



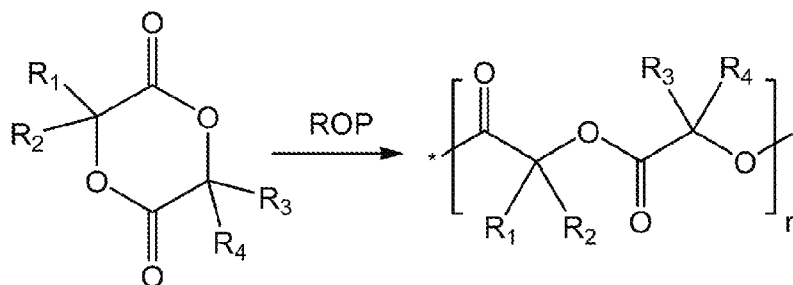
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(54) **Title:** HALOGENATED CYCLIC DIESTERS, RELATED POLYMERS, AND METHODS FOR THEIR PREPARATION AND USE

**FIG. 6**

(57) **Abstract:** Halogenated cyclic diesters, halogenated polymers derived from the cyclic diesters, and methods for making the halo-
genated cyclic diesters and related halogenated polymers.

HALOGENATED CYCLIC DIESTERS, RELATED POLYMERS, AND METHODS FOR THEIR PREPARATION AND USE

CROSS-REFERENCE TO RELATED APPLICATIONS

5 This application claims the benefit of U.S. Patent No. 62/259,514, filed November 24, 2015, and U.S. Patent No. 62/117,900, filed February 18, 2015, each expressly incorporated herein by reference in its entirety.

BACKGROUND OF THE INVENTION

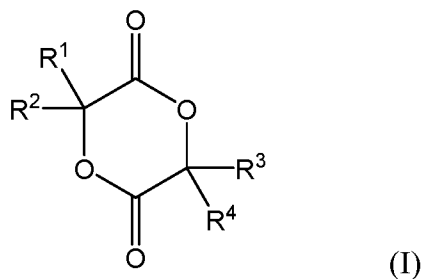
10 Polymers derived from lactic acid and glycolic acid have been extensively used for various biomedical applications due to their biocompatibility and biodegradability. The ability to modify the physiochemical properties, such as degradability, hydrophobicity, and hydrophilicity, of these polymers is a key to expand the spectrum of their uses. Conventional approaches usually involve copolymerization and block copolymer preparations. In contrast, the use of lactic acid and glycolic acid derivatives
15 as monomers for preparing polylactides and polyglycolides is less well known.

Despite advances in the preparation of polylactides and polyglycolides, a need exists for the simple and versatile preparation of polylactides and polyglycolides having improved properties. The present invention seeks to fulfill these needs and provide further related advantages.

20 SUMMARY OF THE INVENTION

The present invention provides halogenated cyclic diesters, halogenated polymers derived from the cyclic diesters, and methods for making the halogenated cyclic esters and related halogenated polymers. In certain embodiments, the present invention provides fluorinated cyclic diesters, fluorinated polymers derived from these cyclic diesters, and
25 methods for making the fluorinated cyclic diesters and related fluorinated polymers.

In one embodiment, the invention provides a cyclic diester having formula (I)

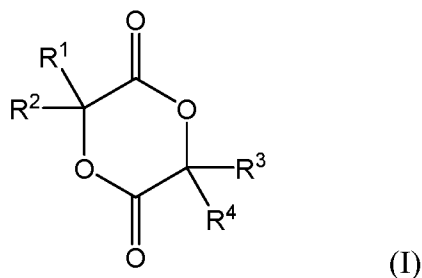


stereoisomers and racemates thereof,

wherein R^1 , R^2 , R^3 , and R^4 are independently selected from hydrogen, C1-C24 alkyl, aryl, fluoro, chloro, and halocarbon, with the proviso that at least one of R^1 , R^2 , R^3 , or R^4 is selected from fluoro, chloro, or halocarbon.

In another embodiment, the invention provides a cyclic diester having formula (I)

5



stereoisomers and racemates thereof,

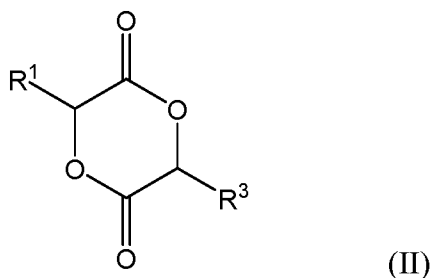
wherein R^1 , R^2 , R^3 , and R^4 are independently selected from hydrogen, C1-C24 alkyl, aryl, fluoro, and fluorocarbon (e.g., C1-C24 fluoroalkyl), with the proviso that at least one of R^1 , R^2 , R^3 , or R^4 is selected from fluoro or fluorocarbon.

10

In certain embodiments, the fluorocarbon is a C1-C24 fluoroalkyl group. In other embodiments, the fluorocarbon is a C1-C12 fluoroalkyl group. In further embodiments, the fluorocarbon is a C1-C6 fluoroalkyl group.

In a further embodiment, the invention provides a cyclic diester having formula

15 (II)



stereoisomers and racemates thereof,

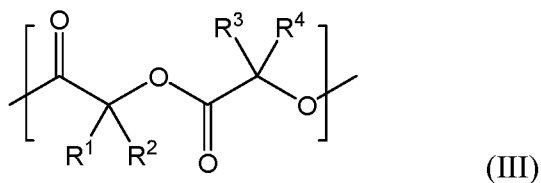
wherein R^1 and R^3 are independently selected from C1-C24 alkyl and fluorocarbon (e.g., C1-C24 fluoroalkyl), with the proviso that at least one of R^1 or R^3 is fluorocarbon.

20

In another aspect, the invention provides polymers prepared from the cyclic diesters of the invention.

In one embodiment, the invention provides a halogenated polymer, comprising a repeating unit having formula (III)

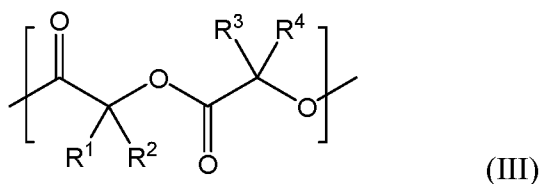
25



wherein

R^1 , R^2 , R^3 , and R^4 are independently selected from hydrogen, C1-C24 alkyl, aryl, fluoro, chloro, and halocarbon, with the proviso that at least one of R^1 , R^2 , R^3 , or R^4 is selected from fluoro, chloro, or halocarbon.

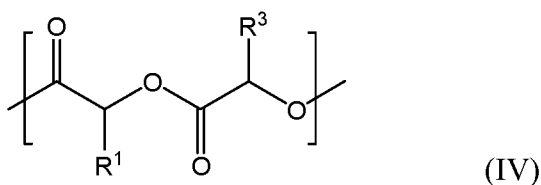
In another embodiment, the invention provides a fluorinated polymer, comprising a repeating unit having formula (III)



wherein

R^1 , R^2 , R^3 , and R^4 are independently selected from hydrogen, C1-C24 alkyl, aryl, fluoro, and fluorocarbon (e.g., C1-C24 fluoroalkyl), with the proviso that at least one of R^1 , R^2 , R^3 , or R^4 is selected from fluoro or fluorocarbon.

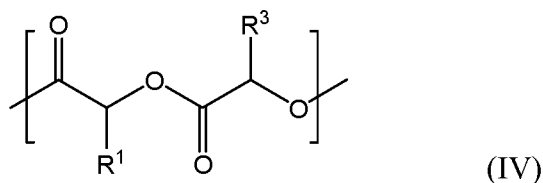
In one embodiment, the invention provides a halogenated polylactic acid, comprising a repeating unit having formula (IV)



wherein

R^1 and R^3 are independently selected from C1-C24 alkyl and halocarbon, with the proviso that at least one of R^1 or R^3 is halocarbon.

In another embodiment, the invention provides a fluorinated polylactic acid, comprising a repeating unit having formula (IV)

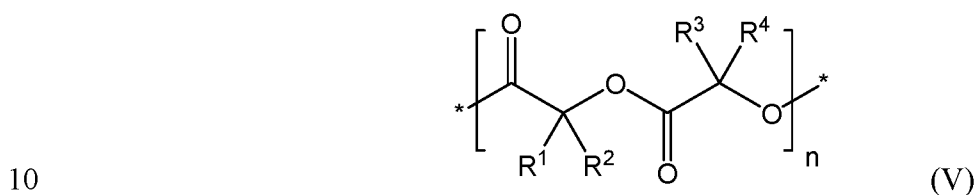


wherein

R^1 and R^3 are independently selected from C1-C24 alkyl and fluorocarbon (e.g., C1-C24 fluoroalkyl), with the proviso that at least one of R^1 or R^3 is fluorocarbon.

5 In certain embodiments, the polymer of the invention further comprises one or more repeating units derived from comonomers suitable for polymerization with a halogenated cyclic diester.

In one embodiment, the invention provides a polymer having formula (V)



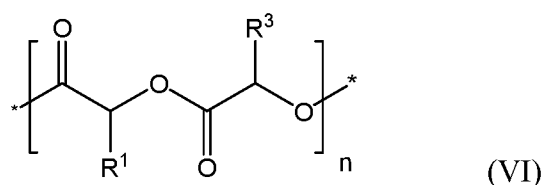
wherein

*represents the terminal groups of the polymer, and

n is an integer from about 10 to about 1000.

In another embodiment, the invention provides a polylactic acid having formula

15 (VI)

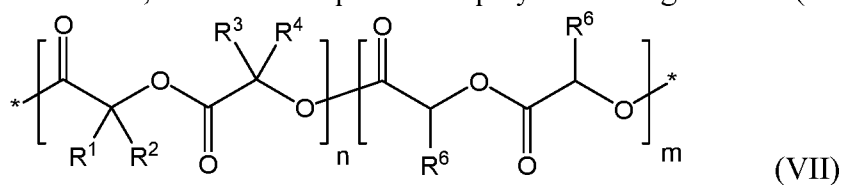


wherein

*represents the terminal groups of the polymer, and

20 n is an integer from about 10 to about 1000.

In one embodiment, the invention provides a polymer having formula (VII)



wherein

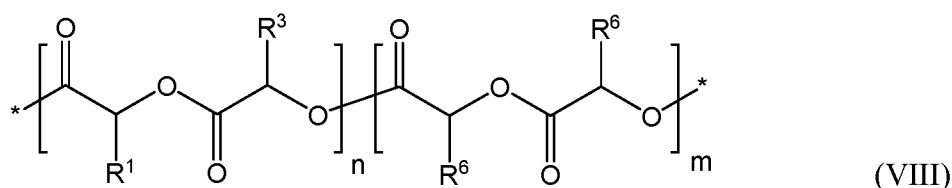
R^6 is hydrogen or methyl,

n is an integer from about 10 to about 1000, and

m is an integer from about 10 to about 1000.

In another embodiment, the invention provides a polylactic acid having formula

5 (VIII)



wherein

R^6 is hydrogen or methyl,

10 n is an integer from about 10 to about 1000, and

m is an integer from about 10 to about 1000.

In certain embodiments, the polymers of the invention are random copolymers. In other embodiments, the polymers of the invention are block copolymers.

In a further aspect of the invention, surfaces coated with a polymer of the invention are provided. In one embodiment, the invention provides a surface of a substrate, wherein at least a portion of the surface is coated with a polymer of the invention. Suitable substrates include drug delivery devices, devices having a degradation-inhibiting coating, devices having a hydrophobic surface with high contact angle, and devices that contact blood. In certain embodiments, the substrate is a medical device, such as a cardiovascular stent.

In another aspect, the invention provides methods for making halogenated polymers. In one embodiment, the method comprises:

subjecting a polymer with an ammonia plasma to provide a polymer functionalized with amino groups;

25 reacting the polymer functionalized with amino groups with a suitably reactive reagent comprising a halocarbon, wherein at least a portion of the amino groups react with the reagent to provide a polymer having at least a portion of the amino groups converted to amine groups covalently coupled to the halocarbon.

In another embodiment, the method comprises:

subjecting a polymer with an ammonia plasma to provide a polymer functionalized with amino groups;

reacting the polymer functionalized with amino groups with a suitably reactive reagent comprising a fluorocarbon (e.g., fluoroalkyl group), wherein at least a portion of the amino groups react with the reagent to provide a polymer having at least a portion of the amino groups converted to amine groups covalently coupled to the fluorocarbon.

DESCRIPTION OF THE DRAWINGS

The foregoing aspects and many of the attendant advantages of this invention will become more readily appreciated as the same become better understood by reference to the following detailed description, when taken in conjunction with the accompanying drawings.

FIGURE 1 is a schematic illustration of a representative preparation of cyclic diesters of the invention from alpha-hydroxy acids and reactive alpha-bromo alkanoyl bromide compounds.

FIGURE 2 is a schematic illustration of a representative preparation of cyclic diesters of the invention starting from the alpha-hydroxy acid: $\text{CF}_3\text{CH}(\text{OH})\text{-C}(=\text{O})\text{OH}$.

FIGURE 3 is a schematic illustration of a representative preparation of cyclic diesters of the invention starting from the alpha-hydroxy acid: $\text{CF}_2(\text{OH})\text{-C}(=\text{O})\text{OH}$.

FIGURE 4 is a schematic illustration of a representative preparation of cyclic diesters of the invention starting from the alpha-hydroxy acid: $(\text{CF}_3)_2\text{C}(\text{OH})\text{-C}(=\text{O})\text{OH}$.

FIGURE 5 is a schematic illustration of a representative preparation of cyclic diesters of the invention starting from the alpha-hydroxy acid: $\text{CF}_3\text{C}(\text{Ph})(\text{OH})\text{-C}(=\text{O})\text{OH}$.

FIGURE 6 is a schematic illustration of a representative preparation of fluorinated polymers of the invention from cyclic diesters.

FIGURE 7 is a schematic illustration of representative preparations of fluorinated polymers of the invention from cyclic diesters prepared from a representative alpha-hydroxy acid: $\text{CF}_3\text{CH}(\text{OH})\text{-C}(=\text{O})\text{OH}$.

FIGURE 8 is a schematic illustration of the preparation of fluorinated polymers of the invention prepared from reaction of suitably reactive fluoroalkyl reagents with amino-containing polymers prepared by treatment of suitable polymers with ammonia plasma.

DETAILED DESCRIPTION OF THE INVENTION

Fluorinated polymers demonstrate excellent inertness in various biological environments and good blood compatibility, and have been used in various biomedical applications, such as prosthetics and drug delivery.

5 In one aspect, the present invention provides halogenated polymers and methods for their preparation. In the halogenated polymers of the invention, the structure of polymer backbone remains unchanged and this in turn results in retention of their hydrolysis characteristics. However, due to the introduction of halogens (i.e., fluorine or chlorine) into these polymers the halogenated (e.g., fluorinated and or chlorinated)
10 polymers of the invention hydrolyze at a reduced rate due to their increased hydrophobicity associated with the replacement of hydrogen in the parent polymers with a halogen (e.g., fluorine or chlorine), thereby improving long-term performance in biological environments.

As used herein, the term "halogenated" or "halogen" refers to a cyclic diester or
15 polymer that includes one or more chlorine and/or fluorine atoms. With reference to the cyclic diesters and polymers of the invention, the term "halogenated" or "halogen" does not refer to cyclic diesters or polymers that include a bromine or an iodine atom.

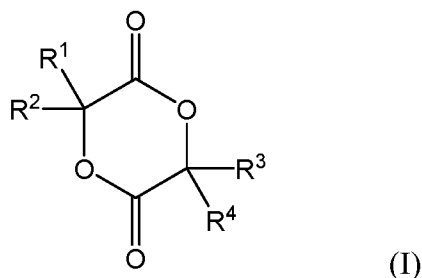
The present invention provides halogenated cyclic diester, halogenated polymers derived from the cyclic diesters, and methods for making the halogenated cyclic esters and
20 related halogenated polymers. In certain embodiments, the present invention provides fluorinated cyclic diesters, fluorinated polymers derived from the cyclic diesters, and methods for making the fluorinated cyclic diesters and related fluorinated polymers.

Cyclic Diesters

In one aspect, the invention provides halogenated cyclic diesters (i.e., cyclic
25 diesters that include one or more halogen substituents also referred to herein as halogen-containing cyclic diesters). The cyclic diesters of the invention can be prepared from alpha-hydroxy acids. See FIGURES 1-5 and 7. The cyclic diesters of the invention can be polymerized to provide polyesters that include fluorine and/or chlorine substituents. See FIGURES 6 and 7. The cyclic diesters of the invention are 6-membered ring
30 compounds. In certain embodiments, the cyclic diester is a lactide or a lactide derivative. In other embodiments, the cyclic diester is a glycolide or a glycolide derivative. The cyclic diesters of the invention have the general structure shown in FIGURE 1 where R¹-R⁴ are as described below. FIGURE 1 is a schematic illustration of a representative

preparation of cyclic diesters of the invention from alpha-hydroxy acids and reactive alpha-bromo alkanoyl bromide compounds.

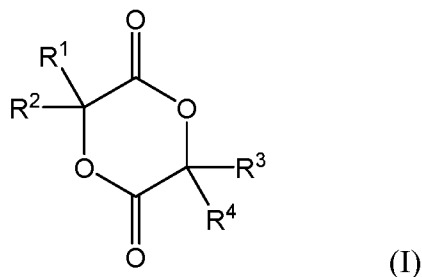
In one embodiment, the cyclic diester of the invention has formula (I)



stereoisomers and racemates thereof, wherein R¹, R², R³, and R⁴ are independently selected from hydrogen, C1-C24 alkyl, aryl, fluoro, chloro, and halocarbon, with the proviso that at least one of R¹, R², R³, or R⁴ is selected from fluoro, chloro, or halocarbon.

As used herein, the term "halocarbon" refers to a substituent group that includes one or more carbons (e.g., C1-C24, C1-C12, or C1-C6) and one or more chlorine or fluorine atoms. The terms "halocarbon" and "halocarbon group" are used interchangeably. Suitable halocarbon groups include one or more chlorine atoms (chloro substituents), one or more fluorine atoms (fluoro substituents), or one or more chlorine atoms and one or more fluorine atoms (chloro and fluoro substituents). Representative halocarbon groups include -CH₂Cl, -CH₂F, and -CH(Cl)F groups, among others.

In another embodiment, the cyclic diester of the invention has formula (I)



stereoisomers and racemates thereof, wherein R¹, R², R³, and R⁴ are independently selected from hydrogen, C1-C24 alkyl, aryl, fluoro, and fluorocarbon (e.g., C1-C24 fluoroalkyl), with the proviso that at least one of R¹, R², R³, or R⁴ is selected from fluoro or fluorocarbon.

As used herein, the term "fluorocarbon" refers to a substituent group that includes one or more carbons (e.g., C1-C24, C1-C12, or C1-C6) and one or more fluorine

atoms. The terms "fluorocarbon" and "fluorocarbon group" are used interchangeably. Suitable fluorocarbon groups include one or more fluorine atoms (fluoro substituents). Representative fluorocarbon groups include $-\text{CH}_2\text{F}$, $-\text{CHF}_2$, and $-\text{CF}_3$ groups, among others. In certain embodiments, the fluorocarbon group is a C1-C24 fluoroalkyl group.

5 In certain embodiments, C1-C24 alkyl is C1-C12 alkyl. In certain embodiments, C1-C24 alkyl is C1-C6 alkyl. Representative alkyl groups include straight chain (e.g., n-propyl), branched (e.g., isopropyl), and cyclo (e.g., C3-C7 cycloalkyl, such as cyclopentyl) groups. In certain embodiments, C1-C24 (or C1-C12 or C1-C6) alkyl is selected from methyl, ethyl, n-propyl, i-propyl, and n-butyl. In certain embodiments, C1-
10 C24 (or C1-C12 or C1-C6) alkyl is methyl.

The alkyl and aryl groups of the cyclic diester may be substituted or unsubstituted. As used herein, the term "substituted C1-C24 alkyl" refers to a C1-C24 alkyl group in which one or more hydrogen atoms is replaced with a non-hydrogen atom. The term "substituted aryl" refers to an aryl group (e.g., phenyl group) in which one or more
15 hydrogen atoms is replaced with a non-hydrogen atom. Representative non-hydrogen atoms include heteroatoms such oxygen, nitrogen, sulfur, and silicon atoms, as well as substituents that include these atoms (e.g., hydroxy, alkoxyl, amino, alkylamino, thiol, thioether).

In certain embodiments, the cyclic diesters of the invention include either a
20 fluorine substituent or a fluoroalkyl substituent. As used herein the term "fluoroalkyl" or "fluoroalkyl group" refers to an alkyl group (i.e., a saturated hydrocarbon group) in which one or more hydrogen atoms is replaced with a fluorine atom (F). As used herein, the terms "fluoro" and "fluorine" are used interchangeably and refer to the substituent F. Representative fluoroalkyl groups include $-\text{CF}_3$, $-\text{CH}_2\text{F}$, $-\text{CHF}_2$, $-\text{CF}_2\text{CF}_3$, $-\text{CH}_2\text{CF}_3$, -
25 CF_2CH_3 , $-\text{CH}_2\text{CHF}_2$, $-\text{CH}_2\text{CH}_2\text{F}$, among others.

In certain embodiments, C1-C24 fluoroalkyl is C1-C12 fluoroalkyl. In certain embodiments, C1-C24 fluoroalkyl is C1-C6 fluoroalkyl.

Representative fluoroalkyl groups include straight chain (e.g., n-propyl), branched (e.g., isopropyl), and cyclo (e.g., C3-C7 cycloalkyl, such as cyclopentyl) groups. In
30 certain embodiments, C1-C24 (or C1-C12 or C1-C6) fluoroalkyl is selected from methyl, ethyl, n-propyl, i-propyl, and n-butyl in which one or more hydrogen atoms is replaced with a fluorine atom. In certain embodiments, the fluoroalkyl is perfluoroalkyl (e.g., trifluoromethyl, pentafluoroethyl, n-perfluoropropyl, n-perfluorobutyl, and n-

perfluoropentyl). In certain embodiments, C1-C24 (or C1-C12 or C1-C6) alkyl is methyl (i.e., trifluoromethyl, difluoromethyl, and fluoromethyl).

In certain embodiments, the fluoroalkyl group(s) of the cyclic diester has a ratio of F:C from about 0.4 to about 3.0. In certain embodiments, the fluoroalkyl group(s) of the cyclic diester has a ratio of F:C of about 0.5. In other embodiments, the fluoroalkyl group(s) of the cyclic diester has a ratio of F:C of about 1.0. In further embodiments, the fluoroalkyl group(s) of the cyclic diester has a ratio of F:C of about 2.0.

In one embodiment of formula (I), R^1 and R^3 are hydrogen and R^2 and R^4 are trifluoromethyl.

In one embodiment of formula (I), R^1 and R^3 are hydrogen, R^2 is methyl, and R^4 is trifluoromethyl.

In one embodiment of formula (I), R^1 and R^2 are hydrogen and R^3 and R^4 are trifluoromethyl.

In one embodiment of formula (I), R^1 , R^2 , and R^3 are hydrogen and R^4 is trifluoromethyl.

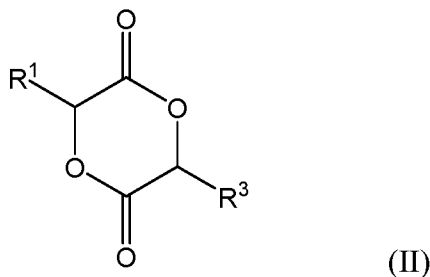
In one embodiment of formula (I), R^1 , R^2 , R^3 , and R^4 are trifluoromethyl.

In one embodiment of formula (I), R^1 and R^2 are hydrogen and R^3 and R^4 are fluoro.

In one embodiment of formula (I), R^1 is hydrogen, R^2 is methyl, and R^3 and R^4 are fluoro.

In one embodiment of formula (I), R^1 , R^2 , R^3 , and R^4 are fluoro.

In another embodiment, the cyclic diester of formula (I) is a lactide having formula (II)



stereoisomers and racemates thereof, wherein R^1 and R^3 are independently selected from C1-C24 alkyl and fluorocarbon (e.g., C1-C24 fluoroalkyl), with the proviso that R^1 and R^3 at least one of R^1 and R^3 is fluorocarbon (e.g., C1-C24 fluoroalkyl). In this embodiment, R^1 and R^3 are as described above for formula (I).

In one embodiment of the lactide of formula (II), R^1 is methyl and R^3 is trifluoromethyl.

In one embodiment of the lactide of formula (II), R^1 is hydrogen and R^3 is trifluoromethyl.

5 In one embodiment of the lactide of formula (II), R^1 and R^3 are trifluoromethyl.

Representative cyclic diesters of the invention have the structures shown in FIGURES 2-5. FIGURE 2 is an illustration of the preparation a representative cyclic diester starting from $CF_3CH(OH)-C(=O)OH$. FIGURE 3 is an illustration of the preparation a representative cyclic diester starting from $CF_2(OH)-C(=O)OH$. FIGURE 4
10 is an illustration of the preparation a representative cyclic diester starting from $(CF_3)_2C(OH)-C(=O)OH$. FIGURE 5 is an illustration of the preparation a representative cyclic diester starting from $CF_3C(Ph)(OH)-C(=O)OH$.

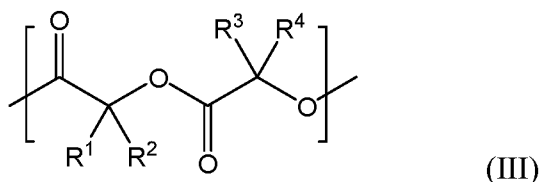
Polymers

In another aspect, the invention provides halogenated polymers. As used herein
15 the terms "halogenated polymer" refers to a polymer that includes one or more chlorine and/or one or more fluorine atoms, and particularly to a polymer that includes repeating units derived from monomers that include one or more halogen atoms (e.g., fluorine and/or chlorine atoms) or halogen-containing substituents (i.e., halocarbon groups, such as chlorocarbon, fluorocarbon, or chloro/fluorocarbon groups). In certain embodiments,
20 the polymers of the invention are prepared from the halogenated cyclic diesters of the invention. In certain embodiments, the halogenated polymers are prepared by ring opening polymerization. In other embodiments, the halogenated polymers are prepared by condensation polymerization.

In one embodiment, the invention provides fluorinated polymers. As used herein
25 the terms "fluorinated polymer" refers to a polymer that includes fluorine atoms, and particularly to a polymer that includes repeating units derived from monomers that include one or more fluorine atoms or fluorine-containing substituents (e.g., fluorocarbon groups, such as fluoroalkyl groups). In one embodiment, the fluorinated polymers of the invention are prepared from the fluorinated cyclic diesters of the invention. In certain
30 embodiments, the fluorinated polymers are prepared by ring opening polymerization. In other embodiments, the fluorinated polymers are prepared by condensation polymerization.

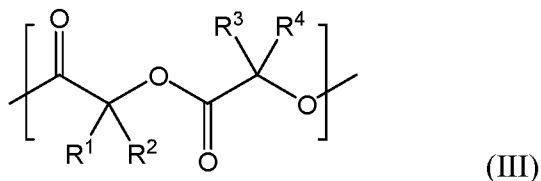
FIGURE 6 is a schematic illustration of a representative preparation of fluorinated polymers of the invention from cyclic diesters. FIGURE 7 is a schematic illustration of representative preparations of fluorinated polymers of the invention from cyclic diesters prepared from a representative alpha-hydroxy carboxylic acid: $\text{CF}_3\text{CH}(\text{OH})\text{-C(=O)OH}$.

- 5 In certain embodiments, the halogenated polymer includes a repeating unit having formula (III)



- 10 wherein R^1 , R^2 , R^3 , and R^4 are independently selected from hydrogen, C1-C24 alkyl, aryl, fluoro, chloro, and halocarbon, with the proviso that at least one of R^1 , R^2 , R^3 , or R^4 is selected from fluoro, chloro, or halocarbon.

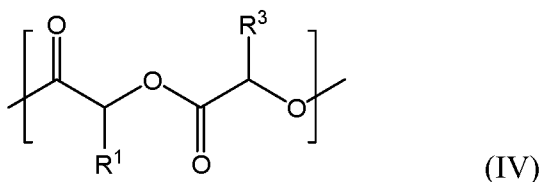
In other embodiments, the fluorinated polymer includes a repeating unit having formula (III)



- 15 wherein R^1 , R^2 , R^3 , and R^4 are independently selected from hydrogen, C1-C24 alkyl, aryl, fluoro, chloro, and halocarbon, with the proviso that at least one of R^1 , R^2 , R^3 , or R^4 is selected from fluoro or fluorocarbon.

In certain embodiments, the halogenated polymer is a polylactic acid that includes a repeating unit having formula (IV)

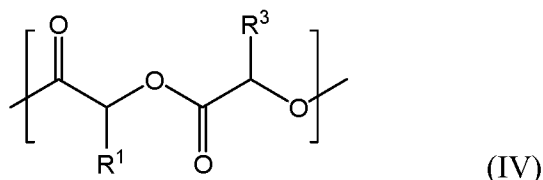
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wherein

R^1 and R^3 are independently selected from C1-C24 alkyl and halocarbon, with the proviso that at least one of R^1 or R^3 is halocarbon.

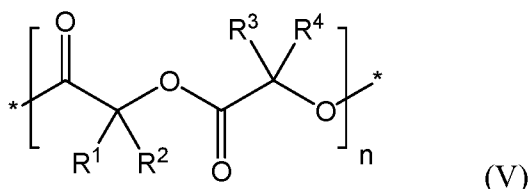
- 25 In other embodiments, the fluorinated polymer is a fluorinated polylactic acid that includes a repeating unit having formula (IV)



wherein R¹ and R³ are independently selected from C1-C24 alkyl and fluorocarbon (e.g., C1-C24 fluoroalkyl), with the proviso that at least one of R¹ and R³ is fluorocarbon. R¹ and R³ are as described above for the cyclic diesters.

In certain embodiments, the invention includes the polymers of formulae (III) and (IV) that further include one or more repeating units derived from comonomers suitable for polymerization with a halogenated (e.g., fluorinated) cyclic diester (e.g., ring opening polymerization or condensation polymerization). Suitable comonomers include cyclic diesters, such as lactides and lactide derivatives (e.g., non-halogenated lactides and non-halogenated lactide derivatives) and glycolides and glycolide derivatives (e.g., non-halogenated glycolides and non-halogenated glycolide derivatives), and other suitable polymerizable esters.

In certain embodiments, the halogenated (e.g., fluorinated) polymer has formula (V)



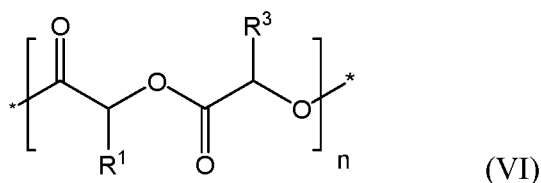
wherein *represents the terminal groups of the polymer, n is an integer from about 10 to about 1000, and R¹, R², R³, and R⁴ are as described above for the cyclic diesters.

The terminal groups of the polymer depend on the nature of the polymerization reaction used to form the polymer. For ring opening polymerizations, the terminal groups are derived from the initiator used in the polymerization. Suitable initiators useful in polymerizing cyclic diesters are known and include water and alcohols. When the initiator is water, one terminal group is –OH and the other is –H. When the initiator is an alcohol (ROH), one terminal group is –OR and the other is –H. Representative alcohols useful as initiators include methanol, 2-propanol, 2-methyl-2-propanol, 1-butanol, 4-phenyl-2-butanol, 1-hexanol, 1-decanol, 1-dodecanol, 1-tetradecanol, 1-hexadecanol, 1-octadecanol, 1-eicosanol, 1-docosanol, 1-pyrene butanol, and benzyl alcohol. In certain

embodiments, the R group of the alcohol includes a functional group that allows for further functionalization of the product polymer.

In certain embodiments, the halogenated (e.g., fluorinated) polymer has formula (VI)

5

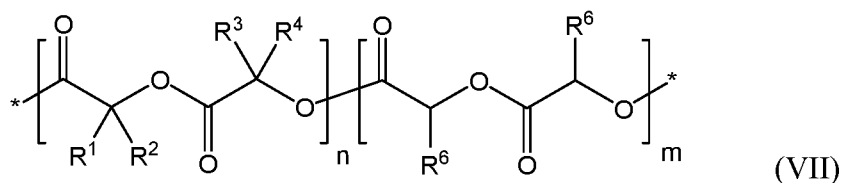


wherein *represents the terminal groups of the polymer as defined above, n is an integer from about 10 to about 1000, and R¹ and R³ are as described above for the cyclic diesters.

As noted above, in certain embodiments, n is an integer from about 10 to about 1000. In other embodiments, n is an integer from about 100 to about 10,000. In further embodiments, n is an integer from about 50 to about 500. In other embodiments, n is an integer from about 50 to about 2000.

In certain embodiments, the halogenated (e.g., fluorinated) polymer has formula (VII)

15



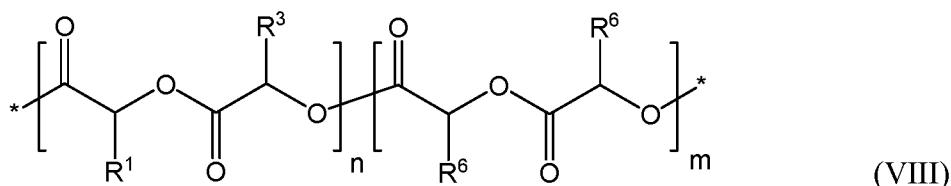
wherein R⁶ is hydrogen or methyl, n is an integer from about 10 to about 1000, m is an integer from about 10 to about 1000, and R¹, R², R³, and R⁴ are as described above for the cyclic diesters.

For the polymers of the invention, the ratio of n:m can vary depending on the desired degree of hydrophobicity and degradability (hydrolysis). In certain embodiments, n:m is about 1:100. In other embodiments, the ratio of n:m is about 100:1. In further embodiments, the ratio of n:m is about 1:1. Other suitable n:m ratios include about 1:2, 1:3, 1:4, 1:5, 1:10, 1:20, 2:1, 3:1, 4:1, 5:1, 10:1, and 20:1.

25

As used herein, the term "about" refers to +/- 5% of the specified value.

In certain embodiments, the fluorinated polymer is a halogenated (e.g., fluorinated) polylactic acid having formula (VIII)



wherein R⁶ is hydrogen or methyl, n is an integer from about 10 to about 1000, and m is an integer from about 10 to about 1000, the ratio of n:m is as described above for formula (VII), and R¹ and R³ are as described above for the cyclic diesters.

As indicated above, certain of the polymers of the invention are homopolymers (i.e., include a single type of repeating unit). In certain embodiments, when the polymer includes two or more different types of repeating units, the polymer of the invention is a random copolymer. In other embodiments, when the polymer includes two or more different types of repeating units, the polymer of the invention is a block copolymer.

The polymers of the invention can be prepared from the cyclic diesters of the invention by polymerization methods. Suitable polymerization methods include polymerization methods known in the art for preparing polymers from cyclic diesters, and include ring opening polymerization methods and condensation polymerization methods. See, for example, U.S. Patent Nos. 6,469,133 and 8,927,682, each expressly incorporated herein by reference in its entirety.

In a representative polymerization method, a cyclic diester and a suitable catalyst are combined in a solvent to provide a reaction mixture, the reaction mixture is heated to polymerize the cyclic ester to form the polymer in the reaction mixture (preferably the mixture is heated to a temperature between about 20°C and 200°C), and the polymer is isolated from the reaction mixture.

Suitable catalysts include those known in the art. Representative catalysts useful for preparing the fluorinated polymers of the invention from cyclic diesters include tin reagents such as Sn(octanoate)₂, Sn(2-ethylhexanoate)₂, Sn(trifluoromethane sulfonate)₂, dibutylSn(2-ethylhexanoate)₂, Sn(phenyl)₄, Sn(bromide)₄, Sn(bromide)₂, Sn(oxide). Other suitable catalysts include 4-(dimethylamino)pyridine (DMAP).

A representative procedure for the polymerization of a cyclic diester to provide a polymer of the invention is described in Example 2.

Polymer-Coated Substrates

In a further aspect, the invention provides substrates and surfaces coated with a polymer of the invention.

In one embodiment, the invention provides a surface of a substrate, wherein at least a portion of the surface is coated with a polymer of the invention (i.e., polymer of formulae (III)-(VIII). In certain embodiments, the substrate is useful as a drug delivery device, a device having a degradation-inhibiting coating, a device having hydrophobic surfaces with high contact angle, and a device that contacts blood. In certain embodiments, the substrate is a medical device, such as a cardiovascular stent.

Ammonia Plasma Process

In another aspect of the invention, a method for making a halogenated polymer is provided. In the method, halocarbon groups are introduced into the polymer.

In one embodiment, the method includes:

subjecting a polymer with an ammonia plasma to provide a polymer functionalized with amino groups;

reacting the polymer functionalized with amino groups with a suitably reactive reagent comprising a halocarbon, wherein at least a portion of the amino groups react with the reagent to provide a polymer having at least of portion of the amino groups converted to amine groups covalently coupled to the halocarbon.

In another embodiment, the method includes:

subjecting a polymer with an ammonia plasma to provide a polymer functionalized with amino (-NH₂) groups;

reacting the polymer functionalized with amino groups with a suitably reactive reagent comprising a fluorocarbon (e.g., fluoroalkyl) group, wherein at least a portion of the amino groups react with the reagent to provide a polymer having at least of portion of the amino groups converted to amine groups covalently coupled to the fluorocarbon groups.

An embodiment of the method is illustrated schematically in FIGURE 8.

Methods for imparting amino groups to a polylactic acid film by ammonia plasma treatment are described in J. Biomedical Materials Research B: Applied Biomaterials, February 2014, Vol. 102B, Issue 2, pages 345-355, expressly incorporated herein by reference in its entirety.

Suitable polymers useful in the method include polymers that can be modified by ammonia plasma to provide a polymer functionalized with amino groups. Polymers that

are advantageously treated by the method of the invention include biocompatible, biodegradable polymers. Representative polymers include polylactic acids, polyglycolic acids, and poly(lactic-co-glycolic) acids.

Suitably reactive reagents comprising a halocarbon group have a reactive group
5 capable of forming a covalent bond with the amino group imparted to the polymer by ammonia plasma. Representative reactive groups are selected from a carboxylic acid, carboxylic acid halide, carboxylic acid ester (NHS and fluorophenyl esters), isocyanate, isothiocyanate, acyl azide, aldehyde, epoxide, oxirane, carbonate, sulfonyl chloride, aryl halide, imidoester, glyoxal, carbodiimide, and anhydride. These reactive groups are
10 covalently coupled to the amine groups by either alkylation or acylation.

Suitably reactive reagents comprising a fluorocarbon (e.g., fluoroalkyl) group have a reactive group capable of forming a covalent bond with the amino group imparted to the polymer by ammonia plasma. Representative reactive groups are selected from a carboxylic acid, carboxylic acid halide, carboxylic acid ester (NHS and fluorophenyl
15 esters), isocyanate, isothiocyanate, acyl azide, aldehyde, epoxide, oxirane, carbonate, sulfonyl chloride, aryl halide, imidoester, glyoxal, carbodiimide, and anhydride. These reactive groups are covalently coupled to the amine groups by either alkylation or acylation.

In certain embodiments, the fluorocarbon is a fluoroalkyl group. In certain
20 embodiments, the fluoroalkyl group is a C1-C24 fluoroalkyl group. In certain embodiments, the C1-C24 fluoroalkyl group is a C1-C12 fluoroalkyl group. In other embodiments, the C1-C24 fluoroalkyl group is a C1-C6 fluoroalkyl group. Representative fluoroalkyl groups include those described above for the cyclic diesters.

In certain embodiments of the method, the polymer subjected to ammonia plasma
25 is a coating on at least a portion of a surface of a substrate. Suitable substrates include drug delivery devices, devices having a degradation-inhibiting coating, devices having a hydrophobic surface with high contact angle, and a device that contacts blood. In certain embodiments, the substrate is a medical device. In certain embodiments, the substrate is a cardiovascular stent.

30 In a further aspect, the invention provides a polymer prepared by the above ammonia plasma method. In one embodiment, the invention provides a surface of a substrate having at least a portion of the surface is coated with a polymer prepared by the above ammonia plasma method.

The following examples are provided for the purpose of illustrating, not limiting the invention.

EXAMPLES

Example 1

5 Preparation and Characterization of a Representative Cyclic Diester

In this example, preparations and characterization of representative cyclic diesters of the invention is described. The preparation is schematically illustrated in FIGURES 2 and 7.

Materials and Methods

10 3,3,3-Trifluorolactic acid (TFLA) and 2-bromopropionyl bromide (2-BPB) were purchased from Matrix Scientific (Columbia, USA) and Sigma-Aldrich, respectively, and were used as received. Proton nuclear magnetic resonance (^1H NMR) analyses were carried out at room temperature in deuterated chloroform (CDCl_3) on a Bruker AV-300 spectrometer with the solvent proton signals being used as chemical shift
15 standards.

Monomer synthesis. Under an argon atmosphere, equal molar amounts of TFLA and 2-BPB were mixed and heated at 75 °C for 12 hours. The evolved HBr gas was directed to a saturated solution of NaHCO_3 for neutralization. At the end of reaction time samples were cooled and dissolved in 100 ml dry acetone. Then two molar
20 equivalents of triethylamine were added dropwise and the mixture was refluxed for 6 h. After filtration of triethylammonium salts, acetone was removed in vacuo and resulting product was dissolved in ethyl acetate and filtered through silica gel. Then solvent was distilled off and remaining product was analyzed by ^1H NMR.

Results

25 2-BPB was first condensed with TFLA to form an intermediate ester, followed by ring closure under basic condition to yield the cyclic diester. The reaction was monitored by thin layer chromatography. ^1H NMR (300 MHz, CDCl_3) spectrum of crude reaction mixture of intermediate ester and cyclized monomer showed characteristic peaks related to both intermediate ester and cyclized monomer. The
30 methyl and methine protons can be identified as a doublet and quartet near δ 1.9 and 4.5, respectively. The peak related to CF_3 group in intermediate ester overlaps by the same group in cyclic dimer at 5.55 ppm.

The formation of fluorine--substituted lactide was evaluated under various synthesis conditions by changing the time and temperature of the reaction (Table 1). Although increasing time and temperature of the synthesis was an attempt to derive the reaction toward formation of the monomer, no significant change in final products was observed. Similar ^1H NMR spectra were obtained for samples prepared at different conditions, implying the flexibility and repeatability of the synthesis method. In addition, no additional byproducts were formed during step one of the reaction and observed impurities were traces of starting materials.

Table 1. Synthetic parameters of the fluorine-substituted lactide monomer.

Sample	Reaction time	Reaction Temperature ($^{\circ}\text{C}$)
1	12h	140
2	12h	60
3	12h	70
4	6 days	70

The present invention provides a versatile approach for synthesis of fluorine-substituted lactide monomer.

Example 2

Representative Method for Polymerizing a Cyclic Diester

In this example, a representative method for polymerizing a cyclic diester to provide a fluorinated polymer of the invention is described.

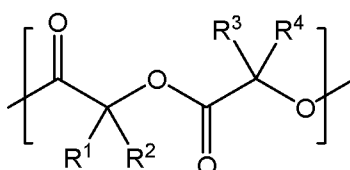
Substituted monomer (0.025 mol) and 1-dodecanol ($1.93\mu\text{mol}$) in a dry three-neck reaction flask are subjected to several cycles of vacuum evacuation and argon flush. A toluene solution of tin (II)(dioctanoate) ($\text{Sn}(\text{Oct})_2$) catalyst (0.03×10^{-5} mol) is added to the reaction flask by syringe and the toluene distilled under vacuum. The reaction mixture is stirred at 140°C for 10h. At the end of the polymerization reaction, the reaction mixture was cooled and the product polymer is dissolved chloroform. The polymer is precipitated from the chloroform solution by the addition excess cold

methanol. The polymer is collected by filtration and dried overnight at 40 °C in a vacuum oven.

CLAIMS

The embodiments of the invention in which an exclusive property or privilege is claimed are defined as follows:

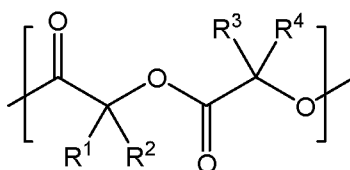
1. A halogenated polymer, comprising a repeating unit having the formula



wherein

R¹, R², R³, and R⁴ are independently selected from hydrogen, C1-C24 alkyl, aryl, fluoro, chloro, and halocarbon, with the proviso that at least one of R¹, R², R³, or R⁴ is selected from fluoro, chloro, or halocarbon.

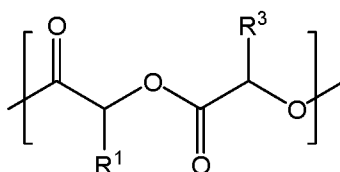
2. A fluorinated polymer, comprising a repeating unit having the formula



wherein

R¹, R², R³, and R⁴ are independently selected from hydrogen, C1-C24 alkyl, aryl, fluoro, and fluorocarbon (e.g., C1-C24 fluoroalkyl), with the proviso that at least one of R¹, R², R³, or R⁴ is selected from fluoro or fluorocarbon.

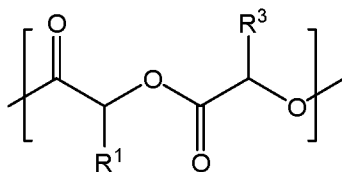
3. A halogenated polylactic acid, comprising a repeating unit having the formula



wherein

R¹ and R³ are independently selected from C1-C24 alkyl and halocarbon, with the proviso that at least one of R¹ or R³ is halocarbon.

4. A fluorinated polylactic acid, comprising a repeating unit having the formula

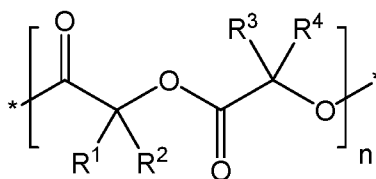


wherein

R^1 and R^3 are independently selected from C1-C24 alkyl and fluorocarbon (e.g., C1-C24 fluoroalkyl), with the proviso that at least one of R^1 or R^3 is fluorocarbon.

5. The polymer of any one of Claims 1-4 further comprising one or more repeating units derived from comonomers suitable for polymerization with a halogenated cyclic diester.

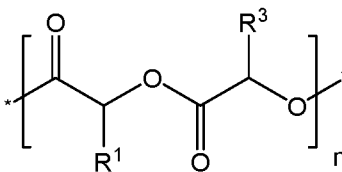
6. The polymer of Claims 1 or 2 having the formula



wherein

*represents the terminal groups of the polymer, and
n is an integer from about 10 to about 1000.

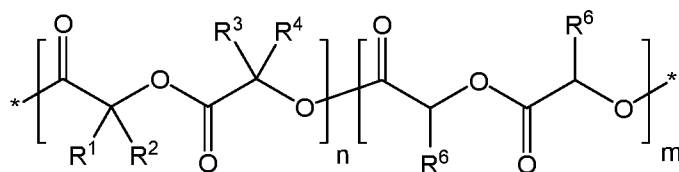
7. The polylactic acid of Claims 3 or 4 having the formula



wherein

*represents the terminal groups of the polymer, and
n is an integer from about 10 to about 1000.

8. The polymer of Claims 1 or 2 having the formula



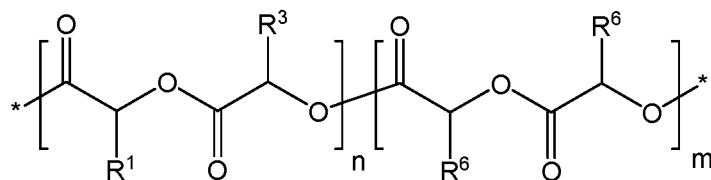
wherein

R^6 is hydrogen or methyl,

n is an integer from about 10 to about 1000, and

m is an integer from about 10 to about 1000.

9. The polylactic acid of Claims 3 or 4 having the formula



wherein

R^6 is hydrogen or methyl,

n is an integer from about 10 to about 1000, and

m is an integer from about 10 to about 1000.

10. The polymer of any one of Claims 1-5, 8, and 9, wherein the polymer is a random copolymer or a block copolymer.

11. A surface of a substrate, wherein at least a portion of the surface is coated with a polymer of any one of Claims 1-10.

12. The surface of Claim 11, wherein the substrate is a drug delivery device, a device having a degradation-inhibiting coating, a device having a hydrophobic surface with high contact angle, or a device that contacts blood.

13. The surface of Claim 11, wherein the substrate is a medical device.

14. The surface of Claim 11, wherein the substrate is a cardiovascular stent.

15. A method for making a halogenated polymer, comprising:
subjecting a polymer with an ammonia plasma to provide a polymer functionalized with amino groups;

reacting the polymer functionalized with amino groups with a suitably reactive reagent comprising a halocarbon, wherein at least a portion of the amino groups react with the reagent to provide a polymer having at least a portion of the amino groups converted to amine groups covalently coupled to the halocarbon.

16. A method for making a fluorinated polymer, comprising:

subjecting a polymer with an ammonia plasma to provide a polymer functionalized with amino groups;

reacting the polymer functionalized with amino groups with a suitably reactive reagent comprising a fluorocarbon (e.g., fluoroalkyl) group, wherein at least a portion of the amino groups react with the reagent to provide a polymer having at least a portion of the amino groups converted to amine groups covalently coupled to fluorocarbon (e.g., fluoroalkyl) groups.

17. The method of Claims 15 or 16 wherein the polymer is selected from the group consisting of a polylactic acid, a polyglycolic acid, and a poly(lactic-co-glycolic) acid.

18. The method of Claim 15, wherein suitably reactive reagent comprising a halocarbon has a reactive group selected from the group consisting of a carboxylic acid, carboxylic acid halide, carboxylic acid ester, isocyanate, isothiocyanate, acyl azide, aldehyde, epoxide, oxirane, carbonate, sulfonyl chloride, aryl halide, imidoester, glyoxal, carbodiimide, and anhydride.

19. The method of Claim 16, wherein suitably reactive reagent comprising a fluorocarbon group has a reactive group selected from the group consisting of a carboxylic acid, carboxylic acid halide, carboxylic acid ester, isocyanate, isothiocyanate, acyl azide, aldehyde, epoxide, oxirane, carbonate, sulfonyl chloride, aryl halide, imidoester, glyoxal, carbodiimide, and anhydride.

20. The method of Claim 16, wherein the fluoroalkyl group is a C1-C24 fluoroalkyl group.

21. The method of Claims 15 or 16, wherein the polymer is a coating on at least a portion of a surface of a substrate.

22. The method of Claim 21, wherein the substrate is a drug delivery device, a device having a degradation-inhibiting coating, a device having a hydrophobic surface with high contact angle, or a device that contacts blood.

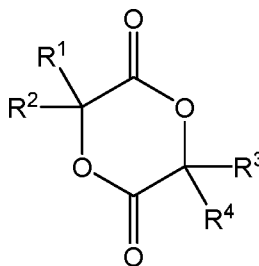
23. The method of Claim 21, wherein the substrate is a medical device.

24. The surface of Claim 21, wherein the substrate is a cardiovascular stent.

25. A polymer obtainable by the process of any one of Claims 15-20.

26. A surface of a substrate having at least a portion of the surface is coated with a polymer obtainable by the process of any one of Claims 15-20.

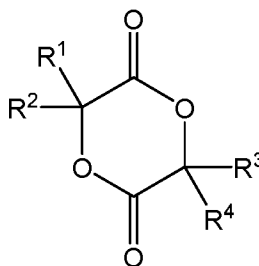
27. A cyclic diester having the formula



stereoisomers and racemates thereof,

wherein R^1 , R^2 , R^3 , and R^4 are independently selected from hydrogen, C1-C24 alkyl, aryl, fluoro, chloro, and halocarbon, with the proviso that at least one of R^1 , R^2 , R^3 , or R^4 is selected from fluoro, chloro, or halocarbon.

28. A cyclic diester having the formula



stereoisomers and racemates thereof,

wherein R^1 , R^2 , R^3 , and R^4 are independently selected from hydrogen, C1-C24 alkyl, aryl, fluoro, and fluorocarbon (e.g., C1-C24 fluoroalkyl), with the proviso that at least one of R^1 , R^2 , R^3 , or R^4 is selected from fluoro or fluorocarbon.

29. The cyclic diester of Claim 28, wherein the C1-C24 fluoroalkyl group is a C1-C12 fluoroalkyl group.

30. The cyclic diester of Claim 28, wherein the C1-C24 fluoroalkyl group is a C1-C6 fluoroalkyl group.

31. The cyclic diester of Claim 28, wherein R^1 and R^3 are hydrogen and R^2 and R^4 are trifluoromethyl.

32. The cyclic diester of Claim 28, wherein R^1 and R^3 are hydrogen, R^2 is methyl, and R^4 is trifluoromethyl.

33. The cyclic diester of Claim 28, wherein R^1 and R^2 are hydrogen and R^3 and R^4 are trifluoromethyl.

34. The cyclic diester of Claim 28, wherein R^1 , R^2 , and R^3 are hydrogen and R^4 is trifluoromethyl.

35. The cyclic diester of Claim 28, wherein R^1 , R^2 , R^3 , and R^4 are trifluoromethyl.

36. The cyclic diester of Claim 28, wherein the C1-C24 alkyl is selected from the group consisting of straight chain, branched, and cyclo alkyl.

37. The cyclic diester of Claim 28, wherein the C1-C24 alkyl is selected from the group consisting of methyl, ethyl, n-propyl, i-propyl, and n-butyl.

38. The cyclic diester of Claim 28, wherein the C1-C24 alkyl is methyl.

39. The cyclic diester of Claim 28, wherein the C1-C24 fluoroalkyl is selected from the group consisting of straight chain, branched, and cyclo fluoroalkyl.

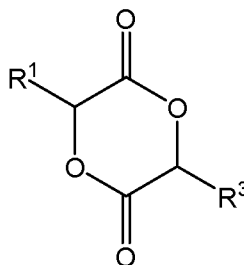
40. The cyclic diester of Claim 28, wherein the C1-C24 fluoroalkyl is a C1-C24 perfluoroalkyl.

41. The cyclic diester of Claim 28, wherein the C1-C24 fluoroalkyl has a ratio of F:C from 0.4 to 3.0.

42. The cyclic diester of Claim 28, wherein the C1-C24 fluoroalkyl is selected from the group consisting of trifluoromethyl, pentafluoroethyl, n-perfluoropropyl, n-perfluorobutyl, and n-perfluoropentyl.

43. The cyclic diester of Claim 28, wherein the C1-C24 fluoroalkyl is trifluoromethyl.

44. A cyclic diester having the formula



stereoisomers and racemates thereof,

wherein R¹ and R³ are independently selected from C1-C24 alkyl and fluorocarbon (e.g., C1-C24 fluoroalkyl), with the proviso that at least one of R¹ or R³ is fluorocarbon.

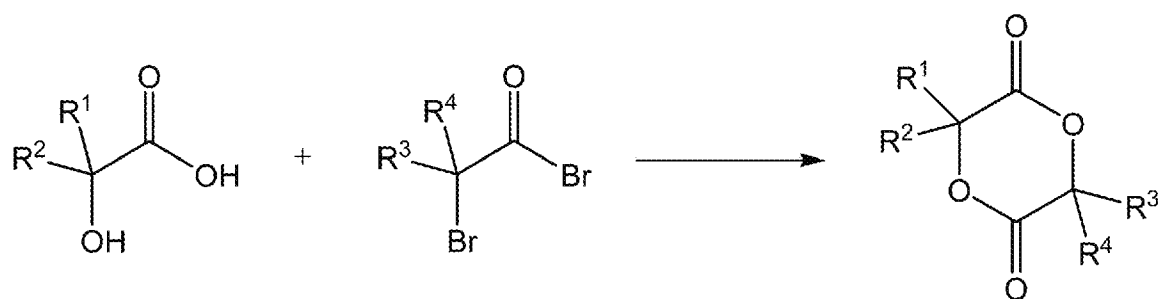
45. The cyclic diester of Claim 44, wherein R¹ is methyl and R³ is trifluoromethyl.

46. The cyclic diester of Claim 44, wherein R¹ is hydrogen and R³ is trifluoromethyl.

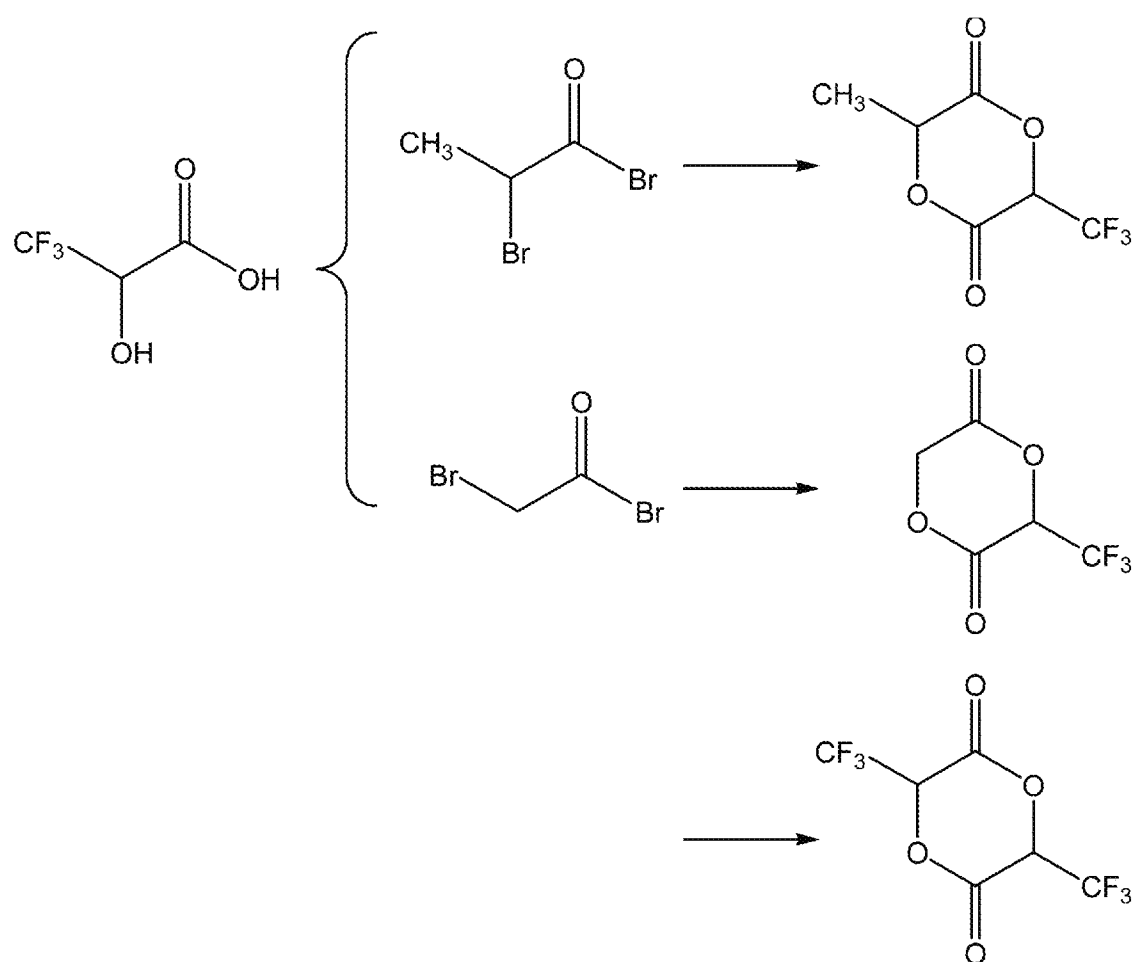
47. The cyclic diester of Claim 44, wherein R¹ and R³ are trifluoromethyl.

48. A fluorinated polymer prepared from a cyclic diester of any one of Claims 28-46.

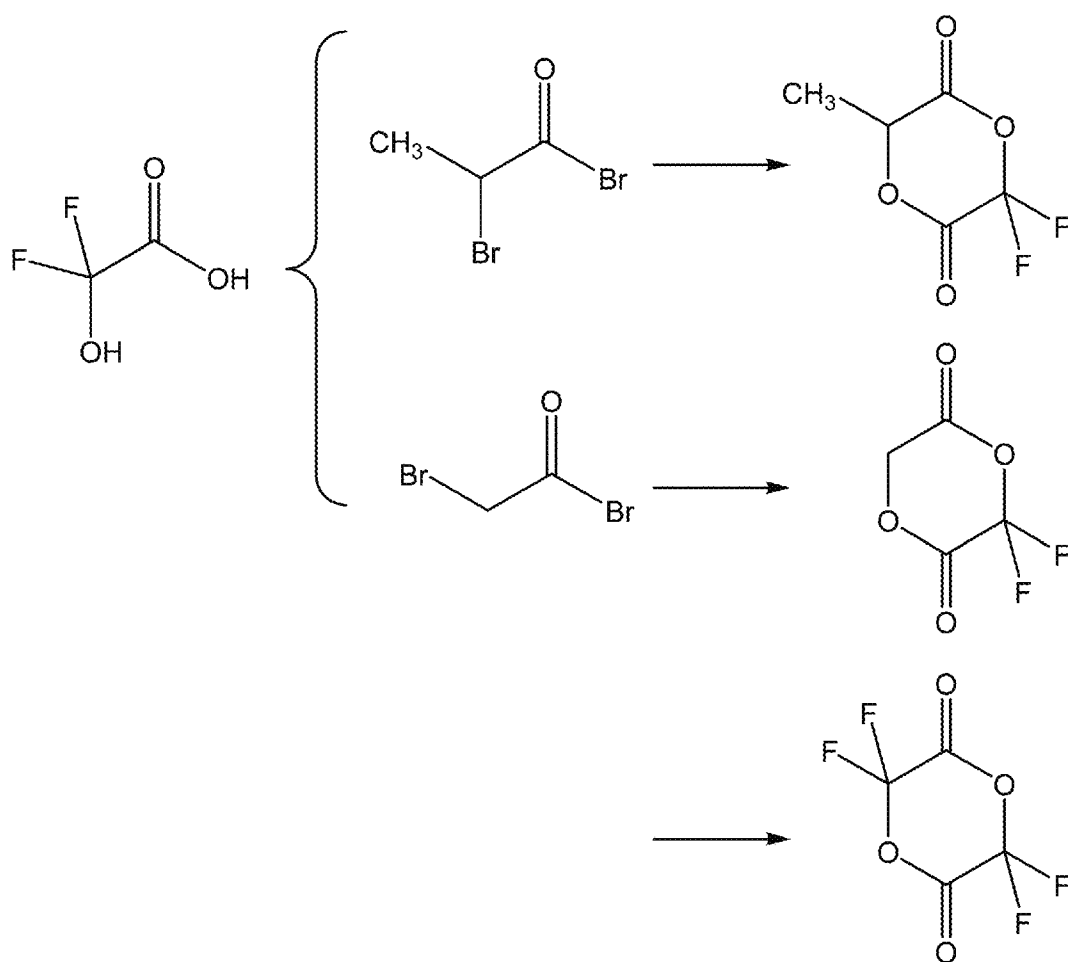
49. A halogenated polymer prepared from a cyclic diester of Claim 27.

1/8***FIG. 1***

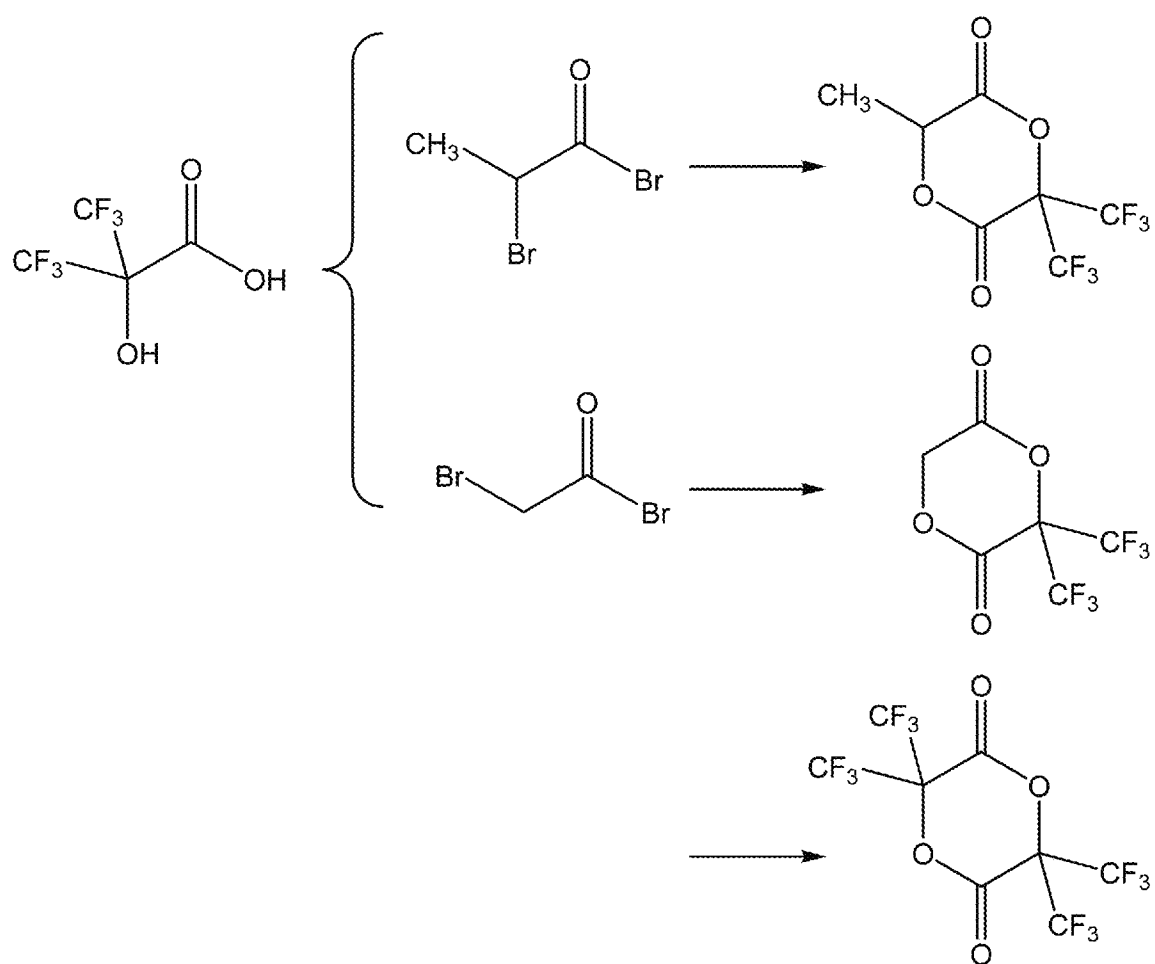
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**FIG. 2**

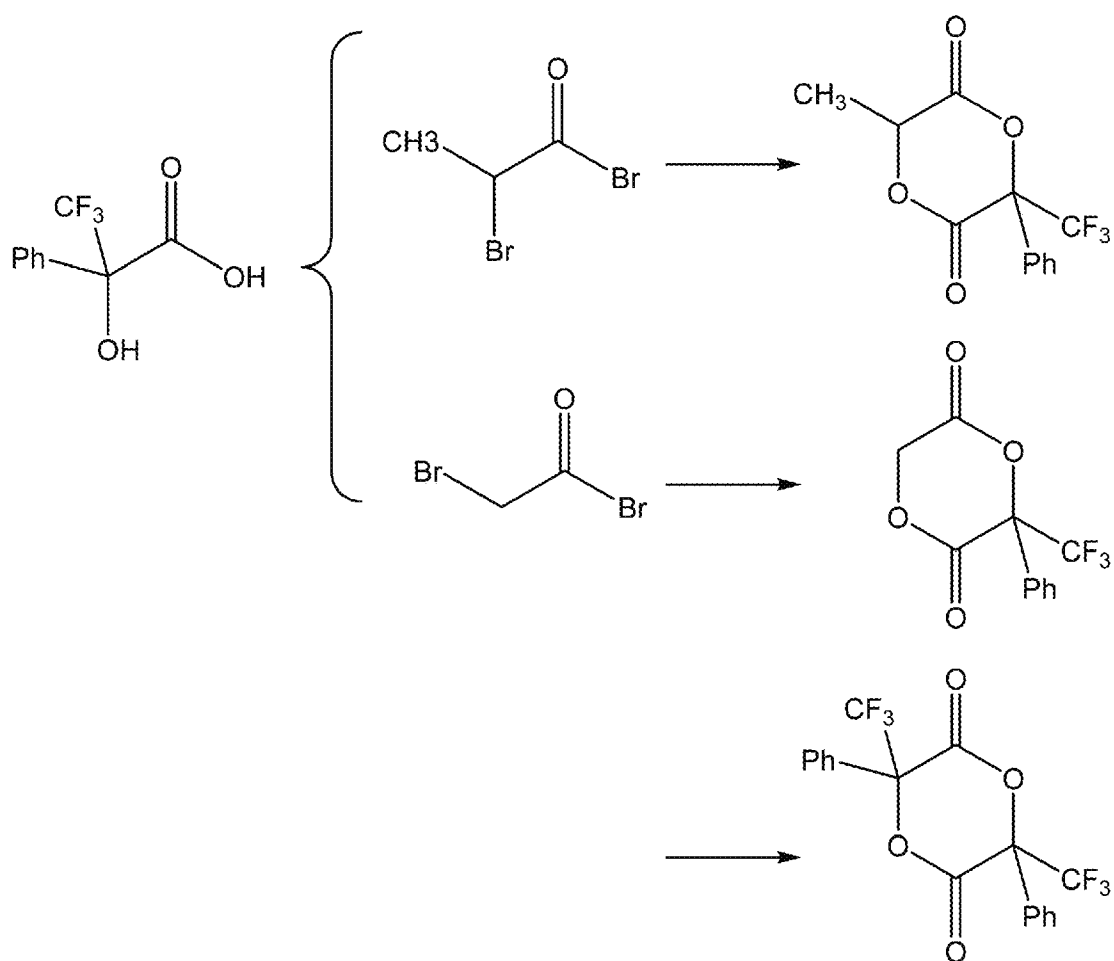
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**FIG. 3**

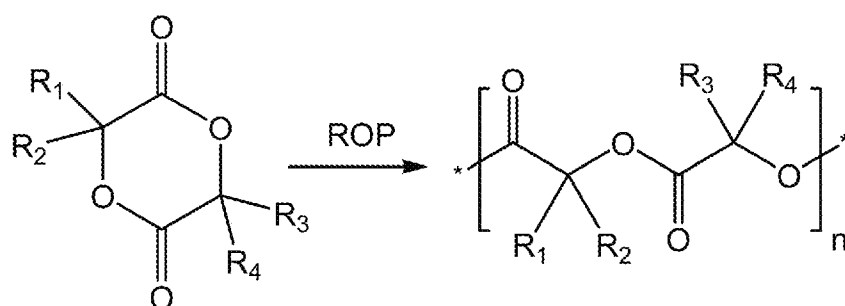
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**FIG. 4**

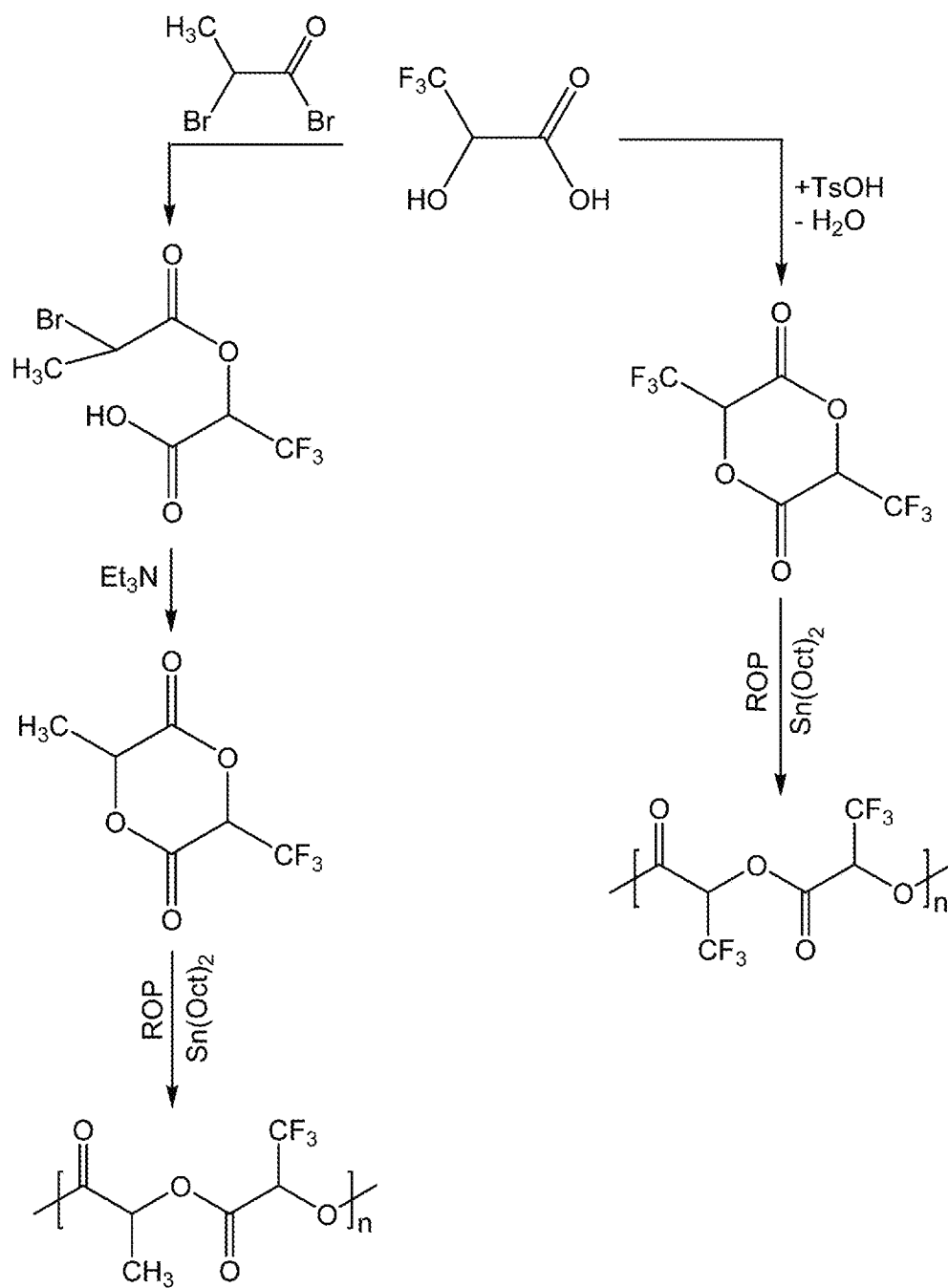
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**FIG. 5**

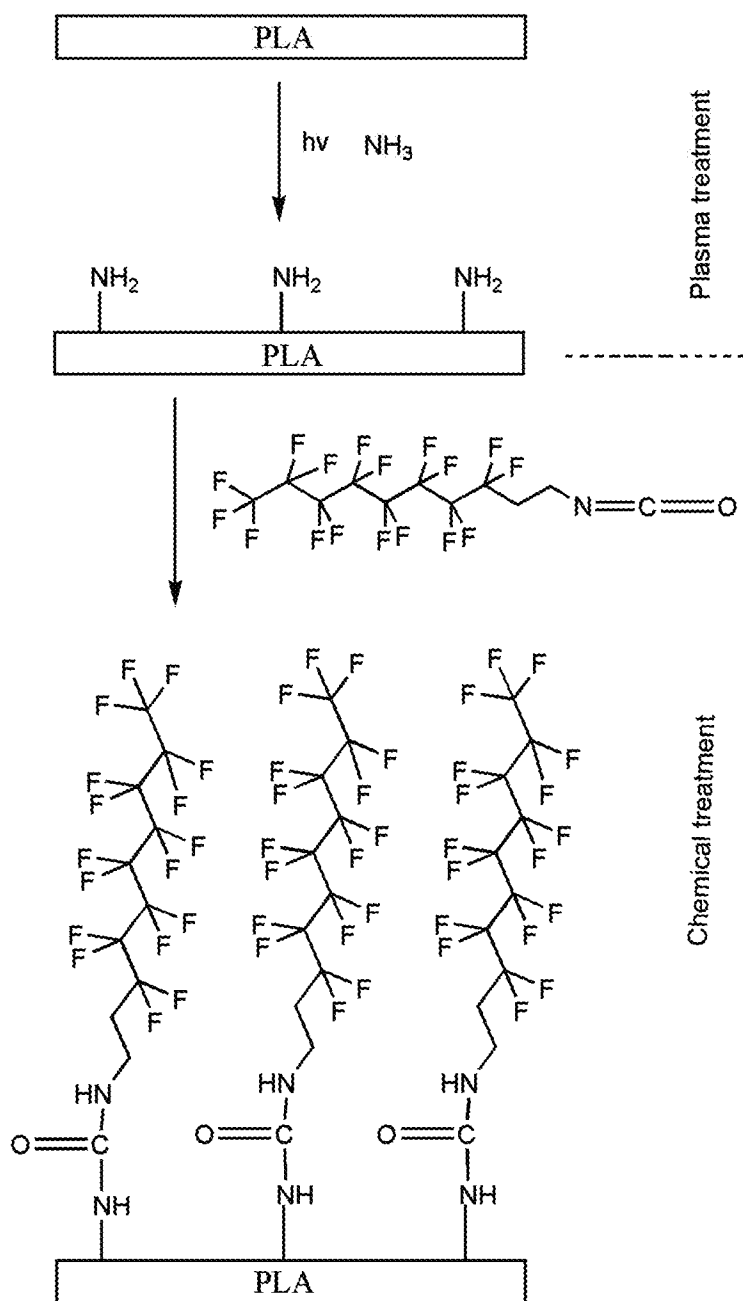
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**FIG. 6**

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**FIG. 7**

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**FIG. 8**

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US16/18529

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - C08G 63/08; C07C 69/67 (2016.01)

CPC - C08G 63/08; C07C 69/67

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)

IPC(8): C08G 63/08; C07C 69/67 (2016.01)

CPC: C08G 63/08; C07C 69/67

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)

PatSeer (US, EP, WO, JP, DE, GB, CN, FR, KR, ES, AU, IN, CA, Other Countries (INPADOC), RU, AT, CH, TH, BR, PH); EBSCO; Google/Google Scholar, IP.com: cyclic, diester, halogenated, fluorinated, polymer, polylactic, block, copolymer, drug, delivery, surface, hydrophobic

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2009/0054619 A1 (BAKER, GL et al.) 26 February 2009; paragraphs [0015]-[0017]	1-4, 5/1-4, 6/1-2, 7/3-4, 8/1-2, 9/3-4
Y	US 2011/0098500 A1 (ISONO, Y et al.) 28 April 2011; paragraphs [0011]-[0012], [0017]	1-4, 5/1-4, 6/1-2, 7/3-4, 8/1-2, 9/3-4
Y	US 7,695,795, B1 (SMITH, DW et al.) 13 April 2010; claim 3	8/1-2, 9/3-4
A	US 2013/0184429 A1 (PUGH, C et al.) 18 July 2013; entire document	1-4, 5/1-4, 6/1-2, 7/3-4, 8/1-2, 9/3-4

☐ 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

"E" earlier application or patent but published on or after the international filing date

"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)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"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

"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

"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

"&" document member of the same patent family

Date of the actual completion of the international search

31 March 2016 (31.03.2016)

Date of mailing of the international search report

24 JUN 2016

Name and mailing address of the ISA/

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents

P.O. Box 1450, Alexandria, Virginia 22313-1450

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US16/18529

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: 10-14, 25-26
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I: Claims 1-9 are directed toward a fluorinated polymer.

Group II: Claims 15-24 are directed toward a method for making a halogenated polymer.

Group III: Claims 27-49 are directed toward a cyclic diester having the recited formulae.

Continued Within the Next Supplemental Box

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-9

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☒ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.

PCT/US16/18529

-Continued from Box No. III: Observations where unity of invention is lacking-

The inventions listed as Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the special technical features of Group I include a fluorinated polymer comprising repeating units having the recited formulae, which are not present in Groups II and III; and the special technical features of Group II include subjecting a polymer with an ammonia plasma to provide a polymer functionalized with amino groups and reacting the polymer functionalized with amino groups with a suitably reactive reagent comprising a halocarbon, wherein at least a portion of the amino groups react with the reagent to provide a polymer having at least a portion of the amino groups converted to amine groups covalently coupled to the halocarbon, which are not present in Groups I and III; and the special technical features of Group III include a cyclic diester having the recited formulae, which are not present in Groups I and II.

The common technical features of Groups I-II are a fluorinated polymer.

These common technical features are disclosed by US 2009/0054619 A1 to Baker, et al. (hereinafter 'Baker'). Baker discloses a fluorinated polymer (formula I; paragraph [0015]).

Since the common technical features are previously disclosed by Baker, these common features are not special and so Groups I-III lack unity.