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— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

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(54) **Title**: ALTERNATING RING-OPENING METATHESIS POLYMERIZATION

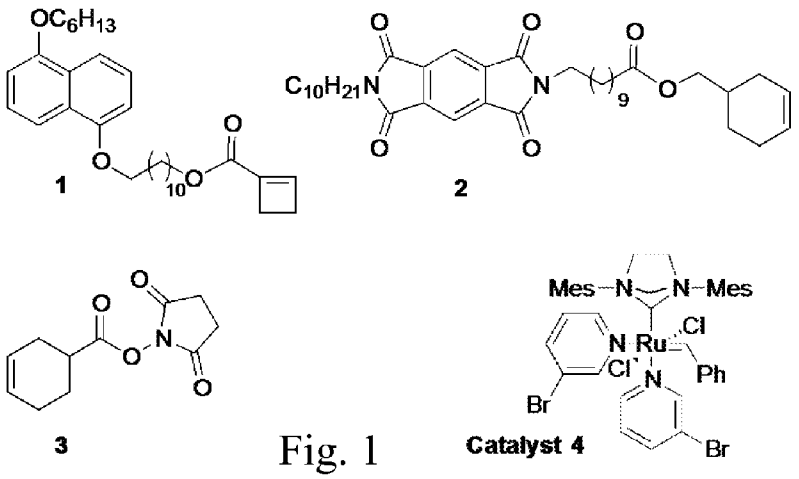

Fig. 1

(57) **Abstract**: The invention relates to the field of polymers and olefin polymerization, and more specifically olefin metathesis polymerization. The invention provides regioregular alternating polymers and methods of synthesizing such polymers. To demonstrate, polymers were synthesized and modified with a FRET pair (Trp/ Dansyl) post-polymerization.

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ALTERNATING RING-OPENING METATHESIS POLYMERIZATION

STATEMENT OF INTEREST

[0001] This invention was made with government support under grant numbers HD038519 and GM097971 awarded by the National Institutes of Health and grant number DBI1039771 awarded by the National Science Foundation. The government has certain rights in the invention.

CROSS REFERENCE TO RELATED APPLICATIONS

[0002] This application claims priority to U.S. Application No. 61/857,189, filed July 22, 2013, and U.S. Application No. 61/858,811, filed July 26, 2013, which are incorporated herein by reference in their entireties.

FIELD OF THE INVENTION

[0003] The invention relates to the field of polymers and olefin polymerization, and more specifically olefin metathesis polymerization.

BACKGROUND

[0004] Copolymers are employed in a wide range of materials, ranging from bulk plastics to specialized coatings, pharmaceutical compositions, and biomedical and electronic devices. Among the most commonly used are block copolymers, which often rely on phase separation of the two blocks for their functional properties, for example in drug delivery nanoparticles, and random copolymers, which incorporate two or more functional moieties that act co-operatively, for example in organic light emitting diodes. Regularly alternating polymers allow for controlled positioning of functional substituents, but they are difficult to access synthetically.

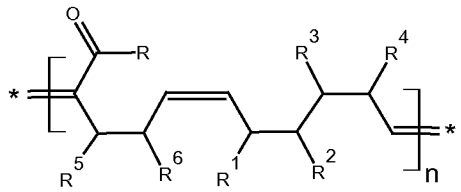
[0005] Regioregular alternating polymers (for example, SAN, styrene-acrylonitrile, an alternating copolymer used in plastics) are generally synthesized by radical polymerization with kinetic control of alternation in the polymerization reaction.[1,2] Recently, ring opening metathesis polymerization (ROMP) and ring opening insertion metathesis polymerization (ROIMP)[3] have been employed to synthesize alternating polymers: Ilker, M. F.; Coughlin, E. B. *Macromolecules* **2002**, *35*, 54-58; Choi, T. L.; Rutenberg, I. M.; Grubbs, R. H. *Angewandte Chemie-Intl. Ed.,* **2002**, *41*, 3839-3841; PCT publication WO 03/070779.

[0006] The existing methods of formation of alternating polymers are limited, and there remains a need for new and more structurally diverse substrates and polymers. The present invention provides substrate and catalyst combinations that can generate a wider range of alternating polymers, having a range of diverse properties.

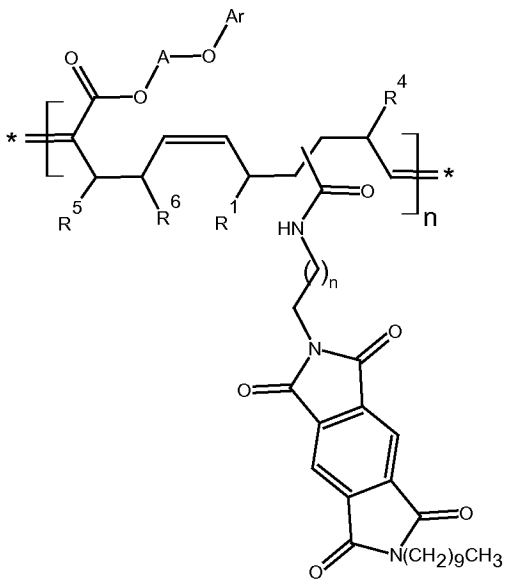
[0007] Herein we address both, the limitation of the NB/COE ROMP, i.e. the formation of COE homoblocks, as well as the intramolecular chain transfer of current AROMP by utilizing CBE/CH monomers containing the DAN-PDI pair to achieve perfectly alternating copolymers. We show that these polymers exhibit a higher intensity charge-transfer absorbance than analogous poly(NB-*alt*-COE) polymers.

BRIEF DESCRIPTION OF THE INVENTION

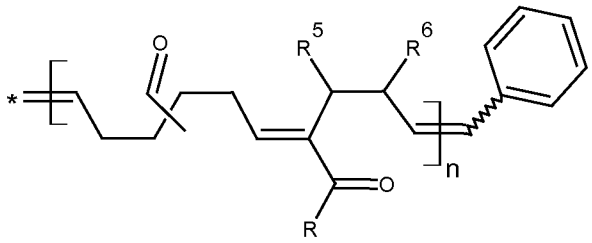
[0008] The invention provides a method for producing an alternating AB copolymer comprising the repeating unit **Ia, Ib**, or **Ic**:



(Ia)

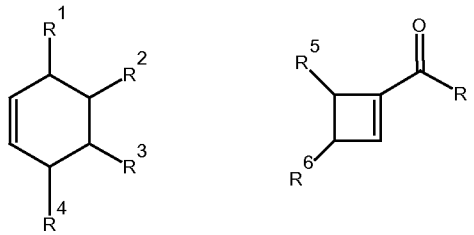


(Ib)



(Ic)

in which the A monomer is derived from a cyclobutene 1-carboxyl or 1-carbonyl derivative **III**, and the B monomer is derived from a cyclohexene derivative **II**.



(II) **(III)**

[0009] The method comprises contacting the cyclohexene derivative **II** with the cyclobutene derivative **III** in the presence of an olefin metathesis catalyst. This polymerization method enables the facile preparation of amphiphilic and bifunctional alternating polymers from simple and readily available starting materials.

BRIEF DESCRIPTION OF THE FIGURES

[0010] Figure 1 shows chemical structures of monomers and catalyst (box) used for AROMP.

[0011] Figure 2 shows partial UV-Vis spectra of the charge-transfer region in chloroform. a) Comparison of alternating copolymers. Upper trace = 3 mM poly(**1**-*alt*-**5**)$_{10}$, middle trace = 100 μM poly(**1**-*alt*-**5**)$_{10}$, lower trace = 3 mM poly(NB-*alt*-COE)-block-poly(COE). b) Plot of charge-transfer absorbance versus concentration of poly(**1**-*alt*-**5**)$_{10}$.

[0012] Figure 3 depicts the ^{1}H-NMR spectrum of 11-(5-(hexyloxy)naphthalen-1-yloxy)undecyl cyclobut-1-enecarboxylate (**1**)

[0013] Figure 4 depicts the ^{13}C-NMR spectrum of 11-(5-(hexyloxy)naphthalen-1-yloxy)undecyl cyclobut-1-enecarboxylate (**1**)

[0014] Figure 5 depicts the ^{1}H-NMR spectrum of 2,5-dioxopyrrolidin-1-yl cyclohex-3-enecarboxylate (**3**).

[0015] Figure 6 depicts the ^{13}C-NMR spectrum of 2,5-dioxopyrrolidin-1-yl cyclohex-3-enecarboxylate (**3**).

[0016] Figure 7 depicts the ^{1}H-NMR spectrum of poly(**1**-*alt*-**2**)$_5$.

[0017] Figure 8 depicts the ^{1}H-NMR spectrum of poly(**1**-*alt*-**3**)$_{10}$.

[0018] Figure 9 depicts the ^{1}H-NMR spectrum of poly(**1**-*alt*-**5**)$_{10}$.

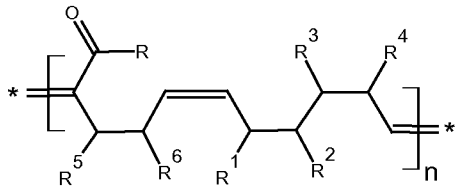
[0019] Figure 10 depicts a partial ^{1}H-NMR spectrum of a) **1**; b) poly(**1**-*alt*-**2**)$_5$; and c) **2**.

[0020] Figure 11 depicts GPC traces of alternating copolymers. a) poly(**1**-*alt*-**2**)$_5$; b) poly(**1**-*alt*-**5**)$_{10}$. Molecular weights and polydispersity indices were measured using UV detection with CH_2Cl_2 as the eluent and a flow rate of 0.700 mL/min on an American Polymer Standards column (Phenogel 5 μ MXL GPC column, Phenomenex). All GPCs were calibrated using poly(styrene) standards and carried out at 30°C.

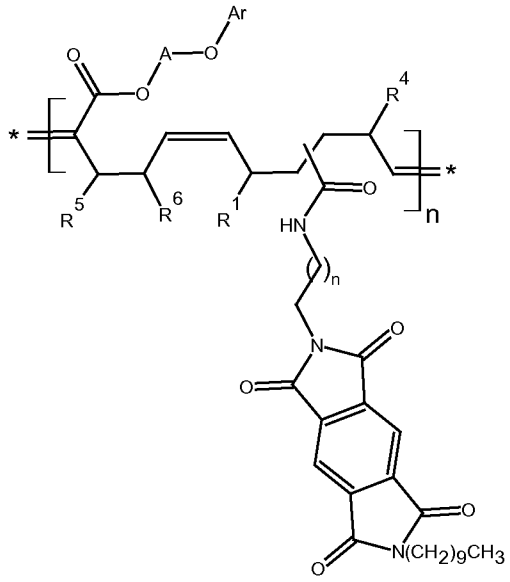
[0021] Figure 12 depicts fluorescence of the polymers. a) The emission spectra of poly(**3′**-*alt*-**4-DH**)$_n$ and poly(**3′-Trp**-*alt*-**4-DH**)$_n$ (1.2 μM in THF) excited at characteristic wavelengths of tryptophan (284 nm) and dansyl fluorophore (335 nm). b) Plot of charge-transfer absorbance of poly(**3′**-*alt*-**4-DH**)$_n$ and poly(**3′-Trp**-*alt*-**4-DH**)$_n$ versus concentration ranging from 0.2 μM and 3 μM. c) Concentration dependence of fluorophores without the backbone showed no emission difference between a two fluorophore mixture and dansyl fluorophore alone.

DETAILED DESCRIPTION OF THE INVENTION

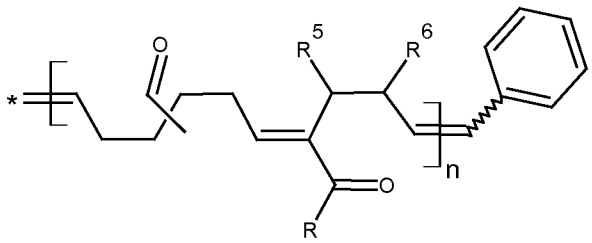
[0022] The invention provides a method for producing an alternating AB copolymer comprising the repeating unit **Ia, Ib** or **Ic**:



Ia

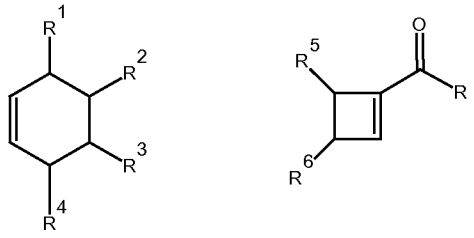


Ib



Ic

which comprises contacting an olefin of structure **II** with a cyclobutene of structure **III**

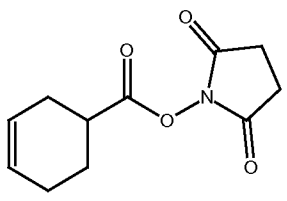


II **III**

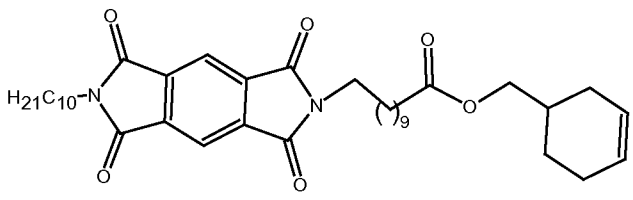
in the presence of an olefin metathesis catalyst. It will be understood that asterisk (*) at the end of a repeating unit can be interpreted as the point of attachment and may be terminated with a functional group as is known in the art. In the above structures, R may be, but is not limited to, H, C_1-C_{20} alkyl, C_2-C_{20} alkenyl, C_3-C_8 cycloalkyl, heterocyclyl, aryl, C_1-C_{20} alkoxy, C_1-C_{20} alkenyloxy, C_3-C_6 cycloalkyloxy, aryloxy, heterocyclyloxy, C_1-C_{20}

alkylamino, C_1-C_{20} alkenylamino, C_3-C_8 cycloalkylamino, heterocyclylamino, or arylamino and may be optionally substituted with up to three substituents selected from halo, CN, NO_2, oxo, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic group. In certain embodiments, the repeating unit, n, is between 2 and 20. Each substituent R^1 through R^6 may independently be, but is not limited to, H, aldehyde, C_1-C_{20} alkyl, C_2-C_{20} alkenyl, C_3-C_6 cycloalkyl, aryl, heterocyclyl, C_1-C_{20} alkoxy, C_1-C_{20} acyloxy, C_2-C_{20} alkenyloxy, C_3-C_6 cycloalkyloxy, aryloxy, heterocyclyloxy, C_1-C_{20} alkylamino, C_2-C_{20} alkenylamino, C_3-C_8 cycloalkylamino, heterocyclylamino, arylamino, or halogen; with the proviso that any carbon-carbon double bonds in R or in R^1 through R^6 are essentially unreactive toward metathesis reactions with the catalyst. It will be also understood that adjacent substitutions of R^1-R^6 may be taken together to form a 5- to 7-membered ring which may be optionally substituted with up to three substituents selected from halo, CN, NO_2, oxo, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic group. In certain embodiments, A may be, but is not limited to C_2-C_{20} alkyl. In another embodiment, A is C_8-C_{12} alkyl. In another embodiment, R^1 through R^6 may be independently be C(O)NH-C_1-C_{20} alkyl-N(R^7)(R^8). Each R^7 and R^8 are independently selected from H, C_2-C_6 alkyl, cycloalkyl, cycloalkenyl, alkyl-O-alkyl, alkyl-O-aryl, alkenyl, alkynyl, aralkyl, aryl and a heterocyclic group; or R^7 and R^8 may be taken together with the nitrogen to which they are attached form a 5- to 7-membered ring which may optionally contain a further heteroatom and may be optionally substituted with up to three substituents selected from halo, CN, NO_2, oxo, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic group.

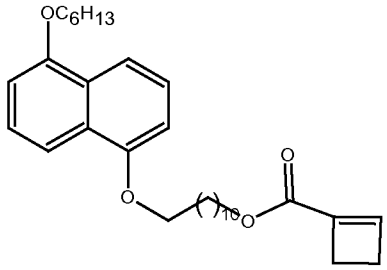
[0023] By way of example, suitable cyclohexene and cyclobutene species include but are not limited to the following:



IIa



IIb



IIIa

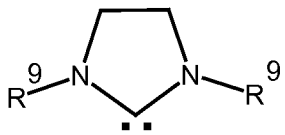
[0024] It will be understood that olefins in the substituents should be essentially unreactive with the metathesis catalyst under the reaction conditions, so that the metathesis polymerization involves the cyclobutene and cyclohexene double bonds exclusively, or nearly so. Generally, any carbon-carbon double bonds in R or in R^1 through R^6 should be trisubstituted or tetrasubstituted, or otherwise rendered unreactive with the catalyst.

[0025] Aryl, as used herein, includes but is not limited to optionally substituted phenyl, naphthyl, anthracenyl, and phenanthryl groups. Heterocycle and heterocyclyl refer to monocyclic and fused polycyclic heteroaromatic and heteroaliphatic ring systems containing at least one N, O, S, or P atom. Aryl and heterocyclic groups may contain from 1 to 60 carbon atoms, and may range from furan, thiophene, and benzene to large chromophores such as phthalocyanines and fullerenes. For some applications, aryl and heterocyclic groups will preferably contain from 1 to 20 carbon atoms.

[0026] It will be apparent that alkyl, alkenyl, cycloalkyl, heterocyclyl, acyl, and aryl moieties in the substituents R and R^1 through R^6 may be substituted with functional groups known to be compatible with the catalyst. Examples include, but are not limited to, C_1-C_4 acyl, acyloxy, acylamino, amido, aryloxy, alkoxy and alkylthio groups; halogens; protected amino groups such as BocNH- and FmocNH-; protected hydroxy groups such as TMSO-, BzO-, and BnO-; and protected carboxyl groups such as -CO_2-*t*-Bu and -CO_2Bn. Accordingly, the terms alkyl, alkenyl, cycloalkyl, acyl, aryl, and heterocyclyl as used herein encompass such substituents.

[0027] The method may be used to prepare block copolymers as well, in which one block comprises the repeating units **Ia**, **Ib**, or **Ic**; the proportion of alternating and block copolymer regions in the polymer being dependent upon the catalyst and substrate. The catalyst may be any olefin metathesis catalyst known in the art, such as those disclosed in WO 03/070779. It is preferably an alkylidene ruthenium complex, and more preferably a

complex of formula $(L)_2(L')X_2Ru=CHR'$, wherein R′ may be, for example, H, C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_3-C_6 cycloalkyl, or aryl. The ligand L is typically a trialkyl phosphines, triarylphosphines, tri(cycloalkyl)phosphines, pyridines, aryl, wherein aryl is optionally substituted with a halogen. L′ is a second ligand, and may be a trialkyl phosphine, triarylphosphine, tri(cycloalkyl)phosphine, or a pyridine. L′ may also be an imidazolin-2-ylidine carbene of formula **IV**:



IV

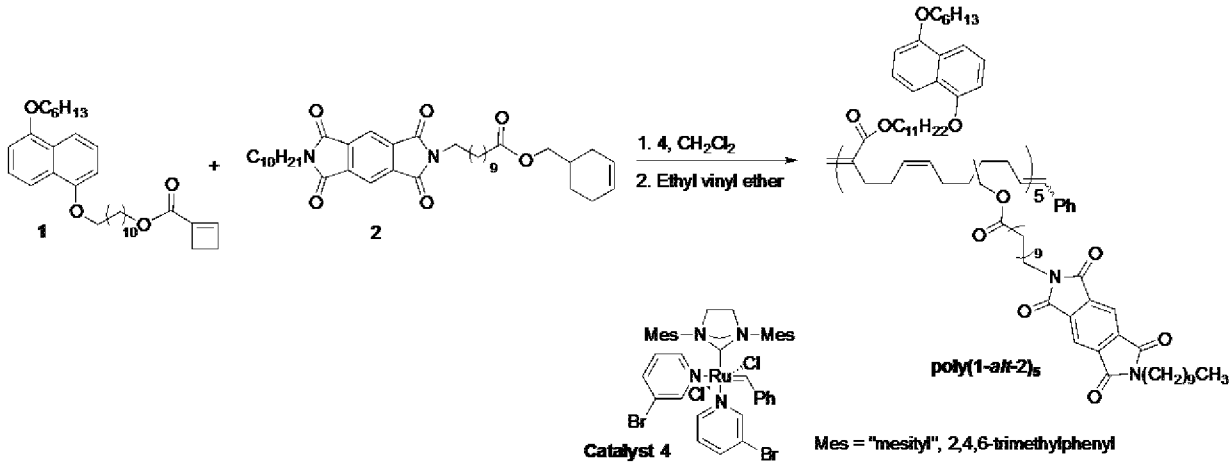
wherein R^9 may be selected from the group, but is not limited to a C_1-C_6 alkyl group or aryl. In certain embodiments, X is a halogen or pseudohalogen such as F, Cl, Br, NO_3, CF_3, or CF_3COO^-.

[0028] In certain embodiments, L is a pyridine, optionally 3-bromopyridine; and L′ is an imidazolin-2-ylidine carbene. In another embodiment, R^9 is preferably mesityl, 2-methylphenyl, 2-ethylphenyl, 2-isopropylphenyl, 2,3-diisopropylphenyl, 2, 6-difluorophenyl, or 3,5-di-*t*-butylphenyl,.

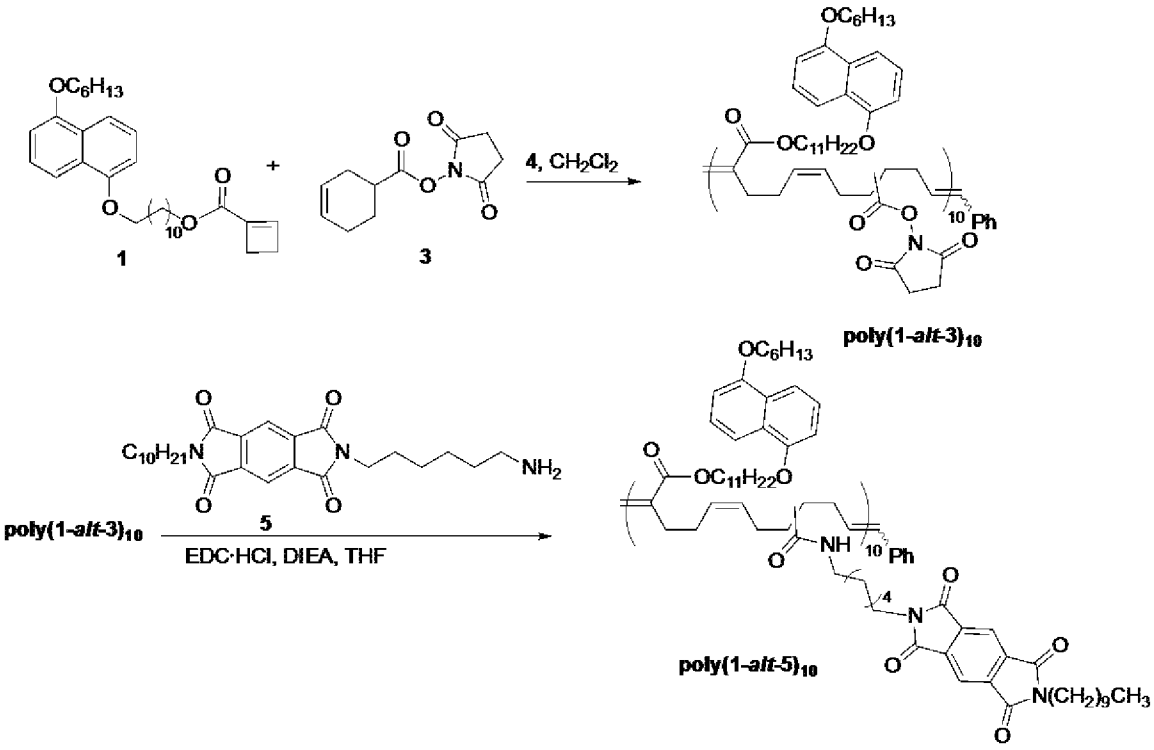
[0029] The invention also provides the following polymer comprising the repeating unit **Ia**, **Ib**, or **Ic**.

[0030] The polymers of the present invention may be prepared according to the representative Schemes 1through 3.

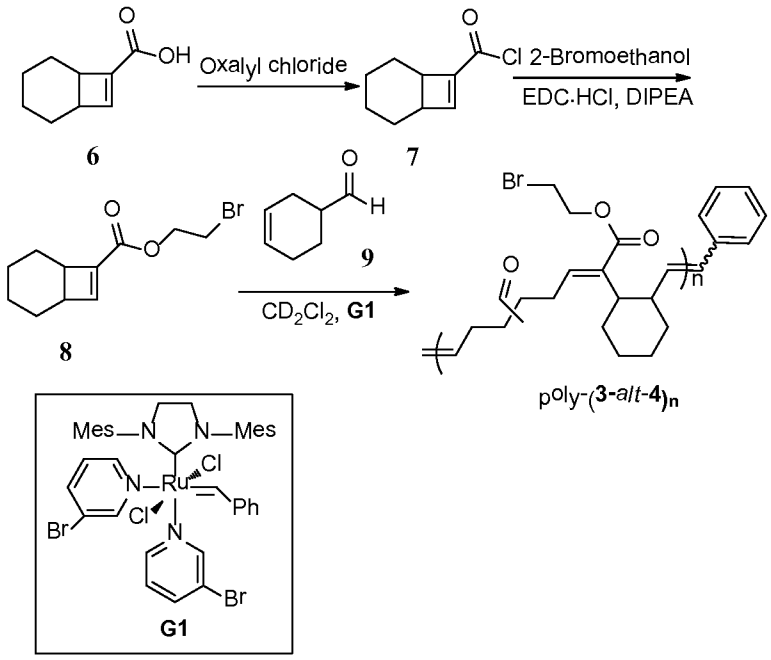
Scheme 1



Scheme 2



Scheme 3



[0031] The target monomers and catalyst are shown in Figure 1. The syntheses of the side-chains are in close analogy to published methods.[4] Based on previous studies,[5] synthetic route 1 (Scheme 1) was first investigated for the alternating copolymerization of the DAN and PDI functionalized CBE and CH monomers, respectively. This route successfully afforded poly(**1**-*alt*-**2**)$_5$. However, longer polymerization times were required due to the significant steric hindrance presented by the side-chain units. This resulted in a decrease in the rate of polymerization inhibiting the formation of higher molecular weight polymers.

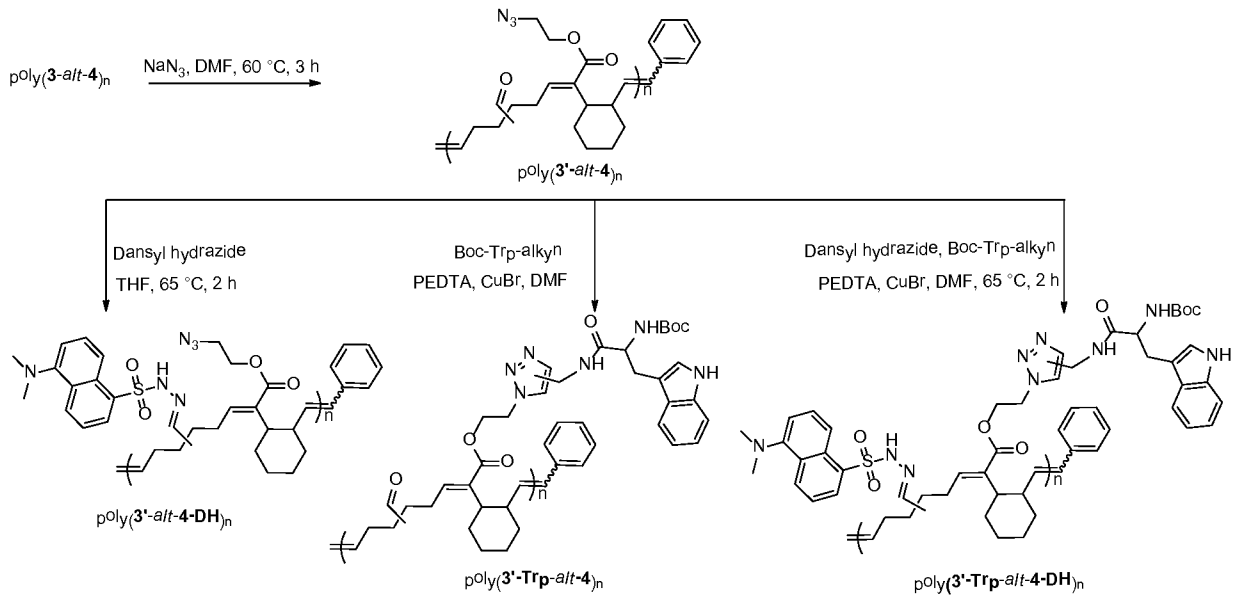
[0032] To minimize steric hindrance and to achieve a higher degree of polymerization, a revised synthetic route was applied using DAN-CBE **1** and a cyclohexene functionalized with *N*-hydroxysuccinimide (NHS) (compound **3**) for AROMP (Scheme 2). The NHS group is less bulky than the PDI, and is not reactive during the polymerization. The PDI ester can then be formed via a post-polymerization functionalization strategy to generate poly(**1**-*alt*-**5**)$_{10}$. This modified route not only allowed for a higher degree of polymerization, but also provided an alternative strategy for the incorporation of the PDI moiety.

[0033] Previous studies on poly(CBE-*alt*-CH)$_n$ revealed signals in the ^{1}H NMR spectrum corresponding to concentration-independent intramolecular backbiting of the enoic ruthenium carbene on the unhindered disubstituted alkenes in the polymer backbone.[5] As a result, polydispersity indices of unfunctionalized poly(CBE-*alt*-CH)$_n$ were larger than 2 and a significant fraction of the polymer was cyclic. In our case, poly(**1**-*alt*-**2**)$_{10}$ and poly(**1**-*alt*-**5**)$_{10}$ did not show any proton resonance signals due to backbiting, had PDIs lower than 1.3, and displayed a monomodal distribution. We hypothesize that backbiting is inhibited by the increased steric hindrance at the enoic carbene and disubstituted alkene in combination with the restricted flexibility of the polymer backbone upon modification with larger substituents. As a consequence, longer AROMP copolymers were obtained than previously reported.

[0034] We designed a new set of cyclobutene derivatives as monomers with bicyclic structures which are very strained and can incorporate rings into the polymeric backbone.[5] Therefore we utilized functional group Br containing bicyclo[4.2.0]oct-7-ene-7-carboxylate and aldehyde containing cyclohexene as the AROMP pair which provides a facile approach to prepare long and completely alternating copolymers with orthogonal functional groups. Post-polymerization modification of Br with an azide group allows click-chemistry while the aldehyde can be coupled to a hydrazide to introduce fluorophores which are not compatible with AROMP reactions.

[0035] The alternating copolymers were further modified according to Scheme 4 to crosslink with dansyl hydrazide (DH) and form poly(**3′**-*alt*-**4-DH**)$_n$; it was coupled with Boc-Trp-alkyn to form poly(**3′-Trp**-*alt*-**4**)$_n$; both fluorophores were introduced in a one-pot reaction to provide poly(**3′-Trp**-*alt*-**4-DH**)$_n$.

Scheme 4



[0036] UV-Vis spectroscopy was utilized to investigate the charge-transfer between the side-chains of the alternating copolymers in solution. The UV-Vis spectrum of poly(**1**-*alt*-**5**)$_{10}$ (3 mM in chloroform) shows a charge-transfer absorbance at the characteristic wavelength (Figure 2a – light blue trace) indicating that the side-chains are able to favorably orient to transfer energy in this system. A concentration study from 3 mM to 100 μM was carried out to determine if these interactions occur inter- or intramolecularly. As shown in Figure 2a, the charge-transfer absorbance signal was persistent even at low concentrations. Moreover, the absorbance followed Beer-Lambert behavior based on the concentration of polymer (Figure 2b), which demonstrated that the charge-transfer is intramolecular. Additionally, the aromatic signals in the ^{1}H NMR spectrum of poly(**1**-*alt*-**5**)$_{10}$ are shifted upfield in comparison to the individual monomers (Figure S10). These shifts further indicate the pi-pi stacking of the donor-acceptor aromatic units, and are consistent with similar shifts previously reported for partially-folded polymers.[6]

[0037] We compared the charge-transfer absorbance of the functionalized poly(CBE-*alt*-CH)s to the previously reported functionalized poly(NB-*alt*-COE)-*b*-COE.[4] As shown in Figure 2, poly(**1**-*alt*-**5**)$_{10}$ exhibits a higher charge-transfer absorbance intensity in comparison

to the NB/COE polymers at the same concentration, which indicates that the new poly(**1**-*alt*-**5**)$_{10}$ polymers more favorably align the aromatic units of the donor and acceptor moieties.

[0038] In conclusion, we have demonstrated the AROMP of CBE and CH monomers containing bulky DAN/PDI side-chains. We attribute inhibition of backbiting to the steric hindrance provided by bulky side-chains around the carbene and the polymer alkenes. UV-Vis spectroscopic analysis shows a charge-transfer absorbance signal for the perfectly alternating copolymers signifying the alignment of the side-chains. The new polymers demonstrate an enhancement of charge-transfer in comparison to previously studied polymers, indicating that the sequence specificity in alternating CBE-CH copolymers provides efficient energy transfer.

[0039] Throughout this application, various publications, reference texts, textbooks, technical manuals, patents, and patent applications have been referred to. The teachings and disclosures of these publications, patents, patent applications and other documents in their entireties are hereby incorporated by reference into this application to more fully describe the state of the art to which the present invention pertains. However, the citation of a reference herein should not be construed as an acknowledgement that such reference is prior art to the present invention.

[0040] It is to be understood and expected that variations in the principles of invention herein disclosed can be made by one skilled in the art and it is intended that such modifications are to be included within the scope of the present invention. The following Examples further illustrate the invention, but should not be construed to limit the scope of the invention in any way.

EXAMPLES

[0041] **11-((5-(hexyloxy)naphthalen-1-yl)oxy)undecan-1-ol.** 11-((5-(hexyloxy)naphthalen-1-yl)oxy)undecan-1-ol was synthesized from 1,5-dihydroxynapthalene, 1-bromo-hexane, and 11-bromo-1-undecanol in two consecutive steps using a catalytic Williamson ether synthesis.[4]

[0042] **Cyclobut-1-enecarboxylic acid.** Cyclobut-1-enecarboxylic acid was prepared according to the procedure for the preparation of 3,3-dimethylcylobutene carboxylic acid as described by Campbell et al.[7] and modified as previously reported.[5] ^{1}H-NMR (400 MHz, $CDCl_3$) δ 10.23 (bs, 1H), 6.94 (t, J = 1.2 Hz, 1H), 2.76 (t, J = 3.2 Hz, 2H), 2.51 (td, J = 3.2 Hz, 1.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 150.1, 138.4, 29.1, 27.5.

[0043] 11-(5-(hexyloxy)naphthalen-1-yloxy)undecyl cyclobut-1-enecarboxylate (1). To a solution of cyclobut-1-enecarboxylic acid (190 mg, 1.94 mmol) and dicyclohexylcarbodiimide (DCC) (417 mg, 2.04 mmol) in CH_2Cl_2 (10 mL) stirred at 0°C for 30 minutes, 11-((5-(hexyloxy)naphthalen-1-yl)oxy)undecan-1-ol (400 mg, 0.97 mmol) and a catalytic amount of dimethylaminopyridine (DMAP) were added. The mixture was allowed to warm to rt over 12 h. CH_2Cl_2 was evaporated under reduced pressure and the crude product was purified by flash chromatography (1:1/hexanes:CH_2Cl_2) to afford **1** in 35% yield: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86 (d, J = 8.2 Hz, 2H), 7.36 (t, J = 7.6 Hz, 2H), 6.84 (d, J = 7.2 Hz, 2H), 6.80 (s, 1H), 4.10 (m, 6H), 2.74 (s, 1H), 2.47 (s, 1H), 1.93 (d, J = 6.3 Hz, 2H), 1.67 (d, J = 6.4 Hz, 1H), 1.58 (d, J = 5.7 Hz, 2H), 1.36 (d, J = 45.9 Hz, 8H), 0.94 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.3, 154.6, 154.6, 146.1, 146.1, 138.8, 126.7, 124.9, 113.9, 113.9, 105.1, 68.0, 64.2, 64.2, 33.9, 32.7, 31.6, 29.5, 29.4, 29.4, 29.4, 29.3, 29.2, 29.0, 28.7, 28.6, 25.9, 25.8, 22.6, 14.0.

[0044] Cyclohex-3-en-1-ylmethyl 3-(6-decyl-1,3,5,7-tetraoxo-6,7-dihydropyrrolo[3,4-*f*] isoindol-2(1*H*,3*H*,5*H*)-yl)propanoate (2). Monomer **2** was prepared from pyromellitic dianhydride and cyclohex-3-en-1-ylmethyl 3-aminopropanoate by methods known in the art.[4]

[0045] 2,5-dioxopyrrolidin-1-yl cyclohex-3-enecarboxylate (3). 3-Cyclohexene-1-carboxylic acid (100 mg, 0.79 mmol), *N*-hydroxysuccinimide (100 mg, 0.87 mmol), and ethyl, dimethylaminopropyl carbodiimide hydrochloride (EDC•HCl) (182 mg, 0.95 mmol) were dissolved in CH_2Cl_2 and cooled in an ice bath. Then DIEA was added to adjust the pH to 8-9. The reaction was stirred for 16 h and washed with 5% Na_2CO_3 (50 mL). The organic phase was dried and condensed, followed by flash chromatography, eluted with 100% CH_2Cl_2 to yield a white solid in 80% yield: ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.88 – 5.44 (m, 2H), 3.01 – 2.80 (m, 1H), 2.76 (s, 4H), 2.42 – 2.22 (m, 2H), 2.17 – 1.92 (m, 3H), 1.90 – 1.62 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 169.2, 126.6, 124.0, 36.6, 26.9, 25.4, 24.6, 23.6.

[0046] 2-(6-aminohexyl)-6-decylpyrrolo[3,4-*f*]isoindole-1,3,5,7(2*H*,6*H*)-tetraone (5). Compound **5** was synthesized from pyromellitic dianhydride, decylamine, and *N*-Boc-1,6-hexanediamine according to methods known in the art.[4]

[0047] 2-Bromoethyl bicyclo[4.2.0]oct-7-ene-7-carboxylate (6). Bicyclo[4.2.0]alkene carboxylic acid was obtained according to the literature with a yield of

62%.[8, 9, 21] The acid (500 mg, 3.3 mmol) was dissolved in 5 mL of CH_2Cl_2 and was cooled in an ice bath when oxalyl chloride (5 mL) was added. The reaction was stirred for 30 min followed by evaporation to yield bicyclo[4.2.0]oct-7-ene-7-carbonyl chloride as off white oil. 2-Bromoethanol (1.2 mg, 10 mmol), EDC•HCl (630 mg, 3.3 mmol), DIPEA (425 mg, 3.3 mmol) were mixed with the acyl chloride oil in 20 mL of CH_2Cl_2. The mixture was stirred for 16 h and was washed with 5% $NaHCO_3$ (3×), 1N HCl (3×) and brine (2×) sequentially and dried over anhydrous $MgSO_4$. The solvent was filtered and removed by evaporation. The crude was subjected to flash silica chromatography (30:70/hexane:CH_2Cl_2) to yield **3** (590 mg, 70%): ^{1}H NMR (500 MHz, CD_2Cl_2): δ 6.91 (d, J = 1.1 Hz, 1H), 4.46 (m, 2H), 3.60 (t, J = 6.1 Hz, 2H), 3.04 (dd, J = 10.3 Hz, J = 5.6 Hz, 1H), 2.77 (td, J = 5.6 Hz, J = 1.1 Hz, 1H), 1.74 (m, 3H), 1.55-1.38 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 151.6, 141.0, 63.0, 40.0, 38.4, 28.6, 23.4, 18.8, 18.2. HRMS (ESI) calcd. for $C_{11}H_{15}BrO_2$ $[M+H]^+$ 258.0255, found 258.0248.

[0048] **Boc-Trp-OH**. Tryptophan (1.00 g, 4.90 mmol) was dissolved in saturated $NaHCO_3$ aqueous solution and cooled in an ice bath. Boc anhydride (2.14 g, 9.80 mmol) was dissolved THF and added dropwise into the tryptophan solution and the reaction was stirred for 10 h. The organic solvent was removed by evaporation and the remaining aqueous solution was washed with CH_2Cl_2 (3×20 mL). The water layer was acidified with 1N HCl to pH=2 and was extracted with CH_2Cl_2 (3×20 mL). The organic layer was dried over $MgSO_4$. The solvent was filtered and removed by evaporation to yield Boc-Trp-OH as a white solid. It was recrystallized in ethyl acetate with hexane and used without further purification.

[0049] **Boc-Trp-alkyn**. BocTrp-OH (500 mg, 1.64 mmol), propagyl amine (82.1 mg, 1.49 mmol), EDC•HCl (347 mg, 1.80 mmol) and DIPEA (233 mg, 1.80 mmol) were mixed in THF. The reaction was stirred for 10 h and THF was removed by evaporation. The residue was dissolved in CH_2Cl_2 and washed sequentially with 5% $NaHCO_3$ (3×), 1N HCl (3×) and brine (2×) and dried over anhydrous $MgSO_4$. The solvent was filtered and removed by evaporation and the crude was subjected to flash silica chromatography (2% MeOH in CH_2Cl_2) to yield Boc-Trp-alkyn (390 mg, 78%). ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.28 (s, 1H), 7.66 (d, J = 7.5 Hz, 1H), 7.38 (d, J = 8.1 Hz, 1H), 7.25 – 7.20 (m, 1H), 7.18 – 7.13 (m, 1H), 7.06 (s, 1H), 6.12 (s, 1H), 5.18 (s, 1H), 4.48 (s, 1H), 3.93 (s, 2H), 3.32 (s, 1H), 3.21 (s, 1H), 2.17 (s, 1H), 1.44 (s, 9H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 171.5, 155.5, 136.2, 127.5, 123.3, 122.3, 119.8, 118.8, 111.3, 110.4, 80.3 79.16, 71.5, 55.0, 29.1, 28.3. ESI (M/Z) $[M+H]^+$ 341.2.

[0050] General Procedure for AROMP

[0051] The NMR tube was evacuated under high vacuum for 15 min, and then was purged with N_2 gas for another 15 min. Under an N_2 atmosphere, a solution of monomer **A** in CD_2Cl_2 (300 μL) was added to the NMR tube. Then a solution of catalyst $(H_2IMes)(3\text{-}Br\text{-}Py)_2(Cl)_2Ru{=}CHPh$ in CD_2Cl_2 (300 μL) was added to the NMR tube. After complete mixing of the solution, the NMR tube was spun for 60 min at an elevated temperature 37°C until the precatalyst had reacted as can be observed by disappearance of ruthenium alkylidene proton at 19 ppm. Monomer **B** (cyclohexene derivative) in CD_2Cl_2 (100 μL) was added to the NMR tube. The reaction was quenched in 8 h with ethyl vinyl ether (50 μL) and the resulting solution was stirred for another 1 h.

[0052] **poly(1-*alt*-2)$_5$**. The reaction was monitored by ^{1}H NMR. The NMR tube was evacuated under high vacuum for 15 min, and then was purged with N_2 gas for another 15 min. Under an N_2 atmosphere, a solution of monomer **1** (29.6 mg, 0.060 mmol) in CD_2Cl_2 (300 μL) was added to the NMR tube. Then a solution of catalyst $(H_2IMes)(3\text{-}Br\text{-}Py)_2(Cl)_2Ru{=}CHPh$ (**4**, 5.3 mg, 6.0 μmol) in CD_2Cl_2 (300 μL) was added to the NMR tube. After complete mixing of the solution, the NMR tube was spun for 60 min at an elevated temperature 37°C until the precatalyst had reacted as can be observed by disappearance of ruthenium alkylidene proton at 19 ppm. Monomer **2** (19.5 mg, 0.030 mmol) in CD_2Cl_2 (100 μL) was added to the NMR tube. The reaction was quenched in 8 h with ethyl vinyl ether (50 μL) and the resulting solution was stirred for another 1 h. The mixture was condensed to give a dark brown oil which was further purified by column chromatography (100:1/CH_2Cl_2:MeOH (methanol)) to yield an orange solid in 55% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.26 – 7.92 (m, 8H), 7.83-7.74 (m, 10H), 7.42 – 7.20 (m, 10H), 6.93 – 6.62 (m, 15H), 5.66 – 5.17 (m, 8H), 4.30 – 3.91 (m, 41H), 3.72 (m, 16H), 3.41 – 3.03 (m, 6H), 2.65 – 1.02 (m, 382H), 0.99 – 0.62 (m, 34H). Mn^{cal}=5748, Mn^{GPC}=3291, Mw^{GPC}=4252, PDI=1.29.

[0053] **poly(1-*alt*-5)$_{10}$**. The reaction was monitored by ^{1}H NMR. The NMR tube was evacuated under high vacuum for 15 min, and then was purged with N_2 gas for another 15 min. Under an N_2 atmosphere, a solution of monomer **1** (29.6 mg, 0.060 mmol) in CD_2Cl_2 (300 μL) was added to the NMR tube. Then a solution of catalyst $(H_2IMes)(3\text{-}Br\text{-}Py)_2(Cl)_2Ru{=}CHPh$ (**4**, 5.3 mg, 6.0 μmol) in CD_2Cl_2 (300 μL) was added to the NMR tube. After complete mixing of the solution, the NMR tube was spun for 60 min at 25 °C until the precatalyst had reacted as can be observed by disappearance of ruthenium alkylidene proton

at 19 ppm. Monomer **3** (26.8 mg, 0.120 mmol) in CD_2Cl_2 (100 μL) was added to the NMR tube. The reaction was quenched in 6 h with ethyl vinyl ether (50 μL) and the resulting solution was stirred for another 1 h. The mixture was condensed to give a dark brown oil which was further purified by column chromatography (100:1/CH_2Cl_2:MeOH) to yield an orange solid in 75% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.84 (m, 20H), 7.32 (m, 20H), 6.98 – 6.56 (m, 30H), 5.33 (m, 13H), 4.11 (s, 3H), 292 – 1.25 (m, 366H), 0.95 (m, 30H). The resulting polymer poly(**1**-*alt*-**3**)$_{10}$ (27.2 mg, 3.7 μmol) was dissolved in dry THF and cooled in an ice bath. EDC•HCl (7.1 mg, 37 μmol), DIEA (9.7 mg, 74 μmol), and 2-(6-aminohexyl)-6-decylpyrrolo[3,4-*f*]isoindole-1,3,5,7(2*H*,6*H*)-tetraone **(5)** (34 mg, 74 μmol) were added. The mixture was stirred for 2 days and then filtered, followed by column chromatography (5:95/acetone/CH_2Cl_2) to yield an orange solid in 20% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.26 – 7.92 (m, 9H), 7.80 (dd, J = 14.4, 6.1 Hz, 20H), 7.42 – 7.18 (m, 20H), 6.93 – 6.62 (m, 30H), 5.66 – 5.17 (m, 12H), 4.30 – 3.91 (m, 59H), 3.72 (dd, J = 14.7, 7.1 Hz, 15H), 3.41 – 3.03 (m, 6H), 2.65 – 0.99 (m, 545H), 0.99 – 0.62 (m, 86H). Mn^{Cal}=10948, Mn^{GPC}=7966, Mw^{GPC}=10221, PDI=1.28.

[0054] **Poly(3-*alt*-4)$_n$.** Under an N_2 atmosphere, **6** (61.8 mg, 0.24 mmol) and **G1** (5.3 mg, 0.006 mmol) were mixed in CD_2Cl_2 (600 μL) in an NMR tube. NMR spectra were acquired at 25°C until the **G1** had completely reacted as determined by the disappearance of its alkylidene α proton signal. Cyclohex-3-enecarbaldehyde **9** (52.7 mg, 0.48 mmol) was added to the NMR tube. When no further propagation occurred, the reaction was quenched with ethyl vinyl ether and stirred for 30 min. The solvent was evaporated, and the alternating copolymer was purified by chromatography on silica gel (97:3/CH_2Cl_2:acetone). ^{1}H NMR (500 MHz, CD_2Cl_2): δ 9.59 (m, 27H), 7.25 (m, 5H), 6.59 (m, 27H), 5.83 (m, 27H), 5.36 (m, 27H), 4.39 (m, 54H), 3.59 (m, 54H), 3.0-1.25 (m, 560H). M_n^{calc} = 9700, M_n^{GPC} = 14823, M_w^{GPC} = 31649, $Đ_M$ = 2.13.

[0055] **Post-polymerization Modification**

[0056] In the first step of post-polymerization modifications the bromide was converted to an azide by mixing poly(**3**-*alt*-**4**)$_n$ and NaN_3 in DMF at 60 °C for 3 hours. Poly(**3'**-*alt*-**4**)$_n$ was obtained after workup. ^{1}H NMR of poly(**3'**-*alt*-**4**)$_n$ showed no significant difference from that of poly(**3**-*alt*-**4**)$_n$, so were the GPC traces. Therefore, we obtained IR spectra which showed a distinctive N_3 vibration signal at around 2200 cm^{-1}.

[0057] Poly(**3′**-*alt*-**4**)$_n$. To a solution of poly(**3**-*alt*-**4**)$_n$ (44.0 mg, 4.51 μmol) in anhydrous DMF (1 mL) was added NaN_3 (23.0 mg, 353 μmol). The mixture was stirred at 60°C for 3 h, and water (5 mL) was added and the mixture was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were washed with water and dried over $MgSO_4$. After filtration, the solvent was evaporated by vacuum to give a yellow oil (31.0 mg, 80 %). ^{1}H NMR (500 MHz, CD_3OD): δ 9.50 (m, 27H), 7.24 (m, 5H), 6.48 (m, 27H), 5.78 (m, 27H), 5.30 (m, 27H), 4.20 (m, 59H), 3.50 (m, 59H), 3.00 - 1.35 (m, 863H). IR (KBr): 3418, 2924, 2854, 2718, 2104, 1716, 1633 cm^{-1}.

[0058] **Poly(3′-*alt*-4-DH)$_n$.** Poly(**3′**-*alt*-**4**)$_n$ (4.7 mg, 0.54 μmol) and dansyl hydrazide (5.5 mg, 21 μmol) were dissolved in THF (2 mL). The mixture was stirred at 65°C for 2 h and the solution was concentrated under vacuum. The residue was purified by LH-20 with eluting solvent as THF. ^{1}H NMR (400 MHz, CD_2Cl_2): δ 8.56 (bs, 47H), 8.42 (bs, 39H), 8.28 (bs, 39H), 8.00 (bs, 47H), 7.54 (bs, 87H), 7.20 (bs, 96H), 6.43 (bs, 27H), 5.68 (bs, 29H), 5.13 (bs, 31H), 4.30 (bs, 137H), 3.46 (bs, 131H), 2.94 (bs, 155H), 2.88 (bs, 243H), 2.86 (s, 172H), 2.80 – 1.01 (m, 1618H). M_n^{calc} = 16369, M_n^{GPC} = 19325, M_w^{GPC} = 34382, $Đ_M$ = 1.78.

[0059] **Poly(3′-Trp-*alt*-4)$_n$.** Under an N_2 atmosphere, poly(**3′** -*alt*-**4**)$_n$ (5.9 mg, 0.67 μmol), Boc-Trp-alkyn (10.6 mg, 25.6 μmol), CuBr (1.7 mg, 0.20 μmol) and PEDTA (6.7 μL) were mixed in THF (1 mL). After stirring for 12 h, the solution was concentrated and the residue was purified by LH-20 with eluting solvent as THF. M_n^{calc} = 16715, M_n^{GPC} = 12472, M_w^{GPC} = 20226, $Đ_M$ = 1.62.

[0060] **Poly(3′ -Trp-*alt*-4-DH)$_n$.** Under an N_2 atmosphere, poly(**3′** -*alt*-**4**)$_n$ (7.0 mg, 0.80 mmol), dansyl hydrazide (8.2 mg, 31 μmol), Boc-Trp-alkyn (12.5 mg, 30.0 mmol), CuBr (2.0 mg, 0.24 mmol) and PEDTA (7.9 μL) were mixed in THF (1 mL). The mixture was stirred at 65°C for 12 h, the solution was concentrated and the residue was purified by LH-20 with eluting solvent as THF. M_n^{calc} = 22491, M_n^{GPC} = 21645, M_w^{GPC} = 38312, $Đ_M$ = 1.747. IR (KBr): 3413, 2929, 2854, 1707, 1690 cm^{-1}.

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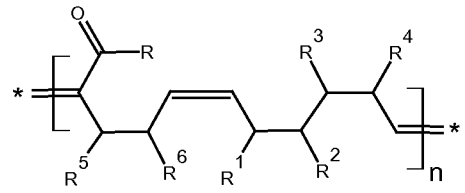
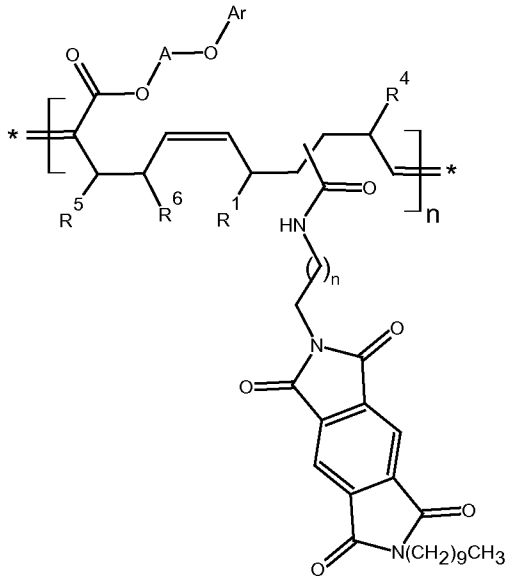
We claim:

1. A method for producing a polymer comprising the repeating unit **(Ia)**, **(Ib)** or **(Ic)**:



(Ia)



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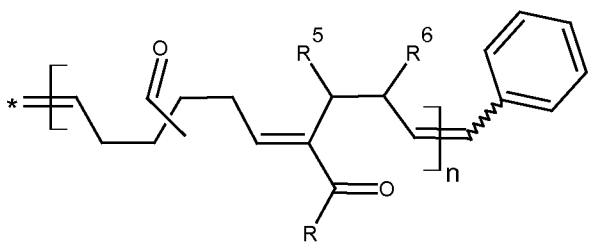
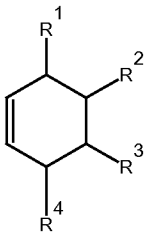
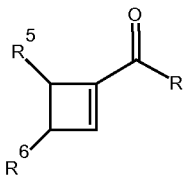


(Ic)

which comprises contacting an olefin of structure **(II)** with a cyclobutene of structure **(III)**



(II)



(III)

in the presence of an olefin metathesis catalyst, wherein

R is selected from the group consisting of H, C_1-C_{20} alkyl, C_2-C_{20} alkenyl, C_3-C_8 cycloalkyl, heterocyclyl, aryl, C_1-C_{20} alkoxy, C_1-C_{20} alkenyloxy, C_3-C_6 cycloalkyloxy, aryloxy, heterocyclyloxy, C_1-C_{20} alkylamino, C_1-C_{20} alkenylamino, C_3-C_8 cycloalkylamino, heterocyclylamino, or arylamino and may be optionally substituted with up to three substituents selected from halo, CN, NO_2, oxo, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic group;

n is a number between 2 and 20;

R^1 through $R^6$are independently selected from the group consisting of H, aldehyde, C_1-C_{20} alkyl, C_2-C_{20} alkenyl, C_3-C_6 cycloalkyl, aryl, heterocyclyl, C_1-C_{20} alkoxy, C_1-C_{20} acyloxy, C_2-C_{20} alkenyloxy, C_3-C_6 cycloalkyloxy, aryloxy, heterocyclyloxy, C_1-C_{20} alkylamino, C_2-C_{20} alkenylamino, C_3-C_8 cycloalkylamino, heterocyclylamino, arylamino, or halogen;

R^1 through R^6 may be taken together to form a 5- to 7-membered ring which may be optionally substituted with up to three substituents selected from halo, CN, NO_2, oxo, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, or a heterocyclic group;

A is a C_2-C_{20} alkyl;

R^7 and R^8 are independently selected from the group consisting of H, C_2-C_6 alkyl, cycloalkyl, cycloalkenyl, alkyl-O-alkyl, alkyl-O-aryl, alkenyl, alkynyl, aralkyl, aryl and a heterocyclic group;

R^7 and R^8 may be taken together with the nitrogen to which they are attached form a 5- to 7-membered ring which may optionally contain a further heteroatom and may be optionally substituted with up to three substituents selected from halo, CN, NO_2, oxo, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic group.

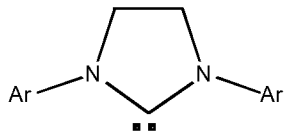
with the proviso that any carbon-carbon double bonds in R or in R^1 through R^6 are essentially unreactive toward metathesis reactions with the catalyst.

2. The method of claim 1, further comprising combining a polymer block comprising repeating units **(Ia)**, **(Ib)** or **(Ic)** into a block copolymer.

3. The method of claim 1, wherein the catalyst is an alkylidene ruthenium complex of formula $(L)(L')X_2Ru=CHR'$ or $(L)_2(L')X_2Ru=CHR'$, wherein
R′ is selected from the group consisting of H, C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_3-C_6 cycloalkyl, and aryl;

L is a ligand selected from the group consisting of trialkyl phosphines, triarylphosphines, tri(cycloalkyl)phosphines, pyridine and substituted pyridine;

L′ is a ligand selected from the group consisting of trialkyl phosphines, triarylphosphines, tri(cycloalkyl)phosphines, pyridine and substituted pyridine, and imidazolin-2-ylidine carbenes of formula



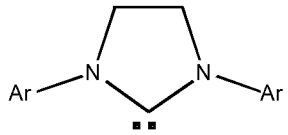
wherein Ar is an ortho-substituted aryl or an aryl; and

X is F, Cl, or Br.

4. The method of claim 2, wherein the catalyst is an alkylidene ruthenium complex of formula $(L)(L')X_2Ru=CHR'$ or $(L)_2(L')X_2Ru=CHR'$, wherein
R′ is selected from the group consisting of H, C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_3-C_6 cycloalkyl, and aryl;

L is a ligand selected from the group consisting of trialkyl phosphines, triarylphosphines, tri(cycloalkyl)phosphines, pyridine and substituted pyridine;

L′ is a ligand selected from the group consisting of trialkyl phosphines, triarylphosphines, tri(cycloalkyl)phosphines, pyridine and substituted pyridine, and imidazolin-2-ylidine carbenes of formula



wherein Ar is an ortho-substituted aryl or an aryl; and

X is F, Cl, or Br.

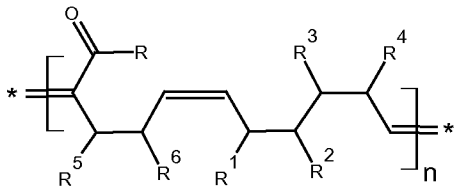
5. The method of claim 3, wherein L is pyridine or substituted pyridine.

6. The method of claim 4, wherein L is 3-bromopyridyl, 3-chloropyridyl or pyridine.

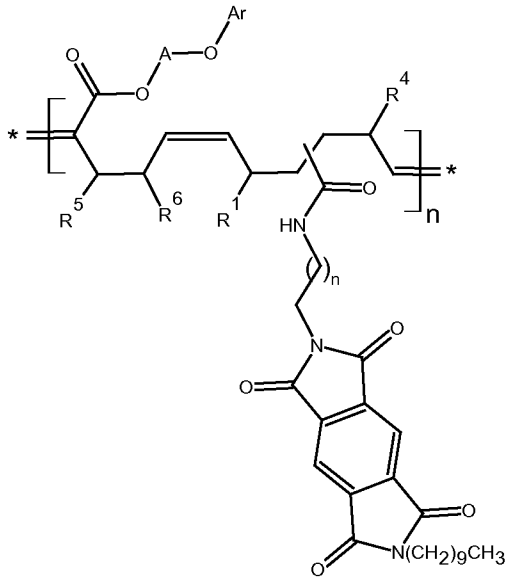
7. The method of any one of claims 3-6, wherein L′ is an imidazolin-2-ylidine carbene and Ar is selected from the group consisting of phenyl, mesityl, 2-methylphenyl, 2-ethylphenyl, 2-isopropylphenyl, 2,3-diisopropylphenyl, 2,6-difluorophenyl, and 3,5-di-*t*-butylphenyl.

8. The method of claim 1 or 2, wherein the catalyst is a molybdenum or tungsten metathesis catalyst.

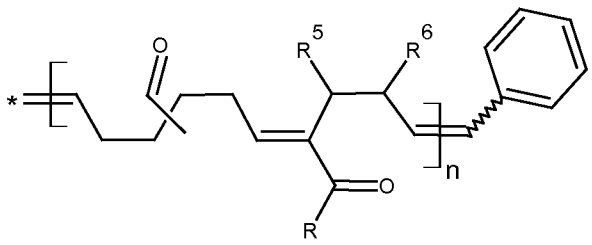
9. A polymer comprising the repeating unit **(Ia)**, **(Ib)** or **(Ic)**:



(Ia)



(Ib)



(Ic)

wherein R is selected from the group consisting of H, C_1-C_{20} alkyl, C_2-C_{20} alkenyl, C_3-C_8 cycloalkyl, heterocyclyl, aryl, C_1-C_{20} alkoxy, C_1-C_{20} alkenyloxy, C_3-C_6 cycloalkyloxy, aryloxy, heterocyclyloxy, C_1-C_{20} alkylamino, C_1-C_{20} alkenylamino, C_3-C_8 cycloalkylamino, heterocyclylamino, or arylamino and may be optionally substituted with up to three substituents selected from halo, CN, NO_2, oxo, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic group;

n is a number between 2 and 20;

R^1 through $R^6$are independently selected from the group consisting of H, aldehyde, C_1-C_{20} alkyl, C_2-C_{20} alkenyl, C_3-C_6 cycloalkyl, aryl, heterocyclyl, C_1-C_{20} alkoxy, C_1-C_{20} acyloxy, C_2-C_{20} alkenyloxy, C_3-C_6 cycloalkyloxy, aryloxy, heterocyclyloxy, C_1-C_{20} alkylamino, C_2-C_{20} alkenylamino, C_3-C_8 cycloalkylamino, heterocyclylamino, arylamino, or halogen;

R^1 through R^6 may be taken together to form a 5- to 7-membered ring which may be optionally substituted with up to three substituents selected from halo, CN, NO_2, oxo, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, or a heterocyclic group;

A is a C_2-C_{20} alkyl;

R^7 and R^8 are independently selected from the group consisting of H, C_2-C_6 alkyl, cycloalkyl, cycloalkenyl, alkyl-O-alkyl, alkyl-O-aryl, alkenyl, alkynyl, aralkyl, aryl and a heterocyclic group;

R^7 and R^8 may be taken together with the nitrogen to which they are attached form a 5- to 7-membered ring which may optionally contain a further heteroatom and may be optionally substituted with up to three substituents selected from halo, CN, NO_2, oxo, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic group.

with the proviso that any carbon-carbon double bonds in R or in R^1 through R^6 are essentially unreactive toward metathesis reactions with the catalyst.

10. The polymer of claim 9, wherein the polymer comprising the repeating unit **(Ia)**, **(Ib)** or **(Ic)** is a cyclic polymer.

11. The polymer of claim 9, wherein polymer comprising the repeating unit **(Ia)**, **(Ib)** or **(Ic)** is a block in a block copolymer.

12. A method of inhibiting microbial growth or inhibiting biofilm formation on a surface comprising the step of contacting one or more microbes with a polymer of claim 9.

13. A method of preparing a therapeutic agent for delivery to a subject comprising combining the therapeutic agent with a polymer of claim 9.

14. The method of claim 13, wherein the therapeutic agent is conjugated to the polymer.

15. The method of claim 13, wherein the therapeutic agent is contained in a micelle comprising the polymer.

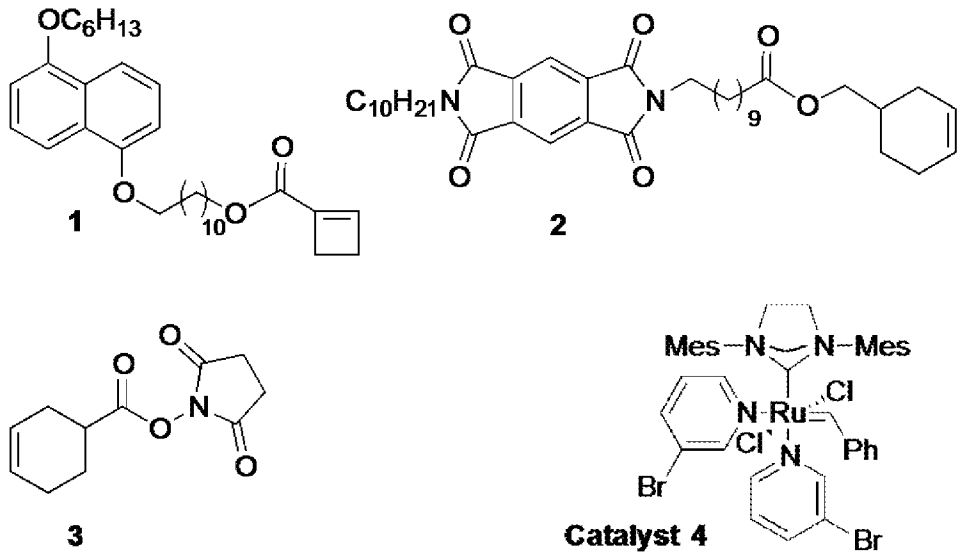

OC6H13
1
C10H21N
2
3
Mes–N N–Mes
Cl
N Ru
Cl N
Ph
Br
Br
Catalyst 4

Fig. 1

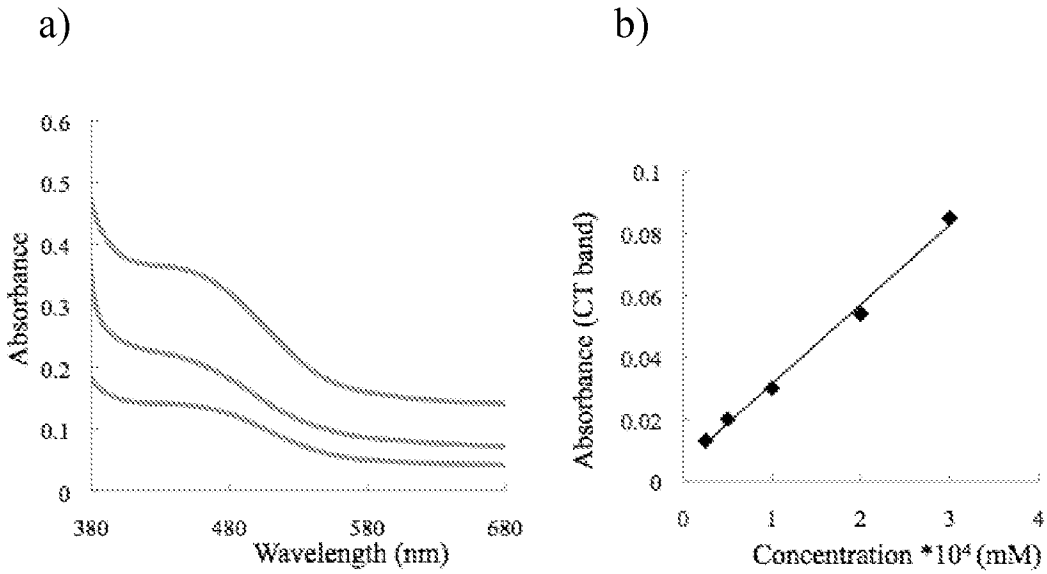

a)
b)
Absorbance
Wavelength (nm)
Absorbance (CT band)
Concentration *10⁴ (mM)

Fig. 2

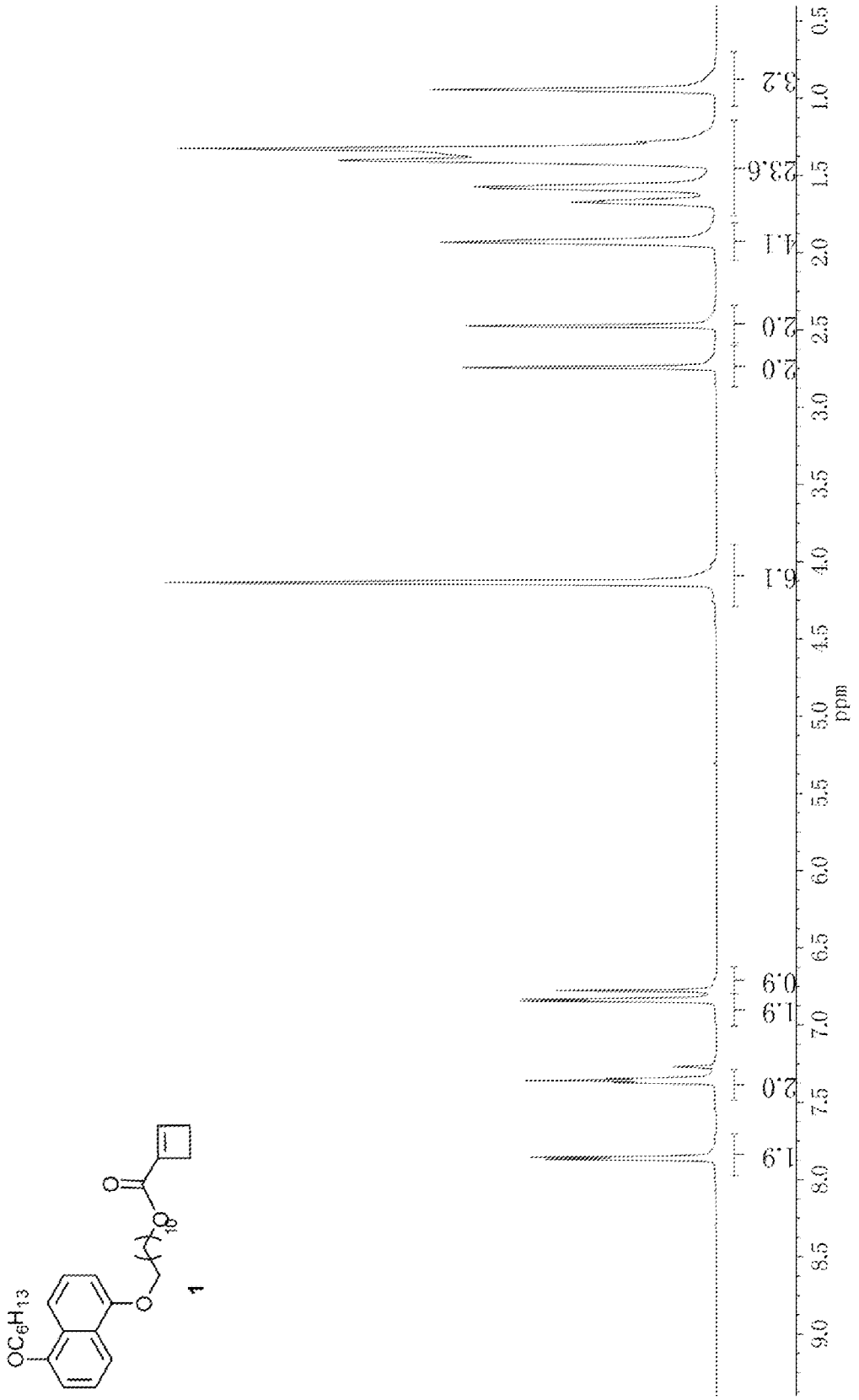

3.2
23.6
4.1
2.0
2.0
6.1
0.9
1.9
2.0
1.9
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
9.0
ppm
OC_6H_{13}
10
1

Fig. 3

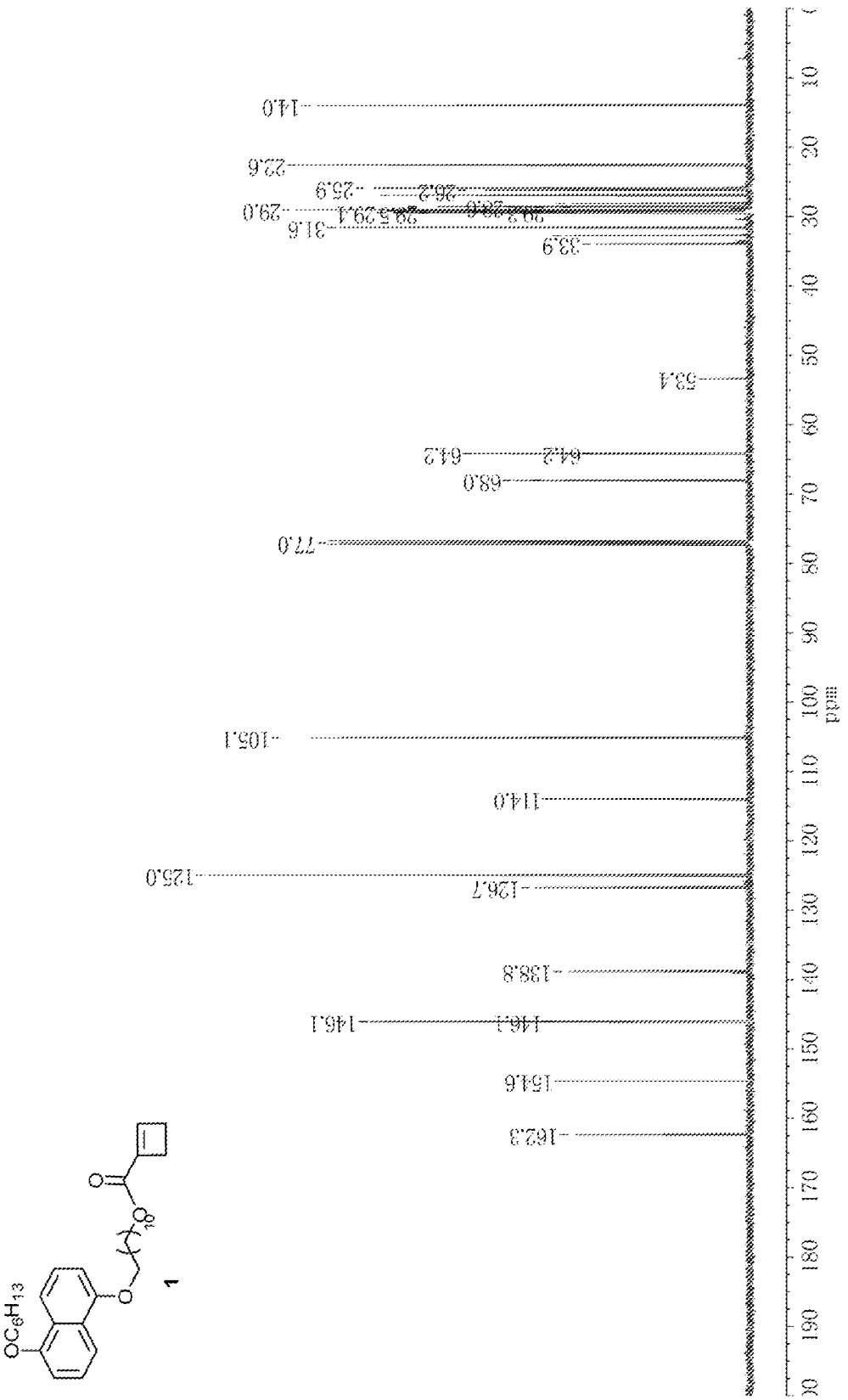

14.0
22.6
25.9
26.2
29.0
29.3
29.4
29.5
31.6
33.9
53.4
64.2
64.2
68.0
77.0
105.1
114.0
125.0
126.7
138.8
146.1
146.1
154.6
162.3
ppm
OC6H13
1

Fig. 4

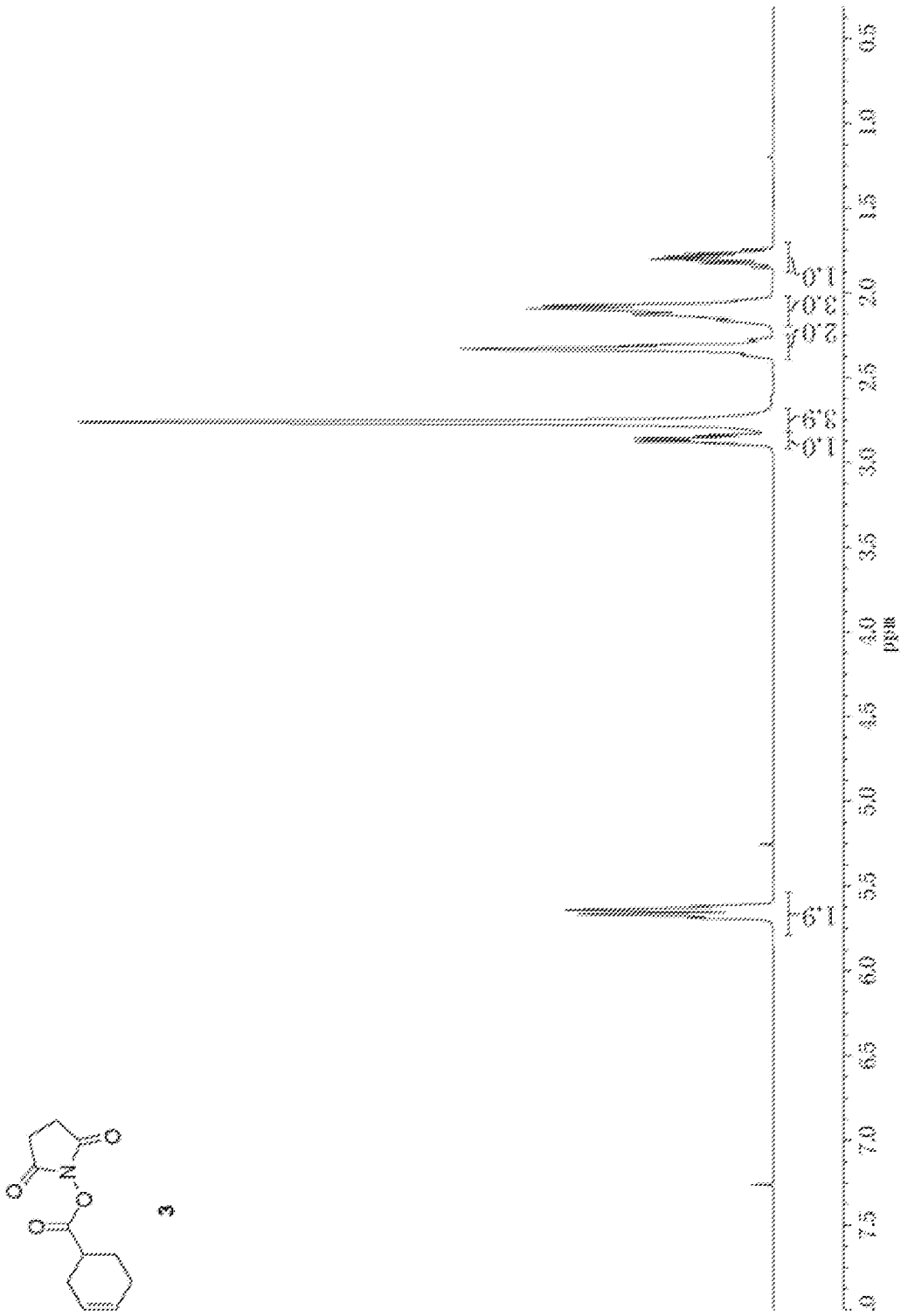


Fig. 5

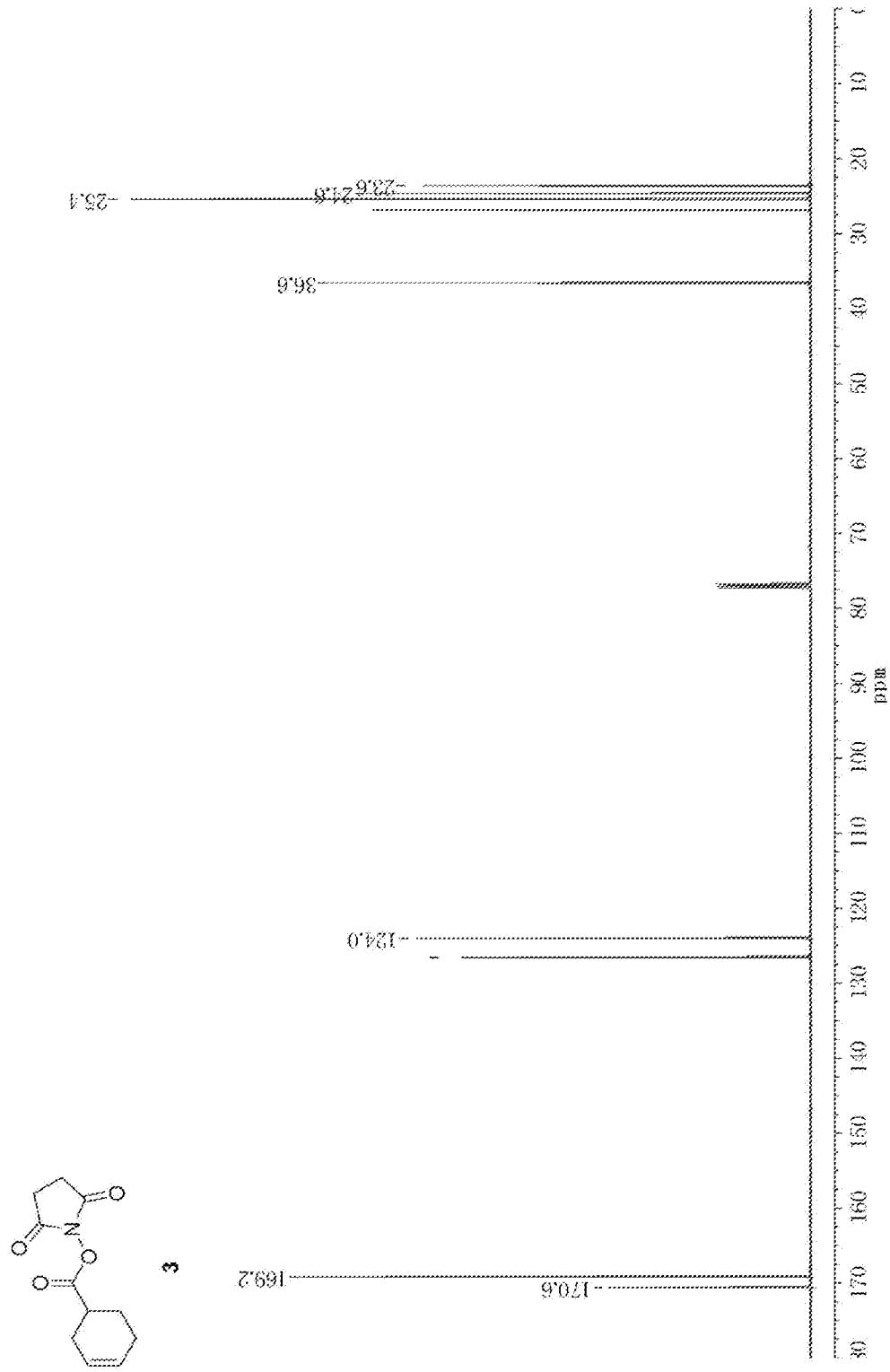


Fig. 6

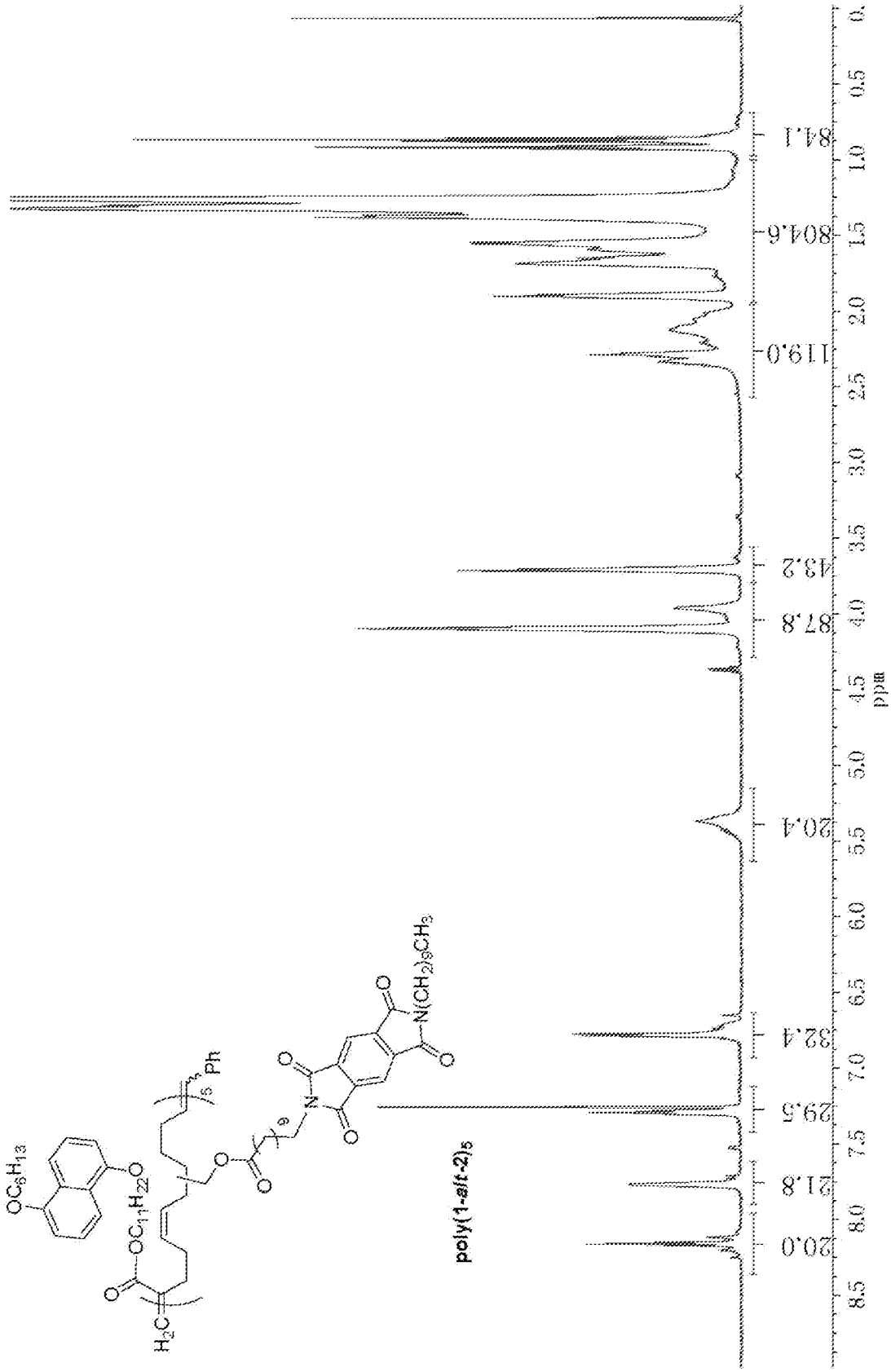


Fig. 7

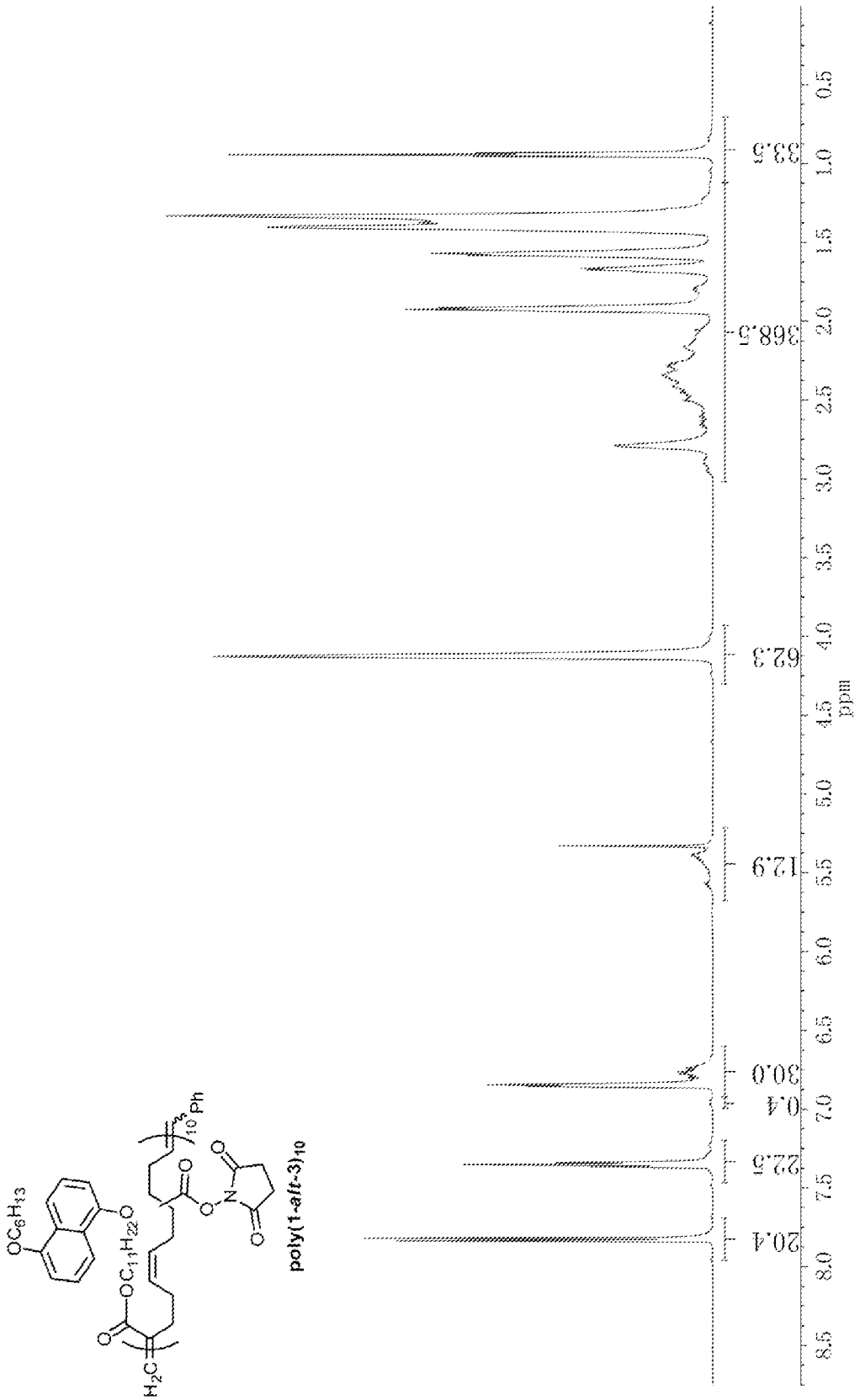


Fig. 8

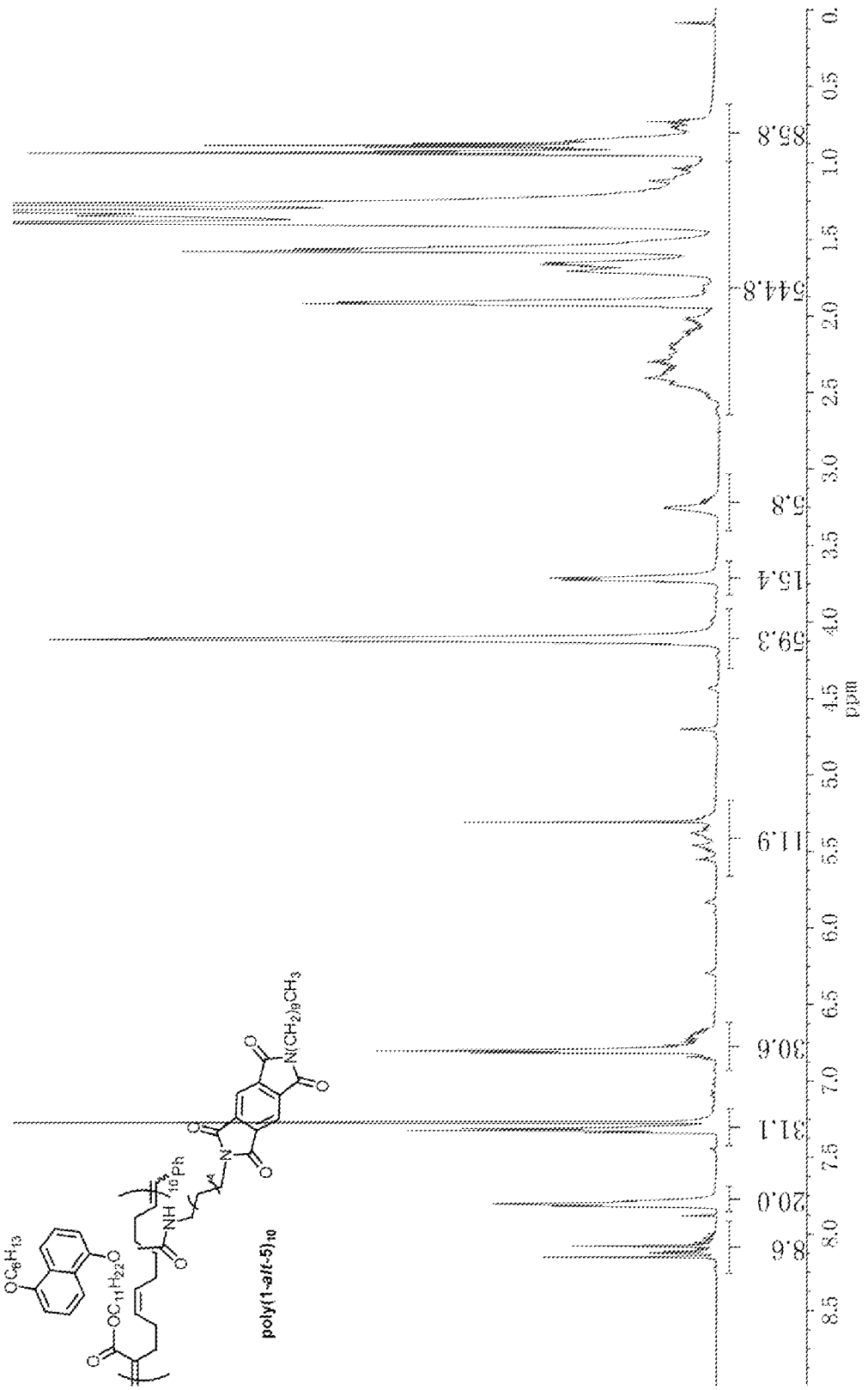

poly(1-alt-5)10
OC8H13
OC11H22O
NH
16Ph
N(CH2)9CH3
85.8
544.8
5.8
15.4
59.3
11.9
30.6
31.1
20.0
8.6
ppm
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.

Fig. 9

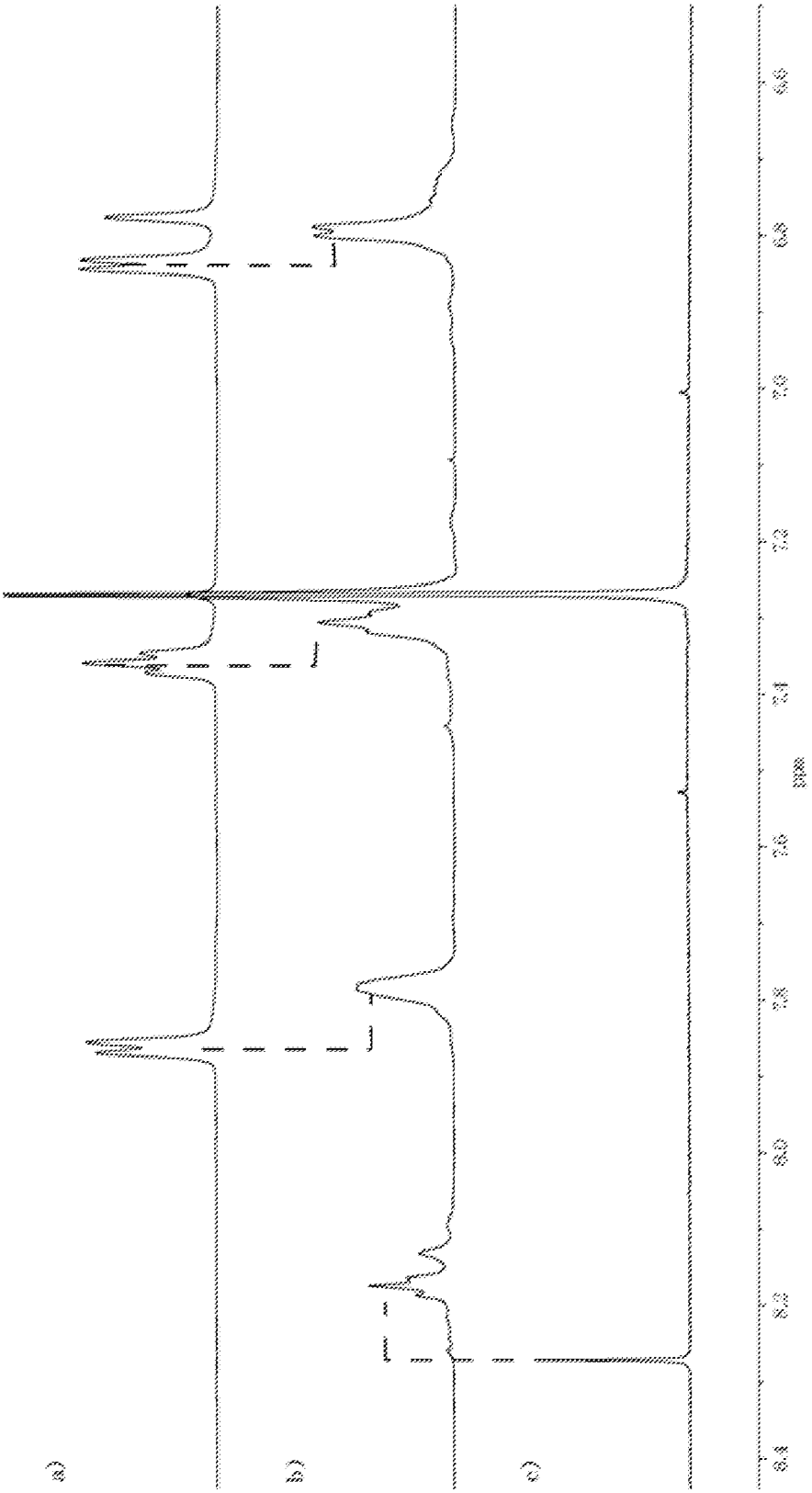
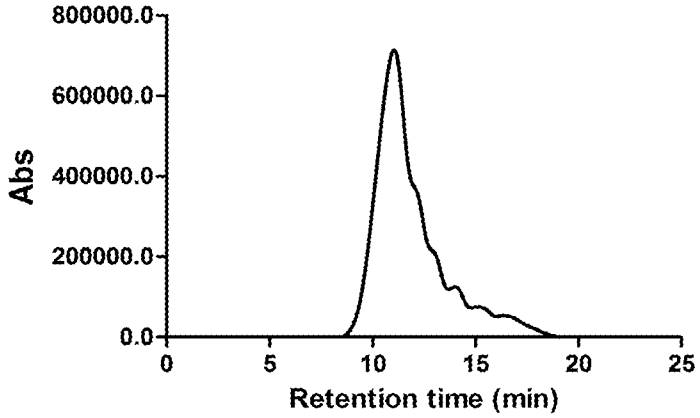


Fig. 10

a)


800000.0
600000.0
400000.0
200000.0
0.0
Abs
0
5
10
15
20
25
Retention time (min)

b)

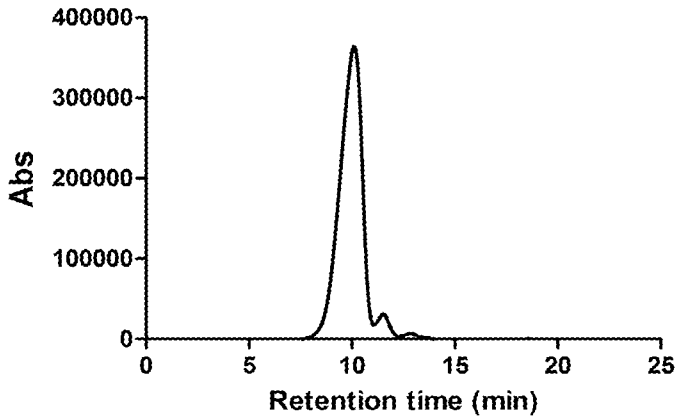
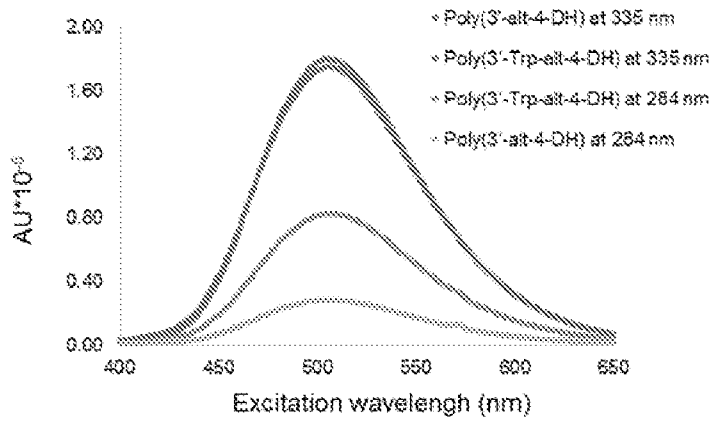
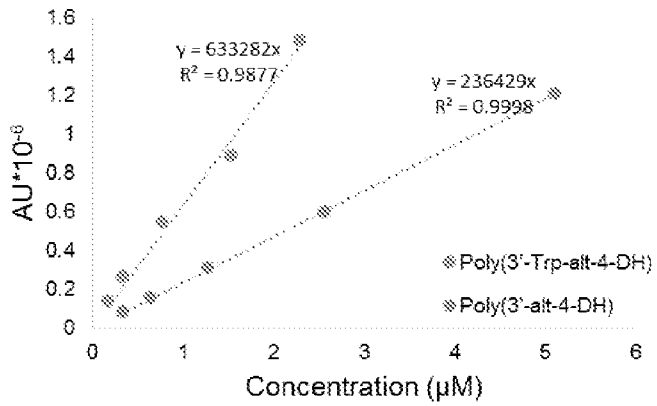

400000
300000
200000
100000
0
Abs
0
5
10
15
20
25
Retention time (min)

Fig. 11

a)


Poly(3'-alt-4-DH) at 335 nm
Poly(3'-Trp-alt-4-DH) at 335 nm
Poly(3'-Trp-alt-4-DH) at 284 nm
Poly(3'-alt-4-DH) at 284 nm
AU*10⁻⁶
2.00
1.60
1.20
0.80
0.40
0.00
400
450
500
550
600
650
Excitation wavelengh (nm)

b)


y = 633282x
R² = 0.9877
y = 236429x
R² = 0.9998
AU*10⁻⁶
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
0
1
2
3
4
5
6
Poly(3'-Trp-alt-4-DH)
Poly(3'-alt-4-DH)
Concentration (μM)

c)

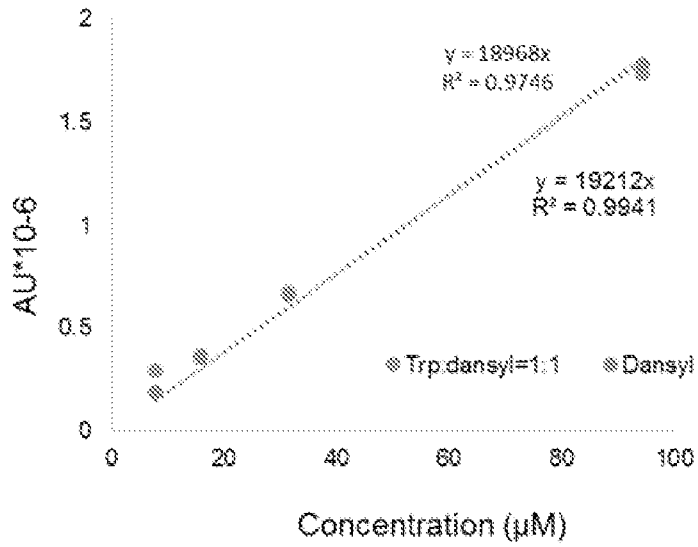

y = 18968x
R² = 0.9746
y = 19212x
R² = 0.9941
AU*10-6
2
1.5
1
0.5
0
0
20
40
60
80
100
Trp:dansyl=1:1
Dansyl
Concentration (μM)

Fig. 12

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 14/47674

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - C08F 299/02; A61K 31/74; C08F 4/80; C08F 232/04 (2014.01)
CPC - A61K 47/48176, C08G 61/08
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: C08F 299/02; A61K 31/74; C08F 4/80; C08F 232/04 (2014.01)
CPC: A61K 47/48176; C08G 61/08

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC: 424/78.08, 525/289, 525/298; 525/268, 525/279, 424/78.31, 525/291, 525/276, 525/278, 525/269, 424/405, 526/171
(See Search Words Below)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PATBASE: Full-text = AU BE BR CA CH CN DE DK EP ES FI FR GB IN JP KR SE TH TW US WO
Google:Patents/Scholar:open-ring polymerization metathesis catalyst ruthenium tungsten ROMP chloropyridine olefin cyclobutene block cyclic copolymers micelle microbial growth inhibitor

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2011/0212046 A1 (SAMPSON et al.) 01 September 2011 (01.09.2011) para [0007]-[0009];[0066]-[0069];[0077]; [0079];[0080];pg 6-7, Scheme V; Figure 5, compound 6b and 6c	1-15

☐ Further documents are listed in the continuation of Box C. ☐

* 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	Date of mailing of the international search report
25 September 2014 (25.09.2014)	29 OCT 2014

Name and mailing address of the ISA/US	Authorized officer:
Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (July 2009)