(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
22 September 2016 (22.09.2016)

WIPO | PCT

(10) International Publication Number
WO 2016/149433 Al

(51) International Patent Classification:
C07D 211/94 (2006.01) *C07C 7/20* (2006.01)
C07D 401/12 (2006.01) *C08F 2/40* (2006.01)
C07D 401/14 (2006.01)

(21) International Application Number:
PCT/US20 16/02273 1

(22) International Filing Date:
17 March 2016 (17.03.2016)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/134,81 1 18 March 2015 (18.03.2015) US

(71) Applicant: **ECOLAB USA INC.** [US/US]; 370 N. Wabasha Street, St. Paul, Minnesota 55102 (US).

(72) Inventors: **MASERE, Jonathan;** c/o Ecolab USA Inc., 7701 Highway 90-A, Sugar Land, Texas 77478 (US). **NEILSON, Andrew;** c/o Ecolab USA Inc., 7701 Highway 90-A, Sugar Land, Texas 77478 (US). **WATSON, Russell;** c/o Ecolab USA Inc., 7701 Highway 90-A, Sugar Land, Texas 77478 (US).

(74) Agent: **DEMASTER, Eric E.;** 655 Lone Oak Drive - ESC-F7, Eagan, Minnesota 55121 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available):* AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available):* ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17 :

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.1 7(H))*

— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.1 7(in))*

Published:

— *with international search report (Art. 21(3))*

WO 2016/149433 A1

(54) Title: THE USE OF STABLE LIPOPHILIC HYDROXYL AMINE COMPOUNDS FOR INHIBITING POLYMERIZATION OF VINYL MONOMERS

(57) Abstract: The present invention generally relates to compounds and methods for inhibiting the radical polymerization of unsaturated compounds, particularly vinyl monomers. More particularly, it relates to the use of stable hydroxyl amines to inhibit the polymerization of unsaturated compounds (e.g., vinyl monomers) wherein said stable hydroxylamine is soluble in organic solvents, particularly hydrocarbon solvents consisting of unsaturated and, therefore, polymerizable constituents.

THE USE OF STABLE LIPOPHILIC HYDROXYLAMINE COMPOUNDS FOR INHIBITING POLYMERIZATION OF VINYL MONOMERS

CROSS-REFERENCE TO RELATED APPLICATION

[0001] This application claims priority to U.S. Patent Application Serial No. 62/134,811 filed on March 18, 2015, the disclosure of which is incorporated herein by reference in its entirety.

FIELD OF THE INVENTION

[0002] The present invention generally relates to compounds and methods for inhibiting the radical polymerization of unsaturated compounds, particularly vinyl monomers. More particularly, it relates to the use of lipophilic N,N-disubstituted hydroxyl amines to inhibit the polymerization of unsaturated compounds (e.g., vinyl monomers) soluble in organic solvents, particularly hydrocarbon solvents.

BACKGROUND OF THE INVENTION

[0003] Unsaturated compounds, particularly vinyl monomers, can undesirably polymerize at various stages of their manufacture, processing, handling, storage, and use. Vinyl monomers can undergo self-initiated polymerization at elevated temperatures even in the absence of polymerization promoters. Thus, undesired thermal polymerization can be a problem during the purification of vinyl aromatic monomers and during sudden process shutdowns. Undesirable polymerization results in product loss because the valuable monomer end product is consumed in the undesired side reaction. Moreover, polymerization reduces production efficiency as the polymer is deposited on process equipment. This fouling of process equipment may require a shutdown to remove the undesired polymer by physical methods.

[0004] The stable free radical, 4-hydroxy-2,2,6,6-i<?ira-methylpiperidinoxy (HTEMPO), has been used extensively to control free radical polymerization of reactive monomers during the purification, handling, transportation and storage. However, to improve its efficacy as an inhibitor, there are two alternatives. Firstly, the dose of HTEMPO can be increased. However, as the concentration is increased, the dissolved HTEMPO will crystallize especially if the ambient temperature under which the solution is used or stored falls. HTEMPO can also crystallize if the solvency of the hydrocarbon media decreases, for instance, a solution comprising aromatic solvents will have a lower

solvency when it comes into contact with aliphatic media. Owing to the low solubility of HTEMPO in aliphatic media, the introduction of an aromatic-based solvent of HTEMPO will result in the precipitation of HTEMPO thereby resulting in the plugging of quills and transfer lines.

[0005] Secondly, the conversion of HTEMPO to its hydroxylamine, HTEMPOL, is the other alternative to increasing its polymer inhibiting efficiency. Unlike HTEMPO that is soluble in aromatic hydrocarbon solvents, HTEMPOL is sparingly soluble in hydrocarbon solvents. In applications that involve aqueous media, the water-soluble HTEMPOL can be used with nominal risk of precipitation whereas it will precipitate in hydrocarbon media. Consequently, the use of HTEMPOL as an inhibitor is restricted to stopping premature polymerization in aqueous media.

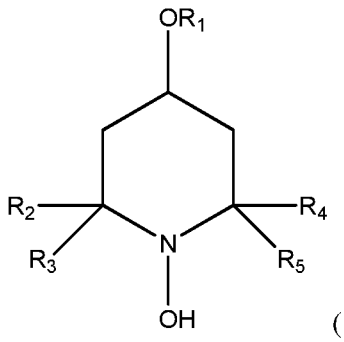
[0006] In prior art, hydrocarbon-soluble hydroxylamines have been used as inhibitors. Due to the presence of hydrogen substituents of the a-carbon atoms relative to the hydroxylamine functional group, said hydroxylamines are therefore unstable. At high operational temperatures associated with the purification and other processes involving vinylic monomers, these unhindered or partially hindered hydroxylamines decompose to yield contaminant byproducts, namely; aldehydes and primary hydroxylamines. As an example, N,N-diethylhydroxylamine will decompose to acetaldehyde and ethylhydroxylamine.

[0007] More particularly, this invention addresses inhibition of polymerization in units typically associated with hydrophobic vinylic monomers such as in distillation towers where aqueous-based inhibitors are not very effective or the poor solubilities of the highly polar inhibitors result in the precipitation or recrystallization of said inhibitors when mixed with hydrocarbon media. In equipment in which a hydrocarbon phase is in contact with an aqueous phase, the currently used hydrophilic hydroxylamines preferentially partition into the aqueous phase rather than the hydrocarbon phase. By contrast, the organic-soluble vinylic species that are liable to polymerization partition into the hydrocarbon phase. Owing to this partitioning tendency, the prior art hydroxylamines are not effective polymerization inhibitors.

[0008] Thus, a need exists for a hydrocarbon soluble, stable free-radical scavenger.

SUMMARY OF THE INVENTION

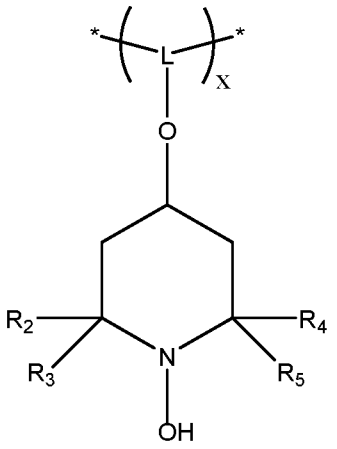
[0009] One aspect of the present invention is a hydroxylamine compound having the structure of Formula 1:



(1)

wherein R_1 is alkyl, aryl, alkaryl, heterocyclo, or -C(0)R_6; R_2, R_3, R_4, and R_5, are independently selected from the group consisting of alkyl, alkylaryl, aryl, heteroaryl, or R_2 and R_3 or R_4 and R_5 together can form a spiro ring; and R_6 is alkyl, alkylaryl, aryl, or heteroaryl.

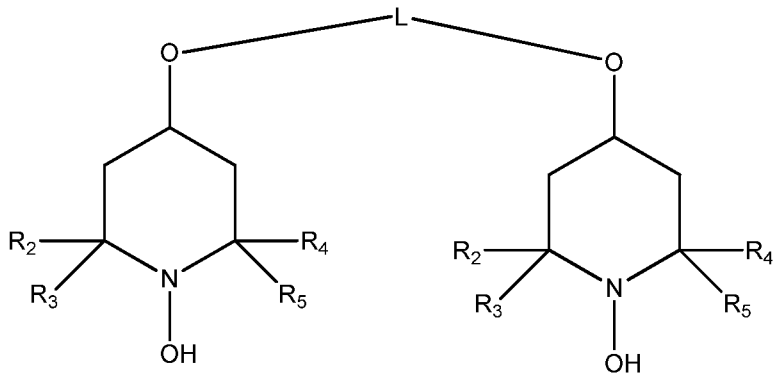
[001 0] Another aspect of the invention is a hydroxylamine oligomer having the structure of Formula 2:



(2)

wherein L is a linker comprising alkylene, arylene, alkarylene, heterocyclo, or diacyl; R_2, R_3, R_4, and R_5, are independently alkyl, alkylaryl, aryl, heteroaryl, or R_2 and R_3 or R_4 and R_5 together can form a spiro ring; and x is an integer greater than 2.

[001 1] Yet another aspect of the invention is a hydroxylamine dimer compound having the structure of Formula 3:



(3)

wherein L is a linker comprising alkylene, arylene, alkarylene, heterocyclo, or diacyl; and R2, R_3, R_4, and R5, are independently alkyl, alkylaryl, aryl, heteroaryl, or R2 and R_3 or R_4 and R_5 together can form a spiro ring.

[0012] Yet another aspect of the invention is a method for inhibiting polymerization of an unsaturated compound comprising an unsaturated carbon-carbon bond comprising contacting the unsaturated compound with the hydroxylamine compound of Formula 1 or the hydroxylamine dimer compound of Formula 2.

[0013] Other objects and features will be in part apparent and in part pointed out hereinafter.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

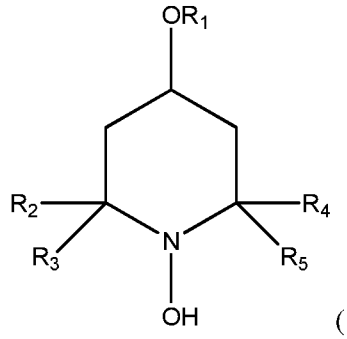
[0014] In place of hydroxylamines that are insoluble in hydrocarbon media and that are unstable at high process temperatures, hydrocarbon-soluble and stable hydroxylamines are disclosed as more efficient scavengers of free radical species that cause unwanted polymerization in hydrocarbon media. Alternative hydroxylamines that are preferentially soluble in hydrocarbon media and not prone to decomposing to contaminants can be used either as stand-alone inhibitors or in combination with other polymerization-inhibiting compounds. These compounds and combinations show highly effective polymer inhibition efficacy.

[0015] The present invention is directed to hydroxylamine compounds, hydroxylamine oligomeric compounds, and methods of use of the hydroxylamine and hydroxylamine oligomeric compounds for inhibiting polymerization of an unsaturated compound comprising an unsaturated carbon-carbon bond in hydrocarbon streams. The unsaturated compound is in contact with an effective amount of a hydroxylamine compound of Formula 1 or a hydroxylamine oligomer of Formula 2 or a dimer compound of Formula 3. Unsaturated hydrocarbons are reactive and liable to undesirable

polymerization under typical processing, transportation and storage conditions. The undesired polymerization of the unsaturated compounds is costly due to the resultant loss of the desired monomer product. Thus, methods for inhibiting this unwanted polymerization are beneficial for said hydrocarbon processes.

[001 6] The hydroxylamines of Formulae 1, 2, and 3 are stable to decomposition at temperatures they are typically exposed to during processing of the unsaturated compounds where they are acting as polymerization inhibitors. The hydroxylamines of Formulae 1, 2, and 3 are also soluble in the hydrocarbons at the concentrations effective for this method. This means that they do no precipitate or crystallize in the system.

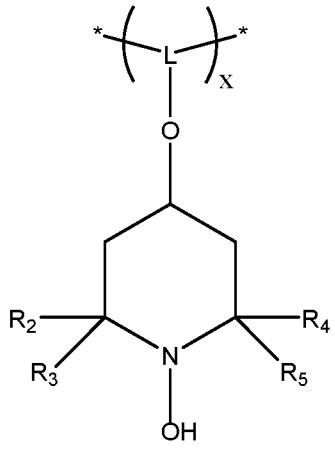
[001 7] One aspect of the invention is a hydroxylamine compound having the structure of Formula 1:



(1)

wherein R_i is alkyl, aryl, alkaryl, heterocyclo, or -C(0)R_6; R2, R3, R_4, and R5, are independently selected from the group consisting of alkyl, alkylaryl, aryl, heteroaryl, or R_2 and R_3 or R_4 and R_5 together can form a spiro ring; and R_6 is alkyl, alkylaryl, aryl, or heteroaryl.

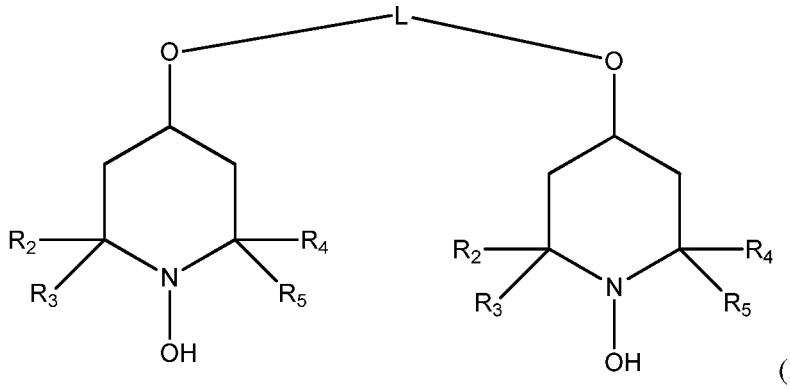
[001 8] Another aspect of the invention is a hydroxylamine oligomer having the structure of Formula 2:



(2)

wherein L is a linker comprising an alkylene, arylene, alkarylene, heterocyclo, or diacyl; R2, R_3, R_4, and R_5 are independently selected from the group consisting of alkyl, alkylaryl, aryl, heteroaryl, or R2 and R_3 or R_4 and R_5 together can form a spiro ring; R_6 is alkyl, alkylaryl, aryl, heteroaryl; and x is an integer greater than 2.

[001 9] Yet another aspect of the invention is a hydroxylamine dimer compound having the structure of Formula 3:



(3)

wherein L is a linker comprising an alkylene, arylene, alkarylene, heterocyclo, or diacyl; R2, R_3, R_4, and R_5, are independently selected from the group consisting of alkyl, alkylaryl, aryl, heteroaryl, or R_2 and R_3 or R_4 and R_5 together can form a spiro ring.

[0020] A further aspect of the invention is a method for inhibiting polymerization of an unsaturated compound comprising an unsaturated carbon-carbon bond comprising contacting the unsaturated compound with the hydroxylamine compound of Formula 1 or the hydroxylamine dimer compound of Formula 2.

[0021] For the compounds of Formulae 1 and 2 and their use in the methods described herein, R_i can be an alkyl, or alkylaryl group of from about 1 to about 18 carbon atoms.

[0022] Further, the compounds of Formulae 1 and 2 and the methods described herein, can have R_i be propyl, butyl, pentyl, or hexyl. Preferably, R_i can be n-butyl, sec-butyl, isobutyl, or tert-butyl.

[0023] Also, the compounds of Formulae 1 and 2 can have R_i be C_i-$C_{i\ 8}$ alkaryl. Preferably, R_1 is benzyl.

[0024] Further, for the compounds of Formulae 1 and 2 and their use in the methods described herein, R_2, R_3, R_4, and R_5, can independently be C1-C9 alkyl. Preferably, R_2, R_3, R_4, and R_5, can independently be C1-C3 alkyl.

[0025] Additionally, for the compounds of Formulae 1 and 2, R_2, R_3, R_4, and R_5, can independently be haloalkyl.

[0026] The compounds of Formulae 1 and 2 can have R_i be n-butyl and R_2 R_3, R_4, and R_5 be methyl.

[0027] Alternatively, compounds of Formulae 1 and 2 can have R_i be benzyl and R_2 R_3, R_4, and R_5 be methyl.

[0028] For the compound of Formula 1, R_6 can be alkyl; preferably, R_6 can be methyl, ethyl, propyl, or butyl.

[0029] For the polymer or oligomer of Formula 2, x can be from 2 to 100; from 2 to 50; or from 2 to 10.

[0030] For the polymer or oligomer of Formula 2, x is selected so that the polymer or oligomer of Formula 2 does not precipitate or crystallize in a hydrocarbon stream.

[0031] For the methods of inhibiting polymerization using the hydroxylamine compound of Formula 1 or the hydroxylamine dimer compound of Formula 2, the unsaturated compound can be a vinyl monomer.

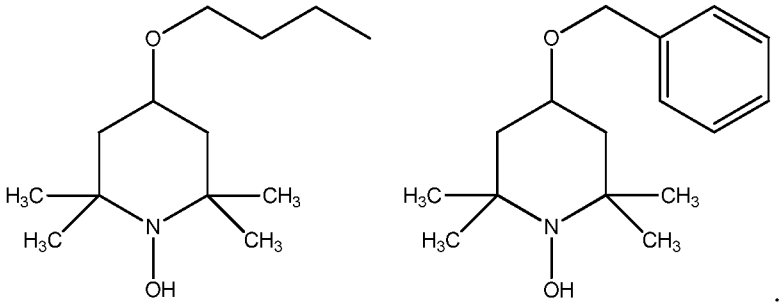
[0032] Further, the unsaturated compound can be ethylene, propylene, acetylene, styrene, vinyl chloride, vinyl alcohol, vinyl acetate, acrylonitrile, acrylate esters, methacrylate esters, acrylic acid, (meth)acrolein, acrolein, butadiene, indene, divinylbenzene, isoprene, acetylene, vinyl acetylene, cyclopentadiene, or a combination thereof. Preferably, the unsaturated compound can comprise acrylate esters, methacrylate esters, styrene, or a combination thereof.

[0033] The polymerization inhibition method can stabilize and inhibit polymerization of an unsaturated compound during a manufacture, a purification, transportation or a storage process.

[0034] The polymerization inhibition method can also stabilize and inhibit polymerization of an unsaturated compound in a primary fractionation process, light ends

fractionation, non-aromatic halogenated vinyl fractionation, process-gas compression, butadiene extraction, propane dehydrogenation, diesel and petrol fuel stabilization, olefin metathesis, styrene purification, hydroxyhydrocarbon purification, or delays the polymerization of resins and compositions comprising ethylenically unsaturated species. Preferably, the polymerization inhibition method can stabilize and inhibit polymerization of an unsaturated compound in a butadiene extraction or styrene purification.

[0035] Preferably for the hydroxylamine compounds of Formula 1, R_1 is n-butyl or benzyl and R_2, R_3, R_4, and R_5 are methyl. These compounds have the structures:



[0036] Methods for preparing compounds of Formulae 1 and 2 are well known in the art and will be apparent to the skilled person. As an illustrative example, 4-alkoxy-2,2,6,6-tetramethyl-l-piperidinols are prepared. This is achieved in a two-step process starting with commercially available 4-hydroxy-TEMPO. In the first step, 4-OH-TEMPO is reacted with an alkylating agent (e.g., n-butyl bromide or benzyl chloride) in the presence of base to give the corresponding 4-alkoxy TEMPO derivative. In the second step, the nitroxide radical is treated with a reducing agent, (e.g., hydrazine hydrate or N,N-diethylhydroxylamine) to give a 4-alkoxy TEMPO hydroxylamine (4-alkoxy TEMPOH).

[0037] Another aspect of the invention is a composition comprising a compound of Formula 1 and a solvent. Suitable organic solvents include pentane, heptane, hexane, benzene, ethylbenzene, toluene, or a combination thereof. The solvents are not restricted to the above-mentioned examples.

[0038] The composition can comprise one or more additional polymerization inhibitors. Compounds that are suitable as additional polymerization inhibitors in the inventive composition include phenols, alkylated phenols, nitrophenols, nitrosophenols, quinones, hydroquinones, quinone ethers, quinone methides, amines, hydroxylamines, and phenothiazines.

[0039] The polymerization inhibitor compositions described herein can be introduced into the monomer to be protected by any conventional method. It can be added

as a concentrate solution in suitable solvents just upstream of the point of desired application by suitable means. In addition, these compounds can be injected separately into the distillation train with the incoming feed, or through separate entry points providing efficient distribution of the inhibitor composition. Since the inhibitor is gradually depleted during operation, it is generally necessary to maintain the appropriate amount of the inhibitor in the distillation apparatus by adding inhibitor during the course of the distillation process. This addition may be carried out either on a generally continuous basis or by intermittently charging inhibitor into the distillation system if the concentration of inhibitor is to be maintained above the minimum required level.

[0040] The effective amount of a compound of Formulae 1, 2, and 3 can be from about 0.1 mmolal to 5 mmolal, from about 0.1 mmolal to 4 mmolal, from about 0.1 mmolal to 3 mmolal, from about 0.1 mmolal to 2 mmolal, from about 0.2 mmolal to 5 mmolal, from about 0.2 mmolal to 4 mmolal, from about 0.2 mmolal to 3 mmolal; preferably, from about 0.2 mmolal to about 2 mmolal.

[0041] The compounds of Formula 1 can be prepared by adding 4-hydroxy-2,2,6,6-tetraalkylpiperidin-l-oxyl to a non-protic polar solvent such as tetrahydrofuran (THF). Then, to the resultant solution, a base was added followed by stirring of the mixture at room temperature. Then, a solution of an alkyl halide in a non-protic polar solvent such as THF was added dropwise into the flask. The reaction mixture was heated until the reaction was completed. Deionized water was added and the layers separated. The organic fraction was isolated, dried over anhydrous magnesium sulfate, and the solvent removed *in vacuo.* This product was added to an aromatic solvent such as toluene and a reducing agent, such as hydrazine hydrate was added and the mixture was heated. Then, the reaction was cooled and washed with water. The organic fraction was isolated, dried over anhydrous magnesium sulfate, and the solvent removed *in vacuo* to give 4-alkoxy-2,2,6,6-tetraalkylpiperidin-l-ol.

[0042] To prepare oligomers and dimers of Formulae 2 and 3, the alkyl halide can be substituted with an alkyl dihalide or another reactant having two or more reactive groups. Additionally, a polymer having a reactive group could be used to react with the adding 4-hydroxy-2,2,6,6-tetraalkylpiperidin-l-oxyl to form a polymer of Formula 2.

[0043] Unless otherwise defined herein, "TEMPO" refers to 2,2,6,6-tetramethylpiperidin- 1-oxyl.

[0044] "4-OH-TEMPO" refers to 4-hydroxy-TEMPO, otherwise known as 4-hydroxy-2,2,6,6-tetramethylpiperidin-l-oxyl or TEMPOL.

[0045] "4-OH-TEMPOH" refers to 4-hydroxy-TEMPO hydroxylamine, otherwise known as 2,2,6,6-tetramethylpiperidin-l,4-diol.

[0046] "4-Bu-TEMPOH" refers to 4-butoxy-TEMPO hydroxylamine, otherwise known as 4-butoxy-2,2,6,6-tetramethyl-l-piperidinol.

[0047] "4-Bn-TEMPOH" refers to 4-benzyloxy TEMPO hydroxylamine, otherwise known as 4-benzyloxy-2,2,6,6-tetramethyl-l-piperidinol.

[0048] Unless otherwise indicated, an alkyl group as described herein alone or as part of another group is an optionally substituted linear saturated monovalent hydrocarbon substituent containing from one to sixty carbon atoms and preferably one to thirty carbon atoms in the main chain or eight to thirty carbon atoms in the main chain, or an optionally substituted branched saturated monovalent hydrocarbon substituent containing three to sixty carbon atoms, and preferably eight to thirty carbon atoms in the main chain. Examples of unsubstituted alkyl groups include methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, i-pentyl, s-pentyl, t-pentyl, and the like.

[0049] "Cycloalkyl" refers to cyclic alkyl groups of from 3 to 10 carbon atoms having single or multiple cyclic rings including fused, bridged, and spiro ring systems. Examples of suitable cycloalkyl groups include, for instance, adamantyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclooctyl, bicyclo[2.2.2]octanyl and the like. Representative cycloalkyl groups include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[2.2.1]heptanyl, bicyclo[2.2.2]octanyl, and the like.

[0050] The terms "aryl" or "ar" as used herein alone or as part of another group (e.g., aralkyl or alkaryl) denote optionally substituted homocyclic aromatic groups, preferably monocyclic or bicyclic groups containing from 6 to 12 carbons in the ring portion, such as phenyl, biphenyl, naphthyl, substituted phenyl, substituted biphenyl or substituted naphthyl. Phenyl and substituted phenyl are the more preferred aryl. The term "aryl" also includes heteroaryl.

[0051] The term "substituted" as in "substituted aryl," "substituted alkyl," and the like, means that in the group in question (i.e., the alkyl, aryl or other group that follows the term), at least one hydrogen atom bound to a carbon atom is replaced with one or more substituent groups such as hydroxy (-OH), alkylthio, phosphino, amido (-$\mathbf{CON(R_AXR_B)}$, wherein $\mathbf{R_A}$ and $\mathbf{R_B}$ are independently hydrogen, alkyl, or aryl), **amino**(-$\mathbf{N(R_A)(R_B)}$, wherein $\mathbf{R_A}$ and $\mathbf{R_B}$ are independently hydrogen, alkyl, or aryl), halo (fluoro, chloro, bromo, or iodo), silyl, nitro (-$N0_2$), an ether (-$\mathbf{OR_A}$ wherein $\mathbf{R_A}$ is alkyl or aryl), an ester (-$\mathbf{OC(0)R_A}$ wherein $\mathbf{R_A}$ is alkyl or aryl), keto (-$\mathbf{C(O)R_A}$ wherein $\mathbf{R_A}$ is alkyl or aryl),

heterocyclo, and the like. When the term "substituted" introduces a list of possible substituted groups, it is intended that the term apply to every member of that group. That is, the phrase "optionally substituted alkyl or aryl" is to be interpreted as "optionally substituted alkyl or optionally substituted aryl."

[0052] "Alkaryl" means an aryl group attached to the parent molecule through an alkylene group. The number of carbon atoms in the aryl group and the alkylene group is selected such that there is a total of about 6 to about 18 carbon atoms in the alkaryl group. A preferred alkaryl group is benzyl.

[0053] "Haloalkyl" refers to an alkyl group as defined herein wherein one of more hydrogen atoms on the alkyl group have been substituted with a halogen. Representative haloalkyl groups include fluromethyl, difluoromethyl, trifluoromethyl, fluoroethyl, difluoroethyl, trifluoroethyl, tetrafluoroethyl, perfluoroethyl, and the like.

[0054] "Vinyl monomer" refers to a monomer comprising at least one carbon-carbon double bond. The monomer can be substituted with various groups, such as acids (e.g., acrylic acid), esters (e.g., acrylate esters), halogen (e.g., vinyl chloride), aryl (e.g., styrene, vinyl toluene, divinylbenzene), cyano (e.g., acrylonitrile), and acetoxy (e.g., vinyl acetate). The monomer can be conjugated (e.g., butadiene, cyclopentadiene, vinyl acetylene, indene, and the like).

[0055] A polymerization "inhibitor" refers to a composition of matter that is able to scavenge radicals in a radical polymerization process. Inhibitors can be used to stabilize monomers and prevent their polymerization or quench polymerization when a desired conversion is achieved. They can also be used to regulate or control the kinetics of a polymerization process.

[0056] Having described the invention in detail, it will be apparent that modifications and variations are possible without departing from the scope of the invention defined in the appended claims.

EXAMPLES

[0057] The foregoing may be better understood by reference to the following examples, which are presented for purposes of illustration and are not intended to limit the scope of the invention.

[0058] All reactions were performed under an atmosphere of nitrogen unless stated otherwise. The reagents 4-hydroxy-TEMPO, potassium tert-butoxide, 1-bromobutane, and benzyl chloride were purchased from Sigma-Aldrich.

Example 1: Synthesis of 4-butQxy-2,2,6,6-tetrainethylpiperidin-l-ol (4-Bu-TEMPOH)

[0059] To a round-bottomed flask equipped with a stir bar was added 4-hydroxy-2,2,6,6-tetramethylpiperidin-l-oxyl ("4-hydroxy-TEMPO", 26.2 g, 152 mmol) and 700 mL of tetrahydrofuran (THF). To the resultant solution, 20.5 g of potassium i<?ri-butoxide (20.5 g, 183 mmol) was added followed by stirring of the mixture at room temperature for two hours. After two hours, a solution of 25.0 g (182 mmol) of 1-bromobutane in 100 mL of THF was added dropwise into the flask. The reaction mixture was refluxed overnight for an approximate duration of 21 hours, then cooled. Deionized water was added and the layers separated. The organic fraction was isolated, dried over anhydrous magnesium sulfate, and the solvent removed *in vacuo.* The residue was taken up in a minimum amount of dichloromethane and chromatographed on 100 g of silica gel using as the mobile phase 20 % ethyl acetate/ hexane. The total yield of 4-butoxy-TEMPO was 4.99 g (38 %).

[0060] To a 250 mL one-neck round-bottomed flask equipped with a stir bar was added a solution of 4-butoxy-TEMPO (4.852 g, 21.26 mmol) in 100 mL of toluene. To this solution was added hydrazine hydrate (1.03 mL, 21.26 mmol), then the reaction mixture was heated at reflux. After one hour, the reaction mixture was cooled to 25°C, and washed with deionized water. The organic fraction was isolated, dried over anhydrous magnesium sulfate, and the solvent removed *in vacuo* to give 4-buloxy-2, 2.6,6-tetramethylpiperidin-l-ol (4-Bu TEMPOH) in a yield of 81%. The structure of the product was confirmed by ^-NMR and ^{13}C-NMR.

Example 2: Synthesis of 4-benzyloxy-2,2,6,6-tetramethylpiperidin-l-ol (4-Bn- TEMPOH)

[0061] To a round-bottomed flask equipped with a stir bar was added 4-hydroxy-2,2,6,6-tetramethylpiperidine 1-oxyl ("1-hydroxy-TEMPO", 10.0 g, 58.1 mmol) and 300 mL of dry tetrahydrofuran (THF). To the resultant solution, 7.9 g (70.4 mmol) of potassium i<?ri-butoxide was added. After stirring for two hours at room temperature, a solution of benzyl chloride (8.1 g, 64.0 mmol) in 100 mL of dry THF was added drop wise over 45 minutes while the system was heated at reflux. After the addition was complete and after a total of 7 hours at reflux, heating was stopped, and the system was allowed to cool and stirred at room temperature overnight. Deionized water (100 mL) was added and the layers were separated. The aqueous phase was extracted three times with 25 mL portions of ethyl acetate. The combined organic phases were washed with a mixture of

100 mL water and 80 mL brine before drying over anhydrous magnesium sulfate. The solvents were removed by rotary evaporation, and the residue was taken up in 25 mL dichloromethane and chromatographed on 120 g of silica gel using as the mobile phase 20 % ethyl acetate/ hexane. The yield of pure eluted product was 5.39 g (35 %), and the impure solid isolated from other fractions was recrystallized from cold hexane, affording material that resulted in an overall yield of 12.03 g (79 %) of pure 1-benzyloxy-TEMPO.

[0062] 1-Benzyloxy-TEMPO (1.001 g, 3.82 mmol) was dissolved in n-hexane to give an orange-colored solution. To this solution was added a stoichiometric excess of N,N-diethylhydroxylamine (DEHA, 2 mL, 19.06 mmol) until the resulting solution turned pale yellow. The solution was washed with deionized water. After recovering and drying the organic layer with anhydrous magnesium sulfate, the solvent was removed to yield 4-benzyloxy-2,2,6,6-tetramethylpiperidin-l-ol (4-Bn-TEMPOH) in a yield of 45 %. The structure of the product was confirmed by ^-NMR and ^{13}C-NMR.

Example 3: Polymerization of Methyl Methacrylate

Comparative Example 3A: Untreated methyl methacrylate

[0063] A solution consisting of 20 ppm of benzoyl peroxide in methyl methacrylate was prepared. Ten mL aliquots of this solution were added to each of twenty-four Ace Glass #15 threaded pressure tubes equipped with PTFE screw caps and fluoroelastomer (FETFE) O-rings. To purge dissolved oxygen, each solution was sparged with nitrogen for 2 minutes, after which the tube was immediately sealed and the solution kept under a nitrogen headspace. Polymerization reactions were carried out by loading the tubes into a heating block that had been preheated to 100°C. After 30 minutes, and every 15 minutes after that, four tubes were retrieved from the block and the polymerization reactions quenched by cooling the tubes in an ice bath. The cooled polymer solutions were immediately diluted with toluene. A proprietary method was used to measure the amount of polymer in the diluted analyte solutions.

Comparative Example 3B: Methyl methacrylate treated with 4-hydroxy-TEMPO (4-OH-TEMPO)

[0064] A solution consisting of 0.58 mmol of 4-hydroxy-TEMPO and 20 ppm of benzoyl peroxide in methyl methacrylate was prepared. Ten mL aliquots of this solution were added to each of twenty-four Ace Glass #15 threaded pressure tubes equipped with PTFE screw caps and fluoroelastomer (FETFE) O-rings. The procedure in Comparative

Example 3A was used to remove oxygen, polymerize the solutions, and measure the amount of polymer formed.

Example 3C: Methyl methacrylate treated with 4-benzyl-2,2,6,6-tetramethylpiperidin-l-ol (4-BnO-TEMPOH)

[0065] A solution consisting of 0.58 mmol of 4-benzyl-2,2,6,6-tetramethylpiperidin-l-ol and 20 ppm of benzoyl peroxide in methyl methacrylate was prepared. Ten mL aliquots of this solution were added to each of twenty-four Ace Glass #15 threaded pressure tubes equipped with PTFE screw caps and fluoroelastomer (FETFE) O-rings. The procedure in Comparative Example 3A was used to remove oxygen, polymerize the solutions, and measure the amount of polymer formed.

Example 3D: Methyl methacrylate treated with 4-butoxy-2,2,6,6-tetramethylpiperidin- 1-ol (4-BuO-TEMPOH)

[0066] A solution consisting of 0.58 mmol of 4-butoxy-2,2,6,6-tetramethylpiperidin-l-ol and 20 ppm of benzoyl peroxide in methyl methacrylate was prepared. Ten mL aliquots of this solution were added to each of twenty-four Ace Glass #15 threaded pressure tubes equipped with PTFE screw caps and fluoroelastomer (FETFE) O-rings. The procedure in Comparative Example 3A was used to remove oxygen, polymerize the solutions, and measure the amount of polymer formed.

[0067] The results of the experiments in Examples 3A-3D is summarized in Table 1:

Table 1: Inhibition of methyl methacrylate polymerization (initiated with 20 ppm benzoyl peroxide) at 100°C under anaerobic conditions in the presence of no inhibitor (blank) or 0.58 mmol of inhibitor.

	Poly(methyl methacrylate) (ppm)			
	Ex. 3A	Ex. 3B	Ex. 3C	Ex. 3D
Time (min)	Blank	4-OH-TEMPO	4-BnO-TMPOH	4-BuO-TMPOH
30	18588	31	5	2
45	48550	34	4	2
60	80231	64	4	2
75	83625	93	4	3
90	93993	144	4	2
105		180	3	5

Example 4: Polymerization of Styrene

Comparative Example 4A: Untreated styrene

[0068] A disposable, prepacked alumina column was used to remove 4-tert-butylcatechol (TBC) from styrene. Nine mL aliquots of freshly de-inhibited styrene were charged into each of twenty-four Ace Glass #15 threaded pressure tubes equipped with PTFE screw caps and fluoroelastomer (FETFE) O-rings. To purge dissolved oxygen, each solution was sparged with nitrogen for 2 minutes, after which the tube was immediately sealed and the solution kept under a nitrogen headspace. Polymerization reactions were carried out by loading the tubes into a heating block that had been preheated to 120°C. After 30 minutes, and every 15 minutes after that, four tubes were retrieved from the block and the polymerization reaction quenched by cooling the tubes in an ice bath. The cooled polymer solutions were immediately diluted with toluene. The amount of polymer formed was determined by precipitation with methanol according to the ASTM D2121 method.

Comparative Example 4B: Styrene treated with 4-hydroxy-TEMPO (4-OH-TEMPO)

[0069] A solution consisting of 0.33 mmol of 4-hydoxy-TEMPO and inhibitor-free styrene was prepared. Nine mL aliquots of this solution were charged into each of twenty-four Ace Glass #15 threaded pressure tubes equipped with PTFE screw caps and fluoroelastomer (FETFE) O-rings. The procedure in Comparative Example 4A was used to remove oxygen, polymerize the solutions, and measure the amount of polymer formed.

Example 4C: Styrene treated with 4-benzyloxy-2,2,6,6-tetramethylpiperidin-l-ol (4-BnO-TEMPOH)

[0070] A solution consisting of 0.33 mmol of 4-benzyloxy-2,2,6,6-tetramethylpiperidin-l-ol and inhibitor-free styrene was prepared. Nine mL aliquots of this solution were charged into each of twenty-four Ace Glass #15 threaded pressure tubes equipped with PTFE screw caps and fluoroelastomer (FETFE) O-rings. The procedure in Comparative Example 4A was used to remove oxygen, polymerize the solutions, and measure the amount of polymer formed.

Example 4D: Styrene treated with 4-butoxy-2,2,6,6-tetramethylpiperidin-l-ol (4-BuO-TMPOH)

[0071] A solution consisting of 0.33 mmol of 4-butoxy-2,2,6,6-tetramethylpiperidin-l-ol and inhibitor-free styrene was prepared. Nine mL aliquots of this solution were charged into each of twenty-four Ace Glass #15 threaded pressure tubes equipped with PTFE screw caps and fluoroelastomer (FETFE) O-rings. The procedure in Comparative Example 4A was used to remove oxygen, polymerize the solutions, and measure the amount of polymer formed.

[0072] The results of the experiments in Examples 4A-4D is summarized in Table 2:

Table 2: Inhibition of styrene polymerization at 120 °C under anaerobic conditions using no inhibitor (blank) or 0.33 mmol of inhibitor.

	Polystyrene (wt. %)			
	Ex. 4A	Ex. 4B	Ex. 4C	Ex. 4D
Time (min)	Blank	4-OH-TEMPO	4-BnO-TMPOH	4-BuO-TMPOH
30	1.96	0.03	0.02	0.004
45	3.24	0.03	0.02	0.004
60	4.72	0.04	0.02	0.003
75	6.36	0.09	0.02	0.012
90	7.78	1.93	2.10	4.00
105	10.57	7.60	4.28	7.80

Example 5: Polymerization of Isoprene

Comparative Example 5A: Untreated isoprene

[0073] A disposable, prepacked alumina column was used to remove 4-tert-butylcatechol (TBC) from isoprene. Freshly de-inhibited isoprene was diluted with heptane in a 1:1 ratio. Fifty mL aliquots of this solution were charged into each of six glass sample containers, which were then placed into six stainless steel pressure vessels. Each vessel was pressurized with 100 psi nitrogen without purging the system. Polymerization reactions were carried out by loading the vessels into a heating block that had been preheated to 120°C. After 60 minutes, and every 60 minutes after that, one vessel was retrieved from the block and the polymerization reaction quenched by cooling the vessel in an ice bath. The vessels were de-pressurized and the polymer content determined gravimetrically by evaporating the volatiles at 170 °C.

Comparative Example 5B: Isoprene treated with 4-hydoxy-TEMPO (4-OH-TEMPO)

[0074] A solution consisting of 1.55 mmol of 4-hydroxy-TEMPO and inhibitor-free isoprene was prepared. The solution was diluted with heptane in a 1:1 ratio. Fifty mL aliquots of this solution were charged into each of six glass containers, which were then placed into six stainless steel pressure vessels. The procedure in Comparative Example 5A was used to remove oxygen, polymerize the solutions, and measure the amount of polymer formed.

Comparative Example 5C: Isoprene treated with 4-benzyloxy-2,2,6,6-tetramethylpiperidin- 1-ol (4-BnO-TEMPOH)

[0075] A solution consisting of 1.55 mmol of 4-benzyloxy-2,2,6,6-tetramethylpiperidin-l-ol and inhibitor-free isoprene was prepared. The solution was diluted with heptane in a 1:1 ratio. Fifty mL aliquots of this solution were charged into each of six glass containers, which were then placed into six stainless steel pressure vessels. The procedure in Comparative Example 5A was used to remove oxygen, polymerize the solutions, and measure the amount of polymer formed.

Example 5D: Isoprene treated with 4-butoxy-2,2,6,6-tetramethylpiperidin-l-ol (4-BuO-TEMPOH)

[0076] A solution consisting of 1.55 mmol of 4-butoxy-2,2,6,6-tetramethylpiperidin-l-ol and inhibitor-free isoprene was prepared. The solution was diluted with heptane in a 1:1 ratio. Fifty mL aliquots of this solution were charged into each of six glass containers, which were then placed into six stainless steel pressure vessels. The procedure in Comparative Example 5A was used to remove oxygen, polymerize the solutions, and measure the amount of polymer formed.

[0077] The results of the experiments in Examples 5A-5D is summarized in Table 3:

Table 3: Inhibition of isoprene polymerization at 120 °C under anaerobic conditions using no inhibitor (blank) or 0.33 mmol of inhibitor.

	Polyisoprene (wt. %)			
	Ex. 5A	Ex. 5B	Ex. 5C	Ex. 5D
Time (min)	Blank	4-OH-TEMPO	4-BnO-TMPOH	4-BuO-TMPOH
60	0.5444	0	0.0036	0.0048
120	1.1616	0.0008	0	0.006
180	2.0124	0.01	0.006	0.0062
240	2.2878	0.0038	0.1628	0.005
300	2.7036	0.5578	0.6656	0.1648
360	3.308	1.193		0.3078

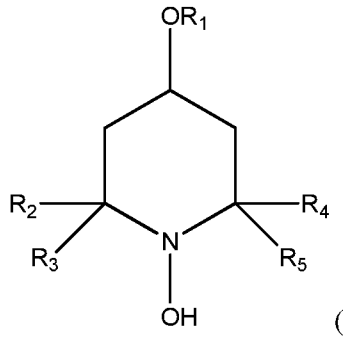
[0078] When introducing elements of the present invention or the preferred embodiments(s) thereof, the articles "a", "an", "the" and "said" are intended to mean that there are one or more of the elements. The terms "comprising", "including" and "having" are intended to be inclusive and mean that there may be additional elements other than the listed elements.

[0079] In view of the above, it will be seen that the several objects of the invention are achieved and other advantageous results attained.

[0080] As various changes could be made in the above compounds and methods without departing from the scope of the invention, it is intended that all matter contained in the above description shall be interpreted as illustrative and not in a limiting sense.

WHAT IS CLAIMED IS:

1. A hydroxylamine compound having the structure of Formula 1:



(1)

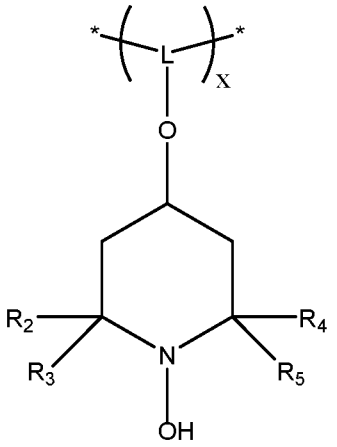
wherein

R_i is alkyl, aryl, alkaryl, heterocyclo, or -C(0)R_6;

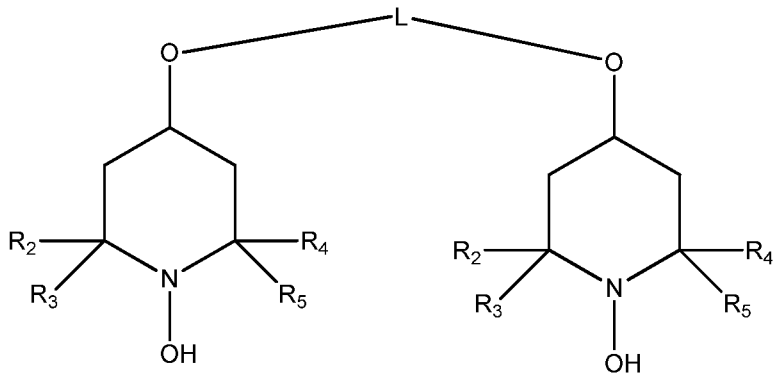
R2, R_3, R_4, and R_5, are independently selected from the group consisting of alkyl, alkylaryl, aryl, heteroaryl, or R_2 and R_3 or R_4 and R_5 together can form a spiro ring; and

R_6 is alkyl, alkylaryl, aryl, or heteroaryl.

2. A hydroxylamine oligomer exemplified but not restricted to the oligomer of Formula 2 or dimer compound of Formula 3:



(2)



(3)

wherein

L is a linker comprising an alkylene, arylene, alkarylene, heterocyclo, or diacyl;

R2, R_3, R_4, and R_5, are independently selected from the group consisting of alkyl, alkylaryl, aryl, heteroaryl, or R2 and R_3 or R_4 and R_5 together can form a spiro ring; and

x is an integer greater than 2.

3. A method for inhibiting polymerization of an unsaturated compound comprising an unsaturated carbon-carbon bond comprising contacting the unsaturated compound with the hydroxylamine compound of claim 1 or the hydroxylamine dimer compound of claim 2.

4. The method of claim 3 wherein the unsaturated compound is a vinyl monomer.

5. The compound or method of any one of claims 1 to 4 wherein R_i is an alkyl, or alkylaryl group of from about 1 to about 18 carbon atoms.

6. The compound or method of claim 5 wherein R_i is propyl, butyl, pentyl, or hexyl.

7. The compound or method of claim 6 wherein R_i is n-butyl, sec-butyl, isobutyl, or tert-butyl.

8. The compound or method of claim 5 wherein R_i is C_i-$C_{i\ 8}$ alkaryl.

9. The compound or method of claim 8 wherein R_i is benzyl.

10. The compound or method of any one of claims 1 to 9 wherein R2, R_3, R4, and R5, are independently C1-C9 alkyl.

11. The compound or method of any one of claims 1 to 10 wherein R2, R_3, R_4, and R5, are independently C1-C3 alkyl.

12. The compound or method of any one of claims 1 to 11 wherein R_2, R_3, R_4, and R_5, are independently haloalkyl.

13. The compound or method of claim 11 wherein R i is n-butyl and R 2 R_3, R^, and R_5 are methyl.

14. The compound or method of claim 11 wherein R i is benzyl and R 2 R_3, R_4, and R_5 are methyl.

15. The method of any one of claims 3 to 13 wherein the unsaturated compound is ethylene, propylene, acetylene, styrene, vinyl chloride, vinyl alcohol, vinyl acetate, acrylonitrile, acrylate esters, methacrylate esters, acrylic acid, (meth)acrolein, acrolein, butadiene, indene, divinylbenzene, isoprene, acetylene, vinyl acetylene, cyclopentadiene, or a combination thereof.

16. The method of claim 15 wherein the unsaturated compound comprises acrylate esters, methacrylate esters, styrene, or a combination thereof.

17. The method of any one of claims 3 to 16 wherein the method stabilizes and inhibits polymerization of an unsaturated compound during a manufacture, a purification, or a storage process.

18. The method of claim 17 wherein the method stabilizes and inhibits polymerization of an unsaturated compound in a primary fractionation process, light ends fractionation, non-aromatic halogenated vinyl fractionation, process-gas compression, butadiene extraction, propane dehydrogenation, diesel and petrol fuel stabilization, olefin metathesis, styrene purification, hydroxyhydrocarbon purification, or delays the polymerization of resins and compositions comprising ethylenically unsaturated species.

19. The method of claim 18 wherein the process is butadiene extraction or styrene purification.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2016/022731

A. CLASSIFICATION OF SUBJECT MATTER
IPC (2016.01) C07D 211/94, C07D 401/12, C07D 401/14, C07C 7/20, C08F 2/40

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 (2016.01) C07D 211/94, C07D 401/12, C07D 401/14, C07C 7/20, C08F 2/40

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)
Databases consulted: THOMSON INNOVATION, Google Patents, CAPLUS, MARPAT, REGISTRY, Google Scholar, DWPI
Search terms used: HTEMPO, HTEMPOL, 2,2,6,6-Tetramethylpiperidin-l-oxyl, 4-hydroxy-2,2,6,6,-tetra-methylpiperidinoxy, polymerization inhibitor, vinyl monomer polymerization.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5290888 A CIBA-GEIGY CORPORATION [US] 01 Mar 1994 (1994/03/01) Coloumn 14,15, Claim 1	1-4,10,11,15-19
Y	Whole document	1-19
Y	CA 2232502 Al James Tyler Merrill 20 Sep 1998 (1998/09/20) Whole document (see especially pages 6, 9(Ex. 5) and Claim 3)	1-19
Y	WO 2007045886 Al A H MARKS AND COMPANY LIMITED [GB] 26 Apr 2007 (2007/04/26) Whole document (see specifically claim 7)	1-19
Y	US 7132540 Bl NOVA MOLECULAR TECHNOLOGIES INC [US] 07 Nov 2006 (2006/11/07) Whole document (see especially coloumn 5, ex. 2 and 3)	1-19

[X] Further documents are listed in the continuation of Box C. [X] 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 ¾¾ to establish the publication date of another citation or other sp „cial TM reason a t (as specified)
"0" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than tire priority date claimed

"T" later document published alter 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
"χ" 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 rnember of the same patent family

Dale of the actual completion of the International search	Date of mailing of the international search report
21 Jun 2016	21 Jun 2016
Name and mailing address of the ISA: Israel Patent Office Technology Park, Bldg.5, Malcha, Jerusalem, 9695101, Israel Facsimile No. 972-2-5651616	Authorized officer Pinchover Miriam Telephone No. 972-2-5651642

Form PCT/ISA/210 (second sheet) (January 2015)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2016/022731

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2008103613 A2 OTHERA HOLDING INC [US] 28 Aug 2008 (2008/08/28) Page 32 (second compound), page 60(example 3), page 78 (compound 43), page 112 (compound 110)	1,5,8-11,14
X	EP 0943665 A1 CIBA SPECIALTY CHEMICALS HOLDING INC [CH] 22 Sep 1999 (1999/09/22) Pages 27-28 (compounds b, k, q)	1,2,5,6,10,11
A	Miyazawa, T. et al, New Method for Preparation of Superoxide Ion by Use of Amino Oxide, J. Org. Chem., December 1985, Vol. 50, No. 25, pages: 5389-5391 31 Dec 1985 (1985/12/31) Whole document	1-19
P,X	WO 2015084843 A1 ECOLAB USA INC?[US] 11 Jun 2015 (2015/06/11) Whole document	1-19

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/US2016/022731

Patent document cited search report	Publication date	Patent family member(s)	Publication Date
US 5290888 A	01 Mar 1994	US 5290888 A	01 Mar 1994
		CA 2047393 A1	21 Jan 1992
		CA 2047393 C	23 Apr 2002
		DE 691 16757 D1	14 Mar 1996
		DE 691 16757 T2	14 Aug 1996
		EP 0467848 A1	22 Jan 1992
		EP 0467848 B1	31 Jan 1996
		JP H04288302 A	13 Oct 1992
		JP 3182535 B2	03 Jul 2001
CA 2232502 A1	20 Sep 1998	CA 2232502 A1	20 Sep 1998
		BE 101 1649 A5	09 Nov 1999
		BR 980093 1 A	04 Apr 2000
		CZ 9800833 A3	14 Oct 1998
		DE 1981 1602 A1	12 Nov l998
		ES 2142274 A1	01 Apr 2000
		ES 2142274 B1	01 Jan 2001
		FR 2761060 A1	25 Sep 1998
		FR 2761060 B1	20 Aug 1999
		ID 20069 A	24 Sep 1998
		IT MI980548 A1	21 Sep 1998
		IT 129875 1 B1	02 Feb 2000
		JP H10330297 A	15 Dec 1998
		NL 1008644 A1	22 Sep 1998
		NL 1008644 C2	15 Dec 1998
		SK 36398 A3	14 Feb 2000
WO 2007045886 A1	26 Apr 2007	WO 2007045886 A1	26 Apr 2007
		EP 1937726 A1	02 Jul 2008
		GB 05213 19 DO	30 Nov 2005
		US 2010168434 A1	01 Jul 2010

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/US2016/022731

Patent document cited search report	Publication date	Patent family member(s)	Publication Date
US 7132540 B1	07 Nov 2006	US 7132540 B1	07 Nov 2006
		US 200300903 1 A1	09 Jan 2003
WO 2008103613 A2	28 Aug 2008	WO 2008103613 A2	28 Aug 2008
		WO 2008103613 A3	30 Jul 2009
		AU 2008218783 A1	28 Aug 2008
		BR PI0807571 A2	01 Jul 2014
		CA 2679066 A1	28 Aug 2008
		CN 101687786 A	31 Mar 2010
		CN 101687786 B	22 May 2013
		CN 103497148 A	08 Jan 2014
		CN 103497148 B	01 Jun 2016
		EP 2125716 A2	02 Dec 2009
		EP 2620429 A1	31 Jul 2013
		JP 20105 19259 A	03 Jun 2010
		US 2008280890 A1	13 Nov 2008
EP 0943665 A1	22 Sep 1999	EP 0943665 A1	22 Sep 1999
		EP 0943665 B1	05 Nov 2003
		AT 253621 T	15 Nov 2003
		AU 756097 B2	02 Jan 2003
		AU 213 1899 A	30 Sep 1999
		BR 9901022 A	28 Dec 1999
		BR 9901022 B1	19 Apr 201 1
		CA 2265990 A1	19 Sep 1999
		CA 2265990 C	22 Jul 2008
		CN 1237501 A	08 Dec 1999
		CN 1106919 C	30 Apr 2003
		DE 69912502 D1	11 Dec 2003
		DE 69912502 T2	23 Sep 2004

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/US2016/022731

Patent document cited search report	Publication date	Patent family member(s)	Publication Date
		DK 0943665 T3	08 Mar 2004
		ES 2209368 T3	16 Jun 2004
		JP 2000025010 A	25 Jan 2000
		JP 4689778 B2	25 May 2011
		TW 1224995 B	11 Dec 2004
		US 6187387 B1	13 Feb 2001
		ZA 9902175 A	20 Sep 1999
WO 2015084843 A1	11 Jun 2015	WO 2015084843 A1	11 Jun 2015
		US 2015152053 A1	04 Jun 2015