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(72) Inventeur/Inventor:

Fried, Herbert E., US

(73) Propriétaire/Owner:

SHELL CANADA LIMITED, CA

(74) Agent: SMART & BIGGAR

(54) Titre : PREPARATION D'ACIDES ALCOXYALCANOÏQUES

(54) Title: PREPARATION OF ALKOXYALKANOIC ACIDS

(57) **Abrégé/Abstract:**

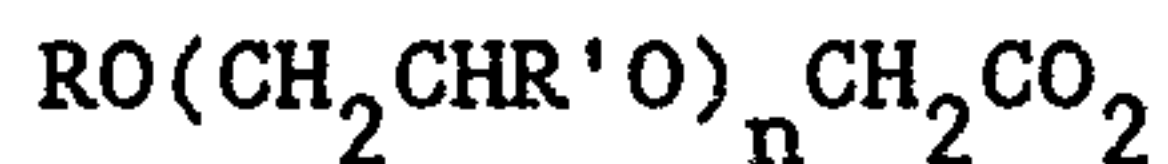
This invention relates to a process for the preparation of an alkoxyalkanoic acid of the formula  $RO(CH_2CHR'O)_nCH_2CO_2$  wherein R is an alkyl group of from 1 to 22 carbon atoms, R' is hydrogen or methyl or mixtures thereof (on the individual molecule) and n is an integer of from 1 to 12, or a salt thereof, which process comprises oxidizing the corresponding alkoxyalkanol using an oxidant in the presence of a solubilized stable free radical nitroxide except for di-tertiary nitroxides.



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## PREPARATION OF ALKOXYALKANOIC ACIDS

This invention relates to a process for the preparation of an alkoxyalkanoic acid of the formula



wherein R is an alkyl group of from 1 to 22 carbon atoms, R' is hydrogen or methyl or mixtures thereof (on the individual molecule) and n is an integer of from 1 to 12, or a salt thereof, which process comprises oxidizing the corresponding alkoxyalkanol using an oxidant in the presence of a solubilized stable free radical nitroxide except for di-tertiary nitroxides.

## PREPARATION OF ALKOXYALKANOIC ACIDS

This invention relates to a process for the preparation of alkoxyalkanoic acids by the oxidation of the corresponding alkoxyalkanols in the presence of a stable free radical nitroxide.

Alkoxyalkanoic acids are useful as anionic detergents. These acids, being composed of only the elements C, H and O, do not pose the environmental problems that other detergents containing heteroatoms such as N, S, and P pose. Commercially, the alkoxyalkanoic acids are prepared in a two-step process of first reacting an alkoxyalkanol with sodium and then reacting the resultant alkoxide with the sodium salt of chloroacetic acid.

It is also known to convert alkoxyalkanols such as methyl carbitol to the corresponding carboxylic acids by oxidizing them with nitric acid. However, not all of the nitric acid can be separated by distillation, and the reaction product contains nitric acid, which is corrosive and therefore undesirable. In addition, cleavage of the ether linkages occurs to a large degree during this process.

Japanese Patent No. 50-96516, issued July 31, 1975, discloses a process for the preparation of carboxylic acid salts by the liquid phase dehydrogenation of alcohols with caustic alkali in the presence of precious metal catalysts, including palladium. This process uses a relatively high temperature, 100°C-270°C. These high temperatures can degrade the ether linkages especially in the highly ethoxylated alcohols.

It is known to use nitroxyl radicals/oxoammonium salts in the oxidation of primary alcohols to produce aldehydes and acids and secondary alcohols to ketones. Journal of Organic Chemistry, vol. 52 (12), pp. 2559-2562; Pure and Applied Chemistry, vol. 62(2), 1990, pp. 217-222; Journal of Organic Chemistry, vol. 55, 1990,

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pp. 462-466. The primary products produced in these processes are aldehydes.

It is generally more difficult to oxidize alkoxyalkanols than alkanols as it is difficult to oxidize alkoxyalkanols without splitting the molecular chain at the ether linkage and thereby produce a large proportion of undesired by-product. It is therefore an object of this invention to produce alkoxyalkanoic acids in high yields and with high selectivities from alkoxyalkanols without producing large amounts of other products such as aldehydes.

It is a further object of this invention to provide a process for the preparation of alkoxyalkanoic acids avoiding the use of highly corrosive, difficult to separate reactants.

It has been found that alkoxyalkanoic acids can be produced in high yields and with high selectivities by using catalytic amounts of a stable free radical nitroxide in the oxidation of the corresponding alkoxy alkanol using conventional oxidants.

Accordingly, this invention provides a process for the preparation of an alkoxyalkanoic acid of the formula

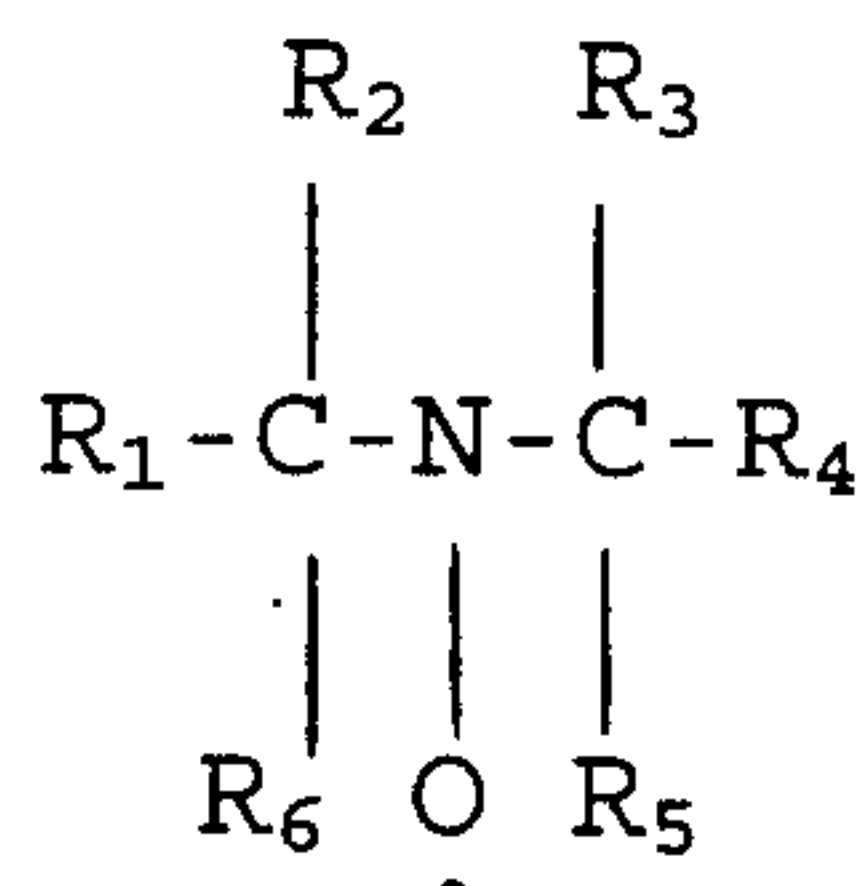


wherein R is an alkyl group of from 1 to 22 carbon atoms, R' is hydrogen or methyl or mixtures thereof (on the individual molecule) and n is an integer of from 1 to 12 or a salt thereof which comprises oxidizing the corresponding alkoxyalkanol using an oxidant in the presence of a solubilized stable free radical nitroxide except for di-tertiary alkyl nitroxides in a neutral to slightly basic medium not adjusted with a bicarbonate salt. Preferably the nitroxide has the formula:

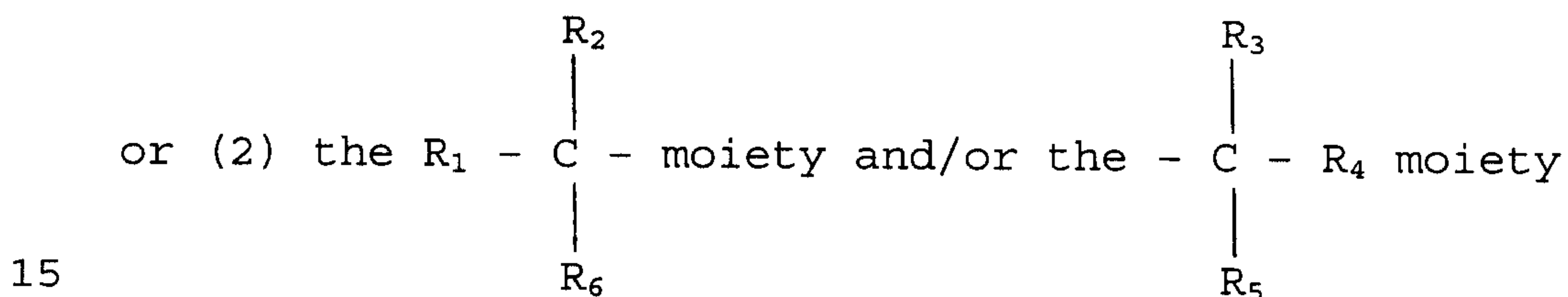


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wherein (1) (a) each of  $R_1$ ,  $R_2$ ,  $R_3$  and  $R_4$  is an alkyl, aryl or  
 5 heteroatom substituted alkyl group having 1 to 15 carbon atoms,  
 and (b)  $R_5$  and  $R_6$  (i) each is an alkyl group having 1 to 15  
 carbon atoms provided that  $R_1$ - $R_6$  are not all alkyl groups, or a  
 substituted alkyl group having 1 to 15 carbon atoms wherein the  
 substituent is halogen, cyano,  $-\text{CONH}_2$ ,  $-\text{OCOCH}_3$ ,  $\text{OCOC}_2\text{H}_5$ ,  
 10 carbonyl, alkenyl,  $-\text{OR}''$  or  $-\text{COOR}''$  wherein  $R''$  is alkyl or  
 aryl, or (ii) together form part of a ring that contains 4 or 5  
 carbon atoms and up to two heteroatoms of O or N,



individually are aryl.

The process is preferably conducted using a chlorine-  
 containing oxidant at a temperature in the range of from  $-10^\circ\text{C}$   
 to  $35^\circ\text{C}$  and thereafter separating out the alkoxyalkanoic acid,  
 20 or a salt thereof.

In the formula  $\text{RO}(\text{CH}_2\text{CHR}'\text{O})_n\text{CH}_2\text{CH}_2\text{OH}$  (I)

$R$  preferably is an alkyl group having 11 to 18 carbon atoms,  
 and  $n$  represents the average number of oxyalkylene groups and  
 preferably is an integer of from 2 to 9.

25 The  $R$  group in the above formula I can be substituted  
 with any substituent which does not interfere with the  
 oxidation of the hydroxy group. Such substituents include

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-OR", -CH<sub>3</sub>, -COOH, CONH<sub>2</sub> and COOR" wherein R" is an alkyl or aryl group. The process of the instant invention is particularly suited to detergent range ethoxylated, or propoxylated alcohols with alkyl chains (R) of 8 to 20, preferably of 11 to 18 carbon atoms. The R' groups on an individual molecule can be hydrogen, methyl or mixtures thereof.

For example, straight ethoxylated, straight propoxylated and mixed ethoxylated-propoxylated detergent alcohols are commercially available. The number of such alkoxylate groups, (CH<sub>2</sub>CHR'O), range from 1 to 20. Commercially, detergent range ethoxylate alcohols are available with an average of 3, 7, 9 and 12 ethoxylate units per molecule. Others can be readily prepared. In a preferred

embodiment, the starting alkoxyalkanol is ethoxylated alcohol which has had the unreacted alcohols and lower ethoethoxylates topped off in order to give an ethoxylate having about four ethylene oxide units per molecule.

5       The term "stable free radical nitroxide" as used herein shall mean a free radical nitroxide that can be prepared by conventional chemical methods and will exist long enough to be used in a subsequent chemical reaction or examined in a static system by normal methods of spectroscopy. Generally, the stable free radical  
10       nitroxides of the present invention have a half life of at least one year. The term "stable free radical" shall also be understood to include the precursor to a stable free radical from which the stable free radical may be produced in situ.

15       The stable free radical nitroxides, as used in the present process, are precursors to oxidating agents, i.e., oxoammonium salts, active for the oxidation of alkoxyalkanols to the corresponding acids. These oxidating agents are generated in situ by the oxidation of a stable free radical nitroxide to an oxoammonium salt with an oxidant, preferably a halogen-containing,  
20       more preferably a chlorine-containing oxidant. The stable free radical nitroxide itself can be obtained by the oxidation of secondary amines or hydroxylamines.

The stable free radical nitroxides which are most suitable for use in the instant invention have the formula:

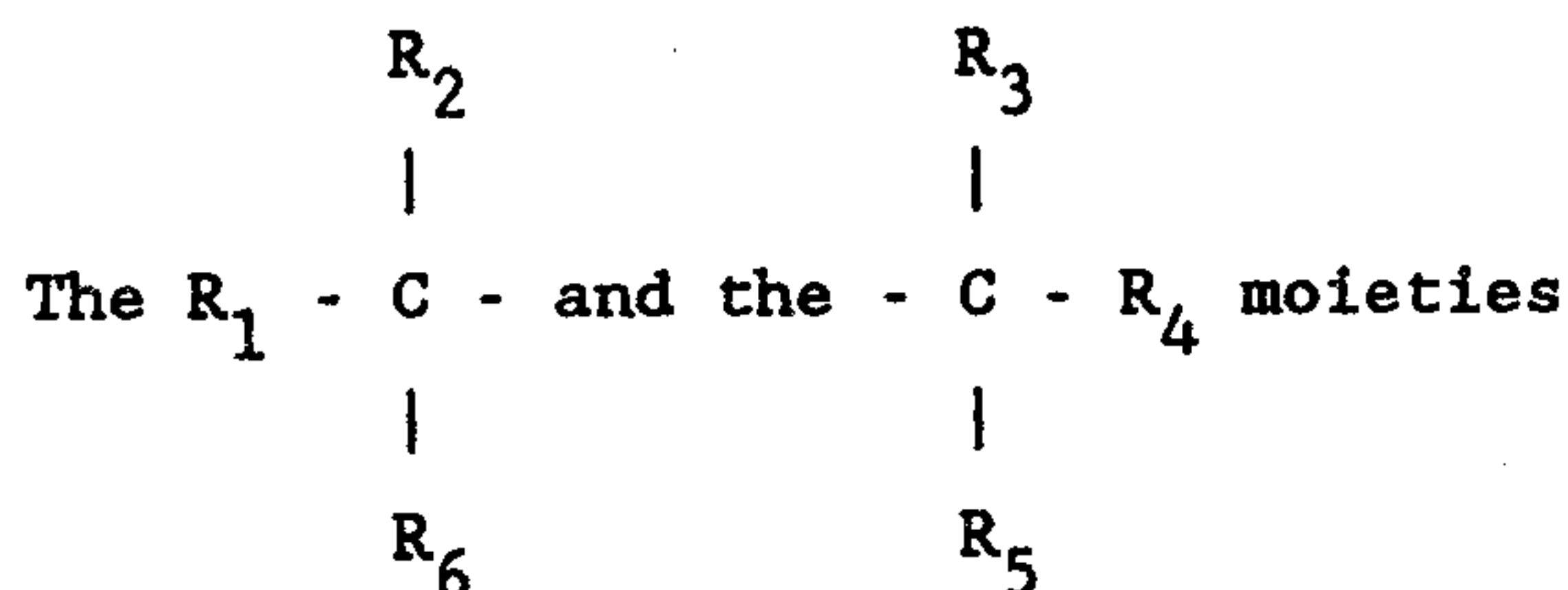


25       wherein each of  $R_1$ ,  $R_2$ ,  $R_3$  and  $R_4$  is an alkyl, aryl or heteroatom substituted aryl or alkyl group and no hydrogen is bound to the remaining valences on the carbon atoms bound to the nitrogen. As used herein, the term "alkyl" is meant to include cycloalkyl. The alkyl (or heteroatom substituted) groups  $R_1$ - $R_4$  may be the same or  
30       different, and preferably contain 1 to 15 carbon atoms.

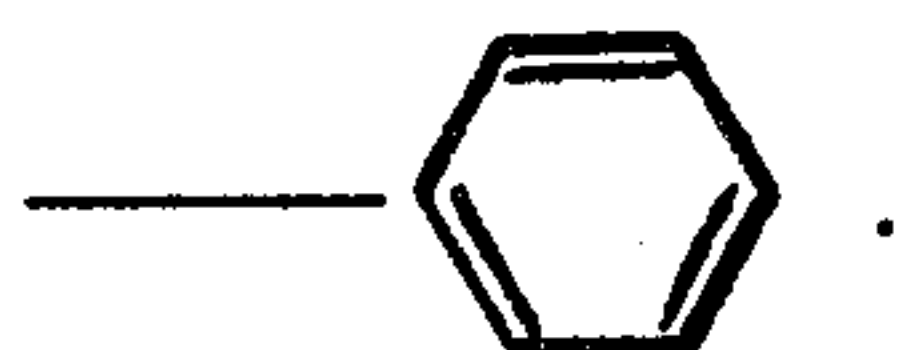


Preferably,  $R_1$ - $R_4$  are methyl, ethyl, or propyl groups. In addition to hydrogen, the heteroatom substituents may include, halogen, oxygen, nitrogen and the like.

5 The remaining valences ( $R_5$  and  $R_6$ ) in formula III above may be satisfied by any atom or group except hydrogen which can bond covalently to carbon, although some groups may reduce the stabilizing power of the nitroxide and are undesirable. When  $R_1$ ,  $R_2$ ,  $R_3$  and  $R_4$  are each alkyl groups, however, at least one of  $R_5$  and  $R_6$  must be a different group. Preferably,  $R_5$  and  $R_6$  are substituted alkyl groups having 1 to 15 carbon atoms wherein the substituent is selected from halogen, cyano,  $-COOR$ , wherein R is alkyl or aryl,  $-CONH_2$ ,  $-OCOC_2H_5$ , carbonyl, or alkenyl where the double bond is not conjugated with the nitroxide moiety, or alkyl groups of 1 to 15 carbon atoms.  $R_5$  and  $R_6$  may also form a ring of carbon atoms and up to two heteroatoms, such as O or N, by  $R_5$  and  $R_6$  together. Examples of suitable compounds having the structure above and in which  $R_5$  and  $R_6$  form part of the ring are piperidiny-1-oxyls and pyrrolidin-1-oxyls. Particular examples wherein  $R_5$  and  $R_6$  above form part of a ring are 2,2,6,6-tetramethyl-piperidine-1-oxyl, 4-hydroxy-2,2,6,6-tetramethyl-piperidine-1-oxyl and 4-oxo-2,2,6,6-tetramethyl-piperidine-1-oxyl.



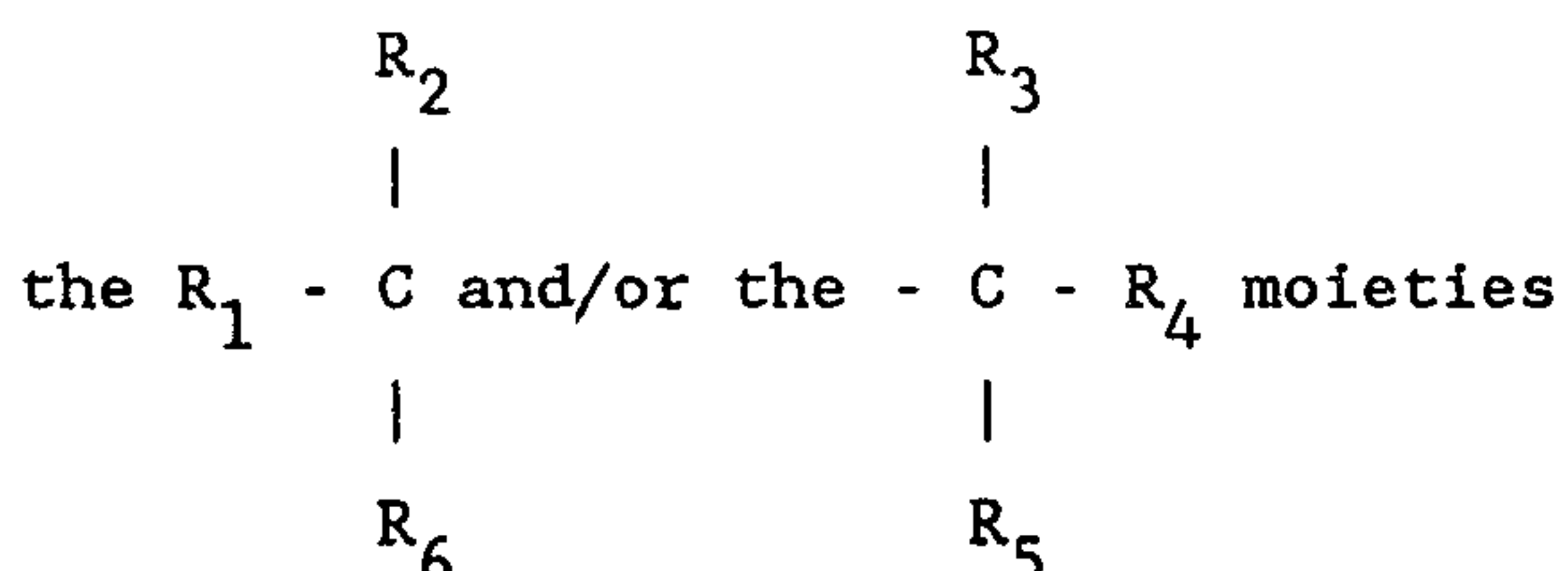
in formula III above can individually be aryl, i.e.,



25 Examples of suitable compounds having the structure above in which



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are individually aryl are diphenylnitroxide, phenyl tertiary butylnitroxide 3-methyldiphenylnitroxide, 2-chlorodiphenylnitroxide and the like. These compounds may be substituted with any

5 substituents which do not interfere with the reaction.

The preferred nitroxides for use in the instant invention are those wherein  $R_5$  and  $R_6$  form a ring structure with the nitrogen, and preferably a six membered ring. Preferably, the nitroxide is selected from the group consisting of 2,2,6,6-tetramethyl-

10 piperidine-1-oxyl, 4-hydroxy-2,2,6,6-tetramethyl-piperidine-1-oxyl, 4-oxo-2,2,6,6-tetramethyl-piperidine-1-oxyl, 2,2,6,6-tetramethyl-piperidine-1-oxyl-4-sulfate, 4-oxo-2,2,6,6-tetramethyl-piperidine, 4-hydroxy-2,2,6,6-tetramethyl-piperidine and mixtures thereof, with

15 2,2,6,6-tetramethyl-piperidine-1-oxyl, 2,2,6,6-tetramethyl-piperidine-1-oxyl-4-sulfate, and 4-hydroxy-2,2,6,6-tetramethyl-pi-

peridine-1-oxyl being particularly preferred.

In one embodiment, the stable free radical nitroxide can be supported on a polystyrene resin such as, for example, by reacting

20 4-hydroxy-2,2,6,6-tetramethyl-piperidine-1-oxyl with chloro-

methyated polystyrene to form a covalently linked resin. The use of a resin-supported nitroxide is advantageous in that by simple filtration, the catalyst can be easily separated from the product.

The chlorine-containing oxidants suitable for use in the instant invention are chlorine-containing compounds which are

25 capable of oxidizing the stable free radical nitroxide to the oxoammonium salt. Suitable chlorine-containing oxidants include chlorine, hypochlorite and N-chloro compounds, with chlorine and hypochlorite being preferred. Suitable hypochlorite oxidants include sodium hypochlorite, which is typically used in an aqueous

30 solution having a concentration of up to 10 %wt, preferably from

2.5 %wt to 5 %wt. When chlorine is used as the oxidant, chlorine is suitably bubbled into the reaction solution.

The amounts and concentrations of the reactants utilized in the process of the instant invention can vary within wide ranges.

5 The amount of stable free radical nitroxide utilized depends on the manner in which the reagents are contacted. The chlorine-containing oxidant is typically added last, i.e. the chlorine-containing oxidant is added slowly to a reaction mixture containing alkoxyalkanol, solvent and nitroxide. When this procedure is used,  
10 the amount of nitroxide is typically in the range of from 500 parts per million to 30,000 parts per million, preferably from 1,000 parts per million to 10,000 parts per million, and more preferably from 1,000 parts per million to 4,000 parts per million, basis the weight of the starting alkoxyalkanol. Alternatively, the chlorine  
15 containing oxidant may be added prior to the addition of the nitroxide, in which case the amount of nitroxide utilized will typically be in the range of from 100 parts per million to 3,000 parts per million. Generally, the amount of chlorine-containing oxidant utilized when the oxidant is sodium hypochlorite will be in  
20 the range of from 2.0 equivalents to 2.5 equivalents, preferably from 2.3 equivalents to 2.5 equivalents, basis the weight of the starting alkoxyalkanol.

The reaction in the instant invention is carried out utilizing a solubilized stable free radical nitroxide. The solvent is  
25 typically a nonaqueous solvent which is to a large extent immiscible in water and in which the alkoxyalkanol is readily soluble. Solvents which are most suitable are those having dielectric constants greater than 2. The solvent may be added to the reaction mixture or, alternatively, the nitroxide may be  
30 dissolved in the solvent prior to addition of the nitroxide to the reaction medium. The solvent is typically selected from the group consisting of ethyl acetate, dichloromethane, acetonitrile, toluene, chlorobenzene, xylene, carbon tetrachloride, chloroform, tetrachloroethylene, diethyl ether, methyl-tert-butyl ether and  
35 mixtures thereof, with ethyl acetate and dichloromethane being

preferred. The amount of solvent utilized in the process is generally from 10:1 to 0.5:1, preferably from 7:1 to 3:1, and more preferably from 4:1 to 3:1, basis the weight of the starting alkoxyalkanol.

5       The reaction is suitably begun in a neutral to slightly basic medium. If the reaction is conducted in a medium which is initially too basic, the start of the oxidation reaction will be extremely slow and lead to longer reaction times. On the other  
10       hand, if the reaction medium is too acidic, the reaction may result in higher amounts of esters than is desirable. Thus, in a preferred embodiment, an acid is added to the reaction mixture either at the beginning of the reaction or after partial completion of the reaction to adjust the pH to a value of 8-9. Suitable acids include hydrochloric acid, sulfuric acid, phosphoric acid and the  
15       like. Alternatively, the pH of the reaction mixture may be adjusted by recycling alkoxyalkanoic acid produced according to the invention. The concentration of the acid will typically be in the range of from 1 %wt to 20 %wt, preferably in the range of from 1 %wt to 10 %wt. The pH of the reaction steadily decreases as the  
20       reaction proceeds and acids are formed. The final pH of the reaction mixture is generally in the range of from 0 to 5. The acid product may be produced at least in part in the form of its alkali metal salt and it is to be understood that the term "acid" as used in the specification and the appended claims is intended to  
25       include the salt form as well as the free acid form.

      The process of the present invention is typically conducted under mild conditions, with good results being obtained using a temperature in the range of from -10°C to 35°C, preferably 0°C to 30°C, more preferably 10°C to 25°C, and most preferably 20°C.  
30       Reaction pressures are not critical and atmospheric pressure is typically used.

      The process of the instant invention can be carried out either batchwise or continuously, using a stirrer equipped reactor or other well known contacting technique to achieve adequate mixing.  
35       Preferred reaction conditions, e.g., temperature, pressure, flow



rates, etc., vary somewhat depending on the specific nitroxide utilized and on the concentration of the nitroxide.

Following the reaction, the product may be separated from the reaction mixture using conventional procedures such as extraction using a suitable extraction solvent such as, for example, ethyl acetate; evaporation wherein the solvent is stripped from the reaction mixture by using heat or vacuum. Phase separation of the acidified solution may be effected at 100°C with water. The reaction product can be purified by a number of conventional means such as high temperature water washing or catalytic hydrogenation.

The products produced by the instant process can be used in a variety of detergent applications. For example, light duty dishwashing liquids, shampoos and heavy duty laundry liquids or powders.

The process of this invention will be further described by the following Examples, wherein the starting alkoxyalkanol was a NEODOL (NEODOL is a TRADEMARK). Ethoxylate 23-3T alcohol which was prepared by ethoxylating a mixture of  $C_{12}$  and  $C_{13}$  substantially straight chain alcohols ( $C_{12}:C_{13} \sim 40:60$ ) to an ethoxylate alcohol having 3 ethylene oxide units per molecule and then topping off the unreacted alcohols and lower ethoxylates so that the final product has three ethylene oxide units per molecule.

#### Example 1

Thirty-one grams of NEODOL. Ethoxylate 23-3T, 0.5 grams of 2,2,6,6-tetramethyl-piperidine-1-oxyl and 125 milliliters of dichloromethane were charged to a 1 liter round bottomed flask. To this mixture was added 282 grams of 5.25 %wt sodium hypochlorite in which the pH was adjusted to 8.6 by the addition of 2.6 grams of 25 %wt sulfuric acid. The reaction temperature was held at 20°C over a six hour period. The results are presented in Table I.

#### Example 2

31.4 grams of NEODOL. Ethoxylate 23-3T, 0.125 grams of 2,2,6,6-tetramethyl-piperidine-1-oxyl and 125 milliliters of dichloromethane were charged to a 1 liter round bottomed flask. To this mixture was added 282 grams of 5.25 %wt sodium hypochlorite in



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which the pH was adjusted to 8.6 by the addition of 2.6 grams of 25 %wt sulfuric acid. The reaction temperature was held at 20°C over a six hour period. The results are presented in Table I.

### Example 3

5           31.7 grams of NEODOL. Ethoxylate 23-3T, 0.125 grams of 2,2,6,6-tetramethyl-piperidine-1-oxyl, 100 milliliters of ethyl acetate, and 5 grams of alkoxyalkanoic acid were charged to a 1 liter round bottomed flask. To this mixture was added 282 grams of 5.25 %wt sodium hypochlorite. The reaction temperature was held at 10 20°C over a four hour period. The results are presented in Table I.

### Comparative Example A

Comparative A was carried out in a manner similar to Example 1 except that di-tert-butyl nitroxide was used as the nitroxide. The 15 results are presented in Table I.

### Comparative Example B

Comparative B was carried out in a manner similar to Example 1 except that no nitroxide was used. The results are presented in Table I.

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Table 1Oxidation of Alkoxyalkanols to Alkoxyalkanoic Acid

	Con- <u>version</u>	% Sel. <u>AEC</u> <sup>1)</sup>	% Sel. <u>Esters</u>	% Sel. <u>Formates</u>	% Sel. Fatty <u>Acids</u>
Example 1	>99	90	5.1	3.2	1.2
Example 2	97	93	7	<1	<1
Example 3	99	89	5.1	3.5	2.4
Comparative Example A	43	<1	97	1	2
Comparative Example B	13	50	38	6	6

1) AEC - alkoxyethoxy acetic acids

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CLAIMS:

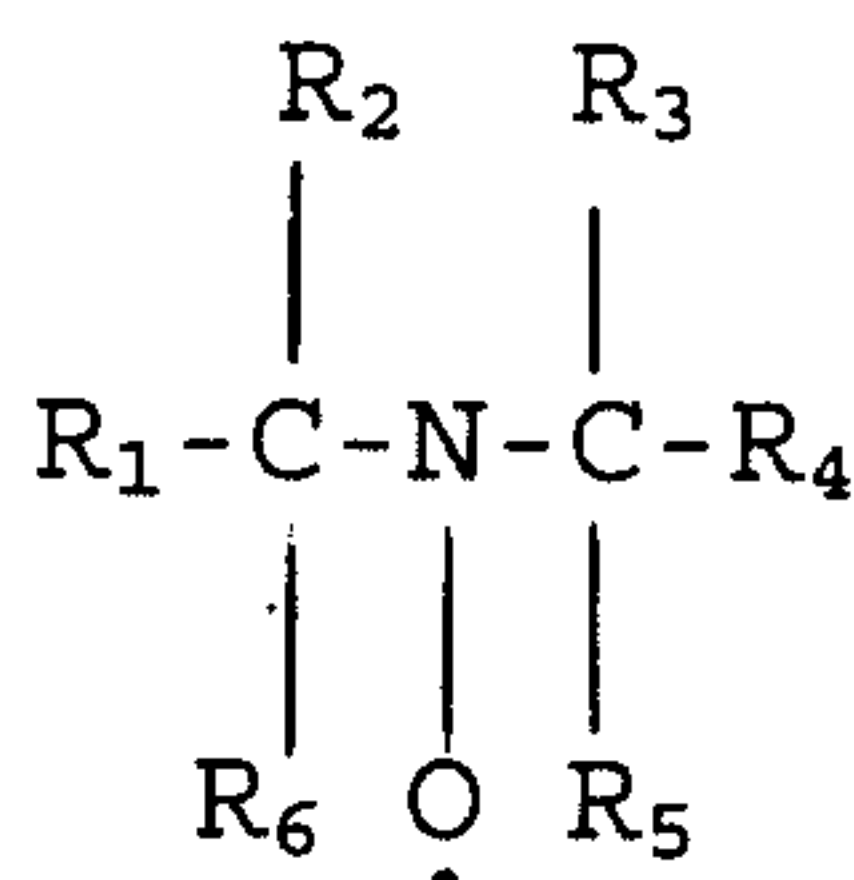
1. A process for the preparation of an alkoxyalkanoic acid of the formula



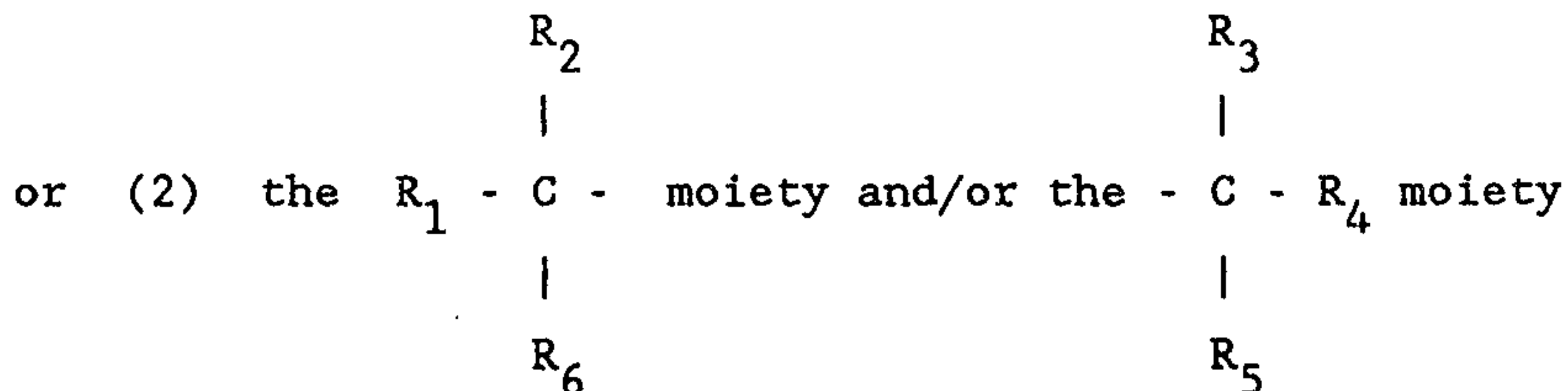
5 wherein R is an alkyl group of from 1 to 22 carbon atoms, R' is hydrogen or methyl or mixtures thereof (on the individual molecule) and n is an integer of from 1 to 12, or a salt thereof, which process comprises oxidizing the corresponding alkoxyalkanol using an oxidant in the presence of a solubilized  
10 stable free radical nitroxide except for di-tertiary alkyl nitroxides in a neutral to slightly basic medium not adjusted with a bicarbonate salt.

2. A process as claimed in claim 1, wherein the solubilized stable free radical nitroxide has the formula:

15



wherein (1) (a) each of R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub> and R<sub>4</sub> is an alkyl, aryl or heteroatom substituted aryl or alkyl group having 1 to 15  
20 carbon atoms, and (b) R<sub>5</sub> and R<sub>6</sub> (i) each is an alkyl group having 1 to 15 carbon atoms provided that R<sub>1</sub>-R<sub>6</sub> are not all alkyl groups, or a substituted alkyl group having 1 to 15 carbon atoms wherein the substituent is halogen, cyano, -CONH<sub>2</sub>, -OCOCH<sub>3</sub>, OCOC<sub>2</sub>H<sub>5</sub>, carbonyl, alkenyl, -OR'' or -COOR'' wherein  
25 R'' is alkyl or aryl, or (ii) together form part of a ring that contains 4 or 5 carbon atoms and up to two heteroatoms of O or N



individually are aryl.

3. A process as claimed in claim 2, wherein in the formula of the solubilized stable free radical nitroxide,  $R_5$  and  $R_6$  together form part of a ring that contains 4 or 5 carbon atoms and up to two heteroatoms of O or N.

4. A process as claimed in claim 3, wherein the solubilized stable free radical nitroxide is a 2,2,6,6-substituted piperidine-1-oxyl.

5. The process of claim 4 wherein the solubilized stable free radical nitroxide is selected from the group consisting of 2,2,6,6-tetramethyl-piperidine-1-oxyl, 4-hydroxy-2,2,6,6-tetramethyl-piperidine-1-oxyl, 4-oxo-2,2,6,6-tetramethyl-piperidine-1-oxyl, 2,2,6,6-tetramethyl-piperidine-1-oxyl-4-sulfate, and mixtures thereof.

6. The process of any one or more of claims 1-5, wherein the stable free radical nitroxide is dissolved in a solvent selected from the group consisting of ethyl acetate, dichloromethane, acetonitrile, toluene, chlorobenzene, xylene, carbon tetrachloride, chloroform, tetrachloroethylene, diethyl ether, methyl-tert-butyl ether and mixtures thereof.

7. The process of claim 6 wherein the solvent is selected from the group consisting of dichloromethane, ethyl acetate and mixtures thereof.

8. The process of any one or more of claims 1-7, wherein said alkoxyalkanol is contacted with said solubilized stable free radical nitroxide, followed by the addition thereto of a halogen-containing oxidant.

9. The process of claim 8 wherein the amount of solubilized stable free radical nitroxide is in the range of from 500 parts per



million to about 30,000 parts per million, basis the weight of the alkoxyalkanol.

10. The process of any one or more of claims 1-7, wherein said alkoxyalkanol is contacted with a halogen-containing oxidant,  
5 followed by the addition thereto of said stable free radical nitroxide.

11. The process of claim 10 wherein the amount of solubilized stable free radical nitroxide is in the range of from 100 parts per million to about 3,000 parts per million, basis the weight of the  
10 alkoxyalkanol.

12. The process of claim 8 or 10 wherein said halogen-containing oxidant is selected from the group consisting of chlorine, hypochlorite and N-chloro compounds.

13. The process of any one or more of claims 1-12 wherein said  
15 process is carried out at a temperature in the range of from -10°C to 35°C and at atmospheric pressure, and the alkoxyalkanoic acid or a salt thereof is separated out thereafter.

14. The process of any one or more of claims 1-3 wherein an acid is added to the reaction mixture during the course of the reaction.

Smart & Biggar  
Ottawa, Canada  
Patent Agents