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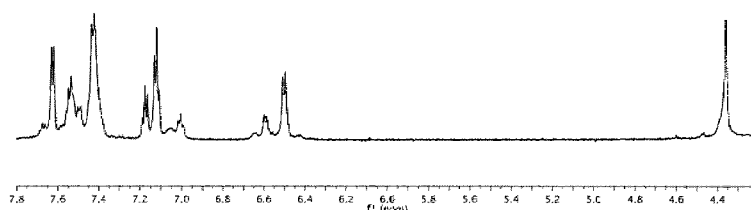
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FIGURE 3



(57) Abstract: The present invention relates to a new class of organic compounds and their use, for example, to sequester metal ions, including actinides (such as uranium and plutonium), precious metals (such as gold, silver and platinum) and all other metals (such as transition metals), from aqueous solutions, such as bodies of water (including but not limited to ocean water, seawater, river water) and all other aqueous solutions. Specifically, the present invention relates to a new class of polydentate organic chelating agents and methods for their use to recover metals from aqueous solutions, such as uranium from seawater.



COMPOUNDS AND METHODS FOR CHELATING METALS IN AQUEOUS SOLUTIONS

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional application, Serial No. 61/217,078, filed on May 27, 2009, which is incorporated herein in its entirety.

TECHNICAL FIELD

[0002] The present invention relates to a new class of organic compounds and their use, for example, to sequester metal ions, including actinides (such as uranium and plutonium), precious metals (such as gold, silver and platinum) and all other metals (such as transition metals), from aqueous solutions, such as bodies of water (including but not limited to ocean water, seawater, river water) and all other aqueous solutions. Specifically, the present invention relates to a new class of polydentate organic chelating agents and methods for their use to recover metals from aqueous solutions, such as uranium from seawater.

BACKGROUND OF INVENTION

[0003] Society relies upon the selective sequestration of metal ions for a broad range of uses, including medical research, water desalinization, and the production of nuclear power. Among metal ions, actinide ions and their corresponding oxides are of particular importance (Gopalan A. *et al.*, Radioactive Waste Management and the Nuclear Fuel Cycle, 17:161 (1993)). Traditionally, these and other metals have been brought to market through commercial mining which extracts metals stored in the earth's crust. Commercial mining, however, has not availed society of the vast supply of actinides and other metals dissolved in the world's bodies of water. Given the current high prices of commodities, the world's seas and oceans are a promising alternative reservoir from which to recover metals. In the case of uranium, for instance, sea water is estimated to

contain 4.5×10^{12} kg of dissolved uranium — approximately 1000 times that available from terrestrial sources.

[0004] At least three challenges, however, have impeded the extraction of uranium from seawater. First is the form of uranium dissolved in seawater. Second is the relative cost-inefficiency of known methods for the extraction of uranium from seawater. Third is the lack of agents that selectively bind uranium and other metal ions in aqueous solution.

[0005] The first of these challenges is the form of naturally-occurring uranium. Due to the highly oxidizing environment of the world's seas, virtually all naturally-occurring uranium in seawater comprises U (VI) in the form of the uranyl cation (UO_2^{2+}). This form of uranium is problematic because of its shape, structure and concentration.

[0006] In terms of its shape, the linear, cylindrical shape of the uranyl cation prevents the use of a number of known chelating ligands, such as ethylenediamine tetraacetic acid (“EDTA”), which effectively targets only spherical cations. Therefore a threshold challenge in the sequestration of uranyl cation is designing chelating agents to target cylindrical cations.

[0007] In terms of its structure, the uranyl cation in seawater forms highly stable tris(carbonato) complexes. The coordination numbers around the metal centers are generally 5 or 6 with the two uranyl oxygens being co-linear and chemically inert. Consequently, any ligand targeting uranium must provide an adequate path to allow for induced-fit binding of the UO_2^{2+} “cylinder.”

[0008] A group of Japanese scientists have attempted to address the structural hurdles (N. Seko, *et al.*, Nuclear Technology, 144:274-278(2003)). These scientists developed a method using fabric surfaces to extract uranium from seawater, but this method is slow and expensive; it requires eight months of submersion in seawater and produces uranium at a cost that is multiples of the highest price that uranium has ever fetched in the marketplace.

[0009] Finally, in terms of its concentration, the low concentration of the uranyl cation in seawater (~3 parts per billion) requires a chelating agent of very high affinity.

In addition, because of the presence of a myriad of other metal ions abundant in seawater, the chelating agent must exhibit high selectivity for the UO_2^{2+} cation.

[0010] The most general approach in developing such selective complexing agents relies on the construction of a ligand cavity of appropriate size and shape with converging donor atoms or groups (Franczyk, T.S. *et al.*, JACS, 114:8138 (1992)).

[0011] Carboxylate ions have strong affinity for binding metal ions. Numerous chelating agents containing carboxylate ions have been reported. For example, EDTA is widely used to sequester di- and tri-valent metal ions such as Ca^{2+} , Cd^{2+} , Mg^{2+} , and Fe^{3+} . Such binding occurs when the electron pairs on oxygens are donated to the empty orbitals of the metal ions.

[0012] The interaction between a metal ion and a carboxylate oxygen follow the principle of hard and soft acids and bases. It has been reported that distal electron pairs of the oxygen atoms are more basic and therefore bind to metal ions more tightly than proximal electron pairs (US Pat. No. 4,861,564 and 4,698,425). In known chelating agents, such as EDTA, nitrilotriacetate, succinate and phthalate, only the proximal, less basic lone pairs are involved in binding the metal ions. However, these chelating agents are ineffective in binding the uranyl cation because of its cylindrical shape.

[0013] Therefore, there is a need to develop chelating agents (ligands) that specifically bind to particular metal ions, such as UO_2^{2+} . In particular, there is a need to isolate such metals from low concentration aqueous solutions, such as seawater.

SUMMARY OF THE INVENTION

[0014] The disclosed embodiments are directed to methods involved in the separation of metal ions from aqueous solution using specifically designed chelating agents.

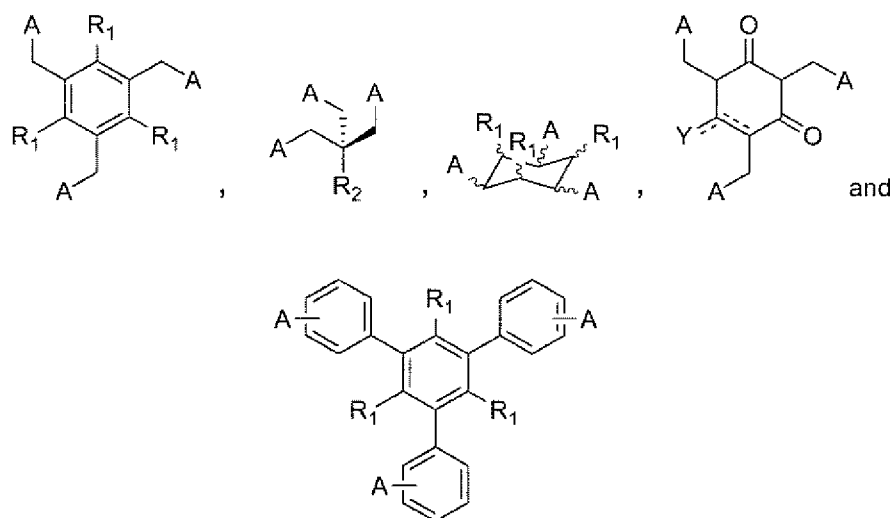
[0015] One object of the present invention is to provide selective chelating agents to separate metal ions, including but not limited to uranium (VI) and dioxouranium (VI) (uranyl, UO_2^{2+}). Such chelating agents should be robust and practical under harsh

conditions and be able to operate over a wide range of environmental conditions and concentrations.

[0016] The architecture of the systems requires subtle tailoring in order to present a pre-organized ligation cavity while retaining adequate flexibility to allow for facile uptake. The ligands must exhibit clefts with enough depth to accommodate the cylindrical shape of the uranyl ion.

[0017] In one aspect, the present invention relates in part to: chelating agent Compounds I to V; to processes for preparing Compounds I to V; ion exchange resins containing Compounds I to V; and extraction of uranyl ion using Compounds I to V, in particular from seawater.

[0018] Accordingly, in one embodiment, a chelating agent is provided having a central core moiety and three pendant groups (A) attached thereto for chelating metal ions from aqueous solution, wherein the chelating agent is selected from the group consisting of:

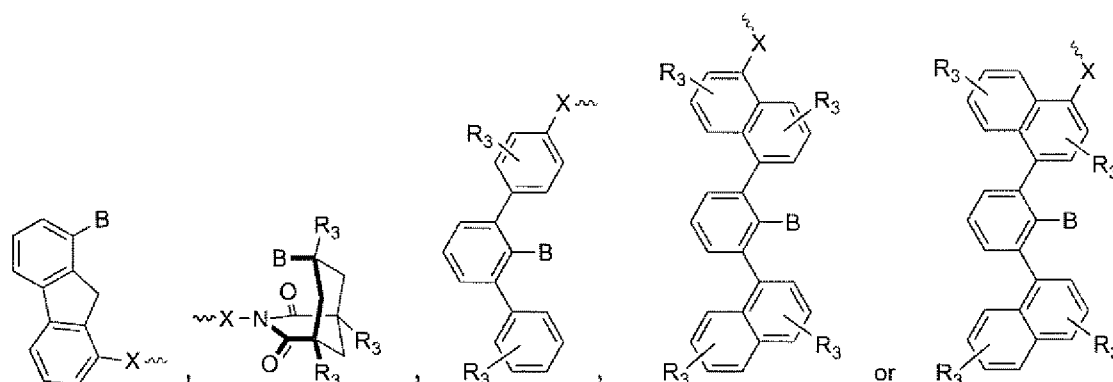


wherein each R_1 is independently hydrogen or unsubstituted C_{1-10} alkyl group;

wherein each R_2 is independently OH, NH_2 or NO_2 ;

wherein each Y is independently H, R_1 or O;

wherein A is independently:



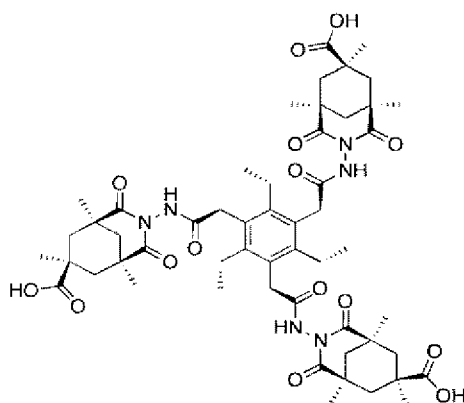
wherein B is , or ;

wherein R_3 is independently H, a substituted or unsubstituted C_{1-8} alkyl group, a substituted or unsubstituted C_{1-8} alkyl group with one or more double bonds, $(C_{1-10}$ alkyl group)-O-(C_{6-10} aryl), $(C_{1-10}$ alkyl group)-O-(C_{1-10} alkyl), or $(C_{1-10}$ alkyl group)(C_{6-10} aryl);

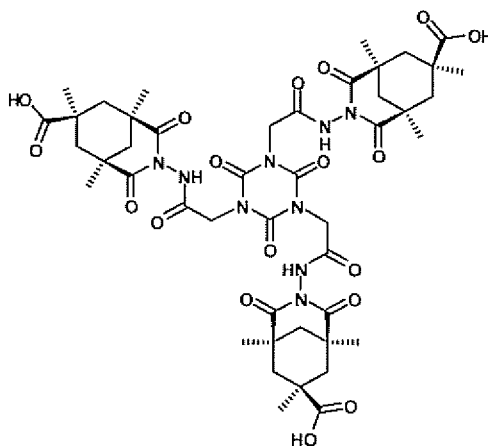
wherein A is covalently attached to the core moiety via X, which is selected from the group consisting of -CONH-, -NHCO-, -OCO-, -COO-, -CH₂O-, -NH-, -O-, -S- and a direct bond; and

wherein each ring structure may further comprise one or more heteroatoms selected from the group consisting of: N, S and O.

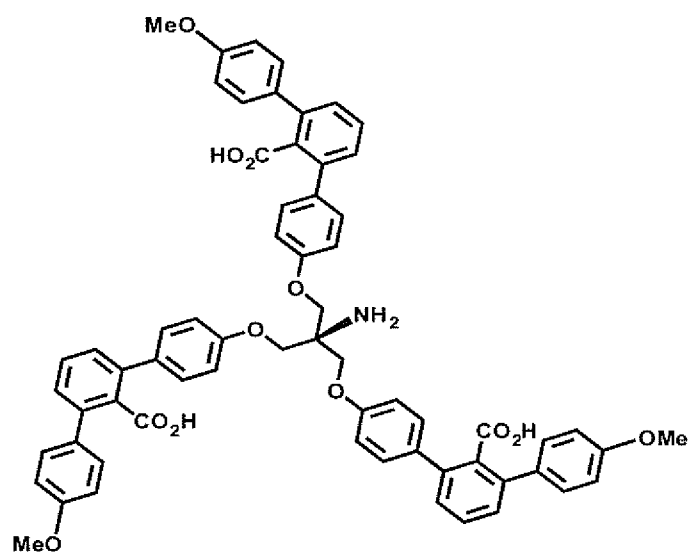
[0019] Such chelating agents may have any of the following Formulas:



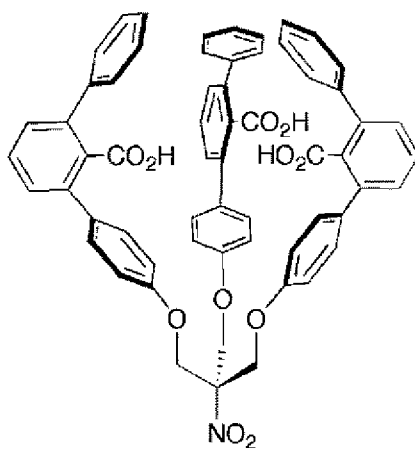
Compound I



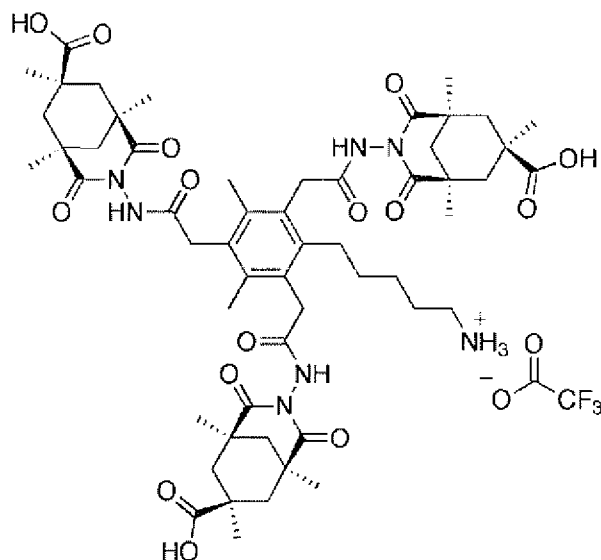
Compound II



Compound III



Compound IV



Compound V

[0020] In another embodiment, the invention is a system for chelating a metal ion comprising at least one chelating agent according to claim 1 bound to a solid support. The chelating agent may be bound to the support at any site of attachment on the core group (i.e. the part of the molecule without A), such as: one of the R_1 , R_2 or R_3 groups via a functional group added thereto.

[0021] In another embodiment, the invention is method of sequestering metal ions from aqueous solution comprising the steps of: preparing a chelating agent according to claim 1; and contacting the chelating agent with an aqueous solution suspected of containing metal ions. Such method may be used to sequester uranyl ions, and in particular to sequester uranyl ions from seawater.

[0022] The method may be carried out by first binding the chelating agent to a solid support or by dissolving it in a non-aqueous solvent before contacting the chelating agent with an aqueous solution. If bound to a solid support, the chelating agent may be bound via the core group, for example at any of the R_1 , R_2 or R_3 moieties which have been derivatized to include a functional group capable of forming a covalent bond with the solid support.

[0023] In still another embodiment, the invention is a method of chelating a uranyl ion from an aqueous solution comprising the steps of: providing a chelating agent comprising an organic core molecule and three pendant groups, each bearing at least one anionic moiety; and contacting the aqueous solution with the chelating agent; wherein the three pendant groups form a stable coordination complex with the uranyl ion via convergence of the anionic moiety with the metal ion.

BRIEF DESCRIPTION OF THE DRAWINGS

[0024] Figure 1 is a ^1H -NMR spectra of uranyl-free Compound IV in $\text{DMSO}-d_6$.

[0025] Figure 2 is a ^1H -NMR spectra of uranyl-free Compound IV in $\text{DMSO}-d_6$ with 3 equivalents TEA.

[0026] Figure 3 is a ^1H -NMR spectra of Compound IV in $\text{DMSO}-d_6$ with uranyl nitrate and 3 equivalents TEA.

[0027] Figure 4 is a ^1H -NMR spectra of uranyl-free Compound I in $\text{MeOD}-d_4$.

[0028] Figure 5 is a ^1H -NMR spectra of Compound I in $\text{MeOD}-d_4$ with uranyl acetate.

[0029] Figure 6 is a ^1H -NMR spectra of Compound I in $\text{MeOD}-d_4$ with uranyl acetate and 3 equivalents of TEA.

DETAILED DESCRIPTION OF THE INVENTION

[0030] The present invention relates to a new class of organic compounds and their use, for example, to sequester metal ions, including actinides (such as uranium and plutonium), precious metals (such as gold, silver and platinum) and all other metals (such as transition metals), from aqueous solutions, such as bodies of water (including but not limited to ocean water, seawater, river water) and all other aqueous solutions. Specifically, the present invention relates to a new class of polydentate organic chelating

agents and methods for their use to recover metals from aqueous solutions, such as uranium from seawater.

[0031] In the description that follows, a number of terms used in the field of chemistry are extensively utilized. In order to provide a clear and consistent understanding of the specification and claims, including the scope to be given such terms, the following non-limiting definitions are provided.

[0032] The term “alkenyl” as used herein refers to an unsaturated, open chain hydrocarbon with one or more carbon-carbon tripple bonds, having the general formula C_nH_{2n-2} that may be bound as a substituent to the central core moiety.

[0033] The term “alkyl” as used herein refers to an alkane group of the formula C_nH_{2n+2} missing one hydrogen. Specifically an alkyl has the general formula C_nH_{2n+1} that may be bound as a substituent to the central core moiety.

[0034] The term “alkylene” as used herein refers to a hydrocarbon chain in which there is one or more carbon-carbon double bonds, having the general formula C_nH_{2n-1} that may be bound as a substituent to the central core moiety.

[0035] The term “aryl” as used herein refers to any functional group or substituent derived from a simple aromatic ring, such as for example phenyl, thiophene or indolyl that may be bound as a substituent to the central core moiety.

[0036] The phrase “central core moiety” as used herein refers to the base structure of the chelating agent to which three chemical entities are bond that surround and sequester the actinide or precious metal cation during chelation.

[0037] The term “heterocyclic” as used herein refers to organic compounds containing at least one atom of carbon, and at least one element other than carbon, such as sulfur, oxygen or nitrogen within a ring structure. These structures may comprise either simple aromatic rings or non-aromatic rings. Examples include, pyridine (C_5H_5N), pyrimidine ($C_4H_4N_2$) and dioxane ($C_4H_8O_2$) that may be bound as a substituent to the central core moiety. As claimed and described herein, each aromatic ring structure depicted without heteroatoms may include them.

[0038] When the terms “one,” “a,” or “an” are used in this disclosure, they mean “at least one” or “one or more,” unless otherwise indicated.

[0039] The phrase “solid support” as used herein refers to any water-insoluble solid matrix to which the chelating agent may be bound, including for example, SephadexTM, dextran, latex particles, macroporous resins and glass beads.

A. Chelating Agents

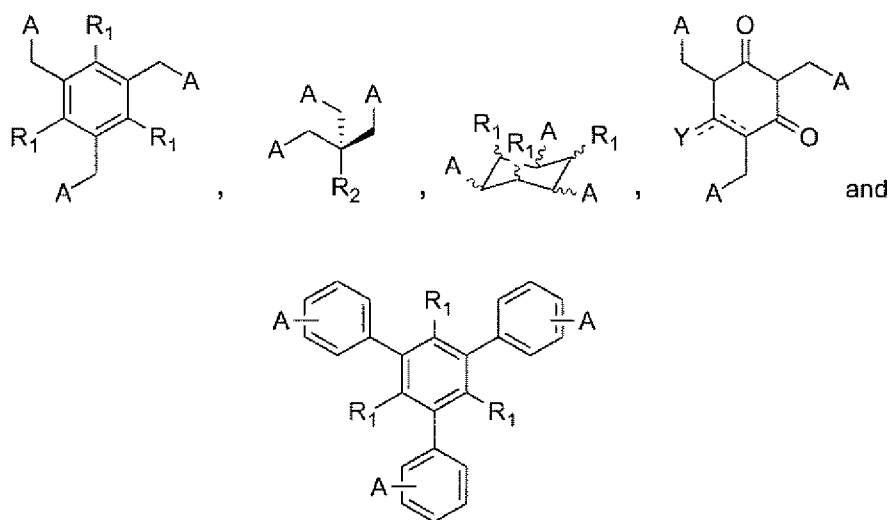
[0040] Pre-organized structures of macrocyclic polydentates are especially good candidates for sequestering actinides and precious metals. The high selectivity of macrocycles is governed mainly by the size of the cyclic interior and the nature the heteroatom donor involved in complexation. The resulting complexes are highly stable due to entropic factors, involved in chelation. Several anionic macrocyclic uranyl ligands are reported, *e.g.*, cyclic acetylacetonates (Alberts, A.H. *et al.*, J. Am. Chem. Soc., 101:3545 (1979)), polycarboxylates (Grey, R.A., *et al.*, J. Org. Chem., 102:5947 (1980)), thiocarbamates (Tabushi, I., *et al.*, J. Am. Chem. Soc., 107:4585 (1985)), Schiff bases (van Staveren, C.J., *et al.*, J. Am. Chem. Soc., 110:4994 (1988)) and calixarenes (Araki, K., *et al.*, Chem. Lett., 829 (1993).) However, the development of polydentate chelating agents for the sequestration of the pseudoplanar hexacoordinate uranyl ion is believed to be unreported.

[0041] The present invention, in part, provides polydentate chelating agents to separate metal ions from aqueous solution, such as uranium (VI) and dioxouranium (VI) (uranyl, [UO₂]²⁺).

[0042] The architecture of the molecules of the present invention requires subtle tailoring in order to present a pre-organized ligation cavity while retaining adequate flexibility to allow for facile uptake. The ligands must exhibit clefts with enough depth to accommodate the cylindrical shape of the uranyl ion.

[0043] Five exemplary polydentate chelating agents with convergent functionalities (*i.e.*, the hydroxamic acid, the carboxylate and the amido-oxime functionalities) are shown below.

[0044] Accordingly, in one embodiment, a chelating agent is provided having a central core moiety and three pendant groups (A) attached thereto for chelating metal ions from aqueous solution, wherein the chelating agent is selected from the group consisting of:

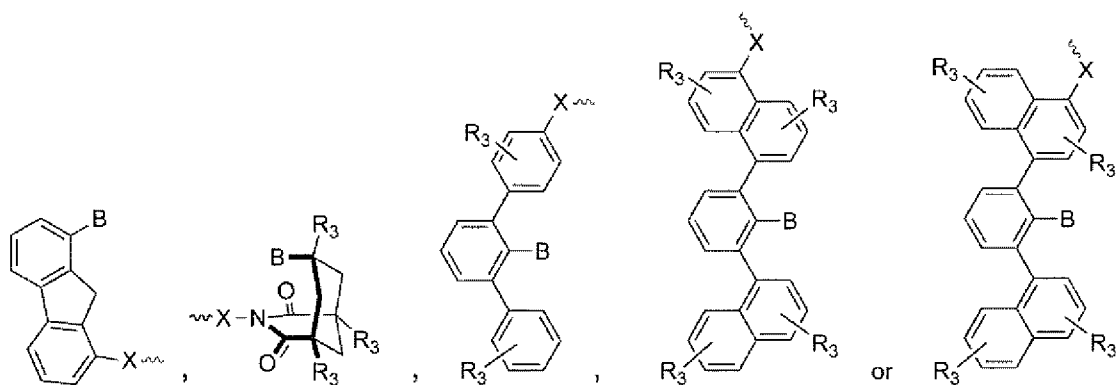


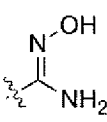
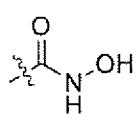
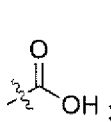
wherein each R_1 is independently hydrogen or unsubstituted C_{1-10} alkyl group;

wherein each R_2 is independently OH, NH_2 or NO_2 ;

wherein each Y is independently H, R_1 or O;

wherein A is independently:



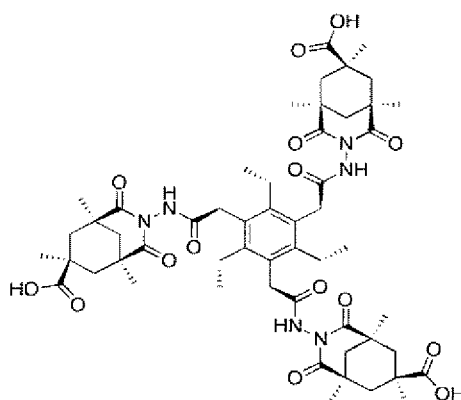
wherein B is ,  or  ;

wherein R₃ is independently H, a substituted or unsubstituted C₁₋₈ alkyl group, a substituted or unsubstituted C₁₋₈ alkyl group with one or more double bonds, (C₁₋₁₀ alkyl group)-O-(C₆₋₁₀ aryl), (C₁₋₁₀ alkyl group)-O-(C₁₋₁₀ alkyl), or (C₁₋₁₀ alkyl group)(C₆₋₁₀ aryl);

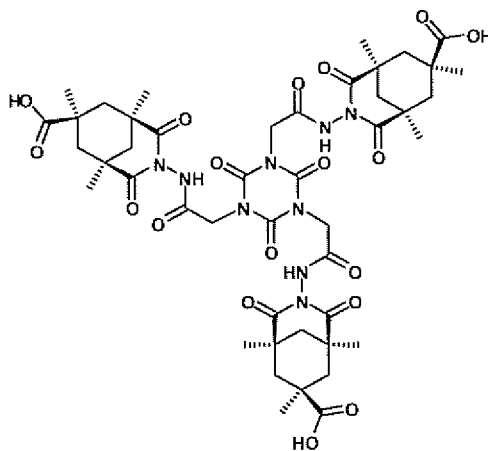
wherein A is covalently attached to the core moiety via X, which is selected from the group consisting of -CONH-, -NHCO-, -OCO-, -COO-, -CH₂O-, -NH-, -O-, -S- and a direct bond; and

wherein each ring structure may further comprise one or more heteroatoms selected from the group consisting of: N, S and O.

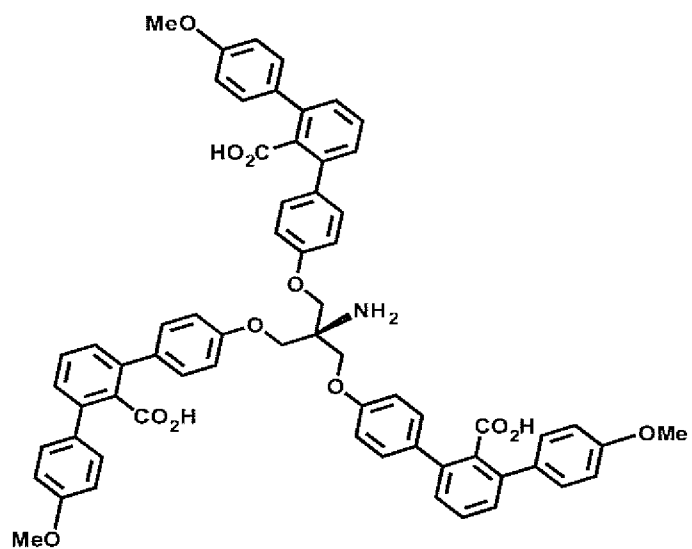
[0045] Such chelating agents may have any of the following Formulas:



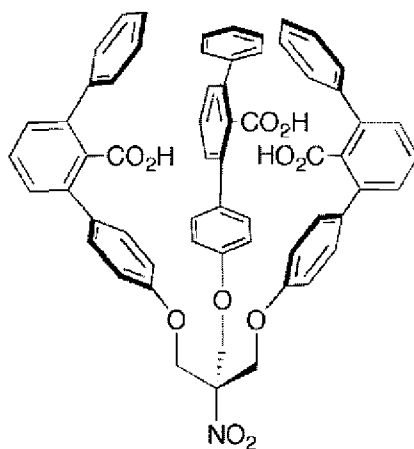
Compound I



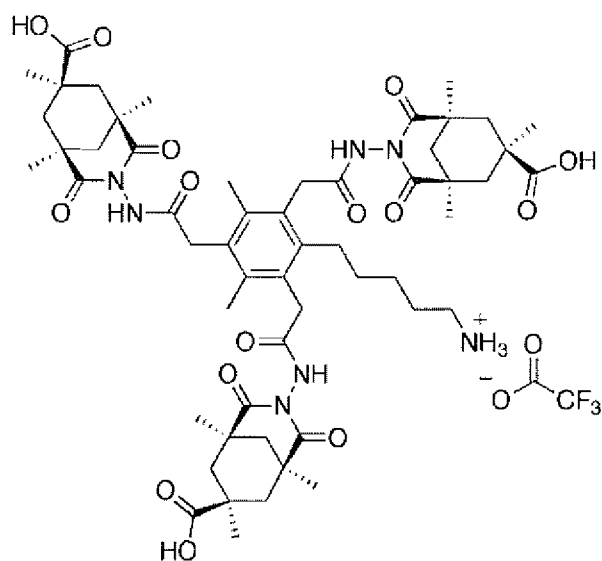
Compound II



Compound III



.Compound IV



Compound V

B. Solid Supports

[0046] The chelating agents of the present invention may be attached to solid supports, such as insoluble polymeric supports, to facilitate separation of the chelated metal ions from the aqueous solution.

[0047] In one embodiment, the chelating agents are attached to the solid support via their core moieties. The attachment may be through hydrophilic or hydrophobic interactions, charge-charge interactions, van der Waal forces or covalent bonding such as through one of the R groups attached to the core moieties (i.e. the part of the chelating agents minus the “A” pendant groups.)

[0048] In sea water desalination using membrane technology (reverse osmosis), seawater is subjected to a number of filtering steps and the overall process results in a concentration of the seawater’s minerals by about a factor of two. This concentrated solution can be passed through a series of selective ion exchange resins coupled to the polydentate chelating agents of the present invention before the solution is returned to the ocean.

[0049] In another embodiment, the chelating agents of the present invention may be attached to commercial macroporous resins such as Amberlite IRC7481. At typical loading levels of approximately 1 meq/gram (wet resin) or 1 M/kg, 1 kg of uranium can be harvested by 4 kg of the resin, which is 100 times more concentrated than the benchmark set by Seko *et al.* (*supra*).

[0050] Solid supports for use in the present invention are well known in the art. These supports are generally water insoluble and include cross-linked dextran (*e.g.* SEPHADEX™, Pharmacia Fine Chemicals, Piscataway, N.J.); agarose; polyvinylchloride, polystyrene, cross-linked polyacrylamide, nitrocellulose, latex particles and glass or polystyrene beads.

[0051] The chelating agents are attached to the solid support via the R₁ and R₂ groups. In order to effect covalent attachment, the R₁ and R₂ groups are functionalized by adding a functional group such as amino, carboxyl, sulfhydryl, amido, etc.

C. Methods of use

[0052] A variety of methods may be used to sequester and recover actinides and precious metals from aqueous solutions using the polydentate chelating agents of the present invention. In one method, the polydentate chelating agent is mixed with an

aqueous solution containing the metal cation and then precipitated from solution by raising or lowering the pH, increasing or decreasing the temperature or raising or lowering the ionic concentration of the solution.

[0053] In another method, the polydentate chelating agent is bound to a solid support and an aqueous solution containing the metal cation is passed over the support. The polydentate chelating agent may be bound to the solid support and thereafter released from the solid support by changing the conditions, such as pH.

[0054] In yet another method, the polydentate chelating agent is solubilized in an organic solvent. The aqueous solution containing the metal cation is mixed vigorously with the organic solvent containing the chelating agent. Once the metal cations are sequestered, the organic layer is separated from the aqueous layer and the metal may be recovered by evaporating the organic solvent.

[0055] In still another embodiment, the invention is a method of chelating a uranyl ion from an aqueous solution comprising the steps of: providing a chelating agent comprising an organic core molecule and three pendant groups, each bearing at least one anionic moiety; and contacting the aqueous solution with the chelating agent; wherein the three pendant groups form a stable coordination complex with the uranyl ion via convergence of the anionic moiety with the metal ion.

EXAMPLES

[0056] The present invention will be understood more readily by reference to the following examples, which are provided by way of illustration and not by way of limitation.

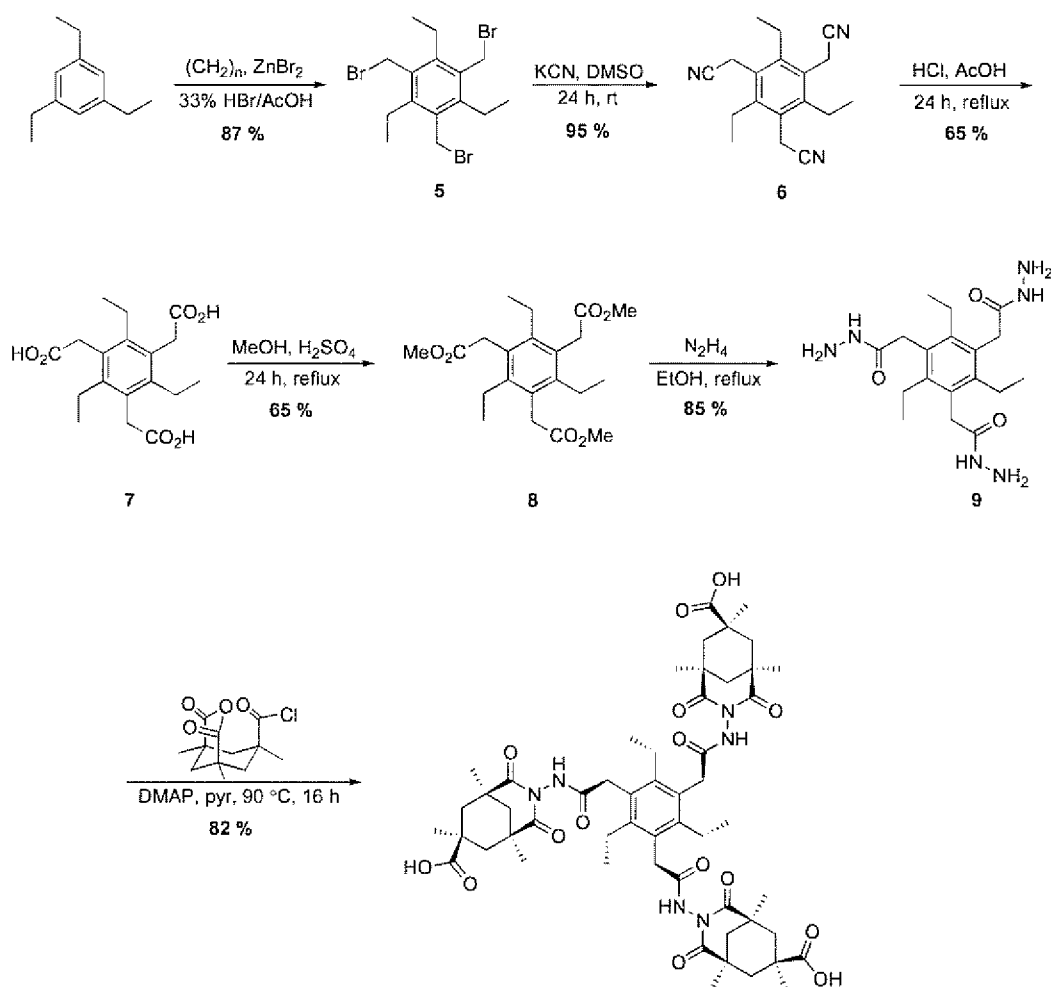
Example 1

Synthetic Method for Preparing Compound 1

[0057] Compound I was synthesized from commercially available 1,3,5-triethylbenzene. Compounds **5**, **6** and **7** were prepared as previously described in Vacca,

A. *et al.*, J. Am. Chem. Soc. 2004, 126:16456, Nativi, C. *et al.*, J. Am. Chem. Soc. 2007, 129:4377 and O'Leary, B.M. *et al.*, J. Am. Chem. Soc. 2001, 123:11519.

[0058] Trimethylester, **8** was prepared by refluxing **7** in methanol with sulfuric acid as a catalyst. Trihydrazide, **9** was prepared by dissolving the corresponding ester, **8** in ethanol with hydrazine and brief heating under reflux. The final uranyl ligand, **Compound I** was prepared from **9** using Kemp's anhydride acid chloride in dry pyridine with DMAP. The uranyl ligand, Compound I was obtained in high purity by subliming off impurities (excess pyridinium chloride).



Compound I

[0059] Compound I is most soluble in methanol or dimethylsulfoxide, and NMR studies were done in these solvents. Figures 4 and 5 show the ^1H -NMR spectra of uranyl-free ligand in MeOD-d_4 and ^1H -NMR of uranyl ligand in MeOD-d_4 with uranyl acetate.

[0060] The application of Compound I as an agent for uranyl ion sequestration was investigated through liquid-liquid extractions. An aqueous solution of uranyl nitrate (1.6 equivalents) in acetate buffer ($\text{pH}=5.0$) was stirred with chloroform solution of Compound I (1 equivalent) and the concentrations of uranium in each phase were determined before and after extraction with Inductively Coupled Plasma Atomic Emission Spectroscopy (ICP-AES). The extraction experiments were run at a series of uranium concentrations: 400 ppm, 40 ppm, and 4 ppm. At 400 ppm, Compound I extracted $55\pm 5\%$ of the aqueous uranyl ion into the organic phase and at 40 ppm $25\pm 5\%$ is extracted. At 4 ppm no uranium was extracted. The uranium can be recovered from the ligand by adding 0.5M HNO_3 . Compound I is highly selective for uranyl. The extraction of uranyl ion at 400 ppm was also carried out in the presence of six ions that dominate the chemistry of seawater: Cl^- , Na^+ , Mg^{+2} , Ca^{+2} , K^+ and SO_4^{-2} . With these ions present at seawater concentrations, Compound I showed no diminished function. Approximately, 55% of the uranyl ion was extracted into the organic phase.

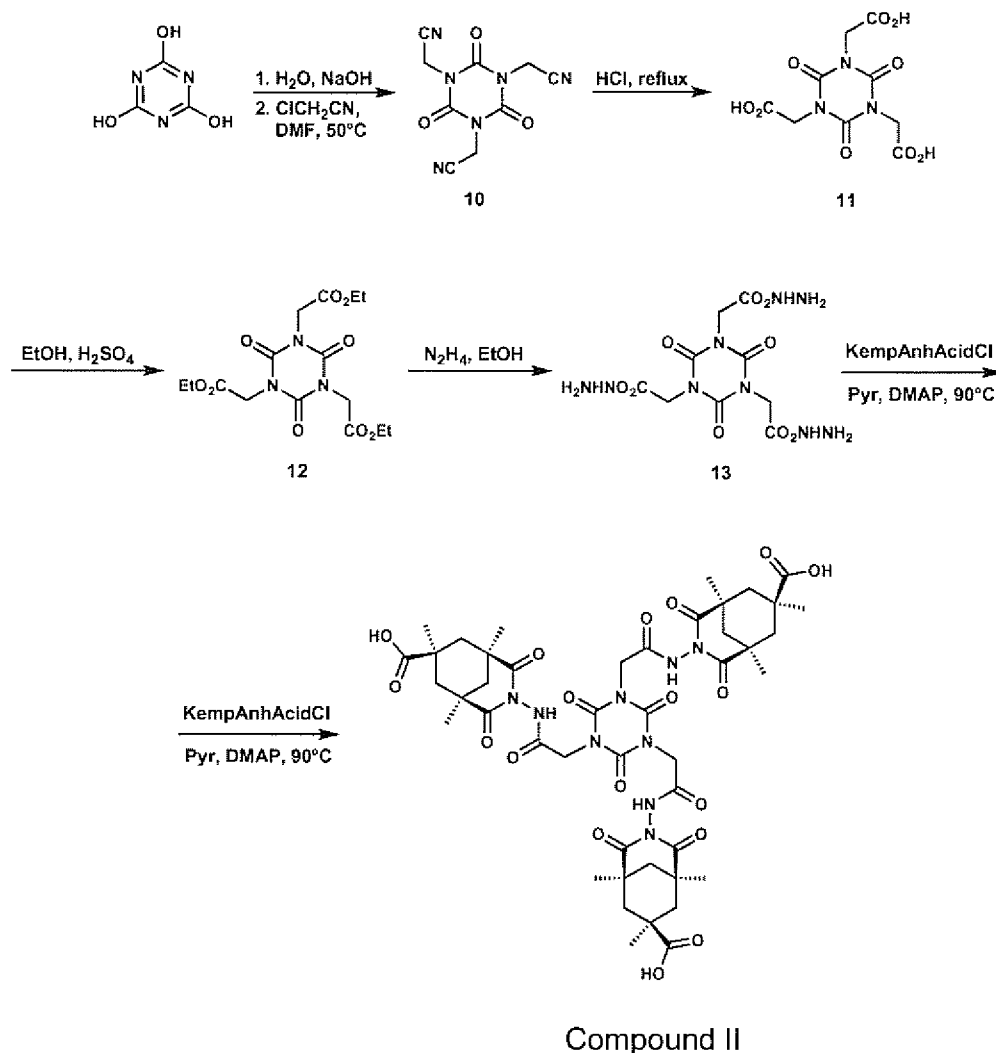
Example 2

Synthetic Method for Preparing Compound 2

[0061] Compounds **10** and **11** were synthesized according to the patent literature (Patent No. GB 988631) starting from the trisodium salt of cyanuric acid. Triacid, **11** (0.456 g, 1.5 mmol) was dissolved in 25 mL dry ethanol, and stirred. To this was added 0.5 mL conc. sulfuric acid dropwise, and the reaction mixture was refluxed for 24 hours. It was then cooled to room temperature, and the solvent removed under reduced pressure. The resulting oil was dissolved in 100 mL dichloromethane, washed with brine (1×50 mL) and water (1×50 mL), dried over Na_2SO_4 and the solvent was removed under reduced pressure. The product **12** was obtained as a white waxy solid 0.570 g (99%).

[0062] Triethyl ester, **12** (0.381 g, 0.984 mmol) was dissolved in 20 mL EtOH. The solution was heated to 60 °C and anhydrous hydrazine (0.6 mL, 9.84 mmol) was added dropwise. The solution was heated to reflux; after 9 hours a white precipitate formed. The suspension was refluxed for an additional 3 hours and cooled to room temperature. The white precipitate was filtered and washed with ethanol. Yield 0.295 g (86 %). The white solid was used without further purification.

[0063] Trihydrazide, **13** (0.100 g, 0.289 mmol), Kemp's anhydride acid chloride (0.250 g, 0.898 mmol) and dimethylamino pyridine (DMAP) (0.010 g, 0.082 mmol) were added to a 10 mL round bottom flask. Dry pyridine (5 mL) was added and the reaction mixture was sonicated briefly to break up the reactants into a fine suspension. The mixture was then stirred and heated to 90 °C under an argon atmosphere for 23 hours. The flask was then cooled to room temperature and the resulting white precipitate was filtered and washed with CH₂Cl₂ to give a white solid (Compound II).



Example 3

Synthetic Method for Preparing Compound 3

[0064] To a vigorously stirred solution of magnesium turnings (1.250 g, 50.50 mmol) in 180 mL of dry THF, bromoanisole (9.430 g, 50.50 mmol) was added slowly and the mixture was then refluxed for 2.5 hours. A cold solution of the 2,6-dichloriodobenzene (6.818 g; 25.00 mmol) with vinylmagnesium bromide (1 equivalent; 32.5 mL of 0.7 M solution in cyclohexane) at -18°C was transferred to the refluxing

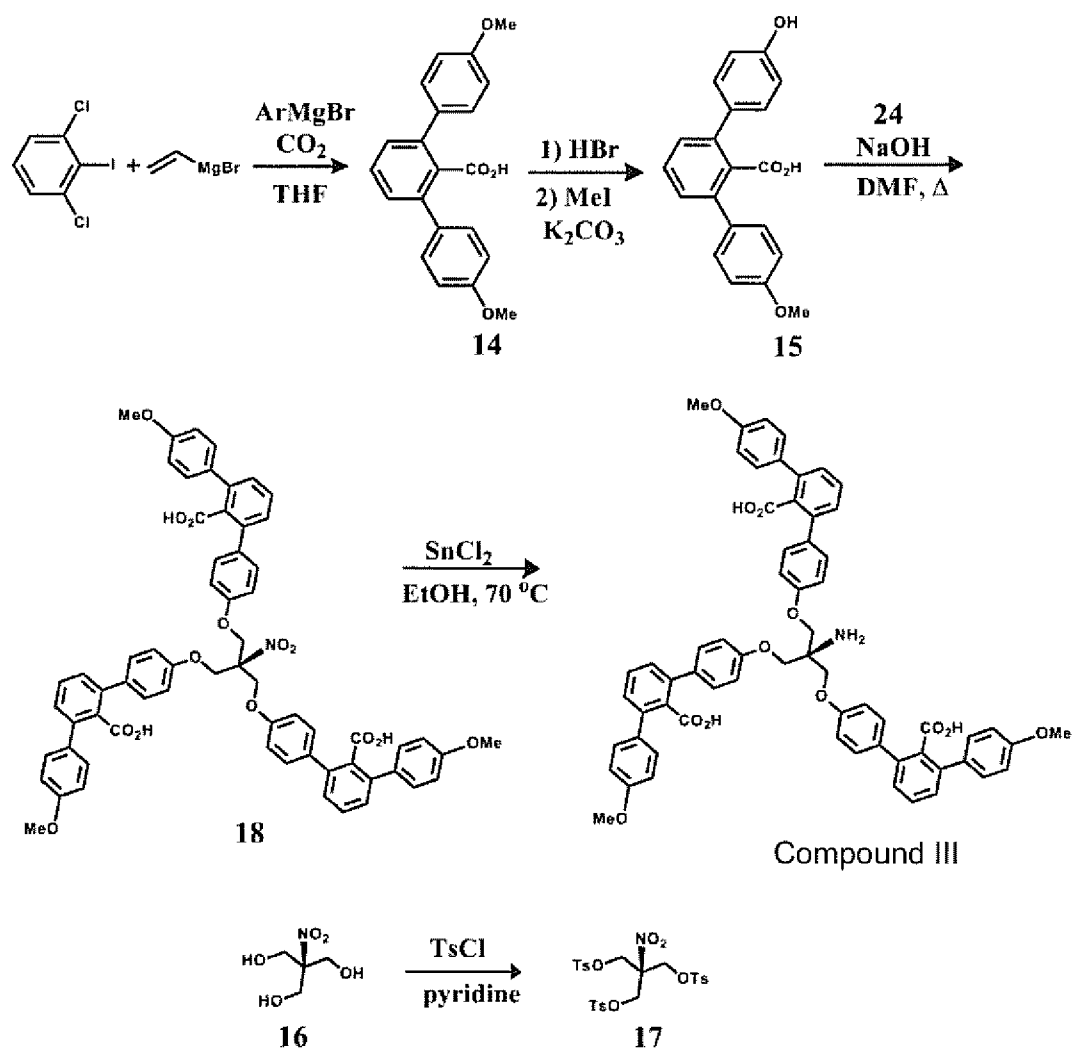
Grignard solution and stirred for 2.5 hours. The reaction mixture was brought to room temperature and CO₂ was bubbled in overnight. It was then quenched with 150 mL of 6N HCl, extracted with Et₂O (3x150 mL) and then washed with water and saturated NaHCO₃. The crude mixture was purified by flash chromatography (silica gel; hexane:CH₂Cl₂ 1:4) and resulted in **14** as a white powder 42.6% (3.56 g).

[0065] A mixture of **14** (3 g, 9 mmol), 14 mL of aqueous hydrobromic acid (d. 1.48), and 14 mL of 33% hydrogen bromide in glacial acetic acid was warmed with vigorous stirring for six hours under a dry carbon dioxide atmosphere. The mixture was then suspended in water. The resulting fine gray precipitate was dissolved in a small volume of 15% sodium hydroxide, filtered, and then precipitated with added concentrated hydrochloric acid. The resulting solid was added to a mixture of potassium carbonate (3.7 g, 27mmol) in DMF (100 mL). Methyl iodide (1.27 g, 9mmol) was added slowly to the mixture at 0°C and stirred at room temperature for 4 hours. The reaction was quenched with 50 mL of 3N HCl and extracted with Et₂O (3x100 mL). The solvent was evaporated leaving the crude product **15**, which was further purified by flash chromatography (silica gel; CH₂Cl₂:Methanol 1:0.05).

[0066] Tris(hydroxymethyl)nitromethane **16** (10.0 g, 66.17 mmol) was dissolved in dry pyridine 60 mL and cooled to 0°C. Tosylchloride (39.2 g, 211.00 mmol) in 80 mL pyridine was slowly added to this solution over 3.5 hours. The reaction mixture was stirred at room temperature overnight and quenched by adding ice. The product was extracted into CH₂Cl₂ and was successively washed with 1M HCl, brine and water. The solvent was evaporated and the resulting white powder was dried over Na₂SO₄. Yield: 22.57 g; 55.6%.

[0067] Tris(para-tolylsulfonylmethyl)nitromethane **17** (3.070 g, 5.0 mmol), and **15** (6.407g, 20 mmol) and NaOH (0.800 g, 20.0 mmol) were dissolved/suspended in 20 mL DMF and the reaction mixture was heated to reflux at 160°C for 17 hours. After cooling to room temperature 100 mL water was added and the precipitate was isolated by filtration. The final product **18** was washed with water and MeOH.

[0068] The final product **18** (5.3 g, 5.0 mmol) and tin(II) chloride (2.84 g, 15 mmol) were combined in ethanol (180 mL) and 37% HCl (50 mL). After being heated at 65°C overnight, the reaction was cooled, and most of the ethanol was removed using a rotary evaporator. Water (50 mL) was added, and the resulting precipitate was filtered, washed with water, and dried under high vacuum to give the product as the hydrochloride salt of Compound III.



Example 4

Synthetic Method for Preparing Compound 4

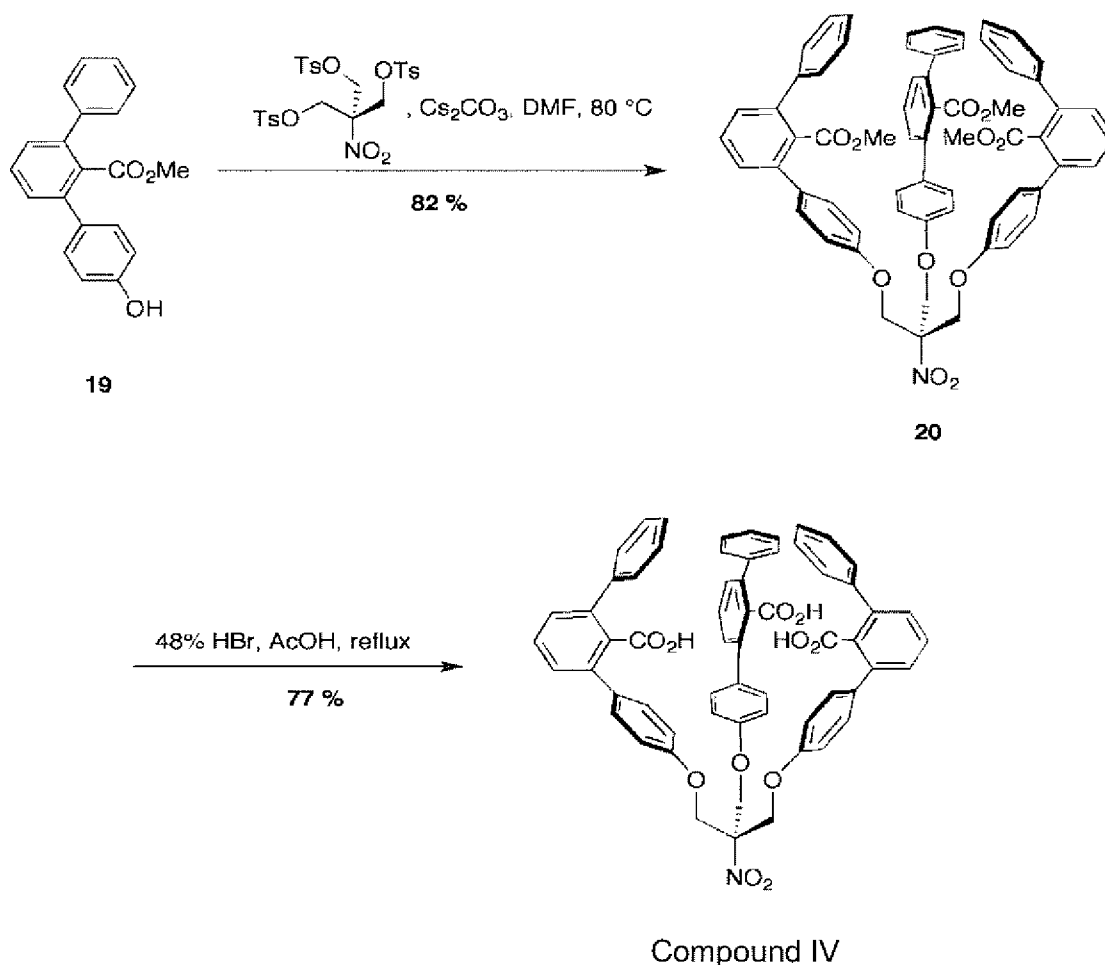
[0069] Approximately 2.343 g, 17 mmol of 4-Hydroxyphenylboronic acid was added to Methyl 3-iodobiphenyl-2-carboxylate, (3.83 g, 11.3 mmol) dissolved in tetrahydrofuran (THF; 77 mL) and 1 M aqueous Na₂CO₃ (31 mL). The mixture was stirred under argon and [PdCl₂(PPh₃)₂] (0.5 g, 0.7 mmol) was added. Air was removed from the reaction mixture by reducing the pressure under vacuum and backfilling with Argon. After repeating this process three times, the reaction mixture was heated to 60 °C. The orange reaction mixture turned black overnight. The resulting black reaction mixture was cooled to room temperature and added to water (150 mL). The organic phase was separated and concentrated under reduced pressure to give a brown/black solid. The solid was triturated with dichloromethane (DCM; 30 mL) and filtered to give a light brown solid. The solid was then collected and triturated with methanol (MeOH; 30 mL) and filtered to give a white solid, terphenyl methyl ester **19**. Yield; 3.27 g (95%). ¹H NMR (600 MHz, MeOD) δ 7.52 (t, J = 7.7, 1H), 7.41 – 7.37 (m, 2H), 7.37 – 7.32 (m, 5H), 7.19 (d, J = 8.6, 2H), 6.81 (d, J = 8.6, 2H), 3.37 (s, 3H).

[0070] Nitro-tritosylate (0.705 g, 0.767 mmol), terphenol methylester, **19** (0.700 g, 2.3 mmol), and cesium carbonate (0.898, 2.76 mmol) was suspended dry dimethylformamide (DMF; 35 mL). The reaction mixture was put under an argon atmosphere and heated to 80 °C for 24 hours. The reaction was cooled to room temperature and poured into 10% HCl (150 mL). The aqueous solution was extracted with diethyl ether (Et₂O; 3 × 125 mL). The organic portions were combined, dried over Na₂SO₄, and concentrated under reduced pressure to give a light brown solid. The brown solid was purified by column chromatography (SiO₂) using dichloromethane (DCM) as the eluent to give a light yellow foam, terphenyl trimer methylester **20**. Yield; 0.608 g (82 %). ¹H NMR (600 MHz, CDCl₃) δ 7.48 (t, J = 7.7, 1H), 7.41 – 7.31 (m, 9H), 6.97 (d, J = 8.7, 2H), 4.73 (s, 2H), 3.38 (s, 3H).

[0071] Terphenyl trimer methylester **20** (0.200g, 0.198 mmol) was dissolved in acetic acid (AcOH; 4.7 mL). The reaction mixture was stirred and hydrobromic acid (48

% HBr in water; 1.2 mL) was added dropwise to give a white suspension. The suspension becomes a yellow solution upon heating. The reaction mixture was heated to reflux overnight giving a white suspension. The suspension was cooled to room temperature, filtered and washed with deionized water giving a white solid. The solid was dried under vacuum to give a white powder, Compound IV. Yield; 0.148g (77%). ^1H NMR (600 MHz, DMSO) δ 12.76 (s, 1H), 7.52 (t, $J = 7.7$, 1H), 7.44 – 7.41 (m, 4H), 7.37 (d, $J = 8.8$, 3H), 7.36 – 7.32 (m, 2H), 7.10 (d, $J = 8.8$, 2H), 4.79 (s, 2H). ESI-TOF high-acc: m/z : 968.3053 ($[\text{MH}]^+$, $\text{C}_{61}\text{H}_{45}\text{NO}_{11}\text{H}^+$, calc. 968.3065).

[0072] Once the ligand, Compound IV, is synthesized and isolated in high purity, several experiments were done to test the ligand's ability to bind uranyl ion. The ligand and the ligand/uranyl complex is most soluble in dimethylsulfoxide (DMSO), so NMR studies were done in this solvent. Figures 1-3 are a series of three NMR spectra. Figure 1 is the free ligand, Figure 2 is the ligand with base (TEA); and Figure 3 is the ligand, base, uranyl nitrate (UO_2NO_3).



Example 5

Synthetic Method for Preparing Compound 5

[0073] Pd(PPh₃)₄ (0.5 g, 0.433 mmol), CuI (0.206 g, 1.08 mmol), and naphthalimide alkyne (2.535 g, 11.89 mmol) were added to a 2-neck round bottom flask equipped with a reflux condenser. The solids were placed under a nitrogen atmosphere. Bromo-*m*-xylene (2 g, 10.8 mmol) and triethyl amine (20 mL) were added via syringe. The reaction mixture was refluxed for 24 hours. The resulting black mixture was cooled to room temperature and the volatiles were removed under reduced pressure. Once dry,

the black residue was dissolved in 1:1 hexanes:dichloromethane and loaded onto a silica column. The eluent was gradually converted from 1:1 hexanes:dichloromethane to 100% dichloromethane. A yellow solid was isolated as product **21**. Yield 2.64 g (76%)

[0074] Alkyne **21** (2.5 g, 7.88 mmol) was placed in a 100 mL round bottom flask and dissolved in 25 mL methanol and 25 mL THF. Pd/C 10% (0.400 g) was added and the reaction mixture was put under a hydrogen atmosphere. The reaction mixture was stirred at room temperature for 24 hours, then filtered through celite and washed with THF to give a light yellow solution. The solution was concentrated to give a white crystalline solid (**22**). Yield 2.435 g (96 %).

[0075] 1,3,5-Dimethylalkyl benzene, **22** (1.5 g, 4.67 mmol), paraformaldehyde (2.203 g, 73.4 mmol), and AcOH/HBr 33% (70 mL) were added to a dry 200 mL round bottom flask. The mixture was stirred while ZnBr₂ (2.620 g, 11.54 mmol) was slowly added and the mixture was heated to 90 °C. After 24 hours, an additional 2.2 g paraformaldehyde and 2.7 g ZnBr₂ was added. The yellow solution was heated an additional 48 hours. The reaction mixture was then cooled to room temperature and concentrated to half the original volume under vacuum. Deionized water was added (100 mL) and the resulting solid was filtered off. The off-white solid was then dissolved in DCM and run through a plug of silica to remove impurities. The DCM was then concentrated to give a white solid (**23**). Yield 2.568 g (92 %).

[0076] Potassium cyanide (0.774 g, 11.9 mmol) was dissolved in 35 mL dry DMSO under an argon atmosphere. The mixture was heated to 50 °C for 10 minutes then tribromomethyl **23** (2.30 g, 3.83 mmol) was added and stirred at 50 °C for 15 minutes. The reaction mixture was cooled to room temperature and stirred 24 hours to yield a yellow/red solution. The reaction mixture was poured onto 80 mL ice water to give an off-white precipitate. The precipitate was filtered and washed with 200 mL deionized water. The resulting off-white solid was placed in a beaker and 200 mL fresh deionized water. The suspension was vigorously stirred for 30 minutes. The suspension was then filtered and washed with 100 mL deionized water. The white solid was dried in a desiccator under vacuum over night to give a white solid (**24**). Yield 1.505 g (90 %).

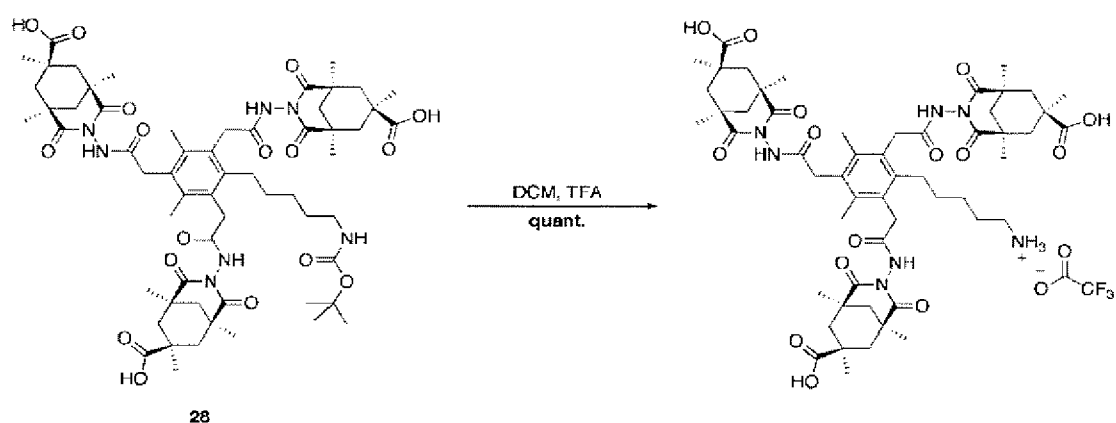
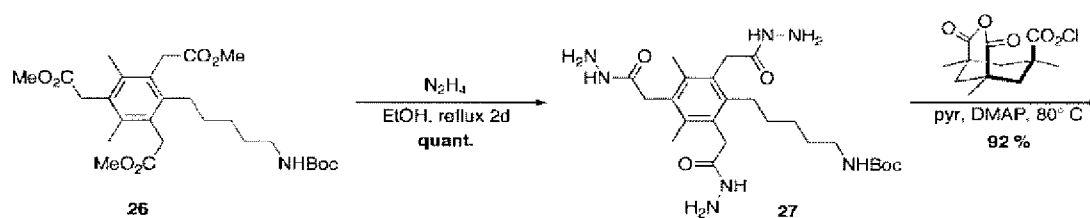
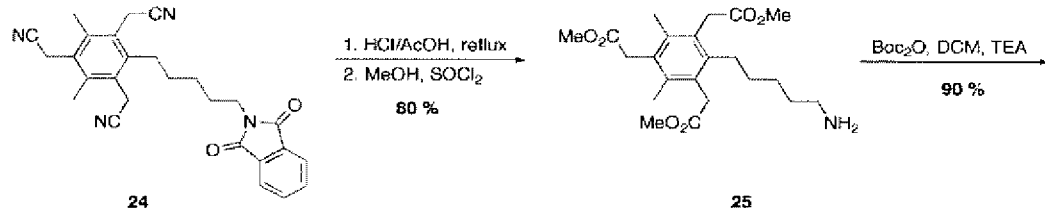
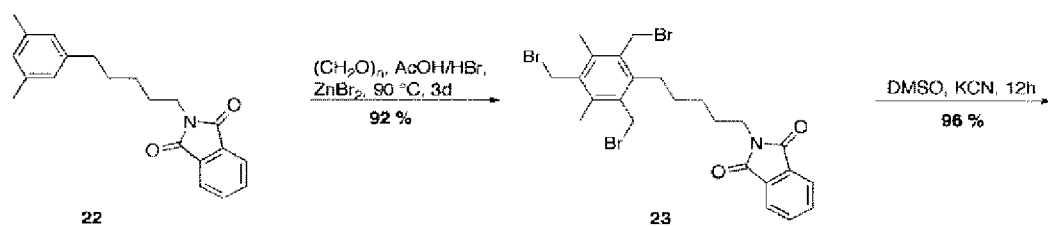
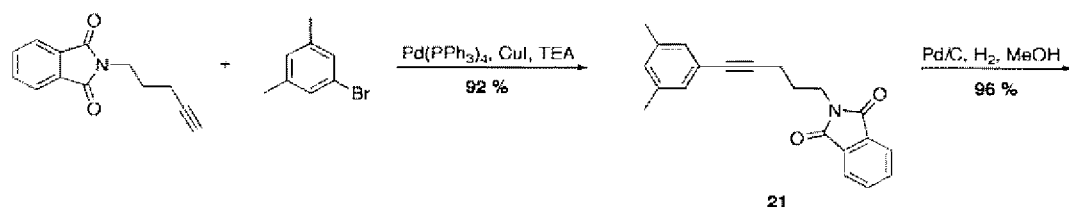
[0077] Tricyanomethyl, **24** (0.100 g, .228 mmol) was added to a 10 mL round bottom flask. Glacial acetic acid (2 mL) and concentrated HCl (2 mL) were added and the reaction mixture was heated to reflux for 22 hours. The yellow solution was then cooled to room temperature and the volatiles were removed under vacuum. The residue was dried in a desiccator under vacuum for 1 hour. The dried solid was then suspended in MeOH (4 mL) and cooled to 0 °C in an ice bath. SOCl₂ was then added dropwise while maintaining the reaction temperature at 0 °C. After addition was complete the reaction mixture was allowed to warm to room temperature. The reaction mixture was then refluxed for 1.5 hours. The reaction was cooled to room temperature and the solvents were removed under vacuum. The resulting off-white residue was dissolved in water and placed in a separatory funnel. The aqueous layer was extracted with Et₂O (3 × 50 mL) then placed in a beaker and basified with NaHCO₃. The basified aqueous solution was then returned to the separatory funnel and extracted with DCM (3 × 50 mL). The combined DCM extracts were dried over Na₂SO₄ and concentrated on a rotary evaporator to give a light brown oil (**25**). Yield 0.074 g (80 %).

[0078] N-boc trimethylester, **26** (0.352 g, 0.694 mmol) was added to a 25 mL round bottom flask with stirbar. EtOH (13 mL) was added and the reaction mixture was warmed to 60° C to solublize the starting material. Hydrazine (0.52 mL, 8.8 mmol) was added dropwise to the reaction mixture. The reaction was then brought to reflux. After 24 hours additional hydrazine (0.52 mL) was added and the reaction mixture was refluxed for an additional 24 hours. After 2 days at reflux, the solvent was removed under vacuum and the resulting white solid (**27**) was used without further purification. Yield 0.350 g (quant.).

[0079] N-boc trihydrazide **27**, (0.150 g, 0.296 mmol), Kemp's anhydride acid chloride (0.256 g, 0.916 mmol), and DMAP (0.010g) were added to a 25 mL round-bottom flask with stirbar. Dry pyridine (14 mL) was then added. The reaction mixture was then put under an argon atmosphere and heated to 90° C overnight. After 19 hours, the reaction mixture was concentrated to dryness on the rotovap. The resulting residue was then dissolved in DCM and washed with 10% HCl. The resulting organics were then stirred over activated carbon. The carbon was then filtered off and the organics were then

washed with 1 M NaOH. The base layer was then washed with DCM. The base layer was then separated and acidified with 2 M HCl which caused a white ppt to form. The ppt was filtered off and dried in the desiccator overnight to give a white solid **28**. Yield 0.174 g (50%).

[0080] N-boc uranyl ligand **28**, (0.100 g, 0.085 mmol) was added to a 50 mL round-bottom flask and dissolved in 24 mL DCM. The solution was stirred and TFA (0.065 mL, 0.85 mmol) was added dropwise. After addition was complete, the reaction mixture was stirred at room temperature for 8 hours. The solvents were removed under vacuum to give off white solid **V**, which will be used without further purification. Yield (quant.).



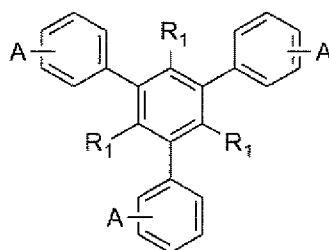
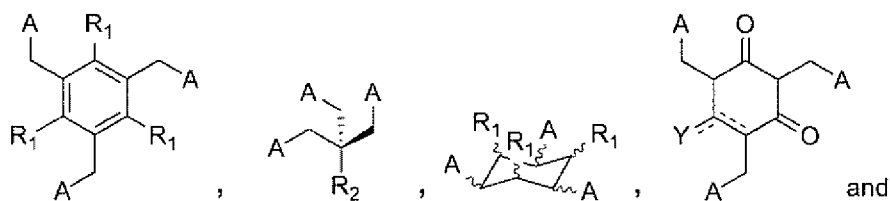
Compound V

[0081] The examples set forth above are provided to give those of ordinary skill in the art a complete disclosure and description of how to make and use the preferred embodiments of the compositions, and are not intended to limit the scope of what the inventors regard as their invention. Modifications of the above-described modes (for carrying out the invention that are obvious to persons of skill in the art) are intended to be within the scope of the following claims. All publications, patents, and patent applications cited in this specification are incorporated herein by reference as if each such publication, patent or patent application were specifically and individually indicated to be incorporated herein by reference.

CLAIMS

We claim:

1. A chelating agent having a central core moiety and three pendant groups (A) attached thereto for chelating metal ions from aqueous solution, wherein the chelating agent is selected from the group consisting of:

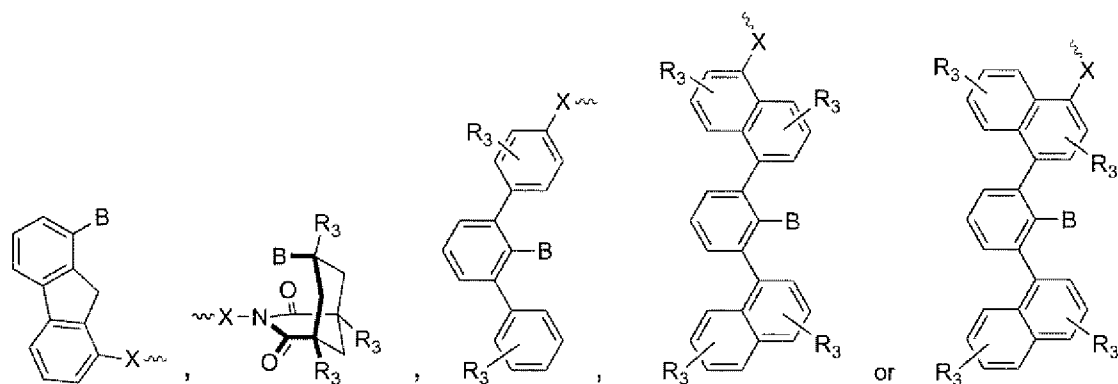


wherein each R_1 is independently hydrogen or unsubstituted C_{1-10} alkyl group;

wherein each R_2 is independently OH, NH_2 or NO_2 ;

wherein each Y is independently H, R_1 or O;

wherein A is independently:



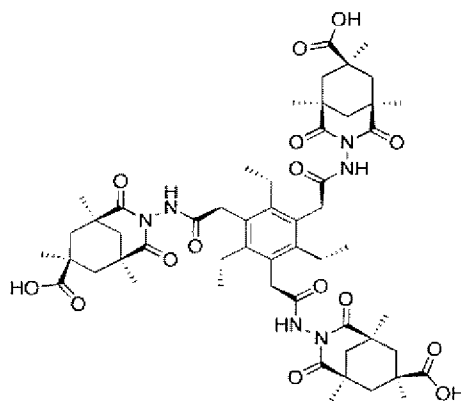
wherein B is , or ;

wherein R_3 is independently H, a substituted or unsubstituted C_{1-8} alkyl group, a substituted or unsubstituted C_{1-8} alkyl group with one or more double bonds, (C_{1-10} alkyl group)-O-(C_{6-10} aryl), (C_{1-10} alkyl group)-O-(C_{1-10} alkyl), or (C_{1-10} alkyl group)(C_{6-10} aryl);

wherein A is covalently attached to the core moiety via X, which is selected from the group consisting of -CONH-, -NHCO-, -OCO-, -COO-, -CH₂O-, -NH-, -O-, -S- and a direct bond; and

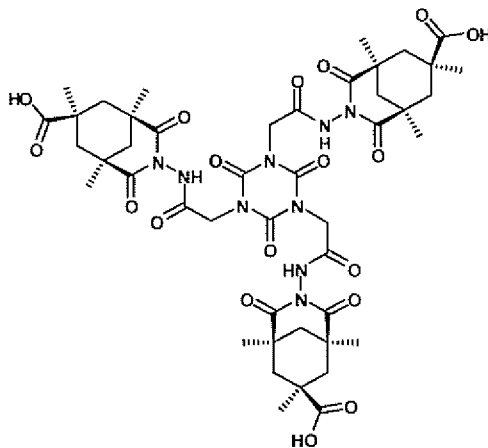
wherein each ring structure may further comprise one or more heteroatoms selected from the group consisting of: N, S and O.

2. A chelating agent given by the formula:



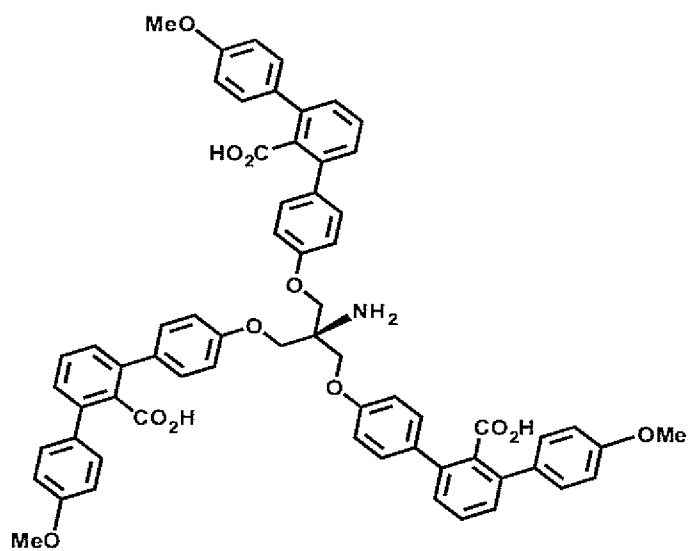
Compound I

3. A chelating agent given by the formula:



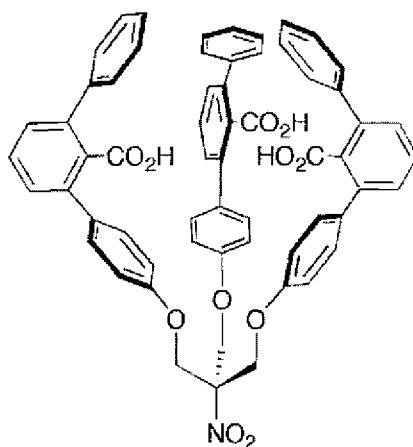
Compound II

4. A chelating agent given by the formula:



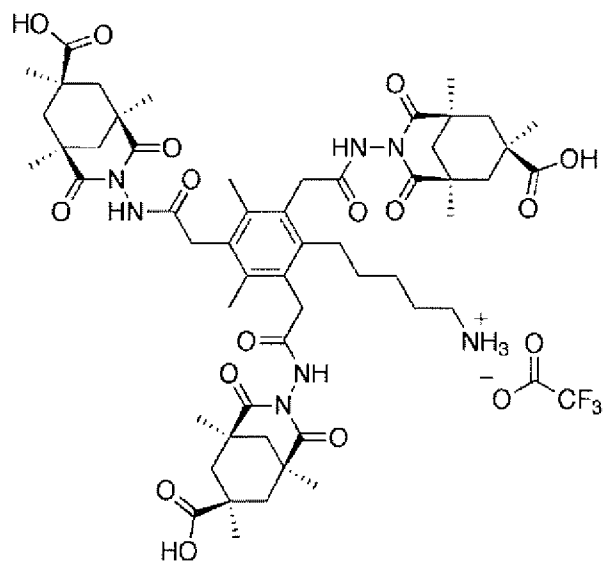
Compound III

5. A chelating agent given by the formula:



Compound IV

6. A chelating agent given by the Formula:



Compound V

7. A system for chelating a metal ion comprising at least one chelating agent according to claim 1 bound to a solid support.

8. The system according to claim 1, wherein the chelating agent is bound to the solid support through at least one of the R_1 , R_2 or R_3 groups via a functional group added thereto.

9. A method of sequestering metal ions from aqueous solution comprising the steps of:

- a) preparing a chelating agent according to claim 1; and
- b) contacting the chelating agent with an aqueous solution suspected of containing metal ions.

10. The method according to claim 9, wherein the metal ions are uranyl ions.

11. The method according to claim 10, wherein the aqueous solution is seawater.

12. The method according to claim 9, wherein the chelating agent is bound to a solid support before step b).

13. The method according to claim 9, wherein the chelating agent is dissolved in a non-aqueous solvent before step b).

14. A method of chelating a uranyl ion from an aqueous solution comprising the steps of:

- a) providing a chelating agent comprising an organic core molecule and three pendant groups, each bearing at least one anionic moiety; and
- b) contacting the aqueous solution with the chelating agent;

wherein the three pendant groups form a stable coordination complex with the uranyl ion via convergence of the anionic moiety with the uranyl ion.

FIGURE 1

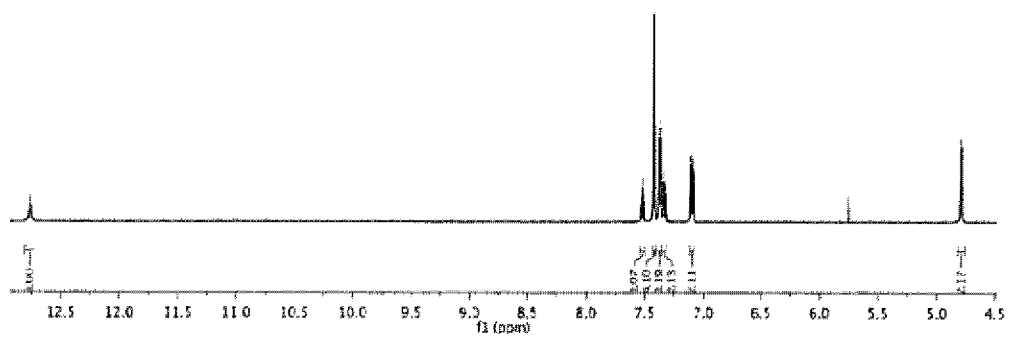


FIGURE 2

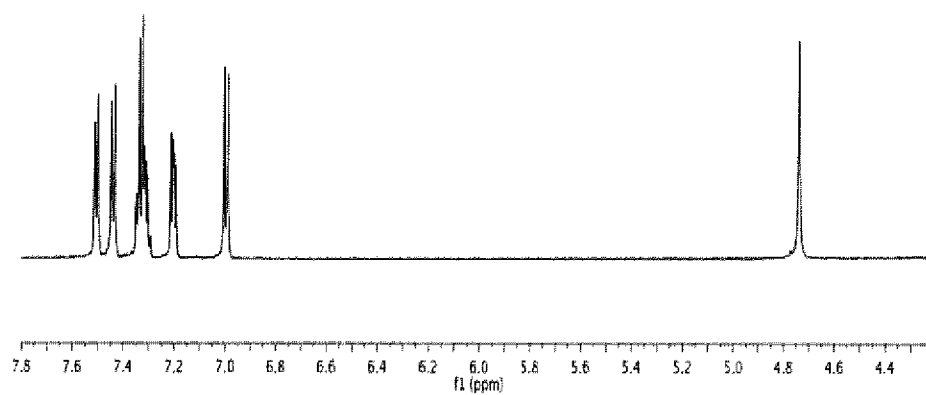


FIGURE 3

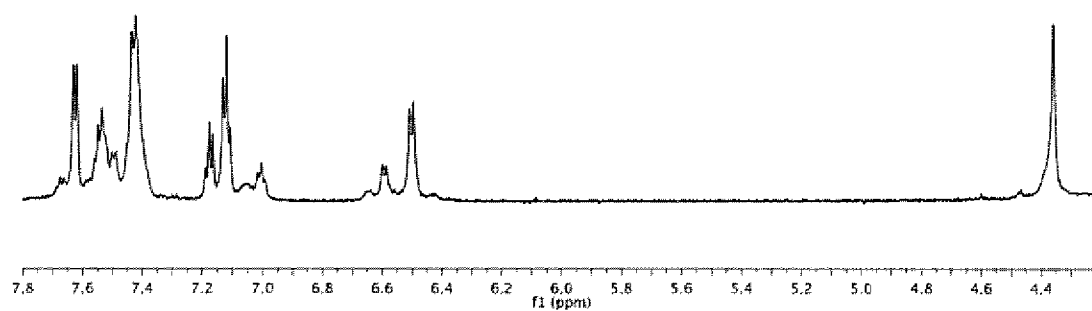


FIGURE 4

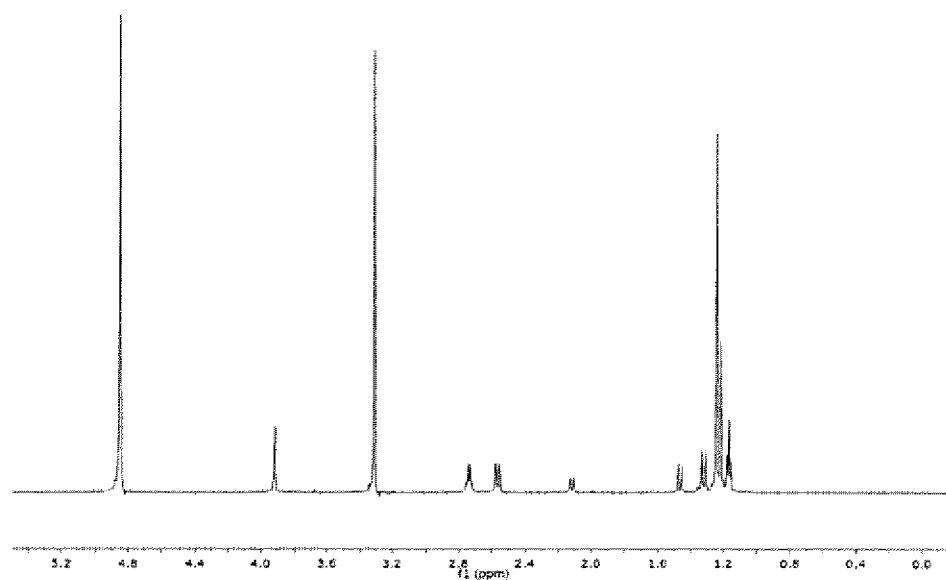


FIGURE 5

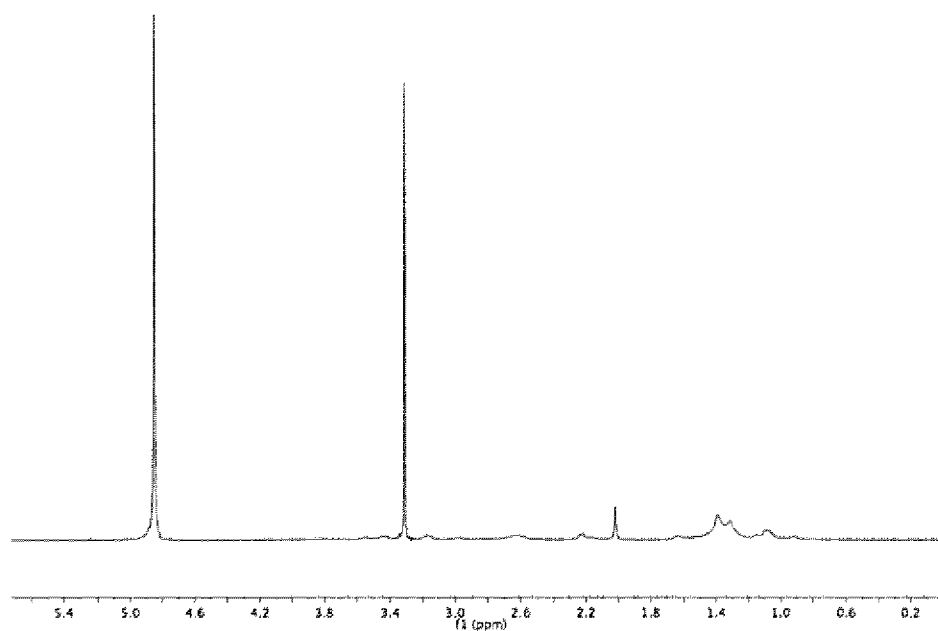


FIGURE 6

