

The Synthesis of Multiarm Poly[(R)-3-hydroxybutyrate] and Its Derivatives

The current invention relates to the generation of a variety of polymeric architectures from PHB - as multiarm PHBs, and then coupling these multiarm PHBs with different polymers
5 such as (2-dimethylamino)ethyl methacrylate (DMAEMA), 2-hydroxyethyl methacrylate (HEMA) and N-isopropylacrylamide (NIPAM) to create novel polymers with different properties such as antimicrobial properties, amphiphilic, thermo-responsive and pH-responsive etc.

10 The listing or discussion of an apparently prior-published document in this specification should not necessarily be taken as an acknowledgement that the document is part of the state of the art or is common general knowledge.

Poly[(R)-3-hydroxybutyrate] (PHB) is a natural biodegradable polyester, which is highly
15 crystalline and hydrophobic, showing a greater hydrophobicity than either poly(lactic acid) or poly(ϵ -caprolactone). PHB is nontoxic and it degrades to D-3-hydroxybutyrate, which is a natural constituent of human blood. As a result of these advantageous properties, PHB may be suitable for a variety of biomedical applications, such as a drug carrier and as a tissue engineering scaffold. Because of its inherent hydrophobicity, PHB is rarely used in
20 applications that require good water solubility, such as polymeric micelles and gels.

There remains a need to develop new and useful polymeric architectures that are suitable to be functionalised for a range of roles.

25 The following drawings that aid to described the current invention are provided.

Figure 1: Depicts block copolymers that make use of the core compounds discussed hereinbefore with poly[(2-dimethylamino)ethyl methacrylate (DMAEMA)].

Figure 2: Synthesis scheme of a PHB-diol.

30 Figure 3: Depicts the molecular weight (M_n) versus time (hours) for the PHB-diol reaction with ethylene glycol, as set out in the synthesis of multiarm PHB (two-arm) experimental section.

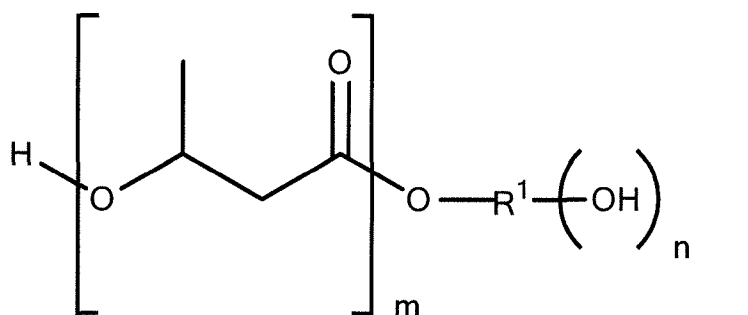
Figure 4: Depicts the reaction of PHB02Br with DMAEMA and its subsequent quaternization.

Figure 5: Depict ^1H NMR spectra of PHB04 series: (A) PHB04, (B) PHB04Br, and (C)
35 PHB04-PDMAEMA.

Figure 6: ^1H NMR (in D_2O) of PHB04-PDMAEMA before (A) and after (B) quaternization.

We have now surprisingly discovered that PHB can be conveniently functionalised to provide a number of platform polymeric architectures that may provide a number of differing functions. For example, said functionalisation may provide antimicrobial polymers, amphiphilic block copolymers, thermoplastic elastomers, shape memory polymers and thermogelling copolymers. Applications of such polymers include biomedical technology (antimicrobial coatings for surgical devices/sterilisation, tissue engineering scaffolds, drug/gene delivery, wound dressing/eye patch, eye drops), as well as in the electronics industry and as a lubricant/rheologic modifier.

Thus, in a first aspect of the invention, there is provided a polymer having formula I:



wherein:

m represents the repeating unit of the polymer;

R¹ represents a straight-chain or branched C₁₋₁₄ alkyl or a C₃₋₁₀ cycloalkyl that are substituted with n hydroxyl groups;

n represents 0 to 8, and wherein

the number average molecular weight of the polymer is from 500 to 80,000 Daltons.

It will be appreciated that the hydroxyl groups may be present on any carbon of R¹ that provides a stable compound. For example, any carbon atom not bonded directly to the ester terminus of the PHB polymeric chain may carry one or more (i.e. one) hydroxyl groups.

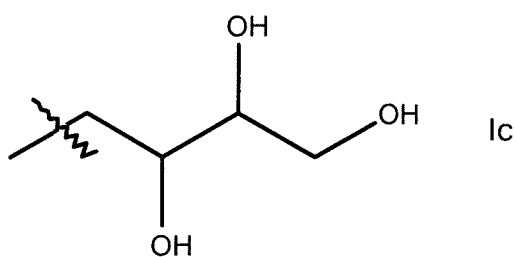
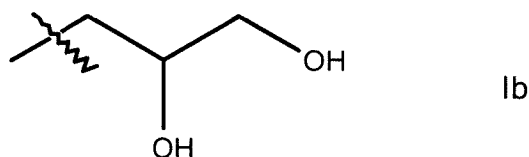
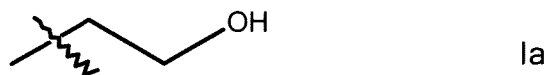
It will also be appreciated that the polymeric backbone of the polymer of formula I is derived from poly[3-hydroxybutyrate]. The methyl group on the repeating unit of poly[3-hydroxybutyrate] is chiral and may exist in the (R)- or (S)- configuration. While the polymer may have a backbone that only contains (R)- or only contain (S)- repeating units, it is explicitly contemplated that the polymeric backbone may contain both (R)- and (S)-

repeating units, whether in a random pattern, a repeating block pattern or in an alternating pattern. For the avoidance of doubt, when used herein "PHB" may be applied to all of the above-mentioned options. In specific embodiments of the invention that may be mentioned herein, the poly[3-hydroxybutyrate] used may be poly[(*R*)-3-hydroxybutyrate].

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In embodiments of the invention:

- (a) the polymer may have a number average molecular weight of from 750 to 60,000 Daltons (e.g. from 1,000 to 30,000 Daltons, such as 1,500 to 10,000 Daltons, such as from 2,000 to 6,000 Daltons);
 - 10 (b) R^1 may represent a straight-chain or branched C_{1-6} alkyl (e.g. a straight-chain C_{2-5} alkyl);
 - (c) n may represent 0 to 5 (e.g. n represents 0 to 4, 0 or 2 to 4, or 3 to 4);
 - (d) R^1 may represent a straight-chain C_{4-6} alkyl and n may represent 0.
- 15 In particular embodiments of the invention, $-R^1(OH)_n$ may represent hexyl or a fragment selected from formula Ia-Ic (e.g. $-R^1(OH)_n$ may represent formula Ib or formula Ic),



where the wavy line represents the point of attachment of the fragment $-R^1(OH)_n$ to the rest of the polymer. For example, when:

- 20 (a) R^1 represents hexyl, the number average molecular weight of the polymer is from 750 to 60,000 Daltons (e.g. from 1,000 to 7,000 Daltons, such as from 1,700 to 2,000 Daltons);

(b) R^1 represents the fragment of formula Ia, the number average molecular weight of the polymer is from 750 to 60,000 Daltons (e.g. from 1,000 to 7,000 Daltons, such as from 2,000 to 2,200 Daltons);

(c) R^1 represents the fragment of formula Ib, the number average molecular weight of the polymer is from 750 to 60,000 Daltons (e.g. from 1,000 to 7,000 Daltons, such as from 6,000 to 6,500 Daltons); and

(d) R^1 represents the fragment of formula Ic, the number average molecular weight of the polymer is from 750 to 60,000 Daltons (e.g. from 1,000 to 7,000 Daltons, such as from 4,500 to 4,700 Daltons).

In particular embodiments that may be mentioned herein, in the polymer of formula I, n may represent 0 or 2 to 4.

It will be appreciated that the resulting polymeric materials are multiarm PHBs that may be used as a platform to build more complex polymeric structures, while retaining the multiarm PHBs as the core architecture. Thus, the polymer of formula I may comprise part of a block copolymer, where one of more of the -OH groups in the compound of formula I instead represents -O- and serves to link the compound of formula I to the other components of said block copolymer. This block copolymer may be produced by:

(a) the copolymerisation of the multiarm PHBs described hereinbefore with suitable di- or polyisocyanate to make polyurethanes (e.g. diphenylmethane diisocyanate, toluene diisocyanate, hexamethylene diisocyanate, isophorone diisocyanate and polymeric diphenylmethane diisocyanate);

(b) following functionalisation with a suitable reversible addition-fragmentation chain-transfer (RAFT) polymerization agent, copolymerisation with a monomer suitable for use in RAFT polymerization to form a RAFT-polymerised block copolymer;

(c) following functionalisation with a suitable atom transfer radical polymerization (ATRP) initiator, copolymerisation with a monomer suitable for use in ATRP polymerization to form a ATRP-polymerised block copolymer.

In keeping with the above, Figure 1 depicts in cartoon fashion the formation of block copolymers that make use of the core compounds discussed hereinbefore with (2-dimethylamino)ethyl methacrylate (DMAEMA). As depicted, the polymeric core may have at least one arm available for functionalisation, but may also have two or more, such as 3 or more arms suitable for functionalisation (i.e. 3 or 4 arms). When the polymer core has more than two arms (i.e. 3 or more arms), the polymeric core the core may be referred to herein as a "star polymer". In addition, the term "star polymer" may also relate to the

resulting block copolymers as described hereinbefore, which may also be referred to herein as “star copolymers”.

While not shown in Fig. 1, the resulting copolymers may themselves be further functionalised, such as by quaternisation, which may also provide particular advantages to the block copolymers made using the core PHB polymers described herein before.

Thus, the core architecture and/or the resulting block copolymers may provide or have one or more of the following advantages:

(i) the polymers may have a higher cationic charge density than linear polymers (e.g. quarternised block copolymers made using star-shaped core PHBs (3- or more-armed PHBs)), which may be useful for antimicrobial and/or gene delivery applications;

(ii) the multiarm PHB polymer provides biodegradability within the core of the block copolymer, where the core PHB structure can be readily hydrolysed and so leads to the formation of shorter branch molecules that may be easier to recycle (this may be particularly advantageous for materials that use star-shaped core structures);

(iii) the star-shaped core structures may provide copolymers that can provide superior performance as a rheologic modifier, breaking the relationship between thickening efficiency, shear stability and viscosity index that limits conventional linear polymethacrylate viscosity modifier technology;

(iv) cationic star copolymers may be less toxic compared to linear polymers with a similar charge density because the branches containing the charges are shorter in size.

In a second aspect of the invention, there is provided a process of preparing a polymer, which process comprises a transesterification reaction to produce a compound of formula I, as defined hereinbefore (e.g. in the first aspect of the invention and its embodiments), comprising reaction of a P3HB having a number average molecular weight of from 20,000 to 200,000 Daltons with an alcohol of formula II,



wherein:

R^1 represents a straight-chain or branched C_{1-14} alkyl, a straight-chain or branched C_{1-14} alkyl substituted with from 0 to 8 hydroxyl groups, a C_{1-10} cycloalkyl or a C_{1-10} cycloalkyl substituted with from 0 to 8 hydroxyl groups, and

the alcohol of formula II is present in a molar excess of from 100 times to 500 times (e.g. 300 times) the molar amount of the P3HB.

When used herein, "P3HB" refers to poly[3-hydroxybutyrate]. As noted hereinbefore, the methyl group on the repeating unit of poly[3-hydroxybutyrate] is chiral and may exist in the (R)- or (S)- configuration. Given this, when used herein "P3HB" may refer to a poly[3-hydroxybutyrate] where the polymer has a backbone that only contains (R)- or only contain (S)- repeating units, as well as a backbone that contains both (R)- and (S)- repeating units, whether in a random pattern, a repeating block pattern or in an alternating pattern. For the In specific embodiments of the invention that may be mentioned herein, the P3HB used may be poly[(R)-3-hydroxybutyrate]. "P3HB" may be used interchangeably with "PHB".

In embodiments of the process, the transesterification reaction may:

(a) be conducted at a temperature of from 100°C to 160 °C for from 1 to 10 days, optionally at a temperature of 140 °C for from 2 to 5 days;

(b) comprise an organic solvent (e.g. diglyme), optionally wherein a concentration of the alcohol of formula II in the organic solvent is from 0.1 M to 1 M (e.g. from 0.4 M to 0.5 M);

(c) further comprise a catalyst (e.g. a tin-based catalyst and/or a titanium-based catalyst, such as dibutyltin dilaurate);

(d) be conducted under an inert atmosphere.

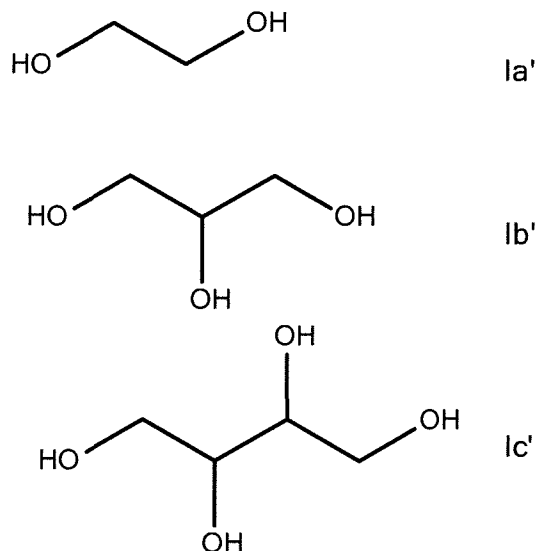
In yet further embodiments of the process, the compound of formula II may be one where:

(i) R^1 represents a straight-chain or branched C_{1-6} alkyl (e.g. a straight-chain C_{2-5} alkyl);

(ii) n may represent 0 to 5 (e.g. n represents 0 to 4, 0 or 2 to 4, or 3 to 4);

(iii) R^1 may represent a straight-chain C_{4-6} alkyl and n may represent 0.

In particular embodiments of the process, in the compound of formula II, R^1OH may represent hexanol or a compound selected from formula Ia'-Ic' (e.g. $-R^1(OH)_n$ may represent formula Ib' or formula Ic'),



For example:

(a) when R^1 represents hexanol, the number average molecular weight of the compound of formula I is from 750 to 60,000 Daltons (e.g. from 1,000 to 7,000 Daltons, such as from 1,700 to 2,000 Daltons);

(b) when R^1OH represents the compound of formula Ia, the number average molecular weight of the compound of formula I is from 750 to 60,000 Daltons (e.g. from 1,000 to 7,000 Daltons, such as from 2,000 to 2,200 Daltons);

(c) when R^1OH represents the compound of formula Ib, the number average molecular weight of the compound of formula I is from 750 to 60,000 Daltons (e.g. from 1,000 to 7,000 Daltons, such as from 6,000 to 6,500 Daltons); and

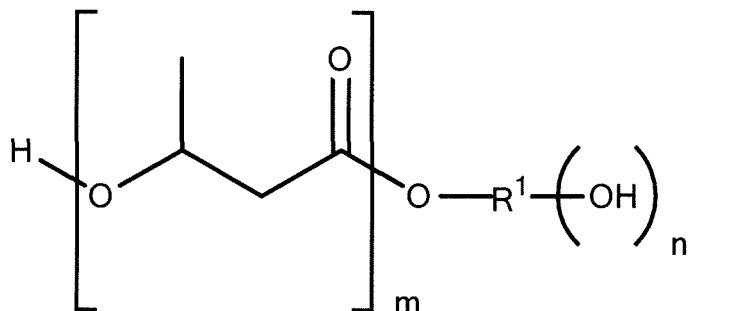
(d) when R^1OH represents the compound of formula Ic, the number average molecular weight of the compound of formula I is from 750 to 60,000 Daltons (e.g. from 1,000 to 7,000 Daltons, such as from 4,500 to 4,700 Daltons).

In particular embodiments that may be mentioned herein, in the polymer of formula I, n may represent 0 or 2 to 4.

It will be appreciated that the process described hereinbefore enables one to make the core polymer architectures described in the context of the first aspect of the invention. However, as indicated hereinbefore, it is possible to make use of these core polymeric structures to form more complex polymers.

Thus, in a third aspect of the invention, there is provided a process to prepare a block copolymer of formula VI that comprises

- (a) reacting a compound of formula I:



- 5 wherein:

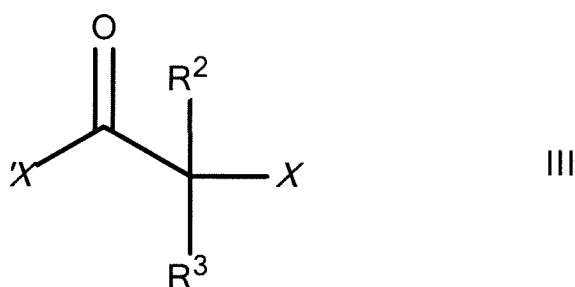
m represents the repeating unit of the polymer;

R¹ represents a straight-chain or branched C₁₋₁₄ alkyl or a C₃₋₁₀ cycloalkyl that are substituted with n hydroxyl groups;

n represents 0 to 8, and wherein

- 10 the number average molecular weight of the polymer is from 500 to 80,000 Daltons,

with a sufficient quantity of a suitable atom transfer radical polymerization (ATRP) initiator of formula III:

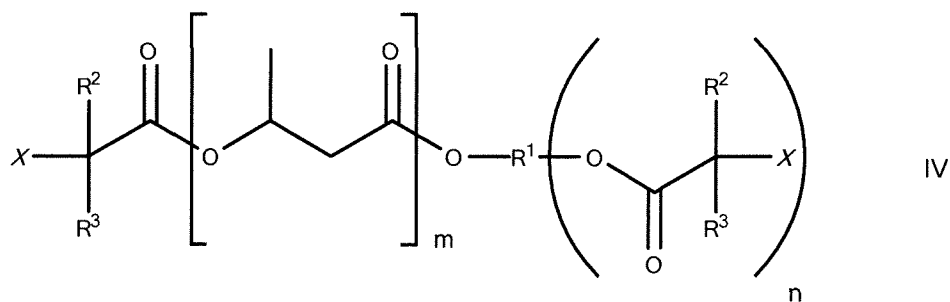


- 15

where X and 'X are independently selected from Cl, Br and I; and

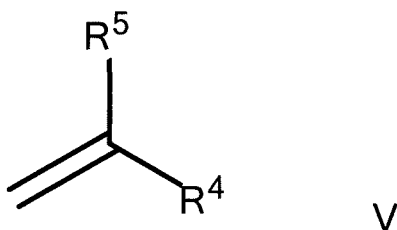
R² and R³ are independently selected from C₁₋₆ alkyl,

to provide a compound of formula IV:



where X, R² and R³ are as defined for the compound of formula III and R¹, m and n are as defined for the compound of formula I (e.g. as above and/or in the first aspect of the invention and its embodiments); and

- 5 (b) reacting the compound of formula IV under ATRP conditions with a monomer compound of formula V:



10 where:

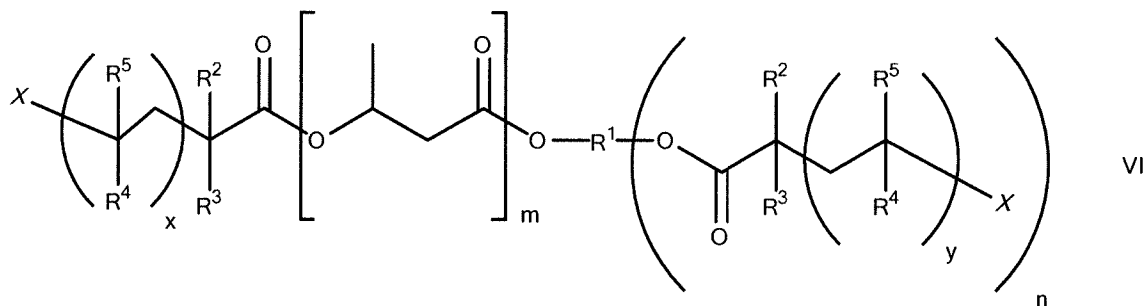
R⁴ represents C₆₋₁₀ aryl, C₅₋₁₀ hetroaryl, C(O)R^{6a}, C(O)OR^{6b} and C(O)NR^{7a}R^{7b};

R⁵ represents H or straight-chain or branched C₁₋₆ alkyl;

R^{6a} and R^{6b} independently represent a straight-chain or branched C₁₋₆ alkyl or straight-chain or branched C₁₋₆ alkyl substituted by one or more of the substituents selected from OR⁸ or NR⁹R¹⁰;

15 R^{7a}, R^{7b}, R⁸, R⁹ and R¹⁰ are independently selected from H or straight-chain or branched C₁₋₆ alkyl,

to provide a compound of formula VI:

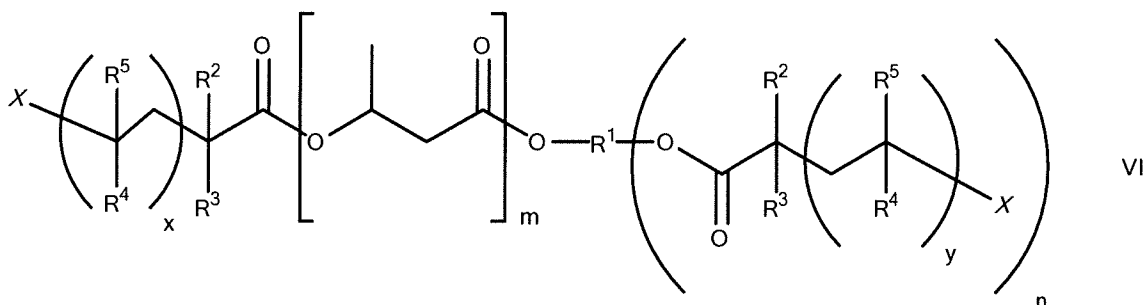


where:

x and y represent a polymeric repeating unit of the monomer of the compound of formula V;
 R^4 and R^5 are as defined for the compound of formula V

- 5 X, R^2 and R^3 are as defined for the compound of formula III; and
 R^1 , m and n are as defined for the compound of formula I (e.g. as above and/or in the first aspect of the invention and its embodiments).

As will be appreciated, the process above provides a range of copolymers. In a fourth
 10 aspect of the invention, said block copolymers are obtained or obtainable by the process of the third aspect of the invention. For example, there may be provided a block copolymer of formula VI:



15 wherein:

m represents a polymeric repeating unit of a first polymeric component;

R^1 represents a straight-chain or branched C_{1-14} alkyl or a C_{3-10} cycloalkyl that are substituted with n ester groups;

n represents 0 to 8;

20 X represents Cl, Br and I;

R^2 and R^3 are independently selected from C_{1-6} alkyl;

R^4 represents C_{6-10} aryl, C_{5-10} hetroaryl, $C(O)R^{6a}$, $C(O)OR^{6b}$ and $C(O)NR^{7a}R^{7b}$;

R^5 represents H or straight-chain or branched C_{1-6} alkyl;

R^{6a} and R^{6b} independently represent a straight-chain or branched C_{1-6} alkyl or straight-chain or branched C_{1-6} alkyl substituted by one or more of the substituents selected from OR^8 or NR^9R^{10} ;

R^{7a} , R^{7b} , R^8 , R^9 and R^{10} are independently selected from H or straight-chain or branched C_{1-6} alkyl,

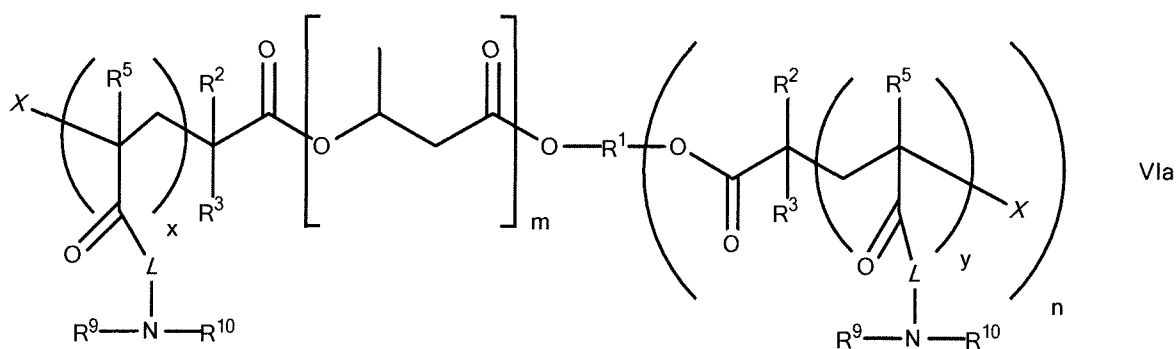
x represents a polymeric repeating unit of a second polymeric component;

y, when present, represents a polymeric repeating unit of a third polymeric component when

n is 1 up to a tenth polymeric component when n is 8; and

the number average molecular weight of the block copolymer is from 15,000 to 200,000 Daltons (e.g. from 20,000 to 150,000 Daltons or from 20,000 to 200,000 daltons).

In certain embodiments, the block copolymer of formula VI may be a block copolymer of formula VIa:



wherein:

m represents a polymeric repeating unit of a first polymeric component;

R^1 represents a straight-chain or branched C_{1-14} alkyl or a C_{3-10} cycloalkyl that are substituted with n ester groups;

n represents 0 to 8;

X represents Cl, Br and I;

R^2 and R^3 are independently selected from C_{1-6} alkyl;

R^5 represents straight-chain or branched C_{1-6} alkyl;

R^9 and R^{10} are independently selected from straight-chain or branched C_{1-6} alkyl,

x represents a polymeric repeating unit of a second polymeric component;

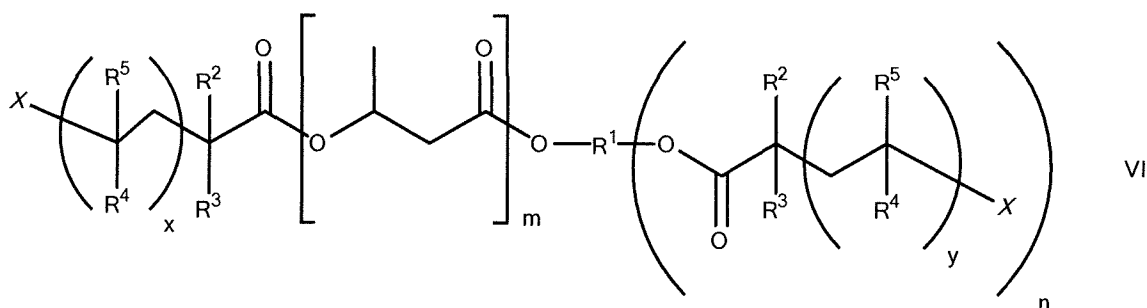
y, when present, represents a polymeric repeating unit of a third polymeric component when n is 1 up to a tenth polymeric component when n is 8;

L represents a straight-chain or branched $-C_{1-6}$ alkylene or a straight-chain or branched $-O-C_{1-6}$ alkylene (e.g. L represents a straight-chain or branched $-O-C_{1-6}$ alkylene); and

5 the number average molecular weight of the block copolymer is from 15,000 to 200,000 Daltons (e.g. from 20,000 to 150,000 Daltons or from 20,000 to 200,000 daltons).

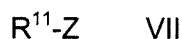
As noted hereinbefore, the resulting copolymers may be further functionalised. Thus, in a fifth aspect of the invention, when R^4 represents $C(O)R^{6a}$ or $C(O)OR^{6b}$, where R^{6a} and R^{6b} independently represent a C_{1-6} straight-chain or branched alkyl substituted by a NR^9R^{10} substituent and R^1 to R^3 , R^5 , and R^7 to R^{10} are as defined in the third aspect of the invention in a compound of formula VI, there is provided a process that comprises:

(i) reacting the compound of formula VI:



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as defined hereinbefore, with a compound of formula VII:



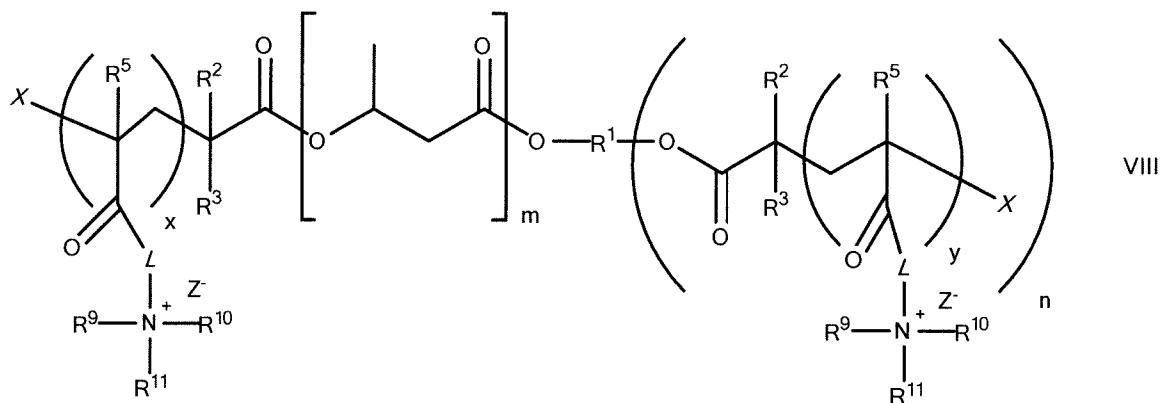
20 where:

R^{11} represents straight-chain or branched C_{1-6} alkyl or straight-chain or branched C_{1-6} alkyl substituted with one or more of C_{6-10} aryl, C_{5-10} heteroaryl and OH; and

Z represents Br, Cl or I,

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to provide a quarternised compound of formula VIII:



where:

L represents a straight-chain or branched -C₁₋₆ alkylene or a straight-chain or branched -O-

5 C₁₋₆ alkylene (e.g. L represents a straight-chain or branched -O-C₁₋₆ alkylene);

R⁹ and R¹⁰ are independently selected from straight-chain or branched C₁₋₆ alkyl;

R¹¹ and Z are as defined for the compound of formula VII hereinbefore;

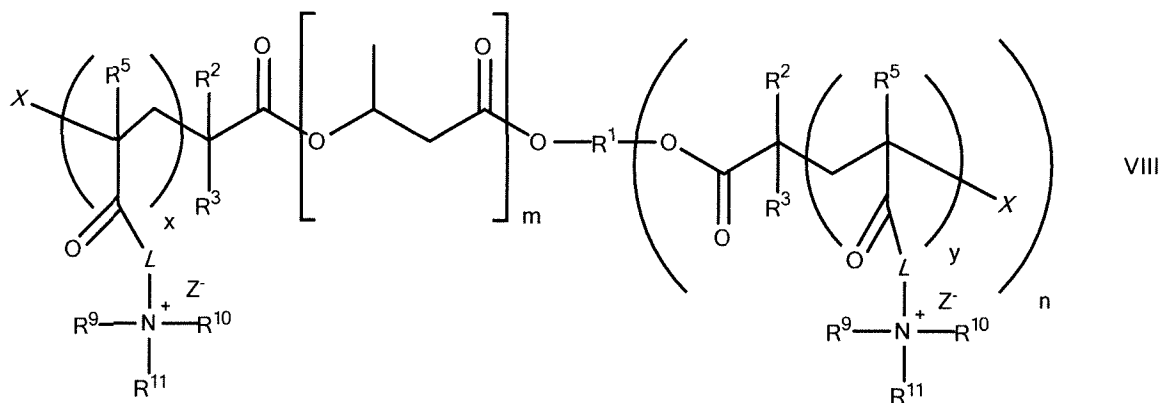
x and y are as defined for the compound of formula VI in the fourth and fifth aspects of the invention;

10 R⁴ and R⁵ are as defined for the compound of formula V in the fourth and fifth aspects of the invention;

X, R² and R³ are as defined for the compound of formula III in the third aspect of the invention; and

15 R¹, m and n are as defined for the compound of formula I in the first or third aspects of the invention (and any of their embodiments).

The resulting functionalised (quaternised) block copolymer of the fifth aspect of the invention is provided as the sixth aspect of the invention as a block copolymer having formula VIII:



wherein:

m represents a polymeric repeating unit of a first polymeric component;

5 R^1 represents a straight-chain or branched C_{1-14} alkyl or a C_{3-10} cycloalkyl that are substituted with n ester groups;

n represents 0 to 8;

X represents Cl, Br and I;

R^2 and R^3 are independently selected from C_{1-6} alkyl;

10 R^5 represents straight-chain or branched C_{1-6} alkyl;

R^9 and R^{10} are independently selected from straight-chain or branched C_{1-6} alkyl,

R^{11} represents straight-chain or branched C_{1-6} alkyl or straight-chain or branched C_{1-6} alkyl substituted with one or more of C_{6-10} aryl, C_{5-10} hetroaryl and OH;

Z represents Br, Cl or I;

15 x represents a polymeric repeating unit of a second polymeric component;

y, when present, represents a polymeric repeating unit of a third polymeric component when n is 1 up to a tenth polymeric component when n is 8;

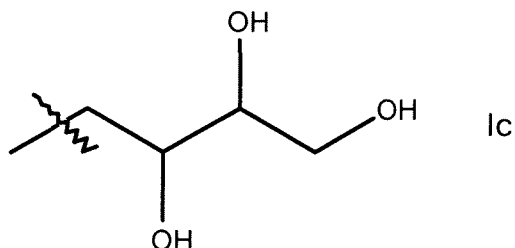
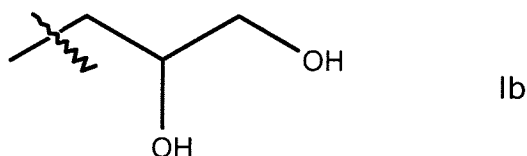
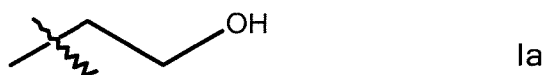
L represents a straight-chain or branched $-C_{1-6}$ alkylene or a straight-chain or branched $-O-C_{1-6}$ alkylene (e.g. L represents a straight-chain or branched $-O-C_{1-6}$ alkylene); and

20 the number average molecular weight of the block copolymer is from 15,000 to 200,000 Daltons (e.g. from 20,000 to 150,000 Daltons or from 20,000 to 200,000 daltons).

In the third to sixth aspects of the invention (and embodiments thereof):

(a) R^1 may represent a straight-chain or branched C_{1-6} alkyl and n represents 0 to

25 5 (e.g. R^1 may represents a straight-chain C_{2-5} alkyl and n represents 0 to 4 or R^1 may represent a straight-chain C_{4-6} alkyl (such as when n is 0), or R^1 may represent hexyl or a fragment selected from formula Ia-Ic,



where the wavy line represents the point of attachment of the fragment to the polymer;

- (b) X represents Cl, or, more particularly, Br;
- (c) R^2 , R^3 and R^5 are independently selected from C_{1-2} alkyl;
- (d) R^{11} represents straight-chain or branched C_{1-3} alkyl or straight-chain or branched C_{1-3} alkyl substituted by phenyl;
- (e) n represents 0 to 4;
- (f) L represents a straight-chain or branched -O- C_{1-2} alkylene;
- (g) the number average molecular weight of the block copolymer is from 15,000 to 165,000 Daltons (e.g. from 55,000 to 163,000 Daltons, such as from 19,000 to 41,000 Daltons).

As described hereinbefore, the copolymerisation process may also be conducted using reversible addition-fragmentation chain-transfer (RAFT) polymerization. Thus, in an seventh aspect of the invention, there is provided a process that comprises functionalising the compound of formula I (as described in the first aspect of the invention and in its embodiments) with a suitable reversible addition-fragmentation chain-transfer (RAFT) polymerization agent to form a RAFT precursor compound and reacting the RAFT precursor compound with a monomer suitable for use in RAFT polymerization to form a RAFT-polymerised block copolymer. Thus in a eighth aspect of the invention, there is provided a block copolymer that is obtained or obtainable from the process of the eighth aspect of the invention.

In a ninth aspect of the invention there is provided a process further comprises reacting the compound of formula I (as described in the first aspect of the invention and in its embodiments) with a suitable di- or polyisocyanate to form a polyurethane. The di- or polyisocyanate may be selected from one or more of the group consisting of diphenylmethane diisocyanate, toluene diisocyanate, hexamethylene diisocyanate, isophorone diisocyanate and polymeric diphenylmethane diisocyanate. Thus in a tenth aspect of the invention, there is provided a block copolymer that is obtained or obtainable from the process of the eighth aspect of the invention.

Non-limiting examples that embody certain aspects of the invention will now be described.

Examples

Materials and Methods

Natural source poly[(*R*)-3-hydroxybutyrate] (P3HB or PHB) was supplied by Aldrich and purified by dissolving it in chloroform followed by filtration and subsequent precipitation in hexane before use. The Mn and Mw of the purified PHB were 6.0×10^4 and 7.1×10^4 g/mol, respectively. Bis(2-methoxyethyl) ether (anhydrous diglyme, 99%), dibutyltin dilaurate (95%), ethylene glycol (99%), 1-hexanol, glycerol (99%), erythritol, triethylamine (TEA), benzyl bromide (Fluka), anhydrous tetrahydrofuran were purchased from Aldrich and used as received.

Example 1

Synthesis of multiarm PHB (one-arm)

PHB with one OH termination (PHB-01) was prepared by transesterification between the natural source PHB and hexanol using dibutyltin dilaurate in diglyme. Typically, 10.5 g (Mn = 6.0×10^4 , 1.77×10^{-4} mol) (1.0 equivalent) of purified PHB was dissolved in 120 mL of diglyme in a 250-mL two-neck round bottom flask, under N₂ atmosphere, at 140 °C. Then, 6.78 mL (0.053 mol) (300 equivalent, ten times in excess) of hexanol was added into the reaction flask. About 0.10 mL of dibutyltin dilaurate was added, and the reaction was continued for 4 days. The resultant PHB-OH was precipitated in diethyl ether and further purified by washing with DI water 4 times. Then, the product was freeze-dried. The yield was 60% and above after isolation and purification.

Example 2**Synthesis of multiarm PHB (two-arm)**

Telechelic hydroxylated PHB (PHB-02) with various molecular weights were prepared by transesterification between the natural source PHB and ethylene glycol using dibutyltin dilaurate in diglyme. The reaction scheme is displayed in Figure 2.

Typically, 10 g ($M_n = 6.0 \times 10^4$, 1.66×10^{-4} mol) (1.0 equivalent) of purified PHB was dissolved in 120 mL of diglyme in a 250-mL two-neck round bottom flask, under N_2 atmosphere, at 140 °C. Then, 2.77 mL (0.05 mol) (300 equivalent, ten times in excess) of ethylene glycol was added into the reaction flask. Dibutyltin dilaurate was dissolved in diglyme, and was added gradually over 2-3 days. Total 0.21 g of dibutyltin dilaurate was added. The resultant PHB-diol was precipitated in diethyl ether and further purified by washing with DI water 4 times. Then, the product was freeze-dried. The yield was 80% and above after isolation and purification.

The progress of the transesterification was monitored by m.w. analysis by using GPC (THF as mobile phase). The diminishing trend of the m.w. over time was plotted in Figure 3. As shown, the molecular weight (M_n) decreased from 60,000 Da to 2,000Da over the course of the transesterification reaction.

Example 3**Synthesis of multiarm PHB (three-arm)**

PHB with 3-OH terminal groups (PHB-03) was prepared by transesterification between the natural source PHB and glycerol using dibutyltin dilaurate in diglyme. Typically, 15.5 g ($M_n = 6.0 \times 10^4$, 2.62×10^{-4} mol) (1.0 equivalent) of purified PHB was dissolved in 300 mL of diglyme in a 250-mL two-neck round bottom flask, under N_2 atmosphere, at 140 °C. Then, 5.75 mL (0.0786 mol) (300 equivalent, ten times in excess) of glycerol was added into the reaction flask. About 0.10 mL of dibutyltin dilaurate was added, and the reaction was continued for 5 days. The resultant PHB-triol was precipitated in diethyl ether and further purified by washing with DI water 4 times. Then, the product was freeze-dried. The yield was 70% and above after isolation and purification.

Example 4**Synthesis of multiarm PHB (four-arm)**

PHB with 4-OH terminal groups (PHB-04) was prepared by transesterification between the
5 natural source PHB and erythritol using dibutyltin dilaurate in diglyme. Typically, 10.4 g (M_n
= 6.0×10^4 , 1.76×10^{-4} mol) (1.0 equivalent) of purified PHB was dissolved in 100 mL of
diglyme in a 250-mL two-neck round bottom flask, under N_2 atmosphere, at 140 °C. Then,
6.75 g (0.0368 mol) (300 equivalent, ten times in excess) of erythritol was added into the
reaction flask. About 0.15 mL of dibutyltin dilaurate was added, and the reaction was
10 continued for 2 days. The resultant PHB-tetra-ol was precipitated in diethyl ether and further
purified by washing with DI water 4 times. Then, the product was freeze-dried. The yield was
80% and above after isolation and purification.

Example 5**Br-Functionalization**

The reaction discussed below is depicted in the first reaction of Figure 4.

Dried multiarm PHB, for example, 1.0 g of PHB-02 (PHB-diol) (M_n = 2055, 4.87×10^{-4} mol)
20 (1.0 equivalent) was dissolved 10 mL of anhydrous tetrahydrofuran (THF) with stirring in a
250-mL two-neck round bottom flask, and placed in an ice bath, under N_2 atmosphere.
Then, 0.33 mL of triethylamine (TEA) (4.8 equivalent) was added to the flask. Then, 0.24 mL
of BiBB (1.95×10^{-3} mol) (4.0 equivalent) in 10 mL anhydrous THF was added drop-wise to
the round bottom flask over a period of 1 h at 4 °C. The mixture was stirred at RT for 24 h.
25 The final reaction mixture was centrifuged to discard the deposition, while the supernatant
was precipitated in diethyl ether. The PHB-02Br was dried under reduced pressure for 2
days. The yield was 60% and above after isolation and purification.

PHB-01, PHB-03 and PHB-04 were reacted in a similar manner to generate PHB-01Br,
30 PHB-03Br and PHB-04Br.

Example 6**Synthesis of multiarm PHB-DMAEMA via Atom-transfer radical-polymerization (ATRP)**

35 The reaction discussed below is depicted in the second reaction of Figure 4.

Multiarm PHB-PDMAEMA, for example, PHB-02-PDMAEMA was synthesized using a molar feed ratio [DMAEMA]/[PHB02Br (0.25 g, $M_n = 2400$ g/mol, 4.16×10^{-4} mol)]/[CuBr]/[HMTETA] of 400 : 1.0 : 2.0 : 2.4. The reaction was performed in 50 mL round bottom flask equipped with a magnetic stirrer bar and under typical conditions for ATRP. DMAEMA, PHB-02Br, and HMTETA were introduced into the flask. About 12 mL of dioxane was added to dissolve the reactants. After complete dissolution, the reaction mixture was degassed by bubbling N_2 for 30 min. Then CuBr was added into the mixture under N_2 atmosphere. The reaction mixture was purged with N_2 for another 1-2 min, before the flask was sealed with a rubber stopper. The polymerization was allowed to proceed under continuous stirring at 50 °C for 24 h. The reaction was stopped by diluting with THF. The catalyst complex was removed by passing the blue dilute polymer solution through a short aluminium oxide column. A colorless solution was obtained. After removal of THF in a rotary evaporator, the PHB-02-PDMAEMA was precipitated in excess n-hexane and dried under reduced pressure for 2 days. The yield was 60% and above after isolation and purification.

PHB-01Br, PHB-03Br and PHB-04Br were reacted in a similar manner to generate PHB-01-PDMAEMA, PHB-03-PDMAEMA and PHB-04-PDMAEMA.

Example 7

Quaternization of PHB-PDMAEMAs

The reaction discussed below is depicted in the third reaction of Figure 4.

Multiarm PHB-PDMAEMA was quaternized with benzyl bromide (BB). Typically, PHB-02-PDMAEMA (2.0 g, $M_n = 7350$ g/mol) was dissolved in 5 mL of THF. Theoretically, about 73 wt. % of the polymer was DMAEMA. Mole of DMAEMA units was 9.3×10^{-3} mol. Then, equimolar of BB (1.1 mL) was added. The reaction was allowed to proceed under continuous stirring at 60 °C for 24 h. After the reaction, 3-5 mL of THF was added to the mixture. It was precipitated in excess of n-hexane, and dried under reduced pressure. The yield was 80% and above after isolation and purification.

PHB-01-PDMAEMA, PHB-03-PDMAEMA and PHB-04-PDMAEMA were reacted in a similar manner to generate other quaternized multiarm PHB-PDMAEMAs (Q-PHB-PDMAEMAs).

Molecular Characterization

GPC measurements were performed on a Waters GPC system equipped with Waters Styragel columns, a Waters-2420 ELS detector, at 40 °C. HPLC grade THF was used as the eluent at a low flow rate of 1.0 mL/min. Monodispersed PMMA standards were used to generate the calibration curve.

Aqueous GPC measurements were performed on a Waters GPC system equipped with Waters Styragel columns, a Waters-2414 refractive index detector, at 37 °C. Acetate buffer solution (pH =4.5) was used as the eluent at a low flow rate of 0.6 mL/min. Monodispersed PEG standards were used to generate the calibration curve.

¹H NMR (400 MHz) spectra were recorded on a Bruker AV-400 NMR spectrometer at room temperature, by accumulation of 16 scans, using CDCl₃ or D₂O as the solvent.

Table 1 lists the GPC results for each of the Multi-arm PHBs produced as described above.

Table 1. GPC results of multiarm PHB

Polymer ID	GPC		
	Mn	Mw	PDI
	Da	Da	
Purified PHB*	59400	70800	1.19
PHB01	1900	2000	1.07
PHB01Br	3300	3700	1.14
PHB01- PDMAEMA#	40800	64200	1.57
PHB02	2100	2300	1.13
PHB02Br	2200	2700	1.20
PHB02- PDMAEMA#	29400	53100	1.80
PHB03	6400	9800	1.54
PHB03Br	9100	14400	1.58
PHB03-	34000	58800	1.73

Polymer ID	GPC		
	Mn	Mw	PDI
	Da	Da	
PDMAEMA [#]			
PHB04	4600	5700	1.23
PHB04Br	-	-	-
PHB04-PDMAEMA [#]	19000	44700	1.73

All samples were characterized by using GPC, THF as mobile phase, except for [#] aqueous, and *CHCl₃ as mobile phase.

5 Number of Arms Calculation (Based on GPC and NMR)

Transesterification of purified PHB yielded shorter PHB chains with different number of hydroxyl arms. Table 2 shows the list of M_n of these PHB as compared to original purified PHB. The molecular weight of single PHB repeating unit (O-CH(CH₃)-CH₂-CO) is 86 g/mol.

- 10 Number of repeating units (m, as shown in Figure 2) of PHB can be calculated by using the GPC M_n minus the m.w. of transesterification agent, and divided by 86 g/mol.

Table 2. GPC Number-averaged molecular weights and "m" of hydroxybutyrate repeating unit

15

Sample ID	Number of hydroxyl end group	GPC M _n	Transesterification agent	M.w. of transesterification agent	m
		Da		Da	
Purified PHB	-	59,400	-	-	
PHB-01	1	1,900	1-hexanol	102.17	21
PHB-02	2	2,100	ethylene glycol	62.07	24
PHB-03	3	6,400	glycerol	92.09	73
PHB-04	4	4,600	erythritol	122.22	52

Number of Br groups attached to multiarm PHBs

To calculate the number of Br in each polymer chain, for example, in PHB-04Br NMR spectrum (as shown in Figures 5A-B), peak **c** ($\delta = 5.25$ ppm) which was assigned to CH in PHB, is set to 52 (based on calculation in Table 2). The integration of peak **a** ($\delta = 1.94$ ppm) which was assigned to $(\text{CH}_3)_2$ next to Br, was recorded in Table 3. The number of Br group attached to the multiarm PHB is calculated by dividing it by 6, since “peak **a**” is the integration result of 6H. The same process was also use to characterise PHB-01Br, PHB-02Br and PHB-03Br.

Table 3 Number of Br-group in multiarm PHB based on NMR analysis

Sample ID	Number of hydroxyl end group	Integration of “peak a”	Number of Br group
PHB-01Br	1	3.5	0.58
PHB-02Br	2	8.27	1.4
PHB-03Br	3	12.50	2.1
PHB-04Br	4	23.21	3.9

From Table 3, it can be seen that the number of Br groups attached in PHB-04Br is the highest. A reason for this may be because new anhydrous THF was used for this reaction.

Number of DMAEMA units in each polymer chain

To calculate the number of DMAEMA units in each polymer chain, for example, in PHB-04-PD NMR spectrum (as shown in Figures 5B-C), peak **b** ($\delta = 1.26$ ppm) which was assigned to CH_3 in PHB, is set to 169 (based on calculation from NMR spectrum of PHB-04Br). Integration of peak **r** ($\delta = 4.07$ ppm) was recorded. This number is divided by 2, since it results from a CH_2 on the DMAEMA unit. To obtain DMAEMA unit per arm, it is further divided by 3.9 (from Table 3). The same process was also use to characterise PHB-01DMAEMA, PHB-02DMAEMA and PHB-03DMAEMA (using the appropriate adaptation of the calculation).

The number of DMAEMA repeating units are listed in Table 4.

Table 4. Number of DMAEMA units in multiarm PHB based on NMR analysis

Sample ID	Number of hydroxyl end group	Integration of "peak r"	Number of DMAEMA units in each arm
PHB-01-PDMAEMA	1	337	291
PHB-02-PDMAEMA	2	464	166
PHB-03-PDMAEMA	3	753	179
PHB-04-PDMAEMA	4	988	127

Degree of quaternization

- 5 The degree of quaternization was determined by NMR analysis qualitatively, using D₂O as solvent.

In Figures 6A and B, the peaks located at 2.27 ppm and 2.99 ppm are attributable to the methyl protons (**t**, N-CH₃) and (**t'**, +N-CH₃) of the non-quaternized and quaternized moieties, respectively. We can conclude that the sample is partially quaternized if both peak **t** and peak **t'** are present. If only peak **t'** is observed, the sample is considered completely quaternized. All the samples were successfully fully quaternized.

Example 715 **Antimicrobial test**

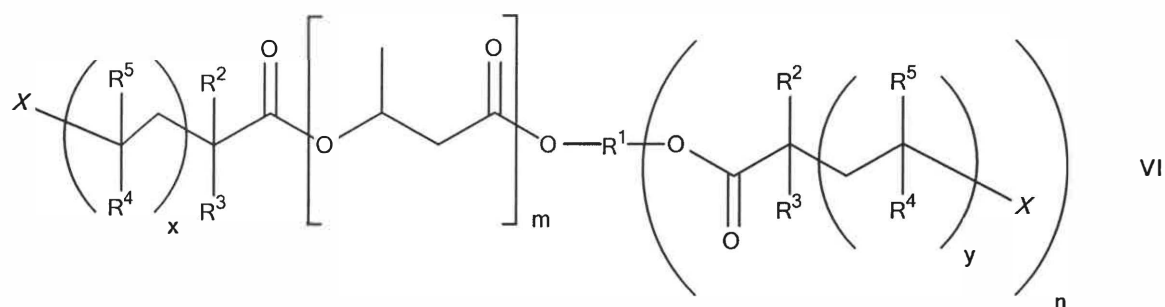
The solutions based on the Q-PHB-PDMAEMA were tested for efficacy in killing clinically significant pathogens: the Gram-negative bacteria (*S. aureus*) and Gram-negative bacteria (*E.coli*). The cationic PHB copolymers showed antimicrobial efficiency that is comparable to those of common antimicrobial peptides (e.g. Melittin, LL-37 etc.). Potential applications of these cationic polymers include antimicrobial coating for surgical devices and drug/gene delivery. Data for the antimicrobial activity of Q-PHB-02-PDMAEMA is provided in Table 5.

Table 5

Sample ID	MIC ($\mu\text{g/mL}$)	
	Gram-positive bacteria	Gram-negative bacteria
	<i>S. aureus</i> (n=2)	<i>E. coli</i> (n=2)
Q-PHB02-PDMAEMA	32	32
Melittin	8	63
LL-37	>250	>250
Indolicidin	130	>250
Magainin I	130	130
Defensin(HNP-1)	>130	>130

CLAIMS

1. A block copolymer having formula VI:



wherein:

m represents a polymeric repeating unit of a first polymeric component;

R¹ represents a straight-chain or branched C₁₋₁₄ alkyl or a C₃₋₁₀ cycloalkyl that are substituted with n ester groups;

n represents 2 to 8;

X represents Cl, Br and I;

R² and R³ are independently selected from C₁₋₆ alkyl;

R⁴ represents C₆₋₁₀ aryl, C₅₋₁₀ heteroaryl, C(O)R^{6a}, C(O)OR^{6b} and C(O)NR^{7a}R^{7b};

R⁵ represents H or straight-chain or branched C₁₋₆ alkyl;

R^{6a} and R^{6b} independently represent a straight-chain or branched C₁₋₆ alkyl or straight-chain or branched C₁₋₆ alkyl substituted by one or more of the substituents selected from OR⁸ or NR⁹R¹⁰;

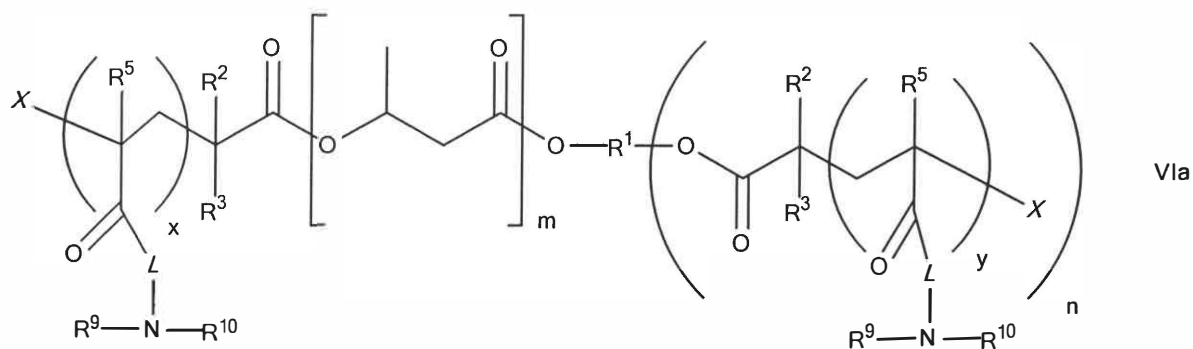
R^{7a}, R^{7b}, R⁸, R⁹ and R¹⁰ are independently selected from H or straight-chain or branched C₁₋₆ alkyl,

x represents a polymeric repeating unit of a second polymeric component;

y, when present, represents a polymeric repeating unit of a third and a fourth polymeric component when n is 2 up to a tenth polymeric component when n is 8; and

the number average molecular weight of the block copolymer is from 15,000 to 200,000 Daltons (e.g. from 20,000 to 150,000 Daltons or from 20,000 to 200,000 daltons).

2. The block copolymer of Claim 1 having the structure of formula VIa:



wherein:

m represents a polymeric repeating unit of a first polymeric component;

R¹ represents a straight-chain or branched C₁₋₁₄ alkyl or a C₃₋₁₀ cycloalkyl that are substituted with n ester groups;

n represents 2 to 8;

X represents Cl, Br and I;

R² and R³ are independently selected from C₁₋₆ alkyl;

R⁵ represents straight-chain or branched C₁₋₆ alkyl;

R⁹ and R¹⁰ are independently selected from straight-chain or branched C₁₋₆ alkyl,

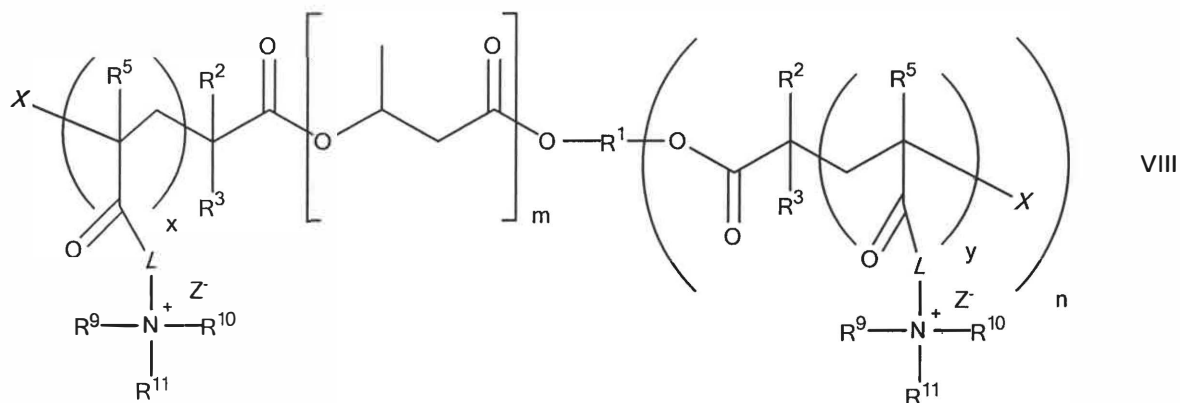
x represents a polymeric repeating unit of a second polymeric component;

y, when present, represents a polymeric repeating unit of a third and fourth polymeric component when n is 2 up to a tenth polymeric component when n is 8;

L represents a straight-chain or branched -C₁₋₆ alkylene or a straight-chain or branched -O-C₁₋₆ alkylene; and

the number average molecular weight of the block copolymer is from 15,000 to 200,000 Daltons (e.g. from 20,000 to 150,000 Daltons or from 20,000 to 200,000 daltons).

3. A block copolymer having formula VIII:



wherein:

m represents a polymeric repeating unit of a first polymeric component;

R¹ represents a straight-chain or branched C₁₋₁₄ alkyl or a C₃₋₁₀ cycloalkyl that are substituted with n ester groups;

n represents 2 to 8;

X represents Cl, Br and I;

R² and R³ are independently selected from C₁₋₆ alkyl;

R⁵ represents straight-chain or branched C₁₋₆ alkyl;

R⁹ and R¹⁰ are independently selected from straight-chain or branched C₁₋₆ alkyl,

R¹¹ represents straight-chain or branched C₁₋₆ alkyl or straight-chain or branched C₁₋₆ alkyl substituted with one or more of C₆₋₁₀ aryl, C₅₋₁₀ heteroaryl and OH;

Z represents Br, Cl or I;

x represents a polymeric repeating unit of a second polymeric component;

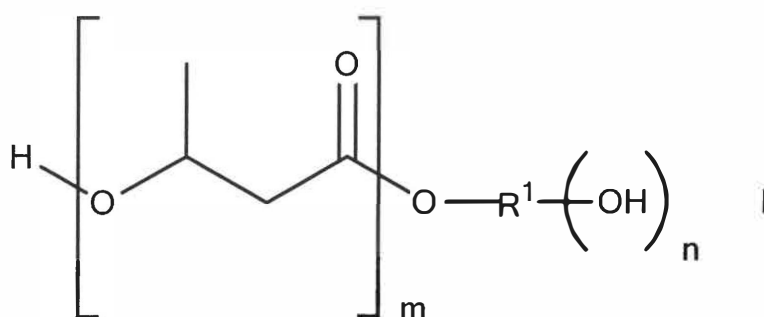
y, when present, represents a polymeric repeating unit of a third and fourth polymeric component when n is 2 up to a tenth polymeric component when n is 8;

L represents a straight-chain or branched -C₁₋₆ alkylene or a straight-chain or branched -O-C₁₋₆ alkylene; and

the number average molecular weight of the block copolymer is from 15,000 to 200,000 Daltons (e.g. from 20,000 to 150,000 Daltons or from 20,000 to 200,000 daltons).

4. A process to provide a block copolymer of formula VI, the process comprising:

(a) reacting a compound of formula I:



wherein:

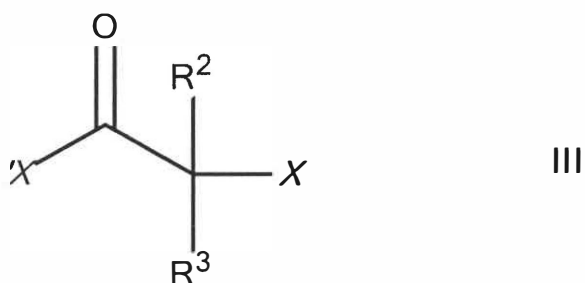
m represents the repeating unit of the polymer;

R^1 represents a straight-chain or branched C_{1-14} alkyl or a C_{3-10} cycloalkyl that are substituted with n hydroxyl groups;

n represents 2 to 8, and wherein

the number average molecular weight of the polymer is from 500 to 80,000 Daltons,

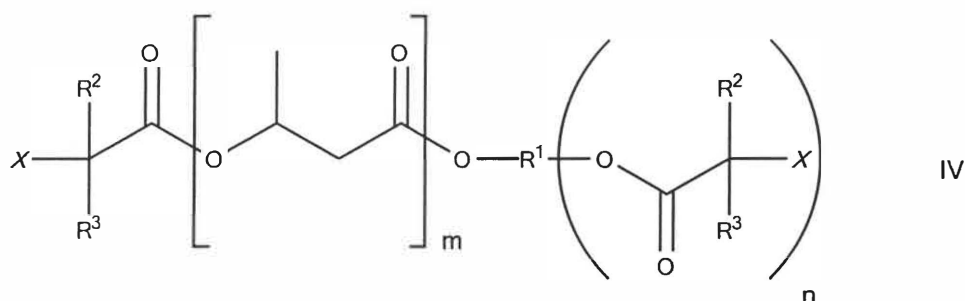
with a sufficient quantity of a suitable atom transfer radical polymerization (ATRP) initiator of formula III:



where X and X' are independently selected from Cl, Br and I; and

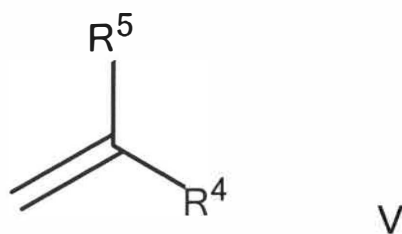
R^2 and R^3 are independently selected from C_{1-6} alkyl,

to provide a compound of formula IV:



where X, R² and R³ are as defined for the compound of formula III and R¹, m and n are as defined for the compound of formula I; and

(b) reacting the compound of formula IV under ATRP conditions with a monomer compound of formula V:



where:

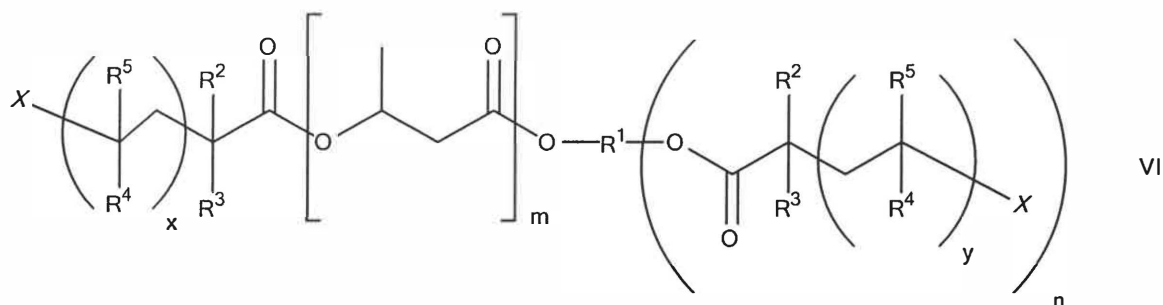
R⁴ represents C₆₋₁₀ aryl, C₅₋₁₀ heteroaryl, C(O)R^{6a}, C(O)OR^{6b} and C(O)NR^{7a}R^{7b};

R⁵ represents H or straight-chain or branched C₁₋₆ alkyl;

R^{6a} and R^{6b} independently represent a straight-chain or branched C₁₋₆ alkyl or straight-chain or branched C₁₋₆ alkyl substituted by one or more of the substituents selected from OR⁸ or NR⁹R¹⁰;

R^{7a}, R^{7b}, R⁸, R⁹ and R¹⁰ are independently selected from H or straight-chain or branched C₁₋₆ alkyl,

to provide a compound of formula VI:



where:

x and y represent a polymeric repeating unit of the monomer of the compound of formula V;

R⁴ and R⁵ are as defined for the compound of formula V

X, R² and R³ are as defined for the compound of formula III; and

R¹, m and n are as defined for the compound of formula I.

5. A process to functionalise the block copolymer of formula VI as defined in Claim 1, wherein when R⁴ represents C(O)R^{6a} or C(O)OR^{6b}, where R^{6a} and R^{6b} independently represent a C₁₋₆ straight-chain or branched alkyl substituted by a NR⁹R¹⁰ substituent, the process comprises:

(i) reacting the compound of formula VI as defined in Claim 1 with a compound of formula VII:

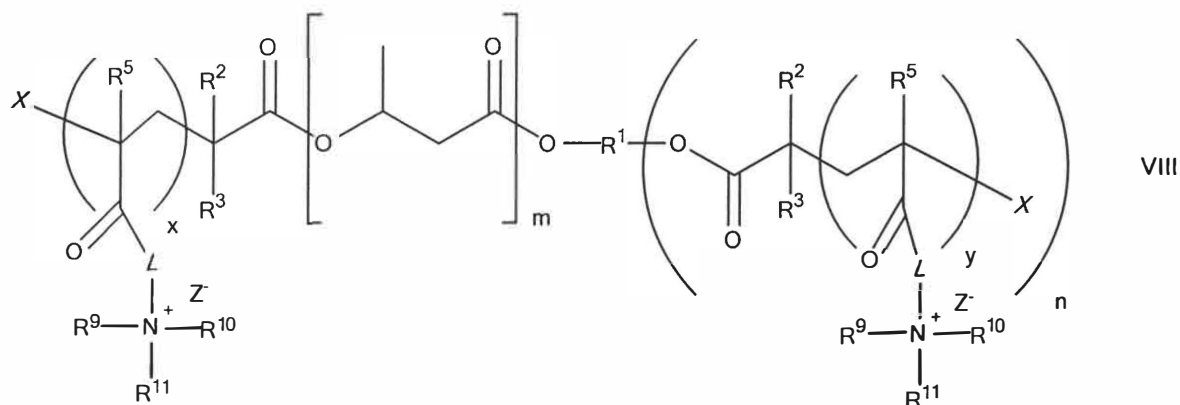


where:

R¹¹ represents straight-chain or branched C₁₋₆ alkyl or straight-chain or branched C₁₋₆ alkyl substituted with one or more of C₆₋₁₀ aryl, C₅₋₁₀ heteroaryl and OH; and

Z represents Br, Cl or I,

to provide a quarternised compound of formula VIII:



where:

L represents a straight-chain or branched $-C_{1-6}$ alkylene or a straight-chain or branched $-O-C_{1-6}$ alkylene, R^9 and R^{10} are independently selected from straight-chain or branched C_{1-6} alkyl;

R^{11} and Z are as defined for the compound of formula VII;

x and y are as defined for the compound of formula VI in Claim 1;

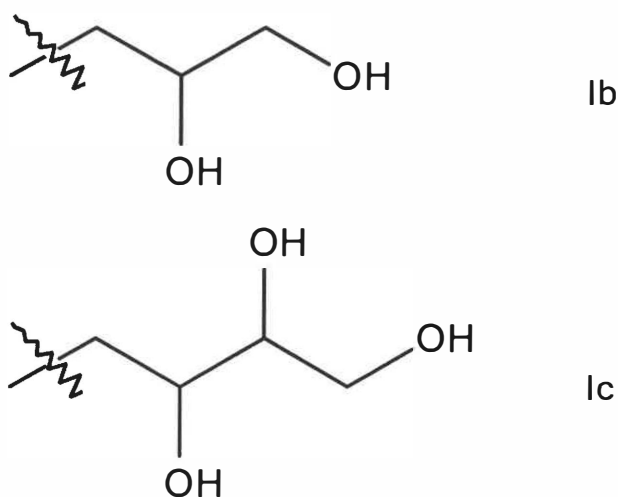
R^4 and R^5 are as defined for the compound of formula V in Claim 4;

X, R^2 and R^3 are as defined for the compound of formula III in Claim 4; and

R^1 , m and n are as defined for the compound of formula I as defined in Claim 1.

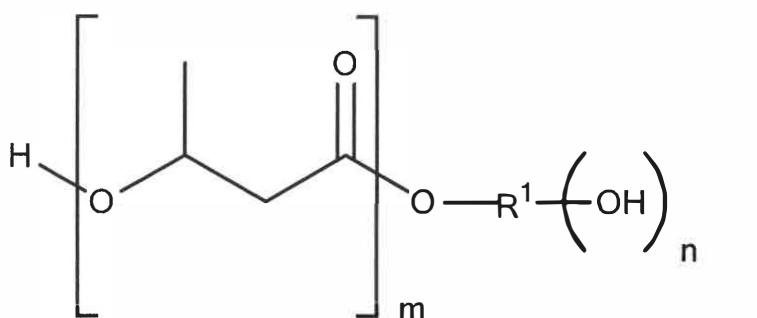
6. The copolymers and processes according to any one of Claims 1 to 5, wherein R^1 represents a straight-chain or branched C_{1-6} alkyl and n represents 2 to 5, optionally wherein R^1 represents a straight-chain C_{2-5} alkyl and n represents 2 to 4 or R^1 represents a straight-chain C_{4-6} alkyl.

7. The copolymers and processes according to Claim 6, wherein R^1 represents hexyl or a fragment selected from formula Ib-Ic,



where the wavy line represents the point of attachment of the fragment to the polymer.

8. The copolymers and processes according to any one of Claims 1 to 7, wherein:
- (a) X represents Cl, or, more particularly, Br; and/or
 - (b) R^2 , R^3 and R^5 are independently selected from C_{1-2} alkyl; and/or
 - (c) R^{11} represents straight-chain or branched C_{1-3} alkyl or straight-chain or branched C_{1-3} alkyl substituted by phenyl; and/or
 - (d) n represents 2 to 4; and/or
 - (e) L represents a straight-chain or branched -O- C_{1-2} alkylene; and/or
 - (f) the number average molecular weight of the block copolymer is from 15,000 to 165,000 Daltons (e.g. from 55,000 to 163,000 Daltons, such as from 19,000 to 41,000 Daltons).
9. A polymer having formula I:



wherein:

m represents the repeating unit of the polymer;

R^1 represents a straight-chain or branched C_{1-14} alkyl or a C_{3-10} cycloalkyl that are substituted with n hydroxyl groups;

n represents 2 to 8, and wherein

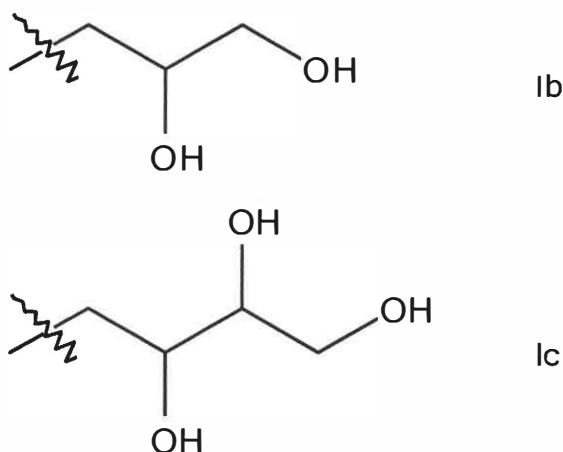
the number average molecular weight of the polymer is from 500 to 80,000 Daltons, optionally wherein:

the polymer has a number average molecular weight of from 1,000 to 10,000 Daltons; and/or

n represents 2 to 4.

10. The polymer according to Claim 9, wherein R^1 represents a straight-chain or branched C_{1-6} alkyl and n represents 2 to 5, optionally wherein R^1 represents a straight-chain C_{2-5} alkyl and n represents 2 to 4 or R^1 represents a straight-chain C_{4-6} alkyl.

11. The polymer according to Claim 10, wherein $-R^1(OH)_n$ represents hexyl or a fragment selected from formula Ib-Ic,



where the wavy line represents the point of attachment of the fragment $-R^1(OH)_n$ to the rest of the polymer.

12. The polymer according to Claim 11, wherein:

(a) when R^1 represents the fragment of formula Ib, the number average molecular weight of the polymer is from 750 to 60,000 Daltons (e.g. from 1,000 to 7,000 Daltons, such as from 6,000 to 6,500 Daltons); and

(b) when R^1 represents the fragment of formula Ic, the number average molecular weight of the polymer is from 750 to 60,000 Daltons (e.g. from 1,000 to 7,000 Daltons, such as from 4,500 to 4,700 Daltons).

13. The polymer of any one Claims 9 to 12, wherein the polymer of formula I comprises part of a block copolymer, where one of more of the -OH groups in the compound of formula I instead represents -O- and serves to link the compound of formula I to the other components of said block copolymer.

14. A process of preparing a polymer, which process comprises a transesterification reaction to produce a compound of formula I, as defined in any one of Claims 9 to 13, comprising reaction of a P3HB having a number average molecular weight of from 20,000 to 200,000 Daltons with an alcohol of formula II,



wherein:

R^1 represents a straight-chain or branched C_{1-14} alkyl, a straight-chain or branched C_{1-14} alkyl substituted with from 2 to 8 hydroxyl groups, a C_{1-10} cycloalkyl or a C_{1-10} cycloalkyl substituted with from 2 to 8 hydroxyl groups, and

the alcohol of formula II is present in a molar excess of from 100 times to 500 times (e.g. 300 times) the molar amount of the P3HB.

15. The process according to Claim 14, wherein:

(a) the transesterification reaction is conducted at a temperature of from 100°C to 160 °C for from 1 to 10 days, optionally at a temperature of 140 °C for from 2 to 5 days; and/or

(b) the transesterification reaction comprises an organic solvent, optionally wherein the solvent is diglyme; and/or

(c) the transesterification reaction further comprises a catalyst, optionally wherein the catalyst is a tin-based catalyst and/or a titanium-based catalyst; and/or

(d) the transesterification reaction is conducted under an inert atmosphere.

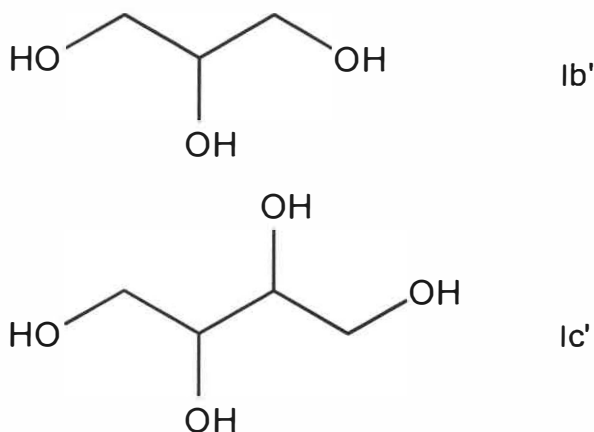
16. The process according to Claim 15(b), wherein the concentration of the alcohol of formula II in the organic solvent is from 0.1 M to 1 M, optionally wherein the concentration is from 0.4 M to 0.5 M.

17. The process according to any one of Claims 14 to 16, wherein R^1 represents a straight-chain or branched C_{1-6} alkyl, or a straight-chain or branched C_{1-6} alkyl substituted with from 2 to 5 hydroxyl groups, optionally wherein:

R^1 represents a straight-chain C_{4-6} alkyl or a straight-chain C_{2-5} alkyl substituted with from 0 to 4 hydroxyl groups; and/or

n represents 2 to 4.

18. The process according to Claim 17, wherein R^1OH represents hexanol or a compound selected from formula Ib'-Ic',



19. The process according to Claim 18, wherein:

(a) when R^1OH represents the compound of formula Ib, the number average molecular weight of the compound of formula I is from 750 to 60,000 Daltons (e.g. from 1,000 to 7,000 Daltons, such as from 6,000 to 6,500 Daltons); and

(b) when R^1OH represents the compound of formula Ic, the number average molecular weight of the compound of formula I is from 750 to 60,000 Daltons (e.g. from 1,000 to 7,000 Daltons, such as from 4,500 to 4,700 Daltons).

20. A process to provide a block copolymer derived from the compound of formula I as defined in any one of Claims 9 to 13, wherein

(a) the process comprises functionalising the compound of formula I with a suitable reversible addition-fragmentation chain-transfer (RAFT) polymerization agent to form a RAFT precursor compound and reacting the RAFT precursor compound with a monomer suitable for use in RAFT polymerization to form a RAFT-polymerised block copolymer; or

(b) the process comprises reacting the compound of formula I with a suitable di- or polyisocyanate to form a polyurethane, optionally wherein the di- or polyisocyanate is selected from one or more of the group consisting of diphenylmethane diisocyanate, toluene diisocyanate, hexamethylene diisocyanate, isophorone diisocyanate and polymeric diphenylmethane diisocyanate.