

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
3 February 2005 (03.02.2005)

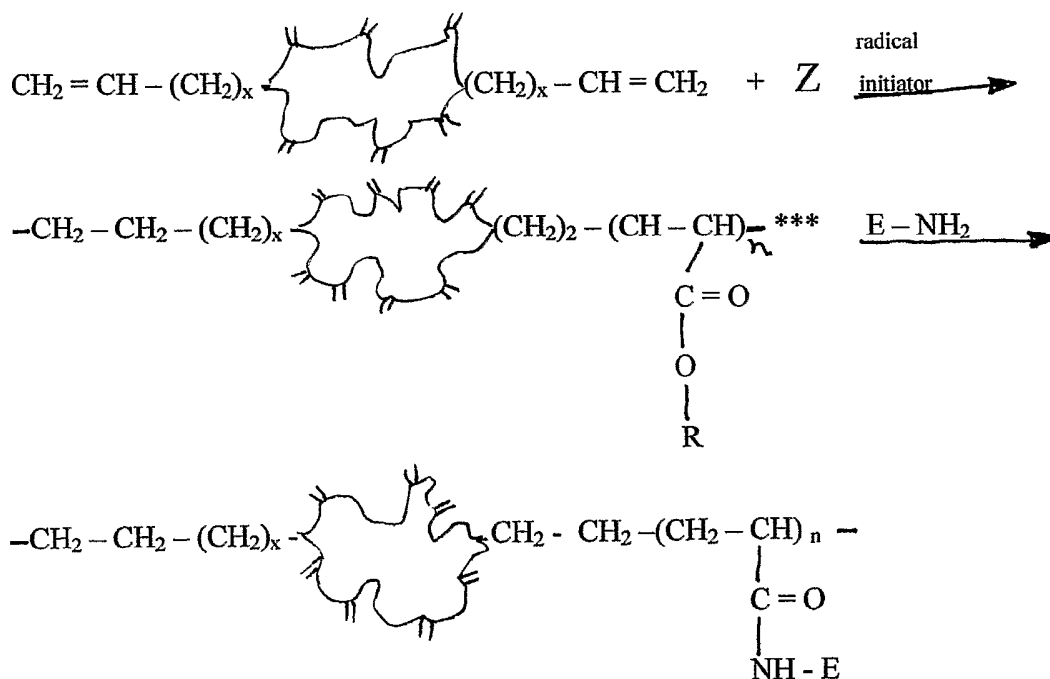
PCT

(10) International Publication Number
WO 2005/010086 A2

- (51) International Patent Classification⁷: C08K
- (21) International Application Number: PCT/US2004/020425
- (22) International Filing Date: 24 June 2004 (24.06.2004)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/488,195 17 July 2003 (17.07.2003) US
10/865,708 10 June 2004 (10.06.2004) US
- (71) Applicant (for all designated States except US): DIAZEM CORPORATION [US/US]; 1406 East Pine Street, Midland, MI 48640 (US).
- (72) Inventors: CABEY, Melvin; 1406 East Pine Street, Midland, MI 48640 (US). KIM, Yung, K.; 2314 Wilmington Drive, Midland, MI 48642 (US).
- (74) Agent: MCKELLAR, Robert, L.; McKellar Stevens, PLLC, 784 South Poseyville Road, Midland, MI 48640 (US).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Declarations under Rule 4.17:
— as to the identity of the inventor (Rule 4.17(i)) for all designations

[Continued on next page]

(54) Title: IMMOBILIZATION METHODS FOR ORGANIC MOLECULES TELOMERS AND POLYMERS ON SOLID SUBSTRATES



(57) Abstract: The immobilization of organic molecules, telomers and polymers on solid substrates. Organic molecules, telomers and polymers are immobilized onto solid substrates, especially particulate materials via covalent bonds that provide greater thermal and organic stability than other methods of immobilization.

WO 2005/010086 A2



-
- *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for all designations*
 - *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations*
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

Published:

- *without international search report and to be republished upon receipt of that report*

TO WHOM IT MAY CONCERN:

Be it known that We, Melvin A. Cabey and Yung K. Kim, both residents of the City of Midland, County of Midland, State of Michigan, have invented a new and useful invention that is

5

**IMMOBILIZATION METHODS FOR ORGANIC MOLECULES
TELOMERS AND POLYMERS ON SOLID SUBSTRATES**

that is described in this specification. This application claims priority from US
10 Provisional application 60/488,195, filed on July 17, 2003 and US Utility application
10/865,708, filed on June 10, 2004.

The invention disclosed and claimed herein deals with the immobilization of organic molecules, telomers and polymers on solid substrates.

15 Organic molecules, telomers and polymers are immobilized onto solid substrates,
especially particulate materials via covalent bonds that provide greater thermal and
organic stability than other methods of immobilization.

BACKGROUND OF THE INVENTION

Immobilization of molecules and/or materials on substrates, such as silicas and
polymeric resinous beads are known. However, covalent bonding immobilization on solid
20 substrates requires reactive functional groups on the molecules to be attached, such as
-SiOR, -SiX, and the like. While R-OH types of functional groups result in
immobilization on solid substrates, the resulting products are not stable because the bond
is an R-O-Si – substrate bond which are known to be chemically unstable, for example,
are readily hydrolyzable. Such bonds are also subject to other chemical attacks.

25 Further, immobilization of molecules and higher molecular weight telomers and
polymers containing no reactive stable, and covalently bondable groups, have been
achieved via adsorption and physical entrapment. These types of immobilized materials
lose their activity due to gradual loss of the immobilized molecules via leaching.

30 Covalently bonded immobilization of non-bondable functional molecules and
higher molecular weight telomers and polymers is very difficult if not impossible. Even if
higher molecular weight telomers and polymers contain bondable functional groups,

referred to as an upper, cake or scum layer, a middle, liquid zone, and a bottom, sedimentary or sludge layer. Waste matter enters the liquid zone at the middle of the tank. The sedimentary layer is formed as heavy solids settle to the bottom of the tank as sediment, or sludge, where they are further decomposed. Some of the sediment, however, will not be biodegradable and will remain at the bottom of the tank. The cake layer is formed as fats and other lighter suspended solids rise to the top of the tank where they too may further decompose.

During proper septic tank operation, only material from the liquid zone is dispensed to the drainage field. The effective volume and rate of flow of the tank determine the tank's settlement rate. The volume of the tank's liquid zone, therefore, is considered the tank's effective volume. In turn, that effective volume is used to determine the fixed design capacity of the tank, which is measured as the ability of the tank to process a particular flow rate of material. With this, the tank will be unable to process material entering the system at an inflow rate over the maximum allowable flow rate.

A septic tank's system capacity, on the other hand, is condition dependent in that it is indicative of the system's ability to continue to process material. The tank's system capacity falls to zero when, for example, particles of the sedimentary or cake layers begin to escape from the tank to the drainage field or the sedimentary and cake layers become so close to one another that the liquid layer is nearly or completely extinguished.

Advantageously, as a result of anaerobic decomposition in the upper and bottom layers, the increase in thickness of the sedimentary and cake layers is substantially less than the rate at which corresponding solids are input into the system. Nonetheless, the bottom, sedimentary or sludge layer and the upper, scum or cake layer do tend to increase progressively in thickness during normal operation of the septic system such that the accumulated solids must eventually be pumped from the system.

Common practice suggests that this pumping be carried out when the volume of the middle liquid zone is reduced to roughly one-third of the total height of the three layers. When that need for pumping will be reached, however, is dependent on the mix and overall volume of waste that is input to the system and the effectiveness of the biological decomposition occurring in the septic tank. Pumping may be considered necessary based on the absolute location of the top layer, the absolute location of the bottom layer, or a combination of these factors that have reduced the volume of the middle, liquid zone to a given extent. Notably, as the volumes of solids increase in the septic tank, the effectiveness of the biological decomposition tends to

As a result, the covalently immobilized materials provide a large number of chemically reactive functional groups that can be used to covalently immobilize a large number of molecules, including enzymes, that are useful for many applications.

Thus, what is disclosed and claimed herein is a method of covalently bonding a
5 material selected from the group consisting of organic molecules, telomers, and
polymers, on solid substrates, the process comprising contacting the solid substrate with
an alkenyl containing silane containing organofunctional moieties and allowing the
organofunctional moieties to react with the solid substrate to provide an alkenyl
functional group bound to the solid substrate to form a first product.

10 Thereafter, contacting the first product from just above with a material
selected from the group consisting of organic molecules, telomers, and polymers,
in the presence of free radicals, to covalently bond the material to the solid substrate.

Another embodiment of this invention is a process in which materials selected
from the groups consisting of organic molecules, telomers, and polymers are covalently
15 reacted, in the presence of a free radicals, with alkenyl groups on silanes, wherein the
silanes also contain organofunctional moieties, to form a first product, and then reacting
the first product of that reaction with a solid substrate using the organofunctional
moieties to bind the solid substrate to the first product.

The methods described and claimed herein are novel and utilize olefinic
20 functional groups, in one embodiment, previously bonded onto the solid substrate to bond
to C-H groups of organic molecules, telomers or polymers via free radical catalyzed
addition reactions to achieve a covalent bonding to the solid substrate. The materials have
a broad range of applications from various analytical and other smaller volume
applications, to large volume industrial applications as are set forth by way of example,
25 *infra*.

Organic molecules, telomers and polymers have previously been immobilized
onto silica and other solid substrates but reactive groups had to be built onto them in
order to bond on the substrate surface.

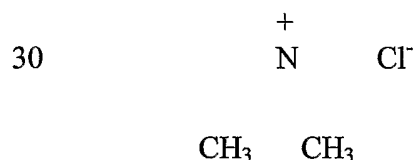
This invention involves the immobilization of organic molecules, telomers, and
30 polymers via stable, covalent bonding wherein the organic molecules, telomers, and
polymers do not normally have reactive groups under ambient conditions. The invention

also involves the use of olefinic functional silanes that are attached to solid substrates, such as silica or other silaceous materials via hydrolysis and subsequent reaction with hydroxyl groups on the substrate. Then, the reaction of the olefinic groups of the silanes, with organic molecules, telomers, or polymers, via free radical catalyzed addition of C-H
 5 groups on them, is undertaken to bond the organic molecules, telomers, and polymers with the olefinic groups.

Olefinic groups on the silanes include vinyl, allyl, hexenyl, and longer chain length olefinic containing molecules. Such olefinic silanes also include one or more hydrolyzable groups such as, for example, alkoxy groups, such as methoxy, ethoxy,
 10 isopropoxy, and the like, halo groups, such as chloro, ester groups such as acetoxy and propoxy, and oximo groups, and the like.

Organic molecules useful in this invention include crown ethers and other aliphatic carbon/hydrogen-containing molecules. Telomers and polymers included in this invention are, for example, polyethylene, polystyrene and almost any other material
 15 containing aliphatic C-H groups, and which also include aliphatic C-H groups on aromatic materials, such as toluene. Telomers are defined as the products of telomerization which is defined as a organic reaction involving addition of fragments of one molecule such as an alcohol, acetal, or chloroform, to the ends of a polymerizing olefin system, for example the reaction of carbon tetrachloride with styrene in the
 20 presence of acetyl peroxide to form the telomers $Cl\{CH(C_6H_5)cCH_2\}_nCCl_3$.

Examples of such Organic molecules, telomers, and polymers are: cellulose, polystyrene, crown ethers, polydimethylsiloxanes, glycol polymers, fatty acids, fatty esters, borate esters, carbohydrates, optically active enantiomers, polyolefins grafted with allylglycidylether, enzymes, polyethyleneimines, vitamins, especially vitamin E,
 25 poly(acrylic acid), poly(acrylic acid) derivatives, non-ionic surfactants, copolymers of allylglycidylether with monomers, organic amines,
 $--CH_2--(CH \text{ ----- } CH)---CH_2--$,



The solid substrates include any of the solid materials exhibiting a reactive
5 surface that can react with the silanes of this invention, that is, a reaction wherein stable
covalent bonding will occur.

In another embodiment of this invention, high molecular weight molecules and
polymers, that contain an aliphatic C-H unit, may be immobilized onto polymeric,
particulate materials such as polyethylene and polystyrene, that contain an aliphatic C-H
10 unit by utilizing the free radical catalyzed addition reaction of the aliphatic C-H group to
a diene such as butadiene or octadiene, as the crosslinker, to achieve a covalent bond.

Any free radical generating technique including peroxides, radiation, mechanical
energy, and the like may be used to catalyze the addition of the aliphatic C-H to the
olefinic functional group.

15 Conditions for reacting the silanes such as chlorosilanes, alkoxy silanes,
acetoxysilanes, and the like, onto the solid substrate are well-known techniques and such
preparations do not need to be set forth herein.

A broad range of final product compositions and structures may be accomplished
by stoichiometric control of the addition of the materials and further reaction of the
20 immobilized materials to additional monomers or polymers, including the same
macromonomers or polymers or a different macromonomer or polymer containing an
aliphatic (C-H group) via use of free radical catalyzed reaction of dienes such as
octadiene.

A wide variety of applications exist for the materials disclosed herein including
25 chromatographic, both liquid, and gas/liquid systems, catalysts for both organic processes
and biological processes, various industrial uses, dairy applications, photographic
applications, optical applications, brewery processes, leather treating, textile applications,
pharmaceutical applications, catalytic materials stabilization, metal capture through
chelation, purification and separation applications, personal care products, household care
30 products, defoamers and antifoams, polymer modifiers, and the like.

Examples

Vinylsilane bonded silicas were prepared by reaction of vinyltrimethoxysilane or vinyltrichlorosilane with various silicas using known procedures.

Example 1

5 About 10 g of vinyl silane bonded silica was suspended in 200 ml of benzene, and there was added to the suspended bonded silica, 7 g of 100,000 molecular weight of polystyrene dissolved in 50 ml of benzene. To this mixture was added 0.8 g of benzoyl peroxide and then it was heated for about 12 hours at 80°C while stirring.

10 The modified bonded silica was isolated using washing and drying techniques to give polystyrene bonded to the silica.

The silica was packed in an HPLC column and a run was made on the HPLC and it showed polystyrene bonded to silica.

Example 2

15 To a mixture of 5 g of vinylsilane bonded to silica as produced in Example 1, there was added 200 ml of benzene, and 2.2 g of 18-crown-6 - ether and 0.2 g of benzoyl peroxide. The mixture was reacted at 80°C for about 12 hours.

Upon isolation and drying of the silica, 18-crown-6 ether bonded to silica was obtained. HPLC showed the 18-crown-6 ether bonded to silica.

Example 3

20 To a mixture of 5 g of vinylsilane bonded silica in 200 ml of benzene, there was added 2 g of (+) - α - tocopherol and 0.05 g of benzoyl peroxide. The mixture was reacted at 65°C for 12 hours.

Upon isolation and drying of the resulting silica, vitamin E immobilized silica was obtained.

25 Example 4

To a mixture of 10 g of polystyrene and 2 g of allylglycidylether in 150 ml of benzene, there was added 0.02 g of benzoyl peroxide. The mixture was reacted at 65°C for 12 hours. Into the reacted mixture there was added 10 g of vinylsilane bonded silica and 0.015 g of benzoyl peroxide. The mixture was reacted at 70°C for 12 hours.

30 Upon isolation and drying of the resulting silica, immobilized allylglycidylether grafted polystyrene on silica was obtained.

Example 5

5 A mixture of 5 g of immobilized allylglycidylether grafted polystyrene on silica from example 4, and 4 g of papain in buffered solution was stirred at 40 to 50°C for 12 hours.

Upon isolation, washing with deionized water, and drying, papain immobilized silica was obtained. It is believed that the reaction involved the epoxy groups reacting
10 with the amino groups of the papain.

Example 6

To a mixture of 150 ml of poly(methyl acrylamide) in water (10%) and 5 g of vinylsilane bonded silica, there was added 0.02 g of benzoyl peroxide. The mixture was reacted at 70°C for 12 hours.

15 Upon isolation and drying of the resulting silica, poly(methylacrylamide) immobilized silica was obtained.

Example 7

Following the procedure of example 1, the following molecules and polymers were immobilized on silica via covalent bonding.

20 polydimethylsiloxane fluid

poly(ethylene glycol)

fatty acid (C₆)

fatty ester (C₂₄)

dextrin

25 papain*

allylglycidylether grafted polyethylene

polyethyleneimine*

poly(diallyldimethylammonium chloride)

poly(vinylmethyl)ketone

30 poly(acrylamide)

poly{bis-(2-chloroethyl)ether-alt-1,3-bis-(3-(dimethylamino)propyl)urea}, quaternized

D – Mannose** and
Heparin**,

wherein * denotes that water was used as a solvent and ** denotes that buffered water was used as the solvent.

5 Example 8

A mixture of 5 g of immobilized allylglycidylether grafted polystyrene on silica from example 4 and 2 g of ampicillin were reacted in 100 ml of benzene at 50°C for 10 hours.

10 Upon isolation, washing with methanol and drying, ampicillin immobilized silica via the reaction of epoxy groups and amino groups of ampicillin, was obtained. An HPLC of the silica showed chirality.

 Example 9

A mixture of 10 g of crosslinked polystyrene beads, 3 g of allylglycidylether, and 0.02 g of benzoyl peroxide in 100 ml of benzene was reacted at 65°C for 12 hours.

15 Upon isolation and drying of polystyrene beads, allylglycidylether grafted polystyrene beads were obtained.

The grafted polystyrene beads were found to react with polyethyleneimine in DFM solution to yield polyethyleneimine immobilized polystyrene beads via the reaction of epoxy groups with amino groups of the polyethyleneimine.

20 Example 10

A mixture of 5 g of poly(methylacrylate) immobilized silica of Example 6 and 3 g of polyethyleneimine in 50 ml of DMF was reacted at 40 to 50°C for 10 hours.

Upon isolation, washing with methanol, and drying, polyethyleneimine immobilized silica, via reaction of ester groups and amino groups, was obtained.

25 Example 11

The immobilized products of example 2, example 5, example 6, and example 10 were selected and tested for chelating capability with copper sulfate, and found to be chelating agents.

 Example 12

A mixture of immobilized allylglycidylether-grafted polystyrene on silica from example 4, and 2 g of 2-(aminomethyl-15-crown-5) was reacted in 100 ml of benzene at 50°C for 10 hours.

5 Upon isolation, washing with methanol and drying, the amino-crown ether-immobilized silica via the reaction of epoxy groups and amino groups of the crown ether is obtained

What is claimed is:

1. A method of covalently bonding a material selected from the group consisting of

- 5
- i organic molecules,
 - ii telomers, and
 - iii polymers,

on solid substrates, the process comprising:

(I) contacting the solid substrate with an alkenyl containing silane
10 containing organofunctional moieties and allowing the organofunctional moieties to react
with the solid substrate to provide an alkenyl functional group bound to the solid
substrate:

(II) contacting the product of (I) with a material selected from the group
consisting of

- i organic molecules,
- 15 ii telomers, and
- iii polymers,

to covalently bond the material to the solid substrate.

20

25

30

2. A method of covalently bonding a material as claimed in claim 1 where, in addition, there is a source of free radicals present.

5 3. A method as claimed in claim 2 wherein the source for the free radical generation is a peroxide.

4. The method as claimed in claim 2 wherein the source for the free radical generation is radiation.

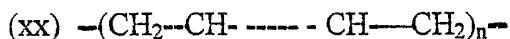
5. The method as claimed in claim 2 wherein the source for the free radicals is
10 mechanical energy.

6. A composition of matter prepared by the process of claim 1.

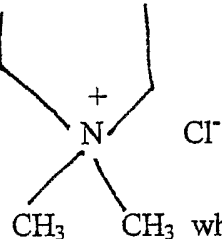
7. A composition of matter prepared by the process of claim 2.

8. A method as claimed in claim 1 wherein (i), (ii), and (iii) are selected from the group consisting of:

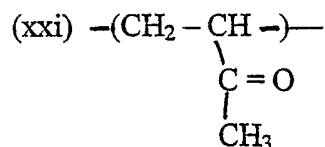
15 (i) cellulose, (ii) polystyrene, (iii) crown ethers, (iv) polydimethylsiloxanes, (v) glycol polymers, (vi) fatty acids, (vii) fatty esters, (viii) borate esters, (ix) carbohydrates, (x) optically active enantiomers, (xi) polyolefins grafted with allylglycidylether, (xii) enzymes, (xiii) polyethyleneimines, (xiv) vitamin E, (xv) poly(acrylic acid) (xvi) poly(acrylic acid) derivatives, (xvii)
20 non-ionic surfactants, (xviii) copolymers of allylglycidylether with monomers, (xix) organic amines,

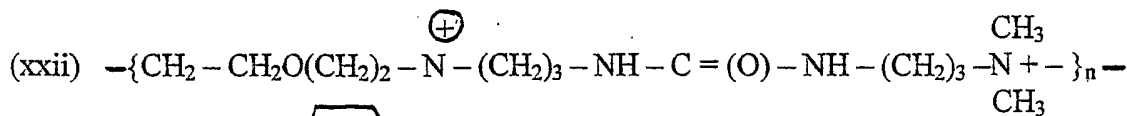


25



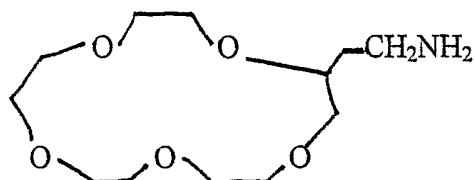
30





5

(xxiii)



(xxiv) alcohols, and (xxv) polyols.

9. A method as claimed in claim 2 wherein (i), (ii), and (iii) are selected from the group consisting of:

10

(i) cellulose, (ii) polystyrene, (iii) crown ethers, (iv)

polydimethylsiloxanes, (v) glycol polymers, (vi) fatty acids, (vii) fatty esters,

(viii) borate esters, (ix) carbohydrates, (x) optically active enantiomers, (xi)

polyolefins grafted with allylglycidylether, (xii) enzymes, (xiii) polyethyleneimines,

(xiv) vitamin E, (xv) poly(acrylic acid) (xvi) poly(acrylic acid) derivatives, (xvii)

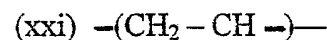
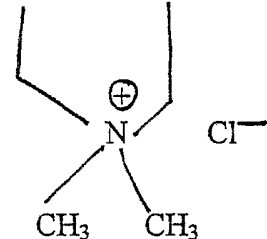
15

non-ionic surfactants, (xviii) copolymers of allylglycidylether with monomers, (xix)

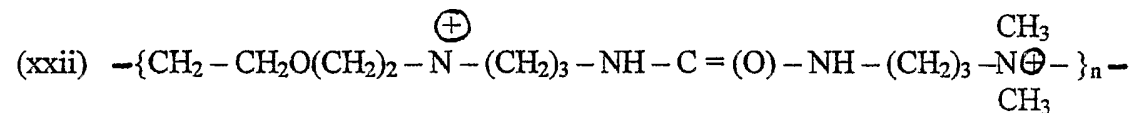
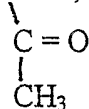
organic amines,



20

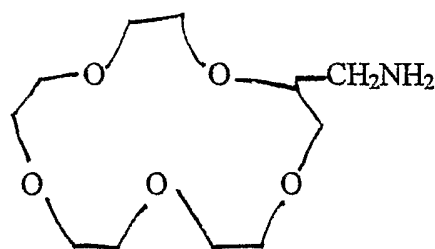


25



30

(xxiii)



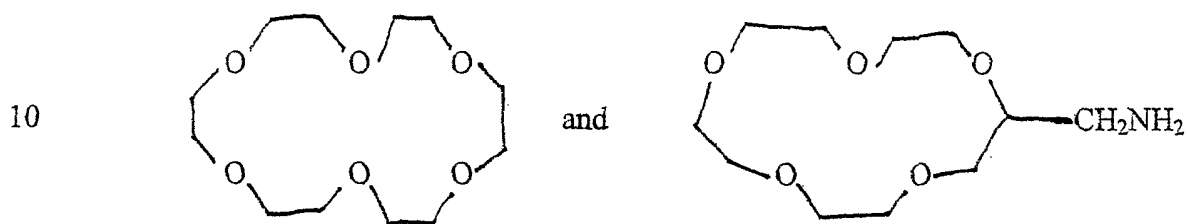
35

(xxiv) alcohols, and (xxv) polyols.

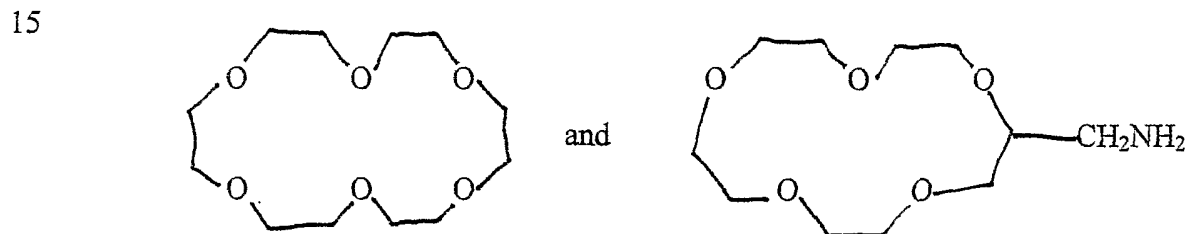
10. A method as claimed in claim 8 wherein the polystyrene is polystyrene grafted with allylglycidylether.

11. A method as claimed in claim 9 wherein the polystyrene is polystyrene grafted with allylglycidylether.

12. A method as claimed in claim 8 wherein the crown ethers are selected from the group consisting of:



13. A method as claimed in claim 9 wherein the crown ethers are selected from the group consisting of:



20

14. A method as claimed in claim 8 wherein the enzyme is papain.

15. A method as claimed in claim 9 wherein the enzyme is papain

16. A method in which materials selected from the groups consisting of

- 25
- (i) organic molecules,
 - (ii) telomers, and
 - (iii) polymers

are (I) covalently reacted, in the presence of a free radical initiator, with an alkenyl group on a silane, wherein the silane also contains organofunctional moieties, and then

(II) reacting the product of (I) with a solid substrate using the organofunctional moieties to bind the solid substrate to the product.

30

17. A composition of matter prepared by the process of claim 16.

18. A personal care product that is a formulated product that includes a composition of claim 6.
19. A personal care product that is a formulated product that includes a composition of claim 7.
- 5 20. A personal care product that is a formulated product that includes a composition of claim 17.
21. A defoamer composition that is a formulated product that includes a composition of claim 6.
22. A defoamer composition that is a formulated product that includes a composition of claim 7.
- 10 23. A defoamer composition that is a formulated product that includes a composition of claim 17.
24. An antifoam product that is a formulated product that includes a composition of claim 6.
- 15 25. An antifoam product that is a formulated product that includes a composition of claim 7.
26. An antifoam product that is a formulated product that includes a composition of claim 17.
27. A method of chelating metals from aqueous solutions, the method comprising, moving the aqueous solution into contact with a composition of claim 6.
- 20 28. A method of chelating metals from aqueous solutions, the method comprising, moving the aqueous solution into contact with a composition of claim 7.
29. A method of chelating metals from aqueous solutions, the method comprising, moving the aqueous solution into contact with a composition of claim 17.
- 25 30. A catalyzed process, wherein the composition of claim 6 is used as the catalyst.
31. A catalyzed process as claimed in claim 30 that is a organic process.
32. A catalyzed process as claimed in claim 30 that is a biological process.
33. A catalyzed process, wherein the composition of claim 7 is used as the catalyst.
34. A catalyzed process as claimed in claim 33 that is a organic process.
- 30 35. A catalyzed process as claimed in claim 33 that is a biological process.
36. A catalyzed process wherein the composition of claim 17 is used as the catalyst.

37. A catalyzed process as claimed in claim 36 that is a organic process.
38. A catalyzed process as claimed in claim 36 that is a biological process.
39. A liquid chromatographic process wherein a composition of claim 6 is used as the chromatographic support.
- 5 40. A liquid chromatographic process wherein a composition of claim 7 is used as the chromatographic support.
41. A liquid chromatographic process wherein a composition of claim 17 is used as the chromatographic support.

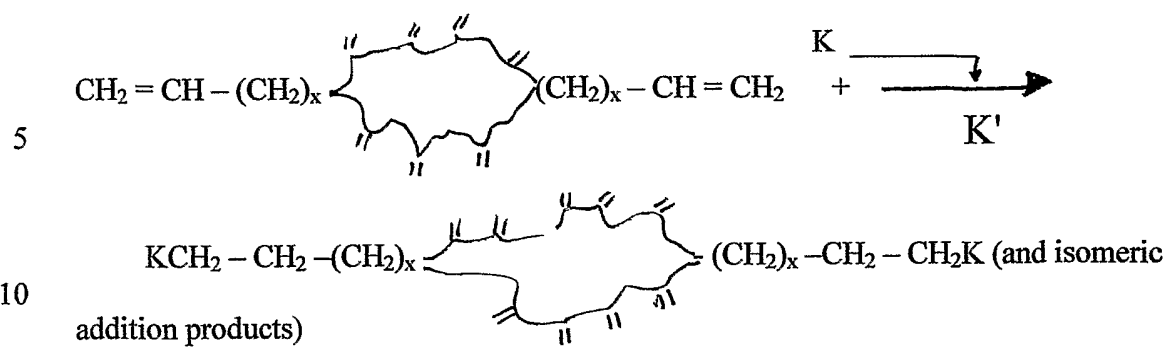


FIG 1

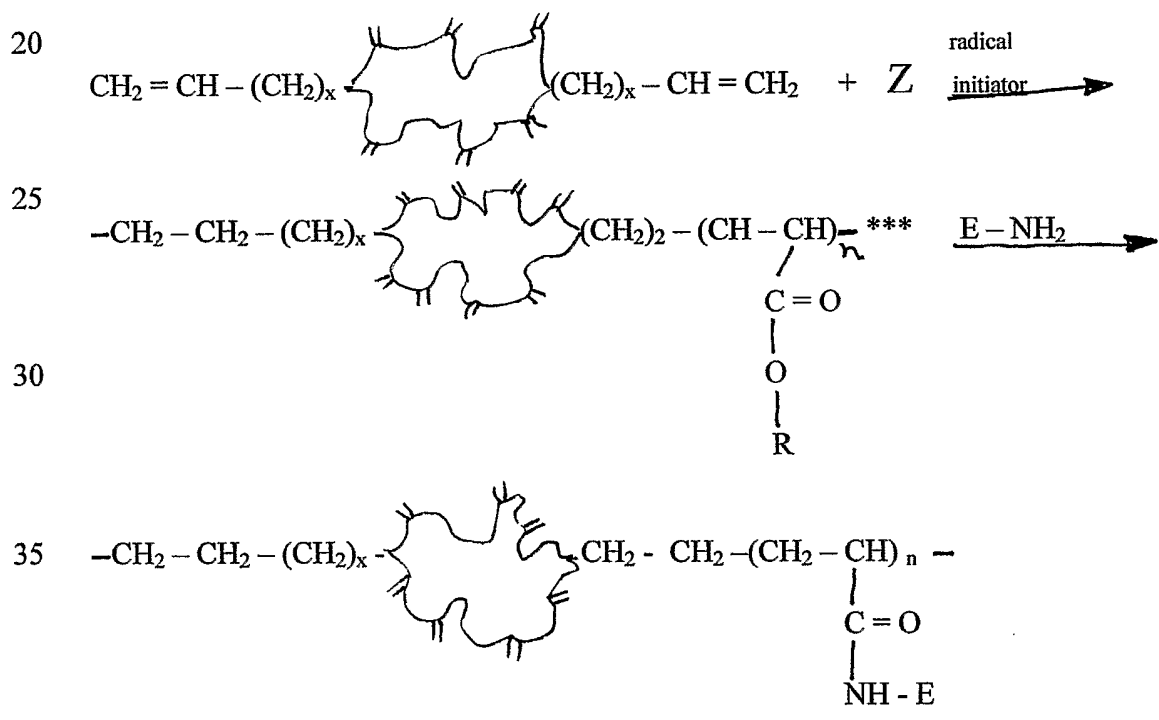


FIG 2

*** = +isomeric addition products