs. The polymerisation proceeds via anionic or cationic kinetic-chain carriers. In other words, the propagating species will either carry a negative or

30 positive charge, and as such there will also be an associated counter cation or counter anion, respectively. For example, in the case of anionic polymerisation, the living

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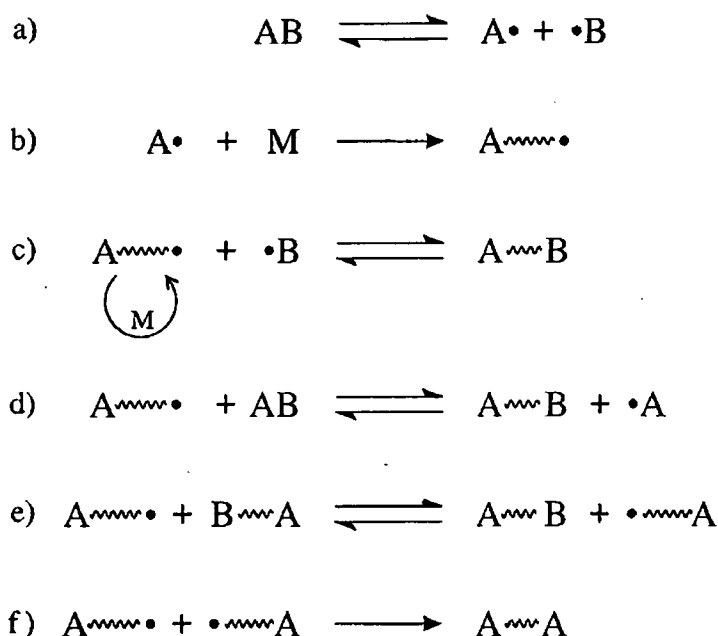
polymerisation agent might be represented as I^-M^+ , where I represents an organo-anion (e.g. an optionally substituted alkyl anion) and M represents an associated countercation, or in the case of living cationic polymerisation, the living polymerisation agent might be represented as I^+M^- , where I represents an organo-cation (e.g. an optionally substituted alkyl cation) and M represents an associated counteranion. Suitable agents for conducting anionic and cationic living polymerisation are well known to those skilled in the art and include, but are not limited to, aprotic acids (eg. Aluminium trichloride, boron trifluoride), protic (Bronstead) acids, stable carbenium-ion salts, organometallic compounds (eg. N-butyl lithium, cumyl potassium) and Ziegler-Natta catalysts (e.g. Triethyl aluminium and titanium tetrachloride).

In one embodiment of the invention, the living polymerisation agent promotes CRP, or in other words the living polymerisation agent is a CRP agent.

In a further embodiment of the invention, the living polymerisation agent promotes Iniferter polymerisation, or in other words the living polymerisation agent is an Iniferter polymerisation agent.

Iniferter polymerisation is a well known form of CRP, and is generally understood to proceed by a mechanism illustrated below in Scheme 1.

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Scheme 1: General mechanism of controlled radical polymerisation with iniferters.

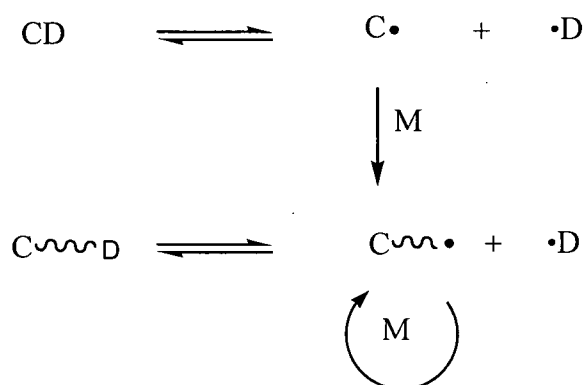
With reference to Scheme 1, the iniferter agent AB dissociates chemically, thermally or
 5 photochemically to produce a reactive radical species A and generally a relatively stable
 radical species B (for symmetrical iniferters the radical species B will be the same as the
 radical species A) (step a). The radical species A can initiate polymerisation of monomer
 M (in step b) and may be deactivated by coupling with radical species B (in step c).
 Transfer to the iniferter (in step d) and/or transfer to dormant polymer (in step e) followed
 10 by termination (in step f) characterise iniferter chemistry.

A living polymerisation agent used in accordance with the invention may therefore be
 represented as AB, where AB can dissociate chemically, thermally or photochemically as
 illustrated above in Scheme 2. Suitable iniferter agents are well known to those skilled in
 15 the art, and include, but are not limited to, dithiocarbonate, disulphide, and thiuram
 disulphide compounds.

In a further embodiment of the invention, the living polymerisation agent promotes SFRP,
 or in other words the living polymerisation agent is a SFRP agent.

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As suggested by its name, this mode of radical polymerisation involves the generation of a stable radical species as illustrated below in Scheme 2.



5

Scheme 2: General mechanism of controlled radical polymerisation with stable free radical mediated polymerisation.

With reference to Scheme 2, SFRP agent CD dissociates to produce an active radical species C and a stable radical species D. The active radical species C reacts with monomer M, which resulting propagating chain may recombine with the stable radical species D. Unlike iniferter agents, SFRP agents do not provide for a transfer step.

A living polymerisation agent used in accordance with the invention may therefore be represented as CD, where CD can dissociate chemically, thermally or photochemically as illustrated above in Scheme 3. Suitable agents for conducting SFRP are well known to those skilled in the art, and include, but are not limited to, moieties capable of generating phenoxy and nitroxy radicals. Where the agent generates a nitroxy radical, the polymerisation technique is more commonly known as nitroxide mediated polymerisation (NMP).

Examples of SFRP agents capable of generating phenoxy radicals include those comprising a phenoxy group substituted in the 2 and 6 positions by bulky groups such as tert-alkyl (e.g. t-butyl), phenyl or dimethylbenzyl, and optionally substituted at the 4 position by an alkyl, alkyloxy, aryl, or aryloxy group or by a heteroatom containing group

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(e.g. S, N or O) such dimethylamino or diphenylamino group. Thiophenoxy analogues of such phenoxy containing agents are also contemplated.

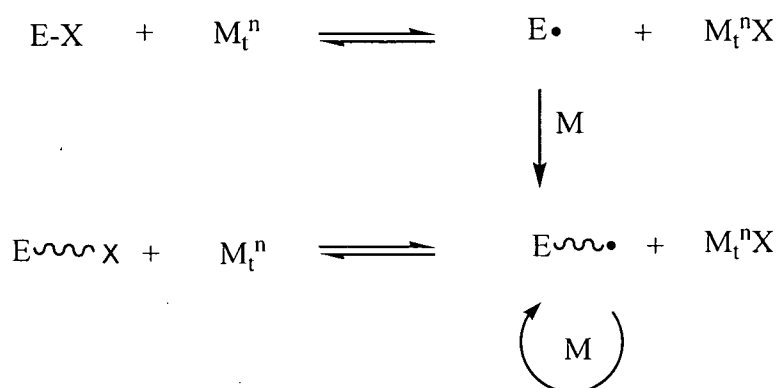
SFRP agents capable of generating nitroxyl radicals include those comprising the substituent R^1R^2N-O- , where R^1 and R^2 are tertiary alkyl groups, or where R^1 and R^2 together with the N atom form a cyclic structure, preferably having tertiary branching at the positions α to the N atom. Examples of such nitroxyl substituents include 2,2,5,5-tetraalkylpyrrolidinoxyl, as well as those in which the 5-membered heterocycle ring is fused to an alicyclic or aromatic ring, hindered aliphatic dialkylaminoxyl and iminoxyl substituents. A common nitroxyl substituent employed in SFRP is 2,2,6,6-tetramethyl-1-piperidinyloxy.

In another embodiment of the invention, the living polymerisation agent promotes ATRP, or in other words the living polymerisation agent is an ATRP agent.

15

ATRP generally employs a transition metal catalyst to reversibly deactivate a propagating radical by transfer of a transferable atom or group such as a halogen atom to the propagating polymer chain, thereby reducing the oxidation state of the metal catalyst as illustrated below in Scheme 3.

20



Scheme 3: General mechanism of controlled radical polymerisation with atom transfer radical polymerisation.

25

With reference to Scheme 3, a transferable group or atom (X, e.g. halide, hydroxyl, C₁-C₆-alkoxy, cyano, cyanato, thiocyanato or azido) is transferred from the organic compound (E) to a transition metal catalyst (M_t, e.g. copper, iron, gold, silver, mercury, palladium, platinum, cobalt, manganese, ruthenium, molybdenum, niobium, or zinc) having oxidation number (n), upon which a radical species is formed that initiates polymerisation with monomer (M). As part of this process, the metal complex is oxidised (M_tⁿ⁺¹X). A similar reaction sequence is then established between the propagating polymer chain and the dormant X end-capped polymer chains.

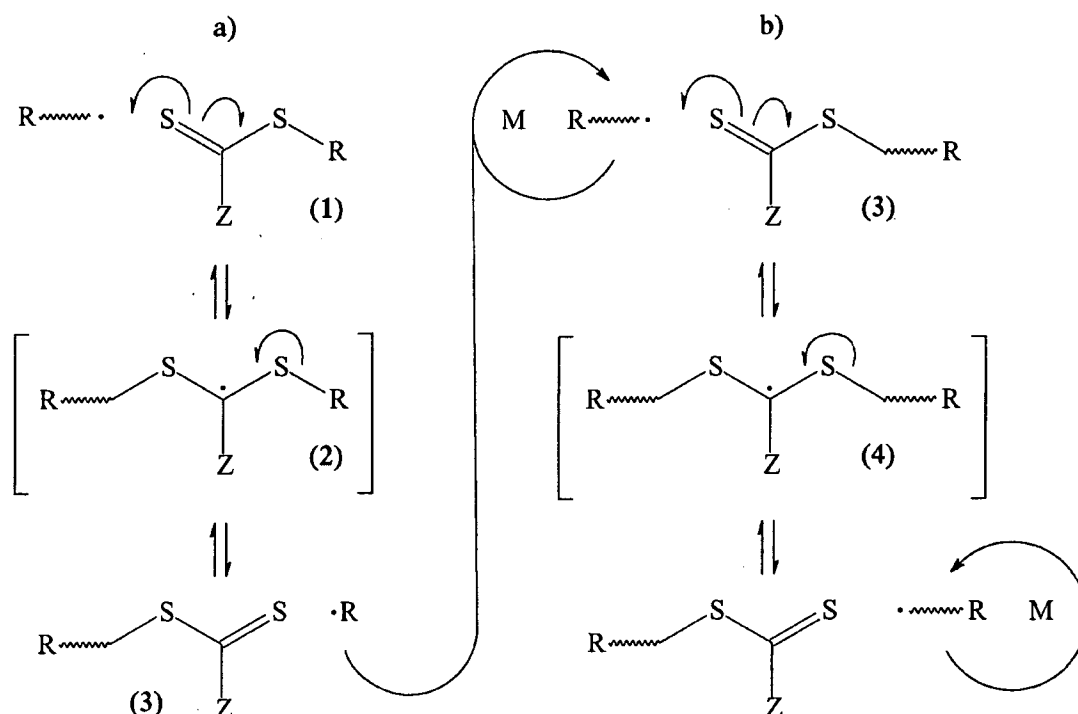
10 A living polymerisation agent used in accordance with the invention may therefore be represented as EX, where E is an organic group (e.g. optionally substituted alkyl, optionally substituted aryl, optionally substituted alkylaryl, or polymer) and X is a transferable atom or group that can participate in a redox cycle with a transition metal catalyst to reversibly generate a radical species and the oxidised metal catalyst as
15 illustrated above in Scheme 3.

Although ATRP requires the presence of a transition metal catalyst to proceed, it is not intended that the transition metal catalyst form part of the "living polymerisation agent" *per se*. However, as will be discussed in more detail below, a suitable catalyst may also be
20 contained within the core of the micelles.

In a further embodiment of the invention, the living polymerisation agent promotes RAFT polymerisation, or in other words the living polymerisation agent is a RAFT agent.

25 RAFT polymerisation is well known in the art and is believed to operate through the mechanism outlined below in Scheme 4.

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Scheme 4: General mechanism of controlled radical polymerisation with reversible addition fragmentation chain transfer polymerisation.

5

With reference to Scheme 4, RAFT polymerisation is believed to proceed through initial reaction sequence (a) that involves reaction of a RAFT agent (1) with a propagating radical. The labile intermediate radical species (2) that is formed fragments to form a temporarily deactivated dormant polymer species (3) together a radical (R) derived from the RAFT agent. This radical can then promote polymerisation of monomer (M), thereby reinitiating polymerisation. The propagating polymer chain can then react with the dormant polymer species (3) to promote the reaction sequence (b) that is similar to reaction sequence (a). Thus, a labile intermediate radical (4) is formed and subsequently fragments to form again a dormant polymer species together with a radical which is capable of further chain growth.

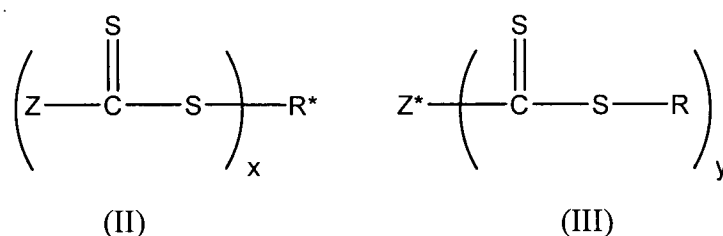
15

RAFT agents suitable for use in accordance with the invention comprise a thiocarbonylthio

group (which is a divalent moiety represented by: -C(S)S-). Examples of RAFT agents are described in Moad G.; Rizzardo, E; Thang S, H. Polymer 2008, 49, 1079-1131 (the entire contents of which are incorporated herein by reference) and include xanthate, dithioester, dithiocarbonate, dithiocarbanate and trithiocarbonate compounds.

5

A RAFT agent suitable for use in accordance with the invention may be represented by general formula (II) or (III):



10

where Z and R are groups, and R* and Z* are x-valent and y-valent groups, respectively, that are independently selected such that the agent can function as a RAFT agent in the polymerisation of one or more ethylenically unsaturated monomers; x is an integer ≥ 1 ; and y is an integer ≥ 2 .

15

In order to function as a RAFT agent in the polymerisation of one or more ethylenically unsaturated monomers, those skilled in the art will appreciate that R and R* will typically be an optionally substituted organic group that function as a free radical leaving group under the polymerisation conditions employed and yet, as a free radical leaving group, retain the ability to reinitiate polymerisation. Those skilled in the art will also appreciate that Z and Z* will typically be an optionally substituted organic group that function to give a suitably high reactivity of the C=S moiety in the RAFT agent towards free radical addition without slowing the rate of fragmentation of the RAFT-adduct radical to the extent that polymerisation is unduly retarded.

25

In formula (II), R* is a x-valent group, with x being an integer ≥ 1 . Accordingly, R* may be mono-valent, di-valent, tri-valent or of higher valency. For example, R* may be an optionally substituted polymer chain, with the remainder of the RAFT agent depicted in

formula (II) presented as multiple groups pendant from the polymer chain. Generally, x will be an integer ranging from 1 to about 20, for example from about 2 to about 10, or from 1 to about 5.

- 5 Similarly, in formula (III), Z^* is a y-valent group, with y being an integer ≥ 2 . Accordingly, Z^* may be di-valent, tri-valent or of higher valency. Generally, y will be an integer ranging from 2 to about 20, for example from about 2 to about 10, or from 2 to about 5.
- 10 Examples of R in RAFT agents used in accordance with the invention include optionally substituted, and in the case of R^* in RAFT agents used in accordance with the invention include a x-valent form of optionally substituted, alkyl, alkenyl, alkynyl, aryl, acyl, carbocyclyl, heterocyclyl, heteroaryl, alkylthio, alkenylthio, alkynylthio, arylthio, acylthio, carbocyclylthio, heterocyclylthio, heteroarylthio, alkylalkenyl, alkylalkynyl, alkylaryl, alkylacyl, alkylcarbocyclyl, alkylheterocyclyl, alkylheteroaryl, alkyloxyalkyl, alkenyloxyalkyl, alkynyloxyalkyl, aryloxyalkyl, alkylacyloxy, alkylcarbocycloxy, alkylheterocycloxy, alkylheteroaryloxy, alkylthioalkyl, alkenylthioalkyl, alkynylthioalkyl, arylthioalkyl, alkylacylthio, alkylcarbocyclylthio, alkylheterocyclylthio, alkylheteroarylthio, alkylalkenylalkyl, alkylalkynylalkyl, alkylarylalkyl, alkylacylalkyl, arylalkylaryl, arylalkenylaryl, arylalkynylaryl, arylacylaryl, arylacyl, arylcarbocyclyl, arylheterocyclyl, arylheteroaryl, alkenyloxyaryl, alkynyloxyaryl, aryloxyaryl, alkylthioaryl, alkenylthioaryl, alkynylthioaryl, arylthioaryl, arylacylthio, arylcarbocyclylthio, arylheterocyclylthio, arylheteroarylthio, and a polymer chain.
- 20
- 25 Examples of R in RAFT agents used in accordance with the invention also include optionally substituted, and in the case of R^* in RAFT agents used in accordance with the invention also include an x-valent form of optionally substituted, alkyl; saturated, unsaturated or aromatic carbocyclic or heterocyclic ring; alkylthio; dialkylamino; an organometallic species; and a polymer chain.
- 30 More specific examples of R in RAFT agents used in accordance with the invention

- 45 -

include optionally substituted, and in the case of R* in RAFT agents used in accordance with the invention include an x-valent form of optionally substituted, C₁-C₁₈ alkyl, C₂-C₁₈ alkenyl, C₂-C₁₈ alkynyl, C₆-C₁₈ aryl, C₁-C₁₈ acyl, C₃-C₁₈ carbocyclyl, C₂-C₁₈ heterocyclyl, C₃-C₁₈ heteroaryl, C₁-C₁₈ alkylthio, C₂-C₁₈ alkenylthio, C₂-C₁₈ alkynylthio, C₆-C₁₈ arylthio, C₁-C₁₈ acylthio, C₃-C₁₈ carbocyclylthio, C₂-C₁₈ heterocyclylthio, C₃-C₁₈ heteroarylthio, C₃-C₁₈ alkylalkenyl, C₃-C₁₈ alkylalkynyl, C₇-C₂₄ alkylaryl, C₂-C₁₈ alkylacyl, C₄-C₁₈ alkylcarbocyclyl, C₃-C₁₈ alkylheterocyclyl, C₄-C₁₈ alkylheteroaryl, C₂-C₁₈ alkyloxyalkyl, C₃-C₁₈ alkenyloxyalkyl, C₃-C₁₈ alkynyloxyalkyl, C₇-C₂₄ aryloxyalkyl, C₂-C₁₈ alkylacyloxy, C₂-C₁₈ alkylthioalkyl, C₃-C₁₈ alkenylthioalkyl, C₃-C₁₈ alkynylthioalkyl, C₇-C₂₄ arylthioalkyl, C₂-C₁₈ alkylacylthio, C₄-C₁₈ alkylcarbocyclylthio, C₃-C₁₈ alkylheterocyclylthio, C₄-C₁₈ alkylheteroarylthio, C₄-C₁₈ alkylalkenylalkyl, C₄-C₁₈ alkylalkynylalkyl, C₈-C₂₄ alkylarylalkyl, C₃-C₁₈ alkylacylalkyl, C₁₃-C₂₄ arylalkylaryl, C₁₄-C₂₄ arylalkenylaryl, C₁₄-C₂₄ arylalkynylaryl, C₁₃-C₂₄ arylacylaryl, C₇-C₁₈ arylacyl, C₉-C₁₈ arylcarbocyclyl, C₈-C₁₈ arylheterocyclyl, C₉-C₁₈ arylheteroaryl, C₈-C₁₈ alkenyloxyaryl, C₈-C₁₈ alkynyloxyaryl, C₁₂-C₂₄ aryloxyaryl, alkylthioaryl, C₈-C₁₈ alkenylthioaryl, C₈-C₁₈ alkynylthioaryl, C₁₂-C₂₄ arylthioaryl, C₇-C₁₈ arylacylthio, C₉-C₁₈ arylcarbocyclylthio, C₈-C₁₈ arylheterocyclylthio, C₉-C₁₈ arylheteroarylthio, and a polymer chain having a number average molecular weight in the range of about 500 to about 80,000, for example in the range of about 500 to about 30,000

20

Where R in RAFT agents used in accordance with the invention include, and in the case of R* in RAFT agents used in accordance with the invention include an x-valent form of, an optionally substituted polymer chain, the polymers chain may be formed by any suitable polymerisation process such as radical, ionic, coordination, step-growth or condensation polymerisation. The polymer chains may comprise homopolymer, block polymer, multiblock polymer, gradient copolymer, or random or statistical copolymer chains and may have various architectures such as linear, star, branched, graft, or brush.

In one embodiment of the invention, R in RAFT agents used in accordance with the invention is an optionally substituted, and in the case of R* in RAFT agents used in accordance with the invention is a x-valent form of an optionally substituted, polymer

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chain. In a further embodiment, the optionally substituted polymer chain is formed of a stimulus responsive polymer as herein defined. In that case, it may be desirable for the stimulus responsive polymer chain of the RAFT agent to be of the same type as the stimulus responsive polymer block that forms part of the copolymer chains used in accordance with the invention (e.g. where the stimulus responsive polymer chain of the RAFT agent and the stimulus responsive polymer block that forms part of the copolymer chains are both p(NIPAAm)).

In particular, it has been found that living polymerisation agents used in accordance with the invention can be effectively and efficiently incorporated within the core of the micelles when they comprise a stimulus responsive polymer chain of the same type as the stimulus responsive polymer block that forms part of the copolymer chains used in accordance with the invention. Living polymerisation agents that comprise a polymer chain are commonly referred to in the art as "macro" living polymerisation agents. Such "macro" living polymerisation agents may conveniently be prepared by polymerising one or more ethylenically unsaturated monomers under the control of a given living polymerisation agent. For example, where the stimulus responsive polymer block that forms part of the copolymer chains is p(NIPAAm), when the reaction being performed is a RAFT mediated polymerisation reaction, it may be desirable to employ a macro RAFT agent where the R or R* groups comprise p(NIPAAm).

Examples of Z in RAFT agents used in accordance with the invention include optionally substituted, and in the case of Z* in RAFT agents used in accordance with the invention include a y-valent form of optionally substituted: F, Cl, Br, I, alkyl, aryl, acyl, amino, carbocyclyl, heterocyclyl, heteroaryl, alkyloxy, aryloxy, acyloxy, acylamino, carbocycloxy, heterocycloxy, heteroaryloxy, alkylthio, arylthio, acylthio, carbocyclthio, heterocyclthio, heteroarylthio, alkylaryl, alkylacyl, alkylcarbocyclyl, alkylheterocyclyl, alkylheteroaryl, alkyloxyalkyl, aryloxyalkyl, alkylacyloxy, alkylcarbocycloxy, alkylheterocycloxy, alkylheteroaryloxy, alkylthioalkyl, arylthioalkyl, alkylacylthio, alkylcarbocyclthio, alkylheterocyclthio, alkylheteroarylthio, alkylarylalkyl, alkylacylalkyl, arylalkylaryl, arylacylaryl, arylacyl,

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arylcarbocyclyl, arylheterocyclyl, arylheteroaryl, aryloxyaryl, arylacyloxy, arylcarbocycloxy, arylheterocycloxy, arylheteroaryloxy, alkylthioaryl, arylthioaryl, arylacylthio, arylcarbocyclylthio, arylheterocyclylthio, arylheteroarylthio, dialkyloxy- ,
 5 diheterocycloxy- or diaryloxy- phosphinyl, dialkyl-, diheterocyclyl- or diaryl-
 phosphinyl, cyano (i.e. -CN), and -S-R, where R is as defined in respect of formula (III).

More specific examples of Z in RAFT agents used in accordance with the invention include optionally substituted, and in the case of Z* in RAFT agents used in accordance with the invention include a y-valent form of optionally substituted: F, Cl, C₁-C₁₈ alkyl,
 10 C₆-C₁₈ aryl, C₁-C₁₈ acyl, amino, C₃-C₁₈ carbocyclyl, C₂-C₁₈ heterocyclyl, C₃-C₁₈ heteroaryl, C₁-C₁₈ alkyloxy, C₆-C₁₈ aryloxy, C₁-C₁₈ acyloxy, C₃-C₁₈ carbocycloxy, C₂-C₁₈ heterocycloxy, C₃-C₁₈ heteroaryloxy, C₁-C₁₈ alkylthio, C₆-C₁₈ arylthio, C₁-C₁₈ acylthio, C₃-C₁₈ carbocyclylthio, C₂-C₁₈ heterocyclylthio, C₃-C₁₈ heteroarylthio, C₇-C₂₄ alkylaryl, C₂-C₁₈ alkylacyl, C₄-C₁₈ alkylcarbocyclyl, C₃-C₁₈ alkylheterocyclyl, C₄-C₁₈ alkylheteroaryl, C₂-C₁₈ alkyloxyalkyl, C₇-C₂₄ aryloxyalkyl, C₂-C₁₈ alkylacyloxy, C₄-C₁₈ alkylcarbocycloxy, C₃-C₁₈ alkylheterocycloxy, C₄-C₁₈ alkylheteroaryloxy, C₂-C₁₈ alkylthioalkyl, C₇-C₂₄ arylthioalkyl, C₂-C₁₈ alkylacylthio, C₄-C₁₈ alkylcarbocyclylthio, C₃-C₁₈ alkylheterocyclylthio, C₄-C₁₈ alkylheteroarylthio, C₈-C₂₄ alkylarylalkyl, C₃-C₁₈ alkylacylalkyl, C₁₃-C₂₄ arylalkylaryl, C₁₃-C₂₄ arylacylaryl, C₇-C₁₈ arylacyl, C₉-C₁₈ arylcarbocyclyl, C₈-C₁₈ arylheterocyclyl, C₉-C₁₈ arylheteroaryl, C₁₂-C₂₄ aryloxyaryl, C₇-C₁₈ arylacyloxy, C₉-C₁₈ arylcarbocycloxy, C₈-C₁₈ arylheterocycloxy, C₉-C₁₈ arylheteroaryloxy, C₇-C₁₈ alkylthioaryl, C₁₂-C₂₄ arylthioaryl, C₇-C₁₈ arylacylthio, C₉-C₁₈ arylcarbocyclylthio, C₈-C₁₈ arylheterocyclylthio, C₉-C₁₈ arylheteroarylthio, dialkyloxy- , diheterocycloxy- or diaryloxy- phosphinyl (i.e. -P(=O)OR^k₂), dialkyl-, diheterocyclyl- or
 25 diaryl- phosphinyl (i.e. -P(=O)R^k₂), where R^k is selected from optionally substituted C₁-C₁₈ alkyl, optionally substituted C₆-C₁₈ aryl, optionally substituted C₂-C₁₈ heterocyclyl, and optionally substituted C₇-C₂₄ alkylaryl, cyano (i.e. -CN), and -S-R, where R is as defined in respect of formula (III).

30 In one embodiment, the RAFT agent used in accordance with the invention is a trithiocarbonate RAFT agent and Z or Z* is an optionally substituted alkylthio group.

In the lists herein defining groups from which Z, Z*, R and R* may be selected, each alkyl, alkenyl, alkynyl, aryl, carbocyclyl, heteroaryl, heterocyclyl, and polymer chain moiety may be optionally substituted. For avoidance of any doubt, where a given Z, Z*, R or R* contains two or more of such moieties (e.g. alkylaryl), each of such moieties may be optionally substituted with one, two, three or more optional substituents as herein defined.

In the lists herein defining groups from which Z, Z*, R and R* may be selected, where a given Z, Z*, R or R* contains two or more subgroups (e.g. [group A][group B]), the order of the subgroups is not intended to be limited to the order in which they are presented. Thus, a Z, Z*, R or R* with two subgroups defined as [group A][group B] (e.g. alkylaryl) is intended to also be a reference to a Z, Z*, R or R* with two subgroups defined as [group B][group A] (e.g. arylalkyl).

The Z, Z*, R or R* may be branched and/or optionally substituted. Where the Z, Z*, R or R* comprises an optionally substituted alkyl moiety, an optional substituent includes where a -CH₂- group in the alkyl chain is replaced by a group selected from -O-, -S-, -NR^a-, -C(O)- (i.e. carbonyl), -C(O)O- (i.e. ester), and -C(O)NR^a- (i.e. amide), where R^a may be selected from hydrogen, alkyl, alkenyl, alkynyl, aryl, carbocyclyl, heteroaryl, heterocyclyl, arylalkyl, and acyl.

Reference herein to a x-valent, y-valent, multi-valent or di-valent "form of..." is intended to mean that the specified group is a x-valent, y-valent, multi-valent or di-valent radical, respectively. For example, where x or y is 2, the specified group is intended to be a divalent radical. In that case, a divalent alkyl group is in effect an alkylene group (e.g. -CH₂-). Similarly, the divalent form of the group alkylaryl may, for example, be represented by -(C₆H₄)-CH₂-, a divalent alkylarylalkyl group may, for example, be represented by -CH₂-(C₆H₄)-CH₂-, a divalent alkyloxy group may, for example, be represented by -CH₂-O-, and a divalent alkyloxyalkyl group may, for example, be represented by -CH₂-O-CH₂-. Where the term "optionally substituted" is used in combination with such a x-valent, y-valent, multi-valent or di-valent groups, that group

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may or may not be substituted or fused as herein described. Where the x-valent, y-valent, multi-valent, di-valent groups comprise two or more subgroups, for example [group A][group B][group C] (e.g. alkylarylalkyl), if viable one or more of such subgroups may be optionally substituted. Those skilled in the art will appreciate how to apply this
5 rationale in providing for higher valent forms.

Depending upon the type of chemical reaction being performed, the micelles may also contain within their core one or more catalysts. If a catalyst is required to perform the chemical reaction, those skilled in the art will be able to select an appropriate catalyst or
10 catalysts for that reaction.

In one embodiment of the invention, the chemical reaction performed is a living polymerisation reaction, and the micelles contain within their core a living polymerisation agent, one or more ethylenically unsaturated monomers as reactants and optionally a
15 catalyst. In a further embodiment, the living polymerisation agent used in the living polymerisation reaction comprises a stimulus responsive polymer, preferably a stimulus responsive polymer that is of the same type as the stimulus responsive polymer block of the copolymer chains that form the core of the micelles.

20 The chemical reaction performed in accordance with the invention may be a condensation polymerisation reaction. Condensation polymerisation is a form of step-growth polymerisation where monomers react to form polymer and in doing so release a low molecular weight species such as water or methanol. To drive the reaction in favour of forming the polymer, the low molecular weight species typically needs to be removed or
25 isolated from the reaction mixture. Where the present invention is used to perform a condensation polymerisation reaction, the low molecular weight species can advantageously be removed or isolated from the reaction mixture by simply being expelled from the micelle core into the liquid medium. Where the low molecular weight species is hydrophilic in character (e.g. water or methanol), its expulsion from the micelle core is
30 believed to be facilitated when an aqueous liquid medium is used.

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Examples of condensation polymers include polyamides, polyacetals, polyesters, and copolymers thereof. Monomers that may be contained within the micelles to form such polymers include dicarboxylic acids (and their ester derivatives), diols, diamines, diacyl chlorides, amino acids, lactones and hydroxy-acids. Those skilled in the art will be able
5 select suitable monomers for preparing the condensation polymers.

Condensation polymerisation reactions are commonly performed using a catalyst. If required, a condensation catalyst may therefore also be contained within the micelles. Examples of condensation catalysts include Lewis acids such as antimony trioxide,
10 titanium oxide and dibutyl tindilaurate.

The liquid medium comprising the micelles may be prepared by any suitable means known to those skilled in the art. For example, an appropriate concentration of the copolymer chains may be combined with the liquid medium so as to undergo micellisation. One or
15 more reactants, and if required other additives such as a catalyst, may then be combined with the liquid medium, whereby these components are preferentially transported through the liquid medium and absorbed within the core of the micelles.

Alternatively, the liquid medium comprising the micelles may be formed by taking
20 advantage of the stimulus responsive feature of the copolymer chains. In particular, the copolymer chains may be combined with the liquid medium such that the stimulus responsive polymer block is appropriately stimulated so as to prevent micellisation of the copolymer chains. One or more reactants, and optionally one or more additives, may each be independently combined with the liquid medium at the same time as, before or after the
25 copolymer chains are combined with the liquid medium. The liquid medium will then comprise the copolymer chains, one or more reactants, and optionally one or more additives without any micelles being formed. The stimulus responsive polymer block may then be subject to an appropriate stimulus such that it undergoes a transition and causes the copolymer chains to undergo micellisation. During micellisation it has been found that the
30 one or more reactants and optionally one or more additives can be effectively and efficiently contained or encapsulated within the core of the micelles.

As a more specific example of this methodology, the stimulus responsive polymer block of the copolymer chains may be a temperature responsive polymer block that is solvated by the liquid medium below its LCST and poorly solvated by the liquid medium above its LCST. In that case, the liquid medium may comprise below the LCST solvated copolymer chains, the one or more reactants and optionally one or more additives. Upon increasing the temperature of the liquid medium to above the LCST, the copolymer chains will become amphipathic and self-assemble into micelles. During micellisation of the copolymer chains the one or more reactants and optionally one or more additives can be effectively and efficiently contained or encapsulated within the core of the micelles.

Where the chemical reaction to be performed involves the use of reactants that may spontaneously react upon coming into contact with each other (e.g. compound A reacting with compound B), it may be desirable to prepare the liquid medium comprising the micelles by one of the methods outlined above such that the micelles only contain reactant A or B. The other reactant may then be combined with the liquid medium, whereby that reactant is preferentially transported through the liquid medium and absorbed within the core of the micelles and consequently react.

Accordingly, in one embodiment of the invention the liquid medium comprising the micelles is formed by combining the copolymer chains and the liquid medium such that the copolymer chains assemble to form micelles, and then combining this composition with one or more reactants.

In a further embodiment, the liquid medium comprising the micelles is formed by combining the liquid medium, the copolymer chains and one or more reactants such that the copolymer chains do not form micelles, and then subjecting the stimulus responsive polymer block of the copolymer chains to a stimulus such that it undergoes a transition and causes the copolymer chains to assemble into micelles (i.e. causes micellisation of the copolymer chains).

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In either of such embodiments, one or more further reactants may be combined with the liquid medium comprising the so formed micelles such that they are transported through the liquid medium and absorbed within the core of the micelles.

- 5 Conventional techniques and apparatus may be used in preparing the liquid medium comprising micelles.

The ability of the copolymer chains used in accordance with the invention to undergo a reversible assembly into micelles (i.e. to reversibly assemble and disassemble) by the
10 stimulus responsive polymer block being subjected to an appropriate stimulus advantageously provides a means for the chemical reaction to be performed in either batch, semi continuous or continuous modes.

For example, as part of a continuous chemical reaction process the micelles may be formed
15 so as to contain the one or more reactants that are subsequently reacted to form a product. The micelles may then be disassembled to release the product into the liquid medium. The product may be isolated from the liquid medium, with the micelles being reformed so as to contain one or more reactants and the chemical reaction take place again. Both the liquid medium and the copolymer chains can therefore advantageously be efficiently and
20 effectively recycled.

Accordingly, in one embodiment the method of the invention further comprises isolating the product from the liquid medium, reforming the micelles containing within their core one or more reactants, and causing the one or more reactants to undergo a reaction and
25 form a product within the core of the micelles. In that case, the micelles may of course be again disassembled in accordance with the invention so as to release the product into the liquid medium.

The one or more reactants contained within the core of the micelles are capable of reacting
30 to form a product within the core of the micelles. The method of the invention therefore comprises a step of causing the one or more reactants to undergo a reaction and form a

product within the core of the micelles. The manner in which a reaction between the one or more reactants is promoted will depend upon the type of reactants used and/or the type of reaction being performed. Those skilled in the art will be able to readily promote a reaction of the one or more reactants for a given chemical reaction being performed. For example, the chemical reaction may be promoted thermally, in which case the liquid medium could simply be heated so as to cause the reaction to take place. Other well known means of promoting chemical reactions include the use of radiation such as radio waves, microwaves, infrared radiation, visible light, ultraviolet radiation, X-rays and gamma rays, ultrasound, pH, bringing two or more reactants into contact with each other, or combinations thereof.

An important feature of the present invention is that the micellar assembled copolymer chains disassemble after the chemical reaction has taken place so as to release the product into the liquid medium. By the "release" of the product into the liquid medium is meant that the micelle disassembles and the product is free to separate from the disassembled copolymer chains. In other words, the micellar assembled copolymer chains do not take part in the chemical reaction such that the product becomes covalently bound thereto. Should this occur, it will be appreciated that the product could not be "released" into the liquid medium.

The copolymer chains used in accordance with the invention are therefore also selected such that they do not take part in the chemical reaction being and form part of the resulting product. Those skilled in the art will be able to select the copolymer chains such that they do not take part in the chemical reaction and become covalently bound to the product.

Where the copolymer chains comprise a reactive moiety that may take part in the chemical reaction to be performed, the reactive moiety can simply be cleaved or deactivated. For example, a RAFT polymerisation reaction may be performed in accordance with the invention using copolymer chains that have themselves been prepared by RAFT polymerisation. In that case, the RAFT agent residue of the copolymer chains may be cleaved or suitably deactivated using techniques well known to those skilled in the art.

Having said this, provided the copolymer chains can assemble into micelles and subsequently disassemble in accordance with the invention, they may nevertheless have a moiety covalently bound thereto that facilitates the chemical reaction taking place. For example, the stimulus responsive polymer block of the copolymer chains may have a catalyst moiety tethered to it. In that case, the stimulus responsive polymer block may be prepared using one or more monomers that having the catalyst moiety tethered thereto, or the stimulus responsive polymer block may be prepared so as to have one or more functional groups that may be subsequently reacted so as to tether the catalyst moiety thereto.

It will be appreciated that despite facilitating the chemical reaction, a catalyst moiety tethered to the copolymer chain will not result in the product becoming covalently bound to the copolymer chains (i.e. the catalyst will not be consumed during the reaction).

Accordingly, where the chemical reaction requires a catalyst, in one embodiment the catalyst is covalently bound to the stimulus responsive polymer block.

Upon being released into the liquid medium, the product may be isolated therefrom using techniques well known in the art such as filtration, precipitation, solvent extraction, centrifugation, and combinations thereof.

Performing a chemical reaction in accordance with the invention can offer a number of advantages compared with performing the same reaction in bulk solvent. For example, it has been found that a polymerisation reaction performed in accordance with the invention can afford a polymer product having a lower polydispersity (PDI) compared with the same polymerisation reaction performed in bulk. Furthermore, the particle size distribution (PSD) of the resulting polymer product can be lower than that which can be prepared using conventional techniques. In particular, the present invention can advantageously be used to prepare polymer particles of various sizes with a near uniform particle size distribution.

As used herein, the term "alkyl", used either alone or in compound words denotes straight chain, branched or cyclic alkyl, preferably C₁₋₂₀ alkyl, e.g. C₁₋₁₀ or C₁₋₆. Examples of straight chain and branched alkyl include methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, *sec*-butyl, *t*-butyl, *n*-pentyl, 1,2-dimethylpropyl, 1,1-dimethyl-propyl, hexyl, 4-methylpentyl, 1-methylpentyl, 2-methylpentyl, 3-methylpentyl, 1,1-dimethylbutyl, 2,2-dimethylbutyl, 3,3-dimethylbutyl, 1,2-dimethylbutyl, 1,3-dimethylbutyl, 1,2,2-trimethylpropyl, 1,1,2-trimethylpropyl, heptyl, 5-methylhexyl, 1-methylhexyl, 2,2-dimethylpentyl, 3,3-dimethylpentyl, 4,4-dimethylpentyl, 1,2-dimethylpentyl, 1,3-dimethylpentyl, 1,4-dimethyl-pentyl, 1,2,3-trimethylbutyl, 1,1,2-trimethylbutyl, 1,1,3-trimethylbutyl, octyl, 6-methylheptyl, 1-methylheptyl, 1,1,3,3-tetramethylbutyl, nonyl, 1-, 2-, 3-, 4-, 5-, 6- or 7-methyloctyl, 1-, 2-, 3-, 4- or 5-ethylheptyl, 1-, 2- or 3-propylhexyl, decyl, 1-, 2-, 3-, 4-, 5-, 6-, 7- and 8-methylnonyl, 1-, 2-, 3-, 4-, 5- or 6-ethyloctyl, 1-, 2-, 3- or 4-propylheptyl, undecyl, 1-, 2-, 3-, 4-, 5-, 6-, 7-, 8- or 9-methyldecyl, 1-, 2-, 3-, 4-, 5-, 6- or 7-ethylnonyl, 1-, 2-, 3-, 4- or 5-propyloctyl, 1-, 2- or 3-butylheptyl, 1-pentylhexyl, dodecyl, 1-, 2-, 3-, 4-, 5-, 6-, 7-, 8-, 9- or 10-methylundecyl, 1-, 2-, 3-, 4-, 5-, 6-, 7- or 8-ethyldecyl, 1-, 2-, 3-, 4-, 5- or 6-propylnonyl, 1-, 2-, 3- or 4-butyloctyl, 1-2-pentylheptyl and the like. Examples of cyclic alkyl include mono- or polycyclic alkyl groups such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, cyclononyl, cyclodecyl and the like. Where an alkyl group is referred to generally as "propyl", butyl" etc, it will be understood that this can refer to any of straight, branched and cyclic isomers where appropriate. An alkyl group may be optionally substituted by one or more optional substituents as herein defined.

The term "alkenyl" as used herein denotes groups formed from straight chain, branched or cyclic hydrocarbon residues containing at least one carbon to carbon double bond including ethylenically mono-, di- or polyunsaturated alkyl or cycloalkyl groups as previously defined, preferably C₂₋₂₀ alkenyl (e.g. C₂₋₁₀ or C₂₋₆). Examples of alkenyl include vinyl, allyl, 1-methylvinyl, butenyl, iso-butenyl, 3-methyl-2-butenyl, 1-pentenyl, cyclopentenyl, 1-methyl-cyclopentenyl, 1-hexenyl, 3-hexenyl, cyclohexenyl, 1-heptenyl, 3-heptenyl, 1-octenyl, cyclooctenyl, 1-nonenyl, 2-nonenyl, 3-nonenyl, 1-decenyl, 3-decenyl, 1,3-butadienyl, 1,4-pentadienyl, 1,3-cyclopentadienyl, 1,3-hexadienyl, 1,4-

hexadienyl, 1,3-cyclohexadienyl, 1,4-cyclohexadienyl, 1,3-cycloheptadienyl, 1,3,5-cycloheptatrienyl and 1,3,5,7-cyclooctatetraenyl. An alkenyl group may be optionally substituted by one or more optional substituents as herein defined.

- 5 As used herein the term "alkynyl" denotes groups formed from straight chain, branched or cyclic hydrocarbon residues containing at least one carbon-carbon triple bond including ethylenically mono-, di- or polyunsaturated alkyl or cycloalkyl groups as previously defined. Unless the number of carbon atoms is specified the term preferably refers to C₂₋₂₀ alkynyl (e.g. C₂₋₁₀ or C₂₋₆). Examples include ethynyl, 1-propynyl, 2-propynyl, and
- 10 butynyl isomers, and pentynyl isomers. An alkynyl group may be optionally substituted by one or more optional substituents as herein defined.

The term "halogen" ("halo") denotes fluorine, chlorine, bromine or iodine (fluoro, chloro, bromo or iodo).

15

- The term "aryl" (or "carboaryl") denotes any of single, polynuclear, conjugated and fused residues of aromatic hydrocarbon ring systems(e.g. C₆₋₂₄ or C₆₋₁₈). . Examples of aryl include phenyl, biphenyl, terphenyl, quaterphenyl, naphthyl, tetrahydronaphthyl, anthracenyl, dihydroanthracenyl, benzanthracenyl, dibenzanthracenyl, phenanthrenyl,
- 20 fluorenyl, pyrenyl, idenyl, azulenyl, chrysenyl. Preferred aryl include phenyl and naphthyl. An aryl group may or may not be optionally substituted by one or more optional substituents as herein defined. The term "arylene" is intended to denote the divalent form of aryl.

- 25 The term "carbocyclyl" includes any of non-aromatic monocyclic, polycyclic, fused or conjugated hydrocarbon residues, preferably C₃₋₂₀ (e.g. C₃₋₁₀ or C₃₋₈). The rings may be saturated, e.g. cycloalkyl, or may possess one or more double bonds (cycloalkenyl) and/or one or more triple bonds (cycloalkynyl). Particularly preferred carbocyclyl moieties are 5-6-membered or 9-10 membered ring systems. Suitable examples include cyclopropyl,
- 30 cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, cyclononyl, cyclodecyl, cyclopentenyl, cyclohexenyl, cyclooctenyl, cyclopentadienyl, cyclohexadienyl,

cyclooctatetraenyl, indanyl, decalynyl and indenyl. A carbocyclyl group may be optionally substituted by one or more optional substituents as herein defined. The term "carbocyclene" is intended to denote the divalent form of carbocyclyl.

- 5 The term "heteroatom" or "hetero" as used herein in its broadest sense refers to any atom other than a carbon atom which may be a member of a cyclic organic group. Particular examples of heteroatoms include nitrogen, oxygen, sulfur, phosphorous, boron, silicon, selenium and tellurium, more particularly nitrogen, oxygen and sulfur.
- 10 The term "heterocyclyl" when used alone or in compound words includes any of monocyclic, polycyclic, fused or conjugated hydrocarbon residues, preferably C₃₋₂₀ (e.g. C₃₋₁₀ or C₃₋₈) wherein one or more carbon atoms are replaced by a heteroatom so as to provide a non-aromatic residue. Suitable heteroatoms include O, N, S, P and Se, particularly O, N and S. Where two or more carbon atoms are replaced, this may be by
- 15 two or more of the same heteroatom or by different heteroatoms. The heterocyclyl group may be saturated or partially unsaturated, i.e. possess one or more double bonds. Particularly preferred heterocyclyl are 5-6 and 9-10 membered heterocyclyl. Suitable examples of heterocyclyl groups may include azridinyl, oxiranyl, thiiranyl, azetidiny, oxetanyl, thietanyl, 2H-pyrrolyl, pyrrolidinyl, pyrrolinyl, piperidyl, piperazinyl,
- 20 morpholinyl, indolinyl, imidazolidinyl, imidazoliny, pyrazolidinyl, thiomorpholinyl, dioxanyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydropyrrolyl, tetrahydrothiophenyl, pyrazolinyl, dioxalanyl, thiazolidinyl, isoxazolidinyl, dihydropyranyl, oxazinyl, thiazinyl, thiomorpholinyl, oxathianyl, dithianyl, trioxanyl, thiadiazinyl, dithiazinyl, trithianyl, azepinyl, oxepinyl, thiepinyl, indenyl, indanyl, 3H-indolyl, isoindoliny, 4H-quinolazinyl,
- 25 chromenyl, chromanyl, isochromanyl, pyranyl and dihydropyranyl. A heterocyclyl group may be optionally substituted by one or more optional substituents as herein defined. The term "heterocyclene" is intended to denote the divalent form of heterocyclyl.

- The term "heteroaryl" includes any of monocyclic, polycyclic, fused or conjugated
- 30 hydrocarbon residues, wherein one or more carbon atoms are replaced by a heteroatom so as to provide an aromatic residue. Preferred heteroaryl have 3-20 ring atoms, e.g. 3-10.

Particularly preferred heteroaryl are 5-6 and 9-10 membered bicyclic ring systems. Suitable heteroatoms include, O, N, S, P and Se, particularly O, N and S. Where two or more carbon atoms are replaced, this may be by two or more of the same heteroatom or by different heteroatoms. Suitable examples of heteroaryl groups may include pyridyl, pyrrolyl, thienyl, imidazolyl, furanyl, benzothienyl, isobenzothienyl, benzofuranyl, isobenzofuranyl, indolyl, isoindolyl, pyrazolyl, pyrazinyl, pyrimidinyl, pyridazinyl, indoliziny, quinolyl, isoquinolyl, phthalazinyl, 1,5-naphthyridinyl, quinoxalinyl, quinazolinyl, quinolinyl, oxazolyl, thiazolyl, isothiazolyl, isoxazolyl, triazolyl, oxadiazolyl, oxatriazolyl, triazinyl, and furazanyl. A heteroaryl group may be optionally substituted by one or more optional substituents as herein defined. The term "heteroarylene" is intended to denote the divalent form of heteroaryl.

The term "acyl" either alone or in compound words denotes a group containing the moiety C=O (and not being a carboxylic acid, ester or amide) Preferred acyl includes C(O)-R^e, wherein R^e is hydrogen or an alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocyclyl, or heterocyclyl residue. Examples of acyl include formyl, straight chain or branched alkanoyl (e.g. C₁₋₂₀) such as acetyl, propanoyl, butanoyl, 2-methylpropanoyl, pentanoyl, 2,2-dimethylpropanoyl, hexanoyl, heptanoyl, octanoyl, nonanoyl, decanoyl, undecanoyl, dodecanoyl, tridecanoyl, tetradecanoyl, pentadecanoyl, hexadecanoyl, heptadecanoyl, octadecanoyl, nonadecanoyl and icosanoyl; cycloalkylcarbonyl such as cyclopropylcarbonyl cyclobutylcarbonyl, cyclopentylcarbonyl and cyclohexylcarbonyl; aroyl such as benzoyl, toluoyl and naphthoyl; aralkanoyl such as phenylalkanoyl (e.g. phenylacetyl, phenylpropanoyl, phenylbutanoyl, phenylisobutyl, phenylpentanoyl and phenylhexanoyl) and naphthylalkanoyl (e.g. naphthylacetyl, naphthylpropanoyl and naphthylbutanoyl]; aralkenoyl such as phenylalkenoyl (e.g. phenylpropenoyl, phenylbutenoyl, phenylmethacryloyl, phenylpentenoyl and phenylhexenoyl and naphthylalkenoyl (e.g. naphthylpropenoyl, naphthylbutenoyl and naphthylpentenoyl); aryloxyalkanoyl such as phenoxyacetyl and phenoxypropionyl; arylthiocarbamoyl such as phenylthiocarbamoyl; arylglyoxyloyl such as phenylglyoxyloyl and naphthylglyoxyloyl; arylsulfonyl such as phenylsulfonyl and naphthylsulfonyl; heterocycliccarbonyl; heterocyclicalkanoyl such as thienylacetyl, thienylpropanoyl, thienylbutanoyl,

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thienylpentanoyl, thienylhexanoyl, thiazolylacetyl, thiadiazolylacetyl and tetrazolylacetyl; heterocyclicalkenoyl such as heterocyclicpropenoyl, heterocyclicbutenoyl, heterocyclicpentenoyl and heterocyclichexenoyl; and heterocyclicglyoxyloyl such as thiazolylglyoxyloyl and thienylglyoxyloyl. The R^e residue may be optionally substituted as
5 described herein.

The term "sulfoxide", either alone or in a compound word, refers to a group -S(O)R^f wherein R^f is selected from hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, heterocyclyl, carbocyclyl, and aralkyl. Examples of preferred R^f include C₁₋₂₀alkyl, phenyl
10 and benzyl.

The term "sulfonyl", either alone or in a compound word, refers to a group S(O)₂-R^f, wherein R^f is selected from hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, heterocyclyl, carbocyclyl and aralkyl. Examples of preferred R^f include C₁₋₂₀alkyl, phenyl
15 and benzyl.

The term "sulfonamide", either alone or in a compound word, refers to a group S(O)NR^fR^f wherein each R^f is independently selected from hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, heterocyclyl, carbocyclyl, and aralkyl. Examples of preferred R^f include C₁₋₂₀alkyl, phenyl and benzyl. In one embodiment at least one R^f is hydrogen. In another
20 embodiment, both R^f are hydrogen.

The term, "amino" is used here in its broadest sense as understood in the art and includes groups of the formula NR^aR^b wherein R^a and R^b may be any independently selected from
25 hydrogen, alkyl, alkenyl, alkynyl, aryl, carbocyclyl, heteroaryl, heterocyclyl, arylalkyl, and acyl. R^a and R^b, together with the nitrogen to which they are attached, may also form a monocyclic, or polycyclic ring system e.g. a 3-10 membered ring, particularly, 5-6 and 9-10 membered systems. Examples of "amino" include NH₂, NHalkyl (e.g. C₁₋₂₀alkyl), NHaryl (e.g. NHphenyl), NHaralkyl (e.g. NHbenzyl), NHacyl (e.g. NHC(O)C₁₋₂₀alkyl, NHC(O)phenyl), Nalkylalkyl (wherein each alkyl, for example C₁₋₂₀, may be the same or
30

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different) and 5 or 6 membered rings, optionally containing one or more same or different heteroatoms (e.g. O, N and S).

The term "amido" is used here in its broadest sense as understood in the art and includes groups having the formula $C(O)NR^aR^b$, wherein R^a and R^b are as defined as above. Examples of amido include $C(O)NH_2$, $C(O)NHalkyl$ (e.g. $C_{1-20}alkyl$), $C(O)NHaryl$ (e.g. $C(O)NHphenyl$), $C(O)NHaralkyl$ (e.g. $C(O)NHbenzyl$), $C(O)NHacyl$ (e.g. $C(O)NHC(O)C_{1-20}alkyl$, $C(O)NHC(O)phenyl$), $C(O)Nalkylalkyl$ (wherein each alkyl, for example C_{1-20} , may be the same or different) and 5 or 6 membered rings, optionally containing one or more same or different heteroatoms (e.g. O, N and S).

The term "carboxy ester" is used here in its broadest sense as understood in the art and includes groups having the formula CO_2R^g , wherein R^g may be selected from groups including alkyl, alkenyl, alkynyl, aryl, carbocyclyl, heteroaryl, heterocyclyl, aralkyl, and acyl. Examples of carboxy ester include $CO_2C_{1-20}alkyl$, CO_2aryl (e.g. $CO_2phenyl$), $CO_2aralkyl$ (e.g. $CO_2benzyl$).

As used herein, the term "aryloxy" refers to an "aryl" group attached through an oxygen bridge. Examples of aryloxy substituents include phenoxy, biphenyloxy, naphthyloxy and the like.

As used herein, the term "acyloxy" refers to an "acyl" group wherein the "acyl" group is in turn attached through an oxygen atom. Examples of "acyloxy" include hexylcarbonyloxy (heptanoyloxy), cyclopentylcarbonyloxy, benzoyloxy, 4-chlorobenzoyloxy, decylcarbonyloxy (undecanoyloxy), propylcarbonyloxy (butanoyloxy), octylcarbonyloxy (nonanoyloxy), biphenylcarbonyloxy (eg 4-phenylbenzoyloxy), naphthylcarbonyloxy (eg 1-naphthoyloxy) and the like.

As used herein, the term "alkyloxycarbonyl" refers to a "alkyloxy" group attached through a carbonyl group. Examples of "alkyloxycarbonyl" groups include butylformate, sec-butylformate, hexylformate, octylformate, decylformate, cyclopentylformate and the like.

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As used herein, the term "arylalkyl" refers to groups formed from straight or branched chain alkanes substituted with an aromatic ring. Examples of arylalkyl include phenylmethyl (benzyl), phenylethyl and phenylpropyl.

- 5 As used herein, the term "alkylaryl" refers to groups formed from aryl groups substituted with a straight chain or branched alkane. Examples of alkylaryl include methylphenyl and isopropylphenyl.

In this specification "optionally substituted" is taken to mean that a group may or may not
10 be substituted or fused (so as to form a condensed polycyclic group) with one, two, three or more of organic and inorganic groups, including those selected from: alkyl, alkenyl, alkynyl, carbocyclyl, aryl, heterocyclyl, heteroaryl, acyl, aralkyl, alkaryl, alkheterocyclyl, alkheteroaryl, alkcarbocyclyl, halo, haloalkyl, haloalkenyl, haloalkynyl, haloaryl, halocarbocyclyl, haloheterocyclyl, haloheteroaryl, haloacyl, haloaryalkyl, hydroxy,
15 hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, hydroxycarbocyclyl, hydroxyaryl, hydroxyheterocyclyl, hydroxyheteroaryl, hydroxyacyl, hydroxyaralkyl, alkoxyalkyl, alkoxyalkenyl, alkoxyalkynyl, alkoxycarbocyclyl, alkoxyaryl, alkoxyheterocyclyl, alkoxyheteroaryl, alkoxyacyl, alkoxyaralkyl, alkoxy, alkenyloxy, alkynyloxy, aryloxy, carbocyclyloxy, aralkyloxy, heteroaryloxy, heterocyclyloxy, acyloxy, haloalkoxy,
20 haloalkenyloxy, haloalkynyloxy, haloaryloxy, halocarbocyclyloxy, haloaralkyloxy, haloheteroaryloxy, haloheterocyclyloxy, haloacyloxy, nitro, nitroalkyl, nitroalkenyl, nitroalkynyl, nitroaryl, nitroheterocyclyl, nitroheteroaryl, nitrocarbocyclyl, nitroacyl, nitroaralkyl, amino (NH₂), alkylamino, dialkylamino, alkenylamino, alkynylamino, arylamino, diarylamino, aralkylamino, diaralkylamino, acylamino, diacylamino,
25 heterocyclamino, heteroarylamino, carboxy, carboxyester, amido, alkylsulphonyloxy, arylsulphenyloxy, alkylsulphenyl, arylsulphenyl, thio, alkylthio, alkenylthio, alkynylthio, arylthio, aralkylthio, carbocyclylthio, heterocyclylthio, heteroarylthio, acylthio, sulfoxide, sulfonyl, sulfonamide, aminoalkyl, aminoalkenyl, aminoalkynyl, aminocarbocyclyl, aminoaryl, aminoheterocyclyl, aminoheteroaryl, aminoacyl, aminoaralkyl, thioalkyl,
30 thioalkenyl, thioalkynyl, thiocarbocyclyl, thioaryl, thioheterocyclyl, thioheteroaryl, thioacyl, thioaralkyl, carboxyalkyl, carboxyalkenyl, carboxyalkynyl, carboxycarbocyclyl,

carboxyaryl, carboxyheterocyclyl, carboxyheteroaryl, carboxyacyl, carboxyaralkyl, carboxyesteralkyl, carboxyesteralkenyl, carboxyesteralkynyl, carboxyestercarbocyclyl, carboxyesteraryl, carboxyesterheterocyclyl, carboxyesterheteroaryl, carboxyesteracyl, carboxyesteraralkyl, amidoalkyl, amidoalkenyl, amidoalkynyl, amidocarbocyclyl, amidoaryl, amidoheterocyclyl, amidoheteroaryl, amidoacyl, amidoaralkyl, formylalkyl, formylalkenyl, formylalkynyl, formylcarbocyclyl, formylaryl, formylheterocyclyl, formylheteroaryl, formylacyl, formylaralkyl, acylalkyl, acylalkenyl, acylalkynyl, acylcarbocyclyl, acylaryl, acylheterocyclyl, acylheteroaryl, acylacyl, acylaralkyl, sulfoxidealkyl, sulfoxidealkenyl, sulfoxidealkynyl, sulfoxidecarbocyclyl, sulfoxidearyl, sulfoxideheterocyclyl, sulfoxideheteroaryl, sulfoxideacyl, sulfoxidearalkyl, sulfonylalkyl, sulfonylalkenyl, sulfonylalkynyl, sulfonylcarbocyclyl, sulfonylaryl, sulfonylheterocyclyl, sulfonylheteroaryl, sulfonylacyl, sulfonylaralkyl, sulfonamidoalkyl, sulfonamidoalkenyl, sulfonamidoalkynyl, sulfonamidocarbocyclyl, sulfonamidoaryl, sulfonamidoheterocyclyl, sulfonamidoheteroaryl, sulfonamidoacyl, sulfonamidoaralkyl, nitroalkyl, nitroalkenyl, nitroalkynyl, nitrocarbocyclyl, nitroaryl, nitroheterocyclyl, nitroheteroaryl, nitroacyl, nitroaralkyl, cyano, sulfate, phosphate, triarylmethyl, triarylamino, oxadiazole, and carbazole groups. Optional substitution may also be taken to refer to where a -CH₂- group in a chain or ring is replaced by a group selected from -O-, -S-, -NR^a-, -C(O)- (i.e. carbonyl), -C(O)O- (i.e. ester), and -C(O)NR^a- (i.e. amide), where R^a is as defined herein.

20

Preferred optional substituents include alkyl, (e.g. C₁₋₆ alkyl such as methyl, ethyl, propyl, butyl, cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl), hydroxyalkyl (e.g. hydroxymethyl, hydroxyethyl, hydroxypropyl), alkoxyalkyl (e.g. methoxymethyl, methoxyethyl, methoxypropyl, ethoxymethyl, ethoxyethyl, ethoxypropyl etc) alkoxy (e.g. C₁₋₆ alkoxy such as methoxy, ethoxy, propoxy, butoxy, cyclopropoxy, cyclobutoxy), halo, trifluoromethyl, trichloromethyl, tribromomethyl, hydroxy, phenyl (which itself may be further substituted e.g., by C₁₋₆ alkyl, halo, hydroxy, hydroxyC₁₋₆ alkyl, C₁₋₆ alkoxy, haloC₁₋₆alkyl, cyano, nitro OC(O)C₁₋₆ alkyl, and amino), benzyl (wherein benzyl itself may be further substituted e.g., by C₁₋₆ alkyl, halo, hydroxy, hydroxyC₁₋₆alkyl, C₁₋₆ alkoxy, haloC₁₋₆ alkyl, cyano, nitro OC(O)C₁₋₆ alkyl, and amino), phenoxy (wherein phenyl itself may be further substituted e.g., by C₁₋₆ alkyl, halo, hydroxy, hydroxyC₁₋₆ alkyl, C₁₋₆ alkoxy,

30

- haloC₁₋₆ alkyl, cyano, nitro OC(O)C₁₋₆ alkyl, and amino), benzyloxy (wherein benzyl itself may be further substituted e.g., by C₁₋₆ alkyl, halo, hydroxy, hydroxyC₁₋₆ alkyl, C₁₋₆ alkoxy, haloC₁₋₆ alkyl, cyano, nitro OC(O)C₁₋₆ alkyl, and amino), amino, alkylamino (e.g. C₁₋₆ alkyl, such as methylamino, ethylamino, propylamino etc), dialkylamino (e.g. C₁₋₆ alkyl, such as dimethylamino, diethylamino, dipropylamino), acylamino (e.g. NHC(O)CH₃), phenylamino (wherein phenyl itself may be further substituted e.g., by C₁₋₆ alkyl, halo, hydroxy, hydroxyC₁₋₆ alkyl, C₁₋₆ alkoxy, haloC₁₋₆ alkyl, cyano, nitro OC(O)C₁₋₆ alkyl, and amino), nitro, formyl, -C(O)-alkyl (e.g. C₁₋₆ alkyl, such as acetyl), O-C(O)-alkyl (e.g. C₁₋₆ alkyl, such as acetyloxy), benzoyl (wherein the phenyl group itself may be further substituted e.g., by C₁₋₆ alkyl, halo, hydroxy hydroxyC₁₋₆ alkyl, C₁₋₆ alkoxy, haloC₁₋₆ alkyl, cyano, nitro OC(O)C₁₋₆alkyl, and amino), replacement of CH₂ with C=O, CO₂H, CO₂alkyl (e.g. C₁₋₆ alkyl such as methyl ester, ethyl ester, propyl ester, butyl ester), CO₂phenyl (wherein phenyl itself may be further substituted e.g., by C₁₋₆ alkyl, halo, hydroxy, hydroxyl C₁₋₆ alkyl, C₁₋₆ alkoxy, halo C₁₋₆ alkyl, cyano, nitro OC(O)C₁₋₆ alkyl, and amino), CONH₂, CONHphenyl (wherein phenyl itself may be further substituted e.g., by C₁₋₆ alkyl, halo, hydroxy, hydroxyl C₁₋₆ alkyl, C₁₋₆ alkoxy, halo C₁₋₆ alkyl, cyano, nitro OC(O)C₁₋₆ alkyl, and amino), CONHbenzyl (wherein benzyl itself may be further substituted e.g., by C₁₋₆ alkyl, halo, hydroxy hydroxyl C₁₋₆ alkyl, C₁₋₆ alkoxy, halo C₁₋₆ alkyl, cyano, nitro OC(O)C₁₋₆ alkyl, and amino), CONHalkyl (e.g. C₁₋₆ alkyl such as methyl ester, ethyl ester, propyl ester, butyl amide) CONHdialkyl (e.g. C₁₋₆ alkyl) aminoalkyl (e.g., HN C₁₋₆ alkyl-, C₁₋₆alkylHN-C₁₋₆ alkyl- and (C₁₋₆ alkyl)₂N-C₁₋₆ alkyl-), thioalkyl (e.g., HS C₁₋₆ alkyl-), carboxyalkyl (e.g., HO₂CC₁₋₆ alkyl-), carboxyesteralkyl (e.g., C₁₋₆ alkylO₂CC₁₋₆ alkyl-), amidoalkyl (e.g., H₂N(O)CC₁₋₆ alkyl-, H(C₁₋₆ alkyl)N(O)CC₁₋₆ alkyl-), formylalkyl (e.g., OHCC₁₋₆alkyl-), acylalkyl (e.g., C₁₋₆ alkyl(O)CC₁₋₆ alkyl-), nitroalkyl (e.g., O₂NC₁₋₆ alkyl-), sulfoxidealkyl (e.g., R(O)SC₁₋₆ alkyl, such as C₁₋₆ alkyl(O)SC₁₋₆ alkyl-), sulfonylalkyl (e.g., R(O)₂SC₁₋₆ alkyl- such as C₁₋₆ alkyl(O)₂SC₁₋₆ alkyl-), sulfonamidoalkyl (e.g., ₂HRN(O)SC₁₋₆ alkyl, H(C₁₋₆ alkyl)N(O)SC₁₋₆ alkyl-), triarylmethyl, triarylmino, oxadiazole, and carbazole.
- The invention will now be described with reference to the following non-limiting examples.

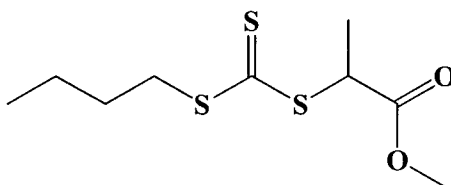
EXAMPLES

Materials

5 All reagents and solvents were of analytical grade and used as received unless otherwise stated. Styrene (STY, 99 %, Aldrich), 2,3,4,5,6-pentafluorostyrene (PFSTY, 99 %, MATRIX Scientific) dimethylacrylamide (DMA, 99 %, Aldrich) and butylacrylate (BA, 99+ %, Aldrich) were passed through a column of basic alumina (activity I) to remove inhibitor. N-isopropylacrylamide (97 %, Aldrich) was recrystallised from hexane prior to
10 use. Azobisisobutyronitrile (AIBN) was recrystallized twice from methanol prior to use. 1,1'-Azobis(cyanocyclohexane) (Vazo88) was recrystallised twice from methanol prior to use. MilliQ Water ($18.2 \text{ M}\Omega\text{cm}^{-1}$) was generated using a Millipore MilliQ-Academic Water Purification System.

15 Example 1

Part (a): Synthesis of chain transfer agent, methyl 2-(butylthiocarbonothioylthio) propanoate



MCEBTTC

20 To a stirred solution of 1-butanethiol (10 mL, 0.093 mol) and triethylamine (14.3 mL, 0.103 mol) in dichloromethane (100 mL) under nitrogen atmosphere was added dropwise carbondisulfide (6.18 mL, 0.103 mol) in dichloromethane (50 mL) over a period of 30 min
25 at 0 °C. The solution gradually turned yellow during the addition. After complete addition the solution was stirred at room temperature for 1 h. Methyl bromopropionate (11.46 mL, 0.103 mol) in dichloromethane (50 mL) was then added dropwise to the solution over a period of 30 min and the solution stirred for 2 h. The dichloromethane was removed under

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nitrogen and the residue dissolved in diethylether. The solution was then washed with cold 10 % HCl solution (3 x 50 mL) and MilliQ water (3 x 50 mL) and then dried over anhydrous MgSO₄. The ether was removed under vacuum and the residual yellow oil was purified by column chromatography (9:1 petroleum ether/ethyl acetate on silica, second
5 band).

¹H NMR (CDCl₃) δ 0.92 (tr, *J* = 7.5 Hz, 3H, CH₃), 1.43 (mult, *J* = 7.5 Hz, 2H, CH₂), 1.62 (d, *J* = 7.5 Hz, 3H, CH₃), 1.65 (quin, *J* = 7.5 Hz, 2H, CH₂), 3.36 (tr, *J* = 7.5 Hz, 2H, CH₂), 3.73 (s, 3H, CH₃), 4.84 (quad, *J* = 7.5 Hz, 1H, CH); ¹³C NMR (CDCl₃) δ 13.55, 16.91,
10 22.02, 29.89, 36.94, 47.68, 52.82, 171.63 (CH-C(=O)-O), 221.99 (S-C(=S)-S)

Part (b): Synthesis of PNIPAM₁₈-SC(=S)SC₄H₉

N-isopropylacrylamide (NIPAM, 2.50 g, 2.21 x 10⁻² mol), AIBN (0.0187 g, 1.14 x 10⁻⁴
15 mol), MCEBTTC (0.302 g, 1.20 x 10⁻³ mol) from part (a) and DMSO (5.02 g) were added to a 50 mL round bottom flask equipped with magnetic stirrer bar. The mixture was deoxygenated by purging with Argon for 20 min then heated at 60 °C for 7 h. The solution was cooled, diluted with dichloromethane and washed with brine. The dichloromethane was then dried over anhydrous MgSO₄, filtered and reduced in volume by rotary
20 evaporation. The polymer was recovered by precipitation into hexane/toluene 90/10, filtered and dried under vacuum for 24 h at 25 °C. (M_n = 1800, PDI = 1.09 (SEC-RI calibrated using PSTY Standards)), (M_n = 2000, MALDI-TOF).

¹HNMR spectrum of PNIPAM₁₈-SC(=S)SC₄H₉. ¹HNMR (300 MHz, CD₃OD): a (δ 0.88,
25 3H), b (δ 3.32, 2H), c (δ 3.63, 3H), d (δ 3.96, 18H), e (δ 1.11, 112H), M_w ~ 2290.

Part (c): Synthesis of PDMA₄₉-SC(=S)SC₄H₉

Dimethylacrylamide (DMA, 9.02 g, 9.10 x 10⁻² mol), AIBN (0.0187 g, 1.1419 x 10⁻⁴ mol),
30 MCEBTTC (0.337 g, 1.34 x 10⁻³ mol) from part (a) and DMSO (18 g) were added to a 50 mL round bottom flask equipped with magnetic stirrer bar. The mixture was deoxygenated

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by purging with Argon for 20 min then heated at 60 °C for 15 h. The solution was cooled, diluted with dichloromethane and washed with brine. The dichloromethane was then dried over anhydrous MgSO₄, filtered and reduced in volume by rotary evaporation. The polymer was recovered by precipitation into hexane/toluene 90/10, filtered and dried under vacuum
5 for 24 h at 25 °C. (M_n = 4840, PDI = 1.11 (SEC-RI calibrated using PSTY Standards))

Part (d): Synthesis of $P(DMA_{49}\text{-}b\text{-}NIPAM_{106})\text{-SC(=S)SC}_4H_9$

N-isopropylacrylamide (NIPAM, 3.11 g, 2.75×10^{-2} mol), AIBN (0.0079 g, 4.84×10^{-5}
10 mol), PDMA₄₉-SC(=S)SC₄H₉ (2.52 g, 5.21×10^{-4} mol) from part (c) and DMSO (5.4 g) were added to a 25 mL round bottom flask equipped with magnetic stirrer bar. The mixture was deoxygenated by purging with Argon for 20 min then heated at 60 °C for 1.5 h. The solution was cooled, diluted with dichloromethane and washed with brine. The dichloromethane was then dried over anhydrous MgSO₄, filtered then reduced in volume by
15 rotary evaporation. The polymer was recovered by precipitation into hexane/toluene 90/10, filtered and dried under vacuum for 24 h at 25 °C. (M_n = 16800, PDI = 1.13) (SEC-Triple Detection)

*Part (e): Synthesis of $P(DMA_{49}\text{-}b\text{-}NIPAM_{106})$: Cleavage of -SC(=S)SC_4H_9 end group from
20 $P(DMA_{49}\text{-}b\text{-}NIPAM_{106})\text{-SC(=S)SC}_4H_9$*

$P(DMA_{49}\text{-}b\text{-}NIPAM_{106})\text{-SC(=S)SC}_4H_9$ (1.75 g, 1.04×10^{-4} mol) from part (d), Vazo88 (0.310 g, 1.27×10^{-3} mol), and DMSO (10 g) were added to a 25 mL round bottom flask equipped with magnetic stirrer bar. The mixture was deoxygenated by purging with Argon
25 for 20 min then heated at 100 °C for 6 h. The solution was cooled, diluted with dichloromethane and washed with brine. The dichloromethane was then dried over anhydrous MgSO₄, filtered then reduced in volume by rotary evaporation. The polymer was recovered by precipitation into hexane/toluene 90/10, filtered and dried under vacuum for 24 h at 25 °C. Quantitative loss of RAFT end-group was determined using SEV with UV
30 detection at 310 nm, which is the absorbance of the RAFT end-group.

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Part (f): Styrene polymerization in the presence of PNIPAM₁₈-SC(=S)SC₄H₉ in P(DMA₄₉-b-NIPAM₁₀₆) micelles in water

A typical polymerisation in micelles is as follows: PNIPAM₁₈-SC(=S)SC₄H₉ (0.02 g, 1.00×10^{-5} mol) from part (b), P(DMA₄₉-b-NIPAM₁₀₆) (0.10 g, 5.95×10^{-6} mol) from part (e), APS (8.7×10^{-4} g, 3.81×10^{-6} mol) and MilliQ water (5 g) was added to a 10 mL schlenk flask equipped with magnetic stirrer. After dissolution of the PNIPAM₁₈-SC(=S)SC₄H₉ and P(DMA₄₉-b-NIPAM₁₀₆), styrene (0.77 g, 7.40×10^{-3} mol) was added to the mixture. The mixture was deoxygenated by purging with Argon for 10 min, then heated at 70 °C.

10 Samples were taken at regular intervals for determination of monomer conversion, molecular weight distribution and particle size. The polymer from the dried final latex was dissolved in tetrahydrofuran then precipitated into methanol prior to analysis by SEC.

Table 1 below gives the amounts of each component used, and the conversion, molecular weight distribution and particle size distribution data for experiments 1 to 8. Experiments 1 to 6 were that for the polymerization of styrene monomer. Experiment 7 was for the polymerization of pentafluorostyrene and experiment 8 was for the polymerization of butyl acrylate within the nanoreactors.

20 **Example 2**

ATRP reaction with BPMODA and P(DMA-b-NIPAM) micelles (2-Ethylbromoisobutyrate as initiator)

25 CuBr₂ (0.004 g, 2×10^{-5} mol) and bis(2-pyridylmethyl)octadecylamine (BPMODA) (0.009 g, 2×10^{-5} mol) were dissolved in 1 mL of MeOH. After the formation of the CuII-BPMODA-complex, the solvent was completely removed. P(DMA-b-NIPAM) from Example 1, part (e) (0.078 g, 7.43×10^{-6} mol) was added to a 15 mL flask and dissolved in 3.5 mL water. Styrene (0.420 g, 4×10^{-3} mol), the initiator 2-ethyl isobutyl bromide (0.004 g, 2×10^{-5} mol) and the CuII-BPMODA-complex were mixed and the green solution was

30 added to the flask. The mixture was purged with Argon for 20 min, heated to 70°C and

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stirred at 70°C for 20 min. Then an aqueous solution of ascorbic acid (0.002 g, 1×10^{-5} mol in 0.4 mL water) was added to the mixture over a period of 5 min. The greenish emulsion turns yellow indicating the formation of a CuI-complex.

- 5 Samples were taken after 30 min, 1h – 6h (every hour) and 23 h for determination of monomer conversion and molecular weight distribution.

amounts: STY:Cu-complex:initiator = 200:1:1

- 10 P(DMA-b-(NIPAM)) = 0.078 g in 3.5 mL water
 CuBr₂ = 2×10^{-5} mol (1)
 BPMODA = 2×10^{-5} mol (1)
 Styrene = 4×10^{-3} mol (200)
 Ebib = 2×10^{-5} mol (1)
 15 Ascorbic acid = 1×10^{-5} mol (0.5) in 0.4 mL water

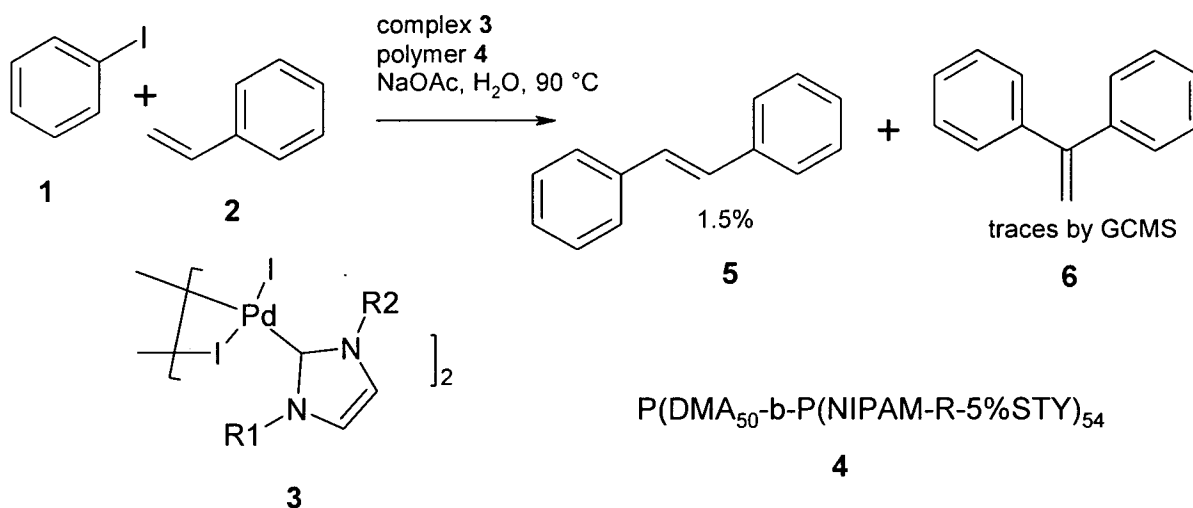
analysis:

Conversion [%]	Mn [g/mol]	PDI	Time [h]
5.0781	2673	1.17	0.5
8.7927	3679	1.18	1
15.8936	6577	1.14	2
--	9019	1.13	3
28.7608	11467	1.11	4
33.6405	12763	1.11	5
35.0675	13571	1.12	6
50.4832	18111	1.15	23

Example 3

Reaction of Iodobenzene (1) and Styrene (2) in the presence of Pd-complex (3) and Polymer (4).

5



The Pd complex of general formula 3 (109 mg of 5.2% THF solution) was placed in a Schlenk tube and evaporated and dried on high vacuum for 1 h to give about 5 μ mol (1 molar %) of complex 3. Compound 2 (85 μ L, 78 mg, 0.75 mmol, 1.5 equiv) and PhI 1 (57 μ L, 102 mg, 0.5 mmol, 1.0 equiv) were added. Polymer 4 (20 mg) and NaOAc (55 mg, 0.67 mmol, 1.34 equiv) were dissolved in 1 mL of demineralized water and added to the Schlenk tube, degassed by vacuum/argon cycle 5 times and mixed at RT for 5 min by stirring on magnetic stirrer. The mixture was placed in the preheated to 90 °C oil bath and stirred for 22 h. The mixture was cooled to RT and extracted with Et₂O (3 $\times$ 5 mL). Organic layer was dried over MgSO₄. The aqueous phase was diluted with brine (1 mL) and extracted with CH₂Cl₂ (3 $\times$ 5 mL) and dried over MgSO₄ to recover the polymer for analyses. The composition of the product and yield of 5 was determined by GCMS using n-C₁₆H₃₄ as internal standard. Et₂O extract content: PhI 1 – traces, Styrene 2 – 0, Stilbene 5 – 1.69 mg, 1,1-diphenylethene 6 – traces. CH₂Cl₂ extract content: PhI 1 – traces, Styrene 2 – 0, Stilbene 5 – 0.99 mg, 1,1-diphenylethene 6 – traces. The yield was 2.68 mg (3 %).

Comparative Example 1*Styrene solution polymerization in the presence of PNIPAM₁₈-SC(=S)SC₄H₉*

5

Styrene (STY, 1.59 g, 1.53×10^{-2} mol), AIBN (3.9×10^{-4} g, 2.38×10^{-6} mol), PNIPAM₁₈-SC(=S)SC₄H₉ (0.040 g, 2.00×10^{-5} mol) from part (b) and 4 mL of DMF were added to a 15 mL Schlenk flask equipped with magnetic stirrer bar. The mixture was deoxygenated by purging with Argon for 20 min then heated at 60 °C for 24 h. Samples were taken at
10 intervals for determination of monomer conversion and molecular weight distribution.
(Time = 24 h, $x = 0.02$, $M_n = 44010$, PDI = 1.59)

Size Exclusion Chromatography (SEC)

15 Size Exclusion Chromatography measurements were performed using a Waters Alliance 2690 Separations Module equipped with an auto-sampler, Differential Refractive Index (RI) detector and a Photo Diode Array (PDA) detector connected in series. HPLC grade tetrahydrofuran was used as eluent at flow rate 1 mL/min. The columns consisted of two 7.8 x 300 mm Waters linear Ultrastaygel SEC columns connected in series.

20

Absolute Molecular Weight Determination by Triple Detection-SEC

Absolute molecular weights of polymers were determined using a Polymer Labs GPC50 Plus equipped with dual angle laser light scattering detector, viscometer and differential
25 refractive index detector. HPLC grade dimethylacetamide containing 0.03 wt-% LiCl was used as eluent at flow rate 1 mL/min. Separations were achieved using two PLGel Mixed B (7.8 x 300 mm) SEC columns connected in series held at a constant temperature of 50 °C. The triple detection system was calibrated using a 2 mg/mL PSTY Standard M_{wt} 110 K in DMAc containing 0.03 wt% LiCl ($dn/dc = 0.160$ and $IV = 0.5809$ mL/g).

30

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Absolute molecular weights of 2,3,4,5,6-pentafluorostyrene copolymers were determined using a Polymer Labs GPC50 with the same detector configuration as above. HPLC grade tetrahydrofuran was used as eluent at flow rate 1 mL/min. Separations were achieved using two PLGel Mixed C (7.8 x 300 mm) SEC columns connected in series held at a constant
5 temperature of 40 °C. The triple detection system was calibrated using a 2 mg/mL PSTY Standard ($M_{wt}=110$ K, $dn/dc = 0.185$ and $IV = 0.4872$ mL/g).

Dynamic Light Scattering (DLS)

10 Dynamic Light Scattering measurements were performed using a Malvern Zetasizer 3000HS. The sample refractive index (RI) was set at 1.59 for polystyrene. The dispersant viscosity and RI were set to 0.89 and 0.89 Ns/m², respectively. The number-average particle diameter was measured for each sample.

15 Matrix Assisted Laser Desorption Ionisation Time of Flight Mass Spectroscopy (MALDI-TOF)

Mass spectrometry analysis of PNIPAM₁₈-SC(=S)SC₄H₉ was performed using a Voyager DE STR MALDI-TOF operated in reflector mode. The matrix used for the analysis was
20 2,5-dihydroxybenzoic acid and silver trifluoroacetate.

Transmission Electron Microscopy (TEM)

A typical TEM grid preparation was as follows: A particle solution was diluted with MilliQ
25 water to approximately 0.05 wt-%. A 10 µL aliquot of the solution was then allowed to air dry onto a formvar precoated copper TEM grid. The particles were characterized using a JEOL-1010 transmission electron microscope utilizing an accelerating voltage of 80 kV with spot size 2, at ambient temperature.

Kinetic Studies

Kinetic data for the RAFT-mediated polymerization of various monomers in the presence of
5 PNIPAM₁₈-SC(=S)SC₄H₉ (0.020 g) from part (b), P(DMA₄₉-b-NIPAM₁₀₆) (0.100 g)
micelles from part (e) and initiated with ammonium persulphate (APS) (0.87 mg) in water
(5 g) is presented below in Table 1. Refer to *part (f)* for a general description of the
experimental procedure followed.

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Table 1

EXPT	Monomer (mass (g))	Time (min)	x	$M_{n,SEC}^a$	PDI ^a	Dh (nm) (PDI)	Nc ($\times 10^{17}$)
1	STY (0.16)	60	0.73	16950	1.09	38 (0.237)	13.5
		90	0.82	26530	1.09	38 (0.292)	
		After precipitation		24340	1.08		
2	STY (0.43)	20	0.10	14790	1.05	36 (0.630)	11.2
		40	0.39	28420	1.06	63 (0.564)	3.59
		60	0.62	43310	1.09	64 (0.113)	4.78
		90	0.80	55550	1.12	70 (0.059)	4.3
		120	0.82	55880	1.14	72 (0.056)	4.12
		After precipitation		56370	1.11		
3	STY (0.77)	30	0.14	19480	1.02	46 (0.383)	7.37
		60	0.42	48540	1.07	84 (0.123)	2.41
		90	0.60	68360	1.08	103 (0.038)	1.78
		120	0.75	78480	1.12	107 (0.026)	1.94
		150	0.84	95550	1.17	114 (0.022)	1.78
		After precipitation		96305	1.08		
4	STY (1.08)	40	0.15	25970	1.04	67 (0.265)	3.05
		60	0.29	42310	1.05	94 (0.133)	1.71
		90	0.42	59630	1.09	114 (0.060)	1.28
		150	0.56	84200	1.11	124 (0.187)	1.30
		180	0.68	93140	1.26	140 (0.039)	1.08
		After precipitation		108140	1.07		
5	STY (1.57)	40	0.10	15530	1.23	54 (0.260)	5.66
		70	0.23	42970	1.12	108 (0.167)	1.27
		100	0.32	54610	1.17	133 (0.111)	0.89
		130	0.39	63940	1.22	153 (0.042)	0.7
		180	0.48	72690	1.31	164 (0.070)	0.69
		After precipitation		90130	1.12		
6 ^b	STY (0.39)	30	0.48	88350	1.32	61 (0.047)	4.03
		60	0.81	141060	1.29	65 (0.022)	4.95
		93	0.86	143650	1.35	66 (0.036)	5.06
		120	0.86	162620	1.28	66 (0.050)	5.07
		After precipitation		175750	1.19		
7	PFSTY (0.78)	15	0.23	52530	1.20	39 (0.204)	15.6
		30	0.51	66180	1.30	69 (0.099)	5.1
		45	0.74	99600	1.26	74 (0.088)	5.88
		60	0.93	138160	1.29	76 (0.09)	6.77
		After precipitation		167480	1.17		
8	BA (0.79)	10	0.06	18860	1.19	39 (0.336)	17.1
		25	0.74	49450	1.57	81 (0.371)	4.46
		40	0.87	60070	1.61	81 (0.239)	5.22
		55	0.90	79940	1.33	88 (0.299)	4.20
		After precipitation		93930	1.25		

^aAbsolute molecular weight values determined using triple detection SEC. ^bMass of PNIPAM₁₈-SC(=S)SC₄H₉ and APS used in this reaction was 0.005 g and 0.22 mg respectively.

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Transmission electron micrographs (TEMs) shown in Figure 2 demonstrate a change in particle diameter with near uniform particle size distributions generated from experiments 1 and 4 (Table 1 above). Refer to *part (f)* above for a general description of the polymerization procedure followed. Scale bar for the TEM relating to experiment 1 is 100 nm and for the TEM relating to experiment 4 is 200 nm.

Throughout this specification and the claims which follow, unless the context requires otherwise, the word "comprise", and variations such as "comprises" and "comprising", will be understood to imply the inclusion of a stated integer or step or group of integers or steps but not the exclusion of any other integer or step or group of integers or steps.

The reference in this specification to any prior publication (or information derived from it), or to any matter which is known, is not, and should not be taken as an acknowledgment or admission or any form of suggestion that that prior publication (or information derived from it) or known matter forms part of the common general knowledge in the field of endeavour to which this specification relates.

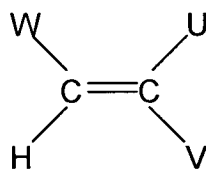
CLAIMS:

1. A method of performing a chemical reaction, the method comprising:
5 providing a liquid medium comprising micelles of assembled copolymer chains, the copolymer chains having a stimulus responsive polymer block that forms the core of the micelles, and a polymer block that is solvated by the liquid medium, wherein the micelles contain within their core one or more reactants;
reacting the one or more reactants to form a product within the core of the micelles;
10 and
subjecting the stimulus responsive polymer block to a stimulus such that it undergoes a transition and causes the micellar assembled copolymer chains to disassemble and release the product into the liquid medium.
- 15 2. The method according to claim 1, wherein the liquid medium is an aqueous liquid medium.
3. The method according to claim 1 or 2, wherein the stimulus responsive polymer block is of a type that in response to the stimulus undergoes a transition from being
20 hydrophobic in character to being hydrophilic in character or vice versa
4. The method according to any one of claims 1 to 3, wherein the stimulus responsive polymer block comprises a temperature responsive polymer that in response to a change in temperature undergoes a transition from being hydrophobic in character
25 to being hydrophilic in character or vice versa.
5. The method according to any one of claims 1 to 4, wherein the stimulus responsive polymer block comprises a homopolymer or copolymer of N-isopropyl acrylamide (NIPAAm).
30
6. The method according to any one of claims 1 to 5, wherein polymer block that is

5 solvated by the liquid medium comprises the polymerised residue of one or more monomers selected from acrylic acid, methacrylic acid, hydroxyethyl methacrylate, hydroxypropyl methacrylate, acrylamide and methacrylamide, hydroxyethyl acrylate, N-methylacrylamide, N,N-dimethylacrylamide and dimethylaminoethyl methacrylate.

7. The method according to any one of claims 1 to 6, wherein the copolymer chains are prepared by controlled radical polymerisation.
- 10 8. The method according to claim 7, wherein the controlled radical polymerisation is selected from iniferter polymerisation, stable free radical mediated polymerisation (SFRP), atom transfer radical polymerisation (ATRP), and reversible addition fragmentation chain transfer (RAFT) polymerisation.
- 15 9. The method according to any one of claims 1 to 8, wherein the one or more reactants are selected from hydrocarbon, alcohol, ether, aldehyde, ketone, carboxylic acid, carbohydrate, amine, amide and heterocyclic compounds.
10. The method according to any one of claims 1 to 9, wherein the one or more
20 reactants react by an addition, elimination, substitution, pericyclic, polymerisation, rearrangement, coupling or redox reaction to form the product.
11. The method according to any one of claims 1 to 8, wherein the one or more reactants comprise ethylenically unsaturated monomers.
- 25 12. The method according to claim 11, wherein the ethylenically unsaturated monomers are polymerised by free radical polymerisation to form the product.
13. The method according to claim 11 or 12, wherein the ethylenically unsaturated
30 monomers comprise those of formula (I):

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(I)

where U and W are independently selected from $-\text{CO}_2\text{H}$, $-\text{CO}_2\text{R}^1$, $-\text{COR}^1$, $-\text{CSR}^1$, $-\text{CSOR}^1$, $-\text{COSR}^1$, $-\text{CONH}_2$, $-\text{CONHR}^1$, $-\text{CONR}^1_2$, hydrogen, halogen and optionally substituted $\text{C}_1\text{-C}_4$ alkyl or U and W form together a lactone, anhydride or imide ring that is optionally substituted, where the optional substituents are independently selected from hydroxy, $-\text{CO}_2\text{H}$, $-\text{CO}_2\text{R}^1$, $-\text{COR}^1$, $-\text{CSR}^1$, $-\text{CSOR}^1$, $-\text{COSR}^1$, $-\text{CN}$, $-\text{CONH}_2$, $-\text{CONHR}^1$, $-\text{CONR}^1_2$, $-\text{OR}^1$, $-\text{SR}^1$, $-\text{O}_2\text{CR}^1$, $-\text{SCOR}^1$, and $-\text{OCSR}^1$;

V is selected from hydrogen, R^1 , $-\text{CO}_2\text{H}$, $-\text{CO}_2\text{R}^1$, $-\text{COR}^1$, $-\text{CSR}^1$, $-\text{CSOR}^1$, $-\text{COSR}^1$, $-\text{CONH}_2$, $-\text{CONHR}^1$, $-\text{CONR}^1_2$, $-\text{OR}^1$, $-\text{SR}^1$, $-\text{O}_2\text{CR}^1$, $-\text{SCOR}^1$, and $-\text{OCSR}^1$;

where the or each R^1 is independently selected from optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted arylalkyl, optionally substituted heteroarylalkyl, optionally substituted alkylaryl, optionally substituted alkylheteroaryl, and an optionally substituted polymer chain.

14. The method according to any one of claims 11 to 13, wherein the ethylenically unsaturated monomers are polymerised by controlled radical polymerisation to form the product.

15. The method according to claim 14, wherein the controlled radical polymerisation is selected from iniferter polymerisation, stable free radical mediated polymerisation (SFRP), atom transfer radical polymerisation (ATRP), and reversible addition fragmentation chain transfer (RAFT) polymerisation.

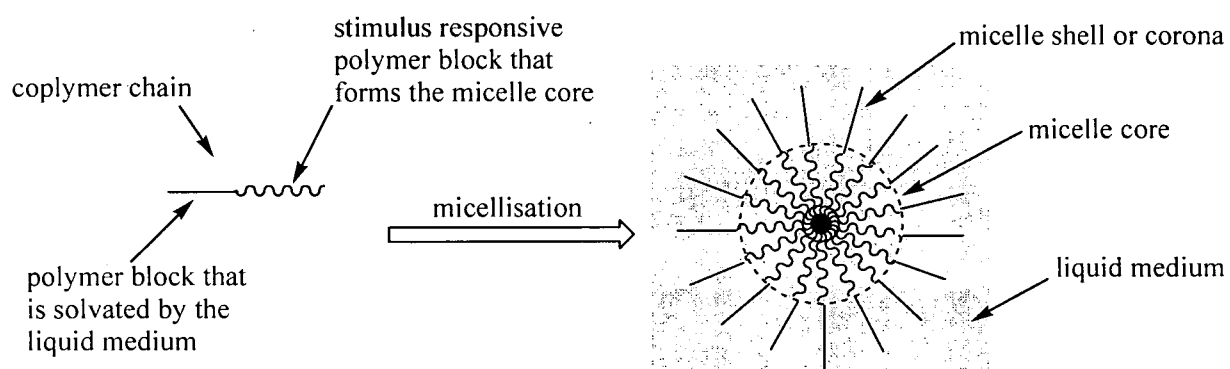
- 78 -

16. The method according to any one of claims 1 to 15, wherein the liquid medium comprising the micelles is provided by combining the copolymer chains and the liquid medium such that the copolymer chains assemble to form micelles, and wherein this resulting composition is combined with the one or more reactants such that they are transported through the liquid medium and absorbed within the core of the micelles.
17. The method according to any one of claims 1 to 15, wherein the liquid medium comprising the micelles is provided by combining the liquid medium, the copolymer chains and one or more reactants such that the copolymer chains do not form micelles, and then subjecting the stimulus responsive polymer block of the copolymer chains to a stimulus such that it undergoes a transition and causes the copolymer chains to assemble into micelles, and wherein the micellisation of the copolymer chains encapsulates the one or more reactants within the core of the micelles.
18. The method according to any one of claims 1 to 17, wherein the stimulus responsive polymer block comprises a temperature responsive polymer, and wherein adjusting the temperature of the liquid medium causes the micellar assembled copolymer chains to disassemble and release the product.
19. The method according to any one of claims 1 to 18, wherein the product formed from the one or more reactants is a polymer.
20. A liquid medium comprising micelles of assembled copolymer chains, the copolymer chains having a stimulus responsive polymer block that forms the core of the micelles and a polymer block that is solvated by the liquid medium, wherein the micelles contain within their core one or more reactants that will react to form a product within the core, and wherein the stimulus responsive polymer block is capable of undergoing a stimulus induced transition that causes the micellar

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assembled copolymer chains to disassemble and release the product into the liquid medium.

21. Use of a liquid medium comprising micelles for producing a product from a chemical reaction, the micelles being formed from assembled copolymer chains, the copolymer chains having a stimulus responsive polymer block that forms the core of the micelles and a polymer block that is solvated by the liquid medium, wherein the micelles are capable of containing within their core one or more reactants that will react to form the product within the core of the micelles, and wherein the stimulus responsive polymer block is capable of undergoing a stimulus induced transition that causes the micellar assembled copolymer chains to disassemble and release the product into the liquid medium.
22. A reactor for performing a chemical reaction, the reactor comprising:
- a liquid medium comprising micelles of assembled copolymer chains, the copolymer chains having a stimulus responsive polymer block that forms the core of the micelles, and a polymer block that is solvated by the liquid medium,
- wherein the micelles contain within their core one or more reactants that are capable of reacting to form a product within the core,
- and wherein the stimulus responsive polymer block is capable of undergoing a stimulus induced transition that causes the micellar assembled copolymer chains to disassemble and release the product into the liquid medium.

**Figure 1**

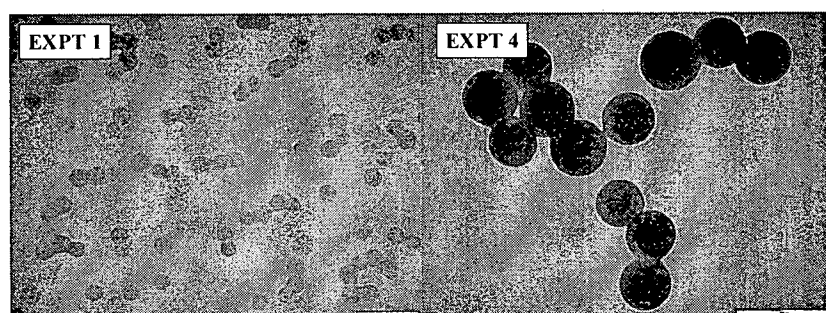


Figure 2

INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU2010/000424

A. CLASSIFICATION OF SUBJECT MATTER

Int. Cl.

C08F 2/00 (2006.01)

C08F 6/00 (2006.01)

C08F 222/38 (2006.01)

B01J 13/14 (2006.01)

C08F 220/42 (2006.01)

C08F 20/56 (2006.01)

C08F 2/20 (2006.01)

C08F 222/00 (2006.01)

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)

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)

EPODOC, WPI, Google Scholar, Patent lens, Google patents

block_polymer, block_co_polymer, co_polymer, Stimulus, ph, temperature_responsive, micelle+, controlled_radical, Living_radical, atom transfer, fragment+, chain_transfer, nanoreactor, Isopropyl_acrylamide

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LIU S <i>et al</i> , "Synthesis of pH-Responsive Shell Cross-Linked Micelles and Their Use as Nanoreactors for the Preparation of Gold Nanoparticles", Langmuir, Vol. 18, No. 22, 2002 page 8350-8357 (Abstract; Introduction; Figure 2; page 8353)	1-4, 6-8, 10, 16-18, 20-22
X	GE Z <i>et al</i> , "Stimuli-Responsive Double Hydrophilic Block Copolymer Micelles with Switchable Catalytic Activity", Macromolecules 2007, Vol 40, No. 10, pages 3538-3546. (Abstract; Introduction; page 3539, left hand side column; page 3544, Scheme 2; page 3545)	1-5, 7-10, 16-18, 20-22
X	NALLANI M <i>et al</i> , "Polymersome Nanoreactors for Enzymatic Ring-Opening Polymerization", Biomacromolecules, Vol. 8, No. 12, 2007, page 3723-3728. (Abstract; page 3723; left column; page 3724, figure 1; page 3725, right column para 3)	1-3, 9-10, 16-17, 19-22

☒ Further documents are listed in the continuation of Box C

☒ See patent family annex

* Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent but published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

05 May 2010

Date of mailing of the international search report

12 MAY 2010

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU2010/000424

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BOUILHAC C <i>et al</i> , "Block Copolymer Micelles as Nanoreactors for Single-Site Polymerization Catalysts", Journal of Polymer Science, Vol 47, Issue 1, pages 197-209. Available on line 24 November 2008 (DOI: 10.1002/pola.23142) (Abstract; page 198, right column; page 199, right column; page 205; scheme 2)	1-3, 7-22
P,X	URBANI <i>et al</i> , "Nanoreactors for Aqueous RAFT-Medicated Polymerisation", Macromolecules, Vol. 42, No. 12, 2009, pages 3884-3886, Published online 07 May 2009 (Whole Document)	1-22
A	WEI H <i>et al</i> , "Self-assembled thermoresponsive micelles of poly(N-isopropylacrylamide-b-methyl methacrylate)", Biomaterials 27 (2006) 2028-2034, Available online 11 October 2005 (Abstract)	
A	MERTOGLU <i>et al</i> , "Stimuli responsive amphiphilic block copolymers for aqueous media synthesised via reversible addition fragmentation chain transfer polymerisation (RAFT)", Polymer 46 (2005) 7726-7740, Available online 23 May 2005 (Abstract)	
A	WO 2008/071661 A1 (UNILEVER N.V) 19 June 2008 (Abstract; page 45, example 6)	

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/AU2010/000424

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report				Patent Family Member			
WO	2008071661	CA	2672382	CN	101605827	EP	2102256
Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.							
END OF ANNEX							