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(54) Title: TETRAIONIC LIQUID SALTS AND METHODS OF USE THEREOF

(57) Abstract: Tetraionic liquid salts and methods of using such tetraionic liquid salts in chromatography systems using, for example, electrospray ionization-mass spectrometry (ESI-MS) detection techniques.



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TETRAIONIC LIQUID SALTS AND METHODS OF USE THEREOF

CROSS-REFERENCE TO RELATED APPLICATION

[0001] This application claims priority to U.S. Patent Application Serial No. 61/266,892, a provisional application filed on 4 December 2009. The disclosure of U.S. Patent Application Serial No. 61/266,892 is incorporated herein by reference in its entirety.

FIELD

[0002] The present invention relates to tetraionic liquid salts and their use in various chromatograph systems using electrospray ionization-mass spectrometry ("ESI-MS") detection techniques.

BACKGROUND

[0003] Room temperature geminal dicationic liquids (or liquid salts) have been shown to possess superior physical properties in terms of thermal stability and volatility compared to traditional ionic liquids. Polycationic liquid salts have been proposed for use as solvents and stationary phases, for example, in gas or liquid chromatography. For example, U.S. Publication Nos. 2006/0025598 and 2008/0027231 report high stability diionic liquid salts and use thereof and U.S. Publication No. 2008/0210858 reports high stability polyionic liquid salts and use thereof.

[0004] Furthermore, detection and quantitation of anions is of great importance in a wide variety of scientific fields. The advent of electrospray ionization allowed routine analysis of ionic components in a liquid sample. By coupling ESI-MS with a separation method, such as liquid chromatography ("LC"), a means to separate and detect most compounds can be accomplished. For example, U.S. Serial Nos. 12/867,139 and 12/867,142 report diionic liquid salts and use in ESI-MS. However, problems exist with ESI-MS, such as background peaks, reduced stability of the ion current, undesirable arcing and necessity of using unconventional solvents. Therefore, a need exists for new compounds and methods of reducing such problems.

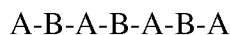
[0005] New methods of anion analysis are of continual interest provided such methods prove advantageous for analytes of importance in a variety of environmental, biochemical or medicinal applications. Several facile and sensitive methods to detect and

quantify anions have been developed to accomplish this task. Currently, ion selective electrodes, conductivity, atomic spectroscopic techniques coupled with flow injection analysis ("FIA"), and ion chromatography have been used for the analysis of anions. However, none of these techniques are completely satisfactory because they are either not universal or lack the ability to provide structural information for complex ions. Inductively coupled plasma mass spectrometry ("ICP-MS") is another method that is known for its high sensitivity and low limits of detection ("LOD"). However, ICP-MS is not applicable for all anions nor does it provide structural information for complex ions because they are destroyed before detection.

[0006] Recently, a new approach for anion detection in the positive mode has been developed. This technique uses cationic ion pairing agents to form complexes with anions which can in turn be detected in the positive mode. The first use of this method was to detect very low levels of perchlorate anions by allowing them to pair with a dicationic reagent in a carrier flow solvent to form a singly positively charged complex detected in the positive mode. This technique was then extended to the detection of a plethora of singly charged anions. This general approach to anion analysis was shown to have many advantages. First, the LODs achieved with this method in the positive mode are much lower than those possible in the negative mode. Second, only small amounts of the ion pairing agents are needed for any analysis and it can be added pre-column or post-column when LC is employed. Third, common solvents such as water, methanol and acetonitrile can be used. Finally, many anions which fall below the low-mass-cut-off ("LMCO") of trapping MS can now be detected since the complexes are brought to a higher mass range by the pairing reagent. Indeed, moving the lower mass detection of any ion away from a region of higher chemical noise into a higher mass region of less noise (upon complexation with the pairing agent) is usually beneficial. For these reasons, detection of anion/cation complexes in the positive mode has proven to be much more sensitive than detection of the native anion in the negative mode. Also, operation in Single Reaction Monitoring ("SRM") mode can further lower LODs.

SUMMARY

[0007] In one embodiment, a tetraionic liquid salt is provided. The tetraionic liquid salt comprises a tetraionic species corresponding in structure to Formula I:



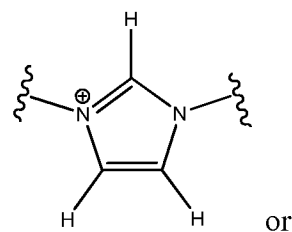
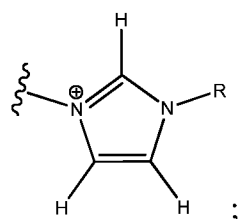
Formula I

and at least one counter-anion,

wherein:

A is selected from the group consisting of optionally substituted protonated tertiary amine of formula $\text{--}\overset{\sim}{\text{N}}\text{RH}^+\text{--}$ or $\text{--}\overset{\sim}{\text{N}}\text{R}_2\text{H}^+\text{--}$, optionally substituted phosphonium

of formula $\text{--}\overset{\sim}{\text{P}}\text{R}_2^+\text{--}$ or $\text{--}\overset{\sim}{\text{P}}\text{R}_3^+\text{--}$, and imidazolium of formula



wherein each R is independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, alkoxy, carbocyclyl, carbocyclylalkyl, heterocyclyl, heterocyclylalkyl and hydroxyalkyl;

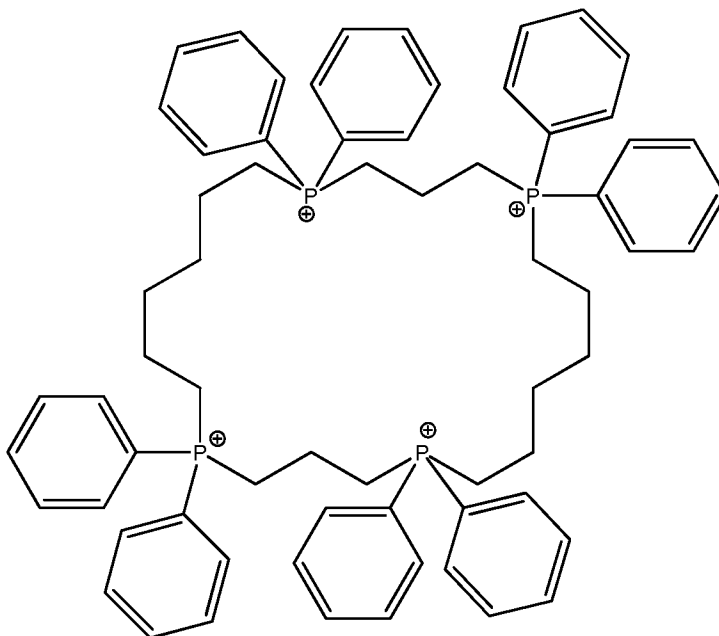
wherein each R group of protonated tertiary amine or phosphonium is optionally substituted with one or more substituents selected from the group consisting of C₁-C₁₅ alkyl, alkenyl, alkynyl, alkoxy, carbocyclyl, carbocyclylalkyl, heterocyclyl, heterocyclylalkyl and hydroxyalkyl;

B is a divalent fragment composed of a chain of one or more moieties selected from the group consisting of C₃-C₂₀-alkylene, C₂-C₂₀-alkenylene, and C₂-C₂₀-alkynylene;

wherein C₃-C₂₀-alkylene, C₂-C₂₀-alkenylene, and C₂-C₂₀-alkynylene optionally contain in the chain one or more heteroatoms selected from the group consisting of O, N, S and Si;

wherein **B** is optionally substituted with one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, and halo.

[0008] In another embodiment, a further tetraionic liquid salt is provided. The tetraionic liquid salt comprises a tetraionic species corresponding in structure to



[0009] In a further embodiment, a solvent is provided comprising at least one tetraionic liquid salt comprising a tetraionic species of Formula I or Formula II, as defined herein.

[0010] In another embodiment, there is provided a method of detecting at least one anion, the method comprising using at least one tetraionic liquid salt comprising a tetraionic species corresponding in structure to Formula I or Formula II, as defined herein.

[0011] In another embodiment, there is provided herein a device useful in chemical separation or analysis comprising a solid support and at least one tetraionic species adsorbed, absorbed or immobilized thereon corresponding in structure to Formula I or Formula II, as defined herein.

[0012] In yet another embodiment, there is provided a method of separating one chemical from a mixture of chemicals comprising the steps of providing a mixture of at least one first chemical and at least one second chemical, exposing said mixture to at least one solid support including at least one tetraionic species adsorbed, absorbed or immobilized thereon corresponding in structure to Formula I or Formula II, as defined herein.

BRIEF DESCRIPTION OF THE DRAWINGS

- [0013] Figure 1 shows structures, names and masses of trivalent anions used herein.
- [0014] Figure 2 shows examples of structures of tetraionic species of Formula I.
- [0015] Figure 3 shows examples of structures of tetraionic species of Formula II.
- [0016] Figure 4 shows examples of tricationic ion pairing agents.

DETAILED DESCRIPTION

[0017] While the specification concludes with the claims particularly pointing out and distinctly claiming the invention, it is believed that the present invention will be better understood from the following description.

A. Definitions

[0018] The term “ammonium” refers to a positively charged polyatomic cation of the

chemical formula $\begin{array}{c} \text{R} \\ | \\ -\text{N}-\text{R}_2^+-\text{R} \\ | \\ \text{R} \end{array}$ or $\begin{array}{c} \text{R} \\ | \\ -\text{N}-\text{R}_3^+ \\ | \\ \text{R} \end{array}$, wherein the R groups are individually H or an organic radical group. Ammonium also embraces positively charged or protonated substituted amines (such as protonated tertiary amine). An “optionally substituted ammonium” is an ammonium wherein the organic radical group, R, is optionally substituted with other organic radical groups.

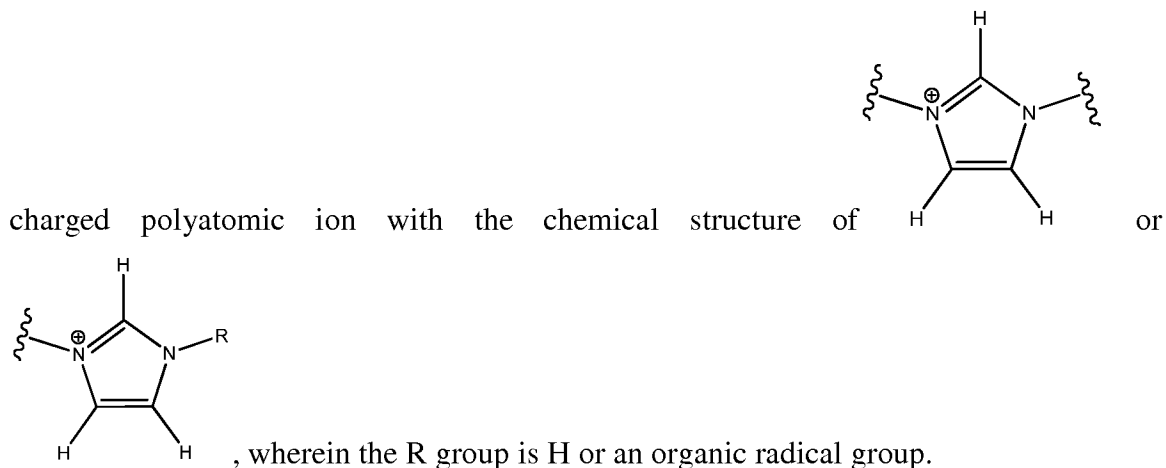
[0019] The term “protonated tertiary amine” refers to a positively charged polyatomic

ion with the chemical formula $\begin{array}{c} \text{R} \\ | \\ -\text{N}-\text{R}_2\text{H}^+-\text{R} \\ | \\ \text{R} \end{array}$ or $\begin{array}{c} \text{R} \\ | \\ -\text{N}-\text{R}_2\text{H}^+ \\ | \\ \text{R} \end{array}$, wherein the R groups are organic radical groups. An “optionally substituted protonated tertiary amine” is a tertiary amine wherein the organic radical group, R, is optionally substituted with other organic radical groups.

[0020] The term “phosphonium” refers to a positively charged polyatomic ion with

the chemical formula $\begin{array}{c} \text{R} \\ | \\ -\text{P}-\text{R}_2^+-\text{R} \\ | \\ \text{R} \end{array}$ or $\begin{array}{c} \text{R} \\ | \\ -\text{P}-\text{R}_3^+ \\ | \\ \text{R} \end{array}$, wherein the R groups are individually H or an organic radical group. An “optionally substituted phosphonium” is a phosphonium wherein the organic radical group, R, is optionally substituted with other organic radical groups.

[0021] The term “imidazolium” or “unsubstituted imidazolium” refers to a positively



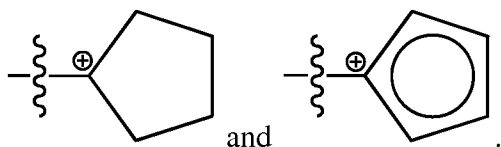
[0022] The term “carbocyclyl” (alone or in combination with another term(s)) means a saturated cyclic (*i.e.*, “cycloalkyl”), partially saturated cyclic (*i.e.*, “cycloalkenyl”), or completely unsaturated (*i.e.*, “aryl”) hydrocarbyl substituent containing from 3 to 14 carbon ring atoms (“ring atoms” are the atoms bound together to form the ring or rings of a cyclic substituent). A carbocyclyl may be a single ring (monocyclic) or polycyclic ring structure.

[0023] A carbocyclyl may be a single ring structure, which typically contains from 3 to 7 ring atoms, more typically from 3 to 6 ring atoms, and even more typically 5 to 6 ring atoms. Examples of such single-ring carbocyclyls include cyclopropyl (cyclopropanyl), cyclobutyl (cyclobutanyl), cyclopentyl (cyclopentanyl), cyclopentenyl, cyclopentadienyl, cyclohexyl (cyclohexanyl), cyclohexenyl, cyclohexadienyl, and phenyl.

[0024] A carbocyclyl may alternatively be polycyclic or contain more than one ring. Examples of polycyclic carbocyclyls include bridged, fused, spirocyclic, and isolated carbocyclyls. In a spirocyclic carbocyclyl, one atom is common to two different rings. An example of a spirocyclic carbocyclyl is spiropentanyl. In a bridged carbocyclyl, the rings share at least two common non-adjacent atoms. Examples of bridged carbocyclyls include bicyclo[2.2.1]heptanyl, bicyclo[2.2.1]hept-2-enyl, and adamantanyl. In a fused-ring carbocyclyl system, multiple rings may be fused together, such that two rings share one common bond. Examples of two- or three-fused ring carbocyclyls include naphthalenyl, tetrahydronaphthalenyl (tetralinyl), indenyl, indanyl (dihydroindenyl),

anthracenyl, phenanthrenyl, and decalinyl. In an isolated carbocyclyl, the rings are separate and independent, as they do not share any common atoms, but a linker exists between the rings.

[0025] The term "carbocyclyl" encompasses protonated carbocyclyls, such as



[0026] The term "heterocyclyl" (alone or in combination with another term(s)) means a saturated (*i.e.*, "heterocycloalkyl"), partially saturated (*i.e.*, "heterocycloalkenyl"), or completely unsaturated (*i.e.*, "heteroaryl") ring structure containing a total of 3 to 14 ring atoms. At least one of the ring atoms is a heteroatom (*i.e.*, N, P, As, O, S and Si), with the remaining ring atoms being independently selected from the group consisting of carbon, oxygen, nitrogen, and sulfur. A heterocyclyl may be a single-ring (monocyclic) or polycyclic ring structure.

[0027] The term "heterocyclyl" encompasses protonated heterocyclyls such as pyridinium, pyridazinium, pyrimidinium, pyrazinium, imidazolium, pyrazolium, thiazolium, oxazolium and triazolium.

[0028] A heterocyclyl may be a single ring, which typically contains from 3 to 7 ring atoms, more typically from 3 to 6 ring atoms, and even more typically 5 to 6 ring atoms. Examples of single-ring heterocyclyls include furanyl, dihydrofuranyl, tetrahydrofuranyl, thiophenyl (thiofuranyl), dihydrothiophenyl, tetrahydrothiophenyl, pyrrolyl, pyrrolinyl, pyrrolidinyl, imidazolyl, imidazolinyl, imidazolidinyl, pyrazolyl, pyrazolinyl, pyrazolidinyl, triazolyl, tetrazolyl, oxazolyl, oxazolidinyl, isoxazolidinyl, isoxazolyl, thiazolyl, isothiazolyl, thiazolinyl, isothiazolinyl, thiazolidinyl, isothiazolidinyl, thiadiazolyl, oxadiazolyl (including 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl (furazanyl) or 1,3,4-oxadiazolyl), oxatriazolyl (including 1,2,3,4-oxatriazolyl or 1,2,3,5-oxatriazolyl), dioxazolyl (including 1,2,3-dioxazolyl, 1,2,4-dioxazolyl, 1,2,3-dioxazolyl or 1,3,4-dioxazolyl), oxathiazolyl, oxathiolyl, oxathiolanyl, pyranyl, dihydropyranyl, thiopyranyl, tetrahydrothiopyranyl, pyridinyl (azinyl), piperidinyl, diazinyl (including pyridazinyl (1,2-diazinyl), pyrimidinyl (1,3-diazinyl), pyrazinyl (1,4-diazinyl)), piperazinyl, triazinyl (including 1,3,5-triazinyl, 1,2,4-triazinyl, and 1,2,3-

triazinyl)), oxazinyl (including 1,2-oxazinyl, 1,3-oxazinyl, or 1,4-oxazinyl)), oxathiazinyl (including 1,2,3-oxathiazinyl, 1,2,4-oxathiazinyl, 1,2,5-oxathiazinyl, or 1,2,6-oxathiazinyl)), oxadiazinyl (including 1,2,3-oxadiazinyl, 1,2,4-oxadiazinyl, or 1,3,5-oxadiazinyl)), morpholinyl, azepinyl, oxepinyl, thiepinyl, and diazepinyl.

[0029] A heterocyclyl may alternatively be polycyclic or contain more than one ring. Examples of polycyclic heterocyclyls include bridged, fused, and spirocyclic heterocyclyls. In a spirocyclic heterocyclyl, one atom is common to two different rings. In a bridged heterocyclyl, the rings share at least two common non-adjacent atoms. In a fused-ring heterocyclyl, multiple rings may be fused together, such that two rings share one common bond. Examples of fused ring heterocyclyls containing two or three rings include indolizinyl, pyranopyrrolyl, 4H-quinolizinyl, purinyl, naphthyridinyl, pyridopyridinyl (including pyrido[3,2-b]-pyridinyl or pyrido[3,4-b]-pyridinyl), and pteridinyl. Other examples of fused-ring heterocyclyls include benzofused heterocyclyls, such as indolyl, isoindolyl (isobenzazolyl, pseudoisoindolyl), indoleninyl (pseudoindalyl), isoindazolyl (benzpyrazolyl), benzazinyl (including quinolinyl (1-benzazinyl) or isoquinolinyl (2-benzazinyl)), phthalazinyl, quinoxalinyl, quinazolinyl, benzodiazinyl (including cinnolinyl (1,2-benzodiazinyl) or quinazolinyl (1,3-benzodiazinyl)), benzopyranyl (including chromanyl or isochromanyl), benzoxazinyl (including 1,2,3-benzoxazinyl, 1,2,4-benzoxazinyl, or 1,3,4-benzoxazinyl), and benzisoxazinyl (including 1,2-benzisoxazinyl or 1,4-benzisoxazinyl).

[0030] As used herein, the term “alkyl” (alone or in combination with another term(s)) refers to an alkane-derived radical containing from 1 to 20 carbon atoms. Alkyl includes straight chain alkyl, branched alkyl and cycloalkyl. Straight chain or branched alkyl groups contain from 1-15 carbon atoms, such as methyl, ethyl, propyl, isopropyl, butyl, *t*-butyl, and the like. Alkyl also includes straight chain or branched alkyl groups that contain or are interrupted by one or more cycloalkyl portions. Examples of this include, but are not limited to, 4-(isopropyl)-cyclohexylethyl or 2-methylcyclopropylpentyl. The alkyl group is attached at any available point to produce a stable compound. The term alkyl is also meant to encompass a fully substituted carbon.

[0031] As used herein, the term “alkenyl” refers to a straight or branched hydrocarbyl group with at least one site of unsaturation, *i.e.* a carbon-carbon, *sp*² double bond. In an

embodiment, alkenyl has from 2 to 15 carbon atoms. In some embodiments, alkenyl is a C₂-C₁₀ alkenyl group or a C₂-C₆ alkenyl group. Examples of alkenyl groups include, but are not limited to, ethylene or vinyl (-CH=CH₂), allyl (-CH₂CH=CH₂), cyclopentenyl (-C₅H₇), and 5-hexenyl (-CH₂CH₂CH₂CH₂CH=CH₂).

[0032] As used herein, the term “alkynyl” refers to a straight or branched carbon-chain group with at least one site of unsaturation, i.e. a carbon-carbon, sp triple bond. In an embodiment, alkynyl has from 2 to 15 carbon atoms. In some embodiments, alkynyl is a C₂-C₁₀ alkynyl group or a C₂-C₆ alkynyl group. Examples of alkynyl groups include acetylenic (-C≡CH) and propargyl (-CH₂C≡CH).

[0033] The term “alkylene” (alone or in combination with another term(s)) refers to a divalent alkane-derived radical containing 1 to 20 carbon atoms, such as 1 to 15 carbon atoms, 3 to 20 carbon atoms, 3 to 12 carbon atoms, or 3 to 9 carbon atoms, from which two hydrogen atoms are taken from the same carbon atom or from different carbon atoms. Examples of alkylene include, but are not limited to, methylene —CH₂—, ethylene —CH₂CH₂—, and the like.

[0034] The term “amino” (alone or in combination with another term(s)) means -NH₂. The term “amino” is meant to encompass a “monosubstituted amino” (alone or in combination with another term(s)) wherein one of the hydrogen radicals is replaced by a non-hydrogen substituent; and a “disubstituted amino” (alone or in combination with another term(s)) wherein both of the hydrogen atoms are replaced by non-hydrogen substituents, which may be identical or different.

[0035] The term “alkoxy” (alone or in combination with another term(s)) means an alkylether, i.e., -O-alkyl. Examples of such a substituent include methoxy (-O-CH₃), ethoxy, *n*-propoxy, isopropoxy, *n*-butoxy, isobutoxy, *sec*-butoxy, *tert*-butoxy, and the like.

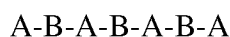
[0036] The term “carbocyclalkyl” (alone or in combination with another term(s)) refers to the group —Z-carbocycl where Z is lower alkylene or substituted lower alkylene group. The term “heterocyclalkyl” (alone or in combination with another term(s)) refers to the group —Z-heterocycl where Z is lower alkylene or substituted lower alkylene group.

[0037] The term “tetraionic salt” is used to describe a salt molecule, although, as the context suggests, it may be used synonymously with “tetraionic liquid” (“TIL”) and “tetraionic liquid salt” (“TILS”). A “tetraionic liquid” or “tetraionic liquid salt” in accordance with the present invention is a liquid comprised of a tetraionic salt. Thus, sufficient tetraionic salt molecules are present such that they exist in liquid form at the temperatures indicated herein. A TIL is either (1) a tetracationic liquid or (2) a tetraanionic liquid.

[0038] A “tetracationic liquid salt” or “tetracationic liquid”, as mentioned above, is either a salt molecule or a liquid comprised of tetracationic salt(s), wherein the tetra cationic salt(s) is formed between a tetracationic species and one or more counter-anions of equal, greater than, or less than opposite charge.

B. Tetraionic Liquid Salts of Formula I

[0039] This invention is directed, in part, to a TILS comprising a tetraionic species and at least one counterion. In one embodiment, the TILS corresponds in structure to Formula I:

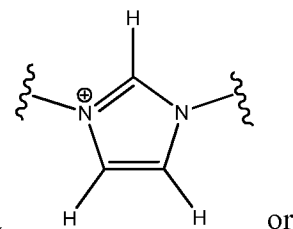
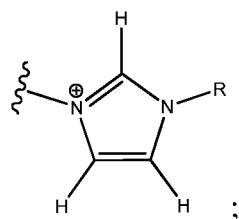


Formula I

and at least one counter-anion, wherein:

A is selected from the group consisting of optionally substituted protonated tertiary amine of formula $\text{--}\zeta\text{--NRH}^+\text{--}\zeta\text{--}$ or $\text{--}\zeta\text{--NR}_2\text{H}^+\text{--}\zeta\text{--}$, optionally substituted phosphonium

of formula $\text{--}\zeta\text{--PR}_2^+\text{--}\zeta\text{--}$ or $\text{--}\zeta\text{--PR}_3^+\text{--}\zeta\text{--}$, and imidazolium of formula



wherein each R is independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, alkoxy, carbocyclyl, carbocyclalkyl, heterocyclyl, heterocyclalkyl and hydroxyalkyl;

wherein each R group of protonated tertiary amine or phosphonium is optionally substituted with one or more substituents selected from the group consisting of C₁-C₁₅ alkyl, alkenyl, alkynyl, alkoxy, carbocyclyl, carbocyclalkyl, heterocyclyl, heterocyclalkyl and hydroxyalkyl;

B is a divalent fragment composed of a chain of one or more moieties selected from the group consisting of C₃-C₂₀-alkylene, C₂-C₂₀-alkenylene, and C₂-C₂₀-alkynylene;

wherein C₃-C₂₀-alkylene, C₂-C₂₀-alkenylene, and C₂-C₂₀-alkynylene optionally contain in the chain one or more heteroatoms selected from the group consisting of O, N, S and Si;

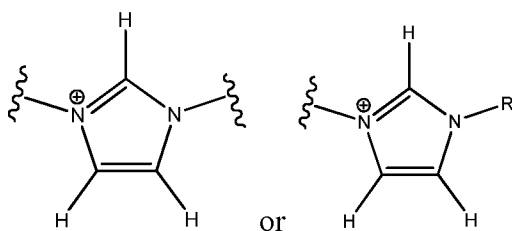
wherein **B** is optionally substituted with one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, and halo.

[0040] In some embodiments, R is alkyl, such as methyl, ethyl, propyl, isopropyl, *n*-butyl, *sec*-butyl, isobutyl, or *t*-butyl. In other embodiments, R is selected from the group consisting of methyl, phenyl, *n*-butyl and propyl. R may be substituted with an organic radical group.

[0041] Each **B** is a bridging group. Each **B** may, where present, be the same or different. In some embodiments, **B** is selected from the group consisting of propylene, butylene, hexylene, decylene, and dodecylene.

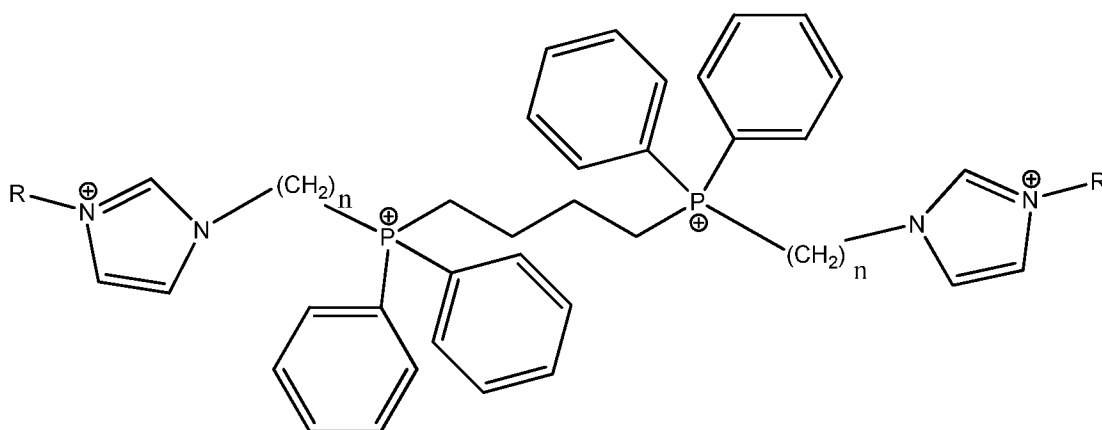
[0042] In some embodiments of Formula I, each **A** is individually selected from the

group consisting of phosphonium of formula $\text{---PR}_2^+ \text{---}$ or ---PR_3^+ , and imidazolium

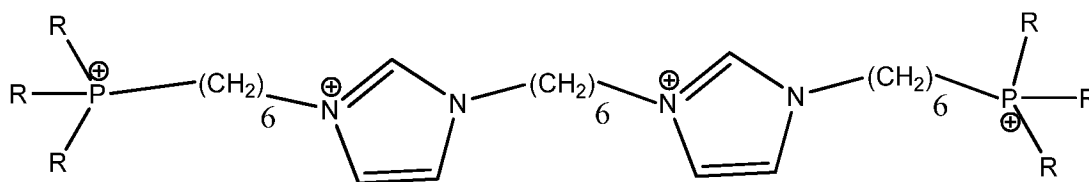
of formula , and **B** is C₃-C₁₂ alkylene. In various embodiments, each **R** is independently alkyl or carbocyclyl. In other embodiments, each

R is independently selected from the group consisting of methyl, ethyl, propyl, isopropyl, *n*-butyl, *sec*-butyl, isobutyl, *t*-butyl and phenyl, and **B** is independently selected from the group consisting of propylene, butylene, hexylene, decylene, and dodecylene. In other embodiments, each **R** is selected from the group consisting of methyl, phenyl, *n*-butyl, isopropyl and propyl.

[0043] Non-limiting examples of such compounds include those selected from the following structures, wherein each **R** is independently selected from the group consisting of methyl, propyl, *n*-butyl and phenyl; and each **B** is individually selected from the group consisting of butylene ($n=4$), hexylene ($n=6$) and dodecylene ($n=12$).

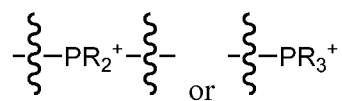


and



[0044] The substitution pattern of various embodiments is given in Figure 2, embodied as compounds D1-D3 and E1 and E2.

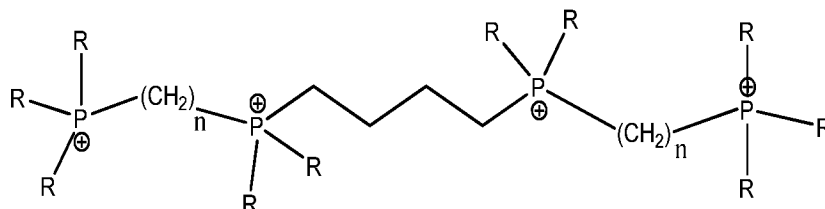
[0045] In some embodiments of Formula I, **A** is phosphonium of formula



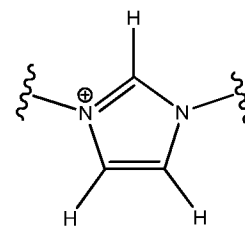
, and **B** is C_3 - C_{12} alkylene. In various embodiments, each **R** is independently alkyl or carbocyclyl. In other embodiments, each **R** is independently selected from the group consisting of methyl, ethyl, propyl, isopropyl, *n*-butyl, *sec*-butyl, isobutyl, *t*-butyl and phenyl, and each **B** is independently selected from the group consisting of propylene, butylene, hexylene, decylene, and dodecylene. In some further

embodiments, each **R** is independently selected from the group consisting of methyl, phenyl, n-butyl, isopropyl and propyl.

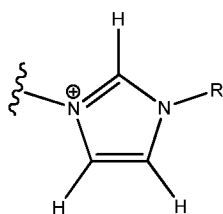
[0046] Non-limiting examples of such compounds include those selected from the following structure, wherein each **R** is independently selected from the group consisting of propyl, isopropyl and phenyl; and each **B** is independently selected from the group consisting of butylene (n=4), hexylene (n=6) and decylene (n=10).



[0047] The substitution pattern of various embodiments is given in Figure 2, embodied as compounds B1-B5 and C1.

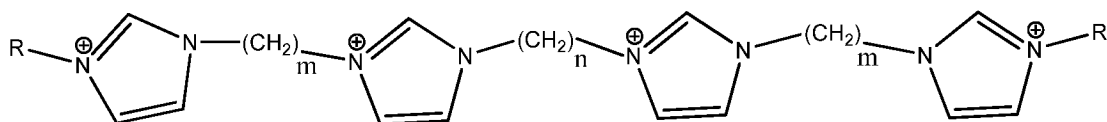


[0048] In some embodiments of Formula I, **A** is



, and **B** is C₃-C₁₂ alkylene. In various embodiments, each **R** is independently alkyl or carbocyclyl. In other embodiments, each **R** is independently selected from the group consisting of methyl, ethyl, propyl, isopropyl, n-butyl, sec-butyl, isobutyl, t-butyl and phenyl, and each **B** is independently selected from the group consisting of propylene, butylene, hexylene, decylene, and dodecylene. In some further embodiments, each **R** is selected from the group consisting of methyl, phenyl, n-butyl, isopropyl and propyl.

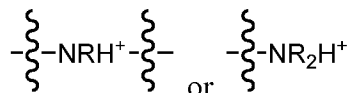
[0049] Non-limiting examples of such compounds include those selected from the following structure, where each **R** is independently selected from the group consisting of methyl and phenyl; and each **B** is independently selected from the group consisting of propylene, butylene, hexylene and decylene.



[0050]

The substitution pattern of various embodiments is given in Figure 2, embodied as compounds A1-A8.

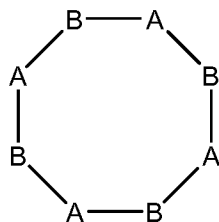
[0051] In some embodiments of Formula I, **A** is optionally substituted tertiary amine



and **B** is C₃-C₁₂ alkylene. In various embodiments, each **R** is independently alkyl or carbocyclyl. In other embodiments, each **R** is independently selected from the group consisting of methyl, ethyl, propyl, isopropyl, *n*-butyl, *sec*-butyl, isobutyl, *t*-butyl and phenyl, and each **B** is independently selected from the group consisting of propylene, butylene, hexylene, decylene, and dodecylene. In some further embodiments, each **R** is selected from the group consisting of methyl, phenyl, *n*-butyl, isopropyl and propyl.

C. Tetraionic Liquid Salts of Formula II

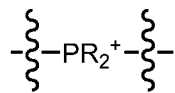
[0052] In another embodiment, the TILS corresponds in structure to Formula II:



Formula II

and at least one counter-anion, wherein:

A is selected from the group consisting of phosphonium of formula



; wherein each **R** is independently selected from the group consisting of alkyl, alkenyl, alkynyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, heterocyclylalkyl, and hydroxyalkyl;

Each **B** is a bridging group. Each **B** may, where present, be the same or different. **B** is a divalent fragment composed of a chain of one or more moieties selected from the group consisting of C₁-C₂₀-alkylene, C₂-C₂₀-alkenylene, C₂-C₂₀-alkynylene, (-CH₂-carbocyclyl-CH₂-), and (-CH₂-carbocyclyl-); wherein C₁-C₂₀-alkylene, C₂-C₂₀-

alkenylene, and C₂-C₂₀-alkynylene optionally contain in the chain one or more heteroatoms selected from the group consisting of O, N, S and Si; wherein **B** is optionally substituted with one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, and halo.

[0053] In some embodiments, **R** is phenyl.

[0054] In some embodiments, **B** is selected from the group consisting of propylene, butylene, and hexylene.

[0055] Non-limiting examples of such compounds include those found in Figure 3.

D. Tetraionic Species Symmetry

[0056] Tetraionic species of the present invention can be classified as symmetric or unsymmetric.

[0057] In some embodiments, the tetraionic species are symmetric.

[0058] By "symmetric", it is meant that the tetraionic species possess symmetric bridging groups **B** and identical ionic groups **A**.

[0059] The tetraionic species can also be center-symmetric. By "center-symmetric", it is meant that the tetraionic species possess a symmetric central bridging group **B** regardless whether the ionic groups **A** are identical.

[0060] In other embodiments, the tetraionic species are unsymmetric.

[0061] By "unsymmetric," it is meant that the monoionic groups **A** are structurally different, or that the bridging groups **B** are unsymmetric, or that the monoionic groups conjugate to the central group in such a manner that the polyionic species is not symmetric. The invention encompasses unsymmetric tetraionic species due to any compositional and/or structural arrangement.

[0062] In some embodiments, an unsymmetric tetraionic species of the invention contains different monoionic groups. For example, **A** can be different cations such as substituted or unsubstituted, saturated or unsaturated, straight or branched aliphatic chain, cyclic group, aromatic group, protonated tertiary amine, phosphonium or imidazolium group.

[0063] The unsymmetric tetraionic salts of the invention can be used in a substantially pure form in any of the applications, *e.g.*, the applications disclosed in this application. As compared to corresponding symmetric tetraionic salts, tetraionic salts

which do not have identical monoionic groups or which include an unsymmetric central group generally have lower melting temperatures, and advantage for “liquid” salts. In addition, the higher the degree of internal structural dissimilarity as compared to corresponding symmetric polyionic salts, generally the lower the melting temperatures will result as compared to those of the corresponding symmetric polyionic salts. The trend can be thought of as a continuum from a symmetric molecule on the one end and a group with all different counterions, all different ions, and different substituents on the other. The former would be expected to have the highest melting point and the latter the relatively lowest. Of course, there can be variations to this trend. For example, a specific counterion might have a greater effect on decreasing melting point than the use of other different ions.

[0064] The unsymmetric tetraionic salts of the invention may also be advantageous for uses as solvents. For example, a tetraionic species having four different **A** groups offers four sets of possible interactions with other molecules in the solution as compared to only one set in the case of a symmetric tetraionic species. Indeed, the more unsymmetric, the more the variety of interactions that can result. Thus, the invention provides a use of a TIL of a substantially pure “unsymmetric” tetraionic salt as describe herein as a solvent.

[0065] The unsymmetric TILSs of the invention can be used in a substantially pure form in any of the applications, *e.g.*, the applications disclosed in this application. The unsymmetric tetraionic salts of the invention can also be used in combination with any of the symmetric tetraionic salts as a mixture. Thus, in one embodiment, the invention provides a TIL of a substantially pure unsymmetric tetraionic salt as described above. In another embodiment, the invention provides a TIL comprising at least one of the unsymmetric polyionic salts as described above and at least one symmetric tetraionic salt of the invention. A person skilled in the art would be able to determine the proportion of the symmetric and unsymmetric TILSs when used as a mixture according to the particular application.

E. Counterions

[0066] The TILs of the present invention are generally salts, although they may exist as ions (+3, -3, +4, -4, *etc.*) in certain circumstances. Thus, in most instances, each ion

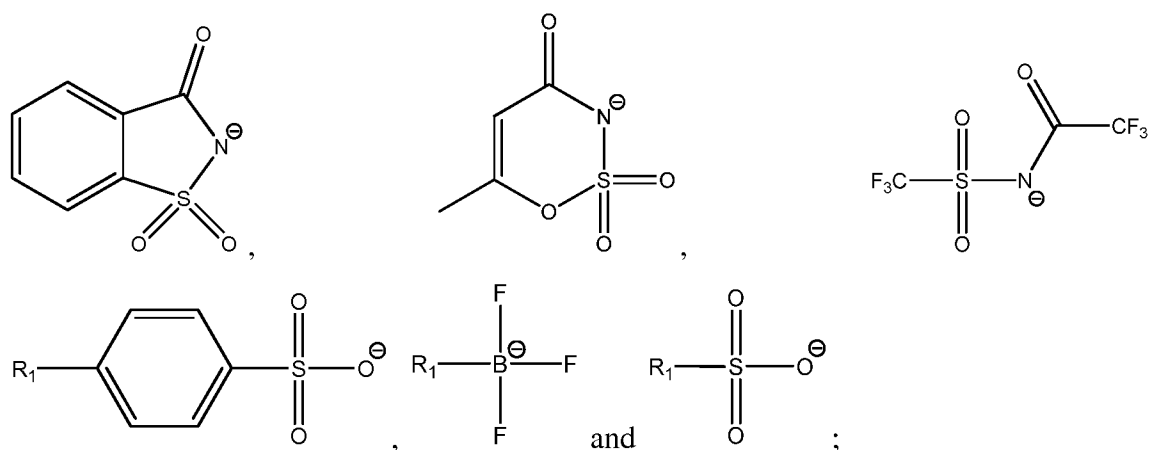
has a counterion, one for each anion or cation. Charge should be preserved in most cases. In the case of a polyanionic ionic liquid, cations are required and in the case of a polycationic ionic liquid, anions are required. The choice of anion can have an effect of the properties of the resulting compound and its utility as a solvent. And, while anions and cations will be described in the context of a single species used, a mixture of cations can be used to form salts with a polyanionic species to form a polyanionic ionic liquid. The reverse is true for polycations. For sake of clarity, the salt-forming ions will be referred to as counterions herein.

[0067] The tetracation of Formulas I and II form a tetraionic salt with counterions having a charge which is opposite to that of the **A** substituent.

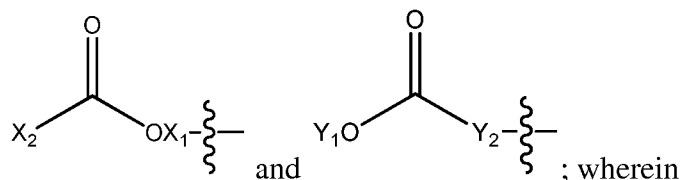
[0068] Anionic counterions can be selected from any of the polyanionic molecules discussed herein useful in the creation of polyanionic ionic liquids. These would include dicarboxylates, disulfonates and disulfates. The corresponding monoionic compounds may also be used including carboxylates, sulfonates, sulfates, phosphonates, and hydroxide. Halogen and halogen-containing compounds that may be used include, without limitation, triflate, NTf_2^- , PF_6^- , BF_4^- , and the like. The counterions should be selected such that the polyionic liquids have good thermal and/or chemical stability and have a solid/liquid transformation temperature and/or a liquid range as described herein. Finally, the ionic groups of the present invention can be substituted or unsubstituted. They may be substituted with halogens, with alkoxy groups, with aliphatic, aromatic or cyclic groups, with nitrogen-containing species, with silicon-containing species, with oxygen-containing species, and with sulfur-containing species. The degree of substitution and the selection of substituents can influence the properties of the resulting material as previously described in discussing the nature of the bridge or chain. Thus, care should be taken to ensure that excessive steric hindrance and excessive molecular weight are avoided, that resulting materials do not lose their overall flexibility and that nothing will interfere with the ionic nature of the two ionic species.

[0069] When **A** is cationic, the counterions are anions which, without limitation, include hydroxide, halogens, mono-carboxylates, mono-sulfonates, mono-sulfates, NTf_2^- , BF_4^- , triflates, or PF_6^- , as well as molecules having anionic groups each selected from, without limitation, carboxylate, sulfate or sulfonate groups. In some embodiments, the at

least one counter-anion of the TILS is independently selected from the group consisting of citrate, sulfanilic acid azochromotrop, trimetaphosphate, nitrilotriacetic tricarboxylate, phosphate, tartrazine, hexanitrocobaltate, pyranine, indigotrisulfonate, hexachlororhodate, tris(2,4-dimethyl-5-sulfophenyl)-phosphine, chromium oxalate, oxalomalic tricarboxylate, phosphoformate, orthovanadate, hexacyanocobaltate, 8-methoxypyrene-1,3,6-trisulfonate, 8-octanoyloxypyrene-1,3,6-trisulfonate, and 8-nonanoyloxypyrene-1,3,6-trisulfonate. In other embodiments, counterions include, without limitation:



[0070] wherein R_1 is selected from the group consisting of hydrogen, alkyl, hydroxyalkyl, carbocyclyl, heterocyclyl, halo, alkoxy, hydroxyl, alkylcarbonyl, alkylcarbonylalkylene, hydroxycarbonyl,



X_1 is C_1 - C_{10} -alkylene;

X_2 is selected from the group consisting of hydrogen, alkyl, alkoxy, amino and hydroxy;

Y_1 is selected from the group consisting of hydrogen and alkyl; and

Y_2 is C_1 - C_{10} -alkylene.

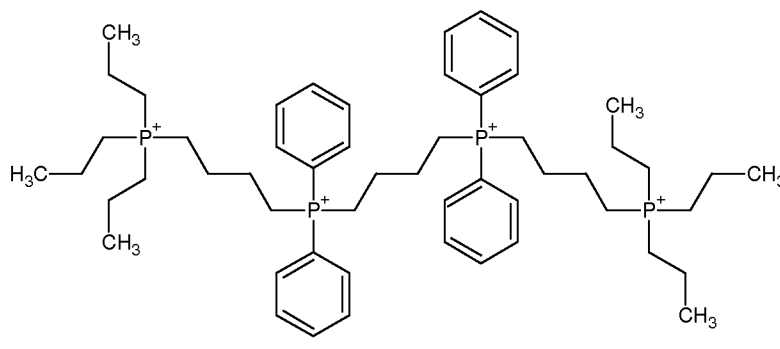
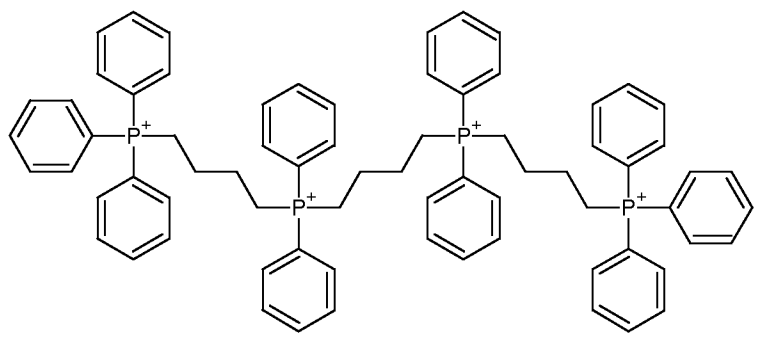
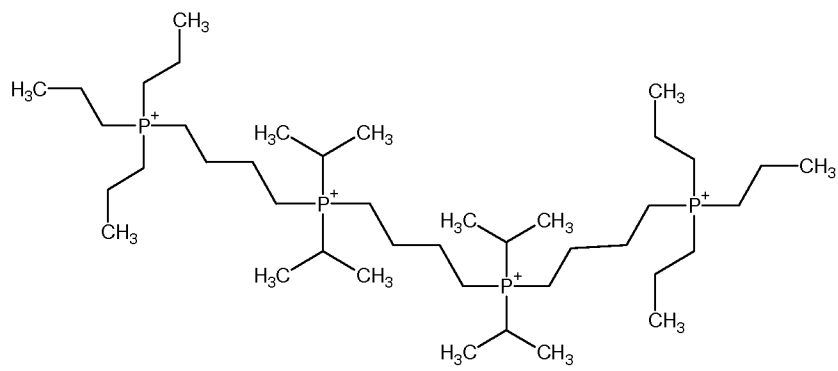
[0071] Counterions can be monoionic, diionic or polyionic ions, or a mixture thereof. They can be the same or different so long as they all have the same type of charge

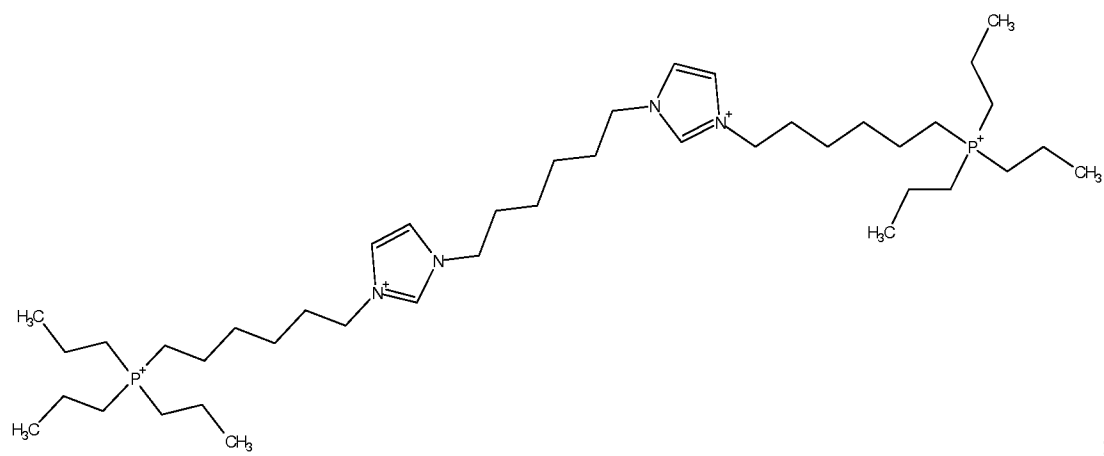
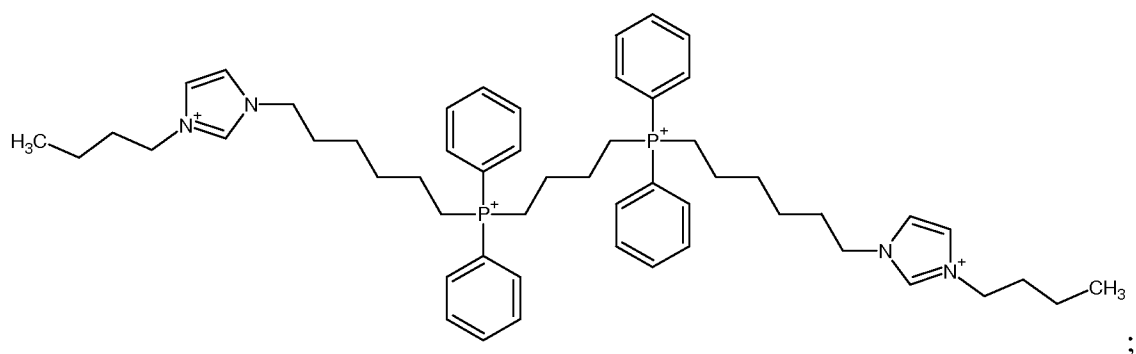
(positive or negative) and the total charge is m . For example, a polyionic liquid can be a mixture of a polycationic liquid and a polyanionic liquid.

F. Example Tetraionic Species

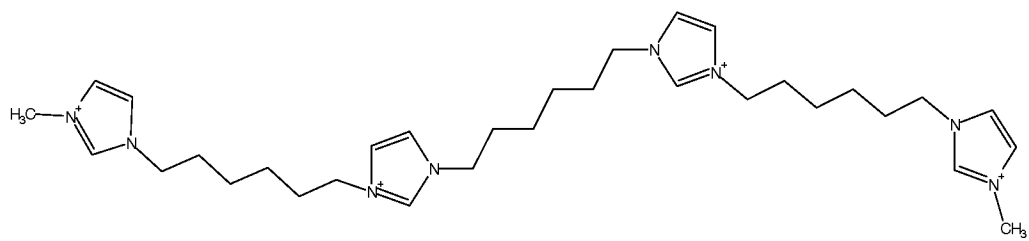
[0072] The present disclosure provides several examples of tetracationic species according to Formula I and Formula II.

[0073] In some embodiments, the tetracationic species is selected from the group consisting of:



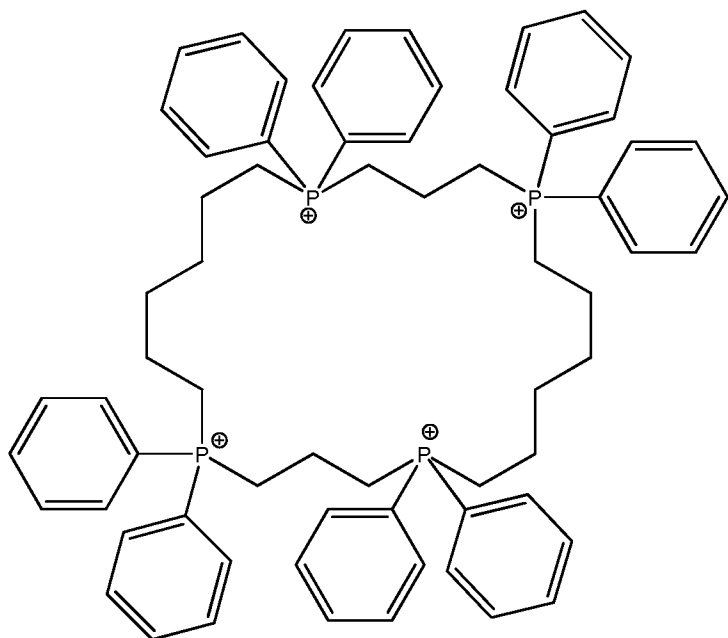


and

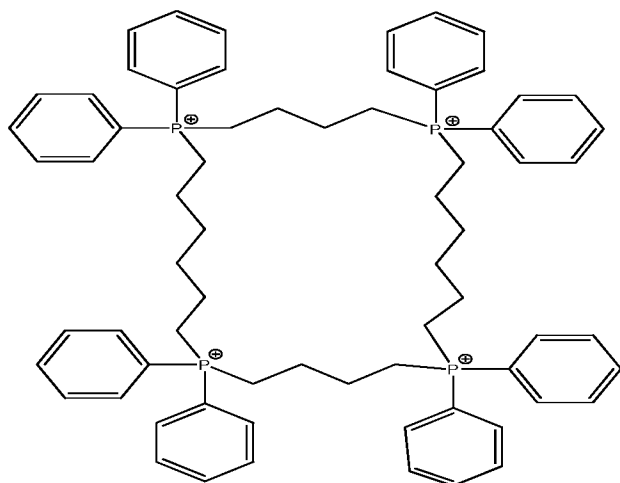


[0074] In other embodiments, the TILS comprises a tetraionic species shown in Figures 2 and 3.

[0075] In a particular embodiment, the TILS comprises a tetraionic species corresponding in structure to



OR



G. Tetraionic liquid Salts as Solvents

[0076] This invention is also directed to solvents comprising one or more TILSs in accordance with the invention.

[0077] In some embodiments, the solvent comprises at least one tetraionic liquid salt comprising a tetraionic species of Formula I or Formula II, as defined herein.

[0078] In some embodiments, the solvent comprises one of the tetraionic species set forth in Figures 2 and 3.

[0079] In other embodiments, the solvent comprises more than one tetraionic species set forth in Figures 2 and 3.

[0080] In another embodiment, one or more TILSs can be used as a solvent for dissolution, suspension or dispersion of solids or liquid mixed therewith or as a reaction solvent for chemical reactions. Both are intended by the term solvent.

[0081] The TILSs of the present invention can be used in pure or in substantially pure form as carriers or as solvents. "Substantially" in this context means no more than about 10% of undesirable impurities. Such impurities can be other undesired tetraionic salts, reaction by-products, contaminants or the like as the context suggests. In an intended mixture of two or more TILSs, neither would be considered an impurity. Because they are non-volatile and stable, they can be recovered and recycled and pose few of the disadvantages of volatile organic solvents. Because of their stability over a wide liquid range they can be used in chemical synthesis that requires both heating and cooling. Indeed, these solvents may accommodate all of the multiple reaction steps of certain chemical syntheses. Of course, these TILs may be used in solvent systems with co-solvents and gradient solvents and these solvents can include, without limitation, chiral ionic liquids, chiral non-ionic liquids, volatile organic solvents, non-volatile organic solvents, inorganic solvents, water, oils, etc. It is also possible to prepare solutions, suspensions, emulsions, colloids, gels and dispersions using the TILs. Tetraionic salts in accordance with the invention may be used in any mixture, including different polycations, different polyanions and mixtures of polycations and polyanions. In addition, one or more of the TILSs of the invention may be mixed with diionic liquid salts as described in U.S. Patent Publication No. 2006/0025598 and 2008/0027231 or triionic liquid salts as described in U.S. Patent Publication No. 2008/0210858, the text of which are hereby incorporated by reference.

[0082] In addition to discrete polyionic liquid salts, it is also possible to produce polymers of these materials. Polymers may include the polyionic liquid salts within the backbone or as pendant groups and they may be cross-linked or non-cross-linked.

H. Methods of Detecting

[0083] There is also provided herein a method of detecting at least one anion, the method comprising using at least one TILS comprising a tetraionic species corresponding in structure to Formula I or Formula II as defined herein. Any tetraionic species described

herein, such as the tetraionic species shown in Figures 2 and 3, is suitable for use in detecting at least one anion.

[0084] In some embodiments, ESI-MS is used to detect the at least one anion. In a particular aspect of this embodiment, ESI-MS is carried out in the positive ion mode.

[0085] In some embodiments, the TILS pairs with a single anion yielding a positively charged complex.

[0086] ESI-MS provides an alternative approach for the analysis of anions and, in particular, complex ions can be detected in their native forms without decomposition. Coupled with separation methods, ESI-MS is capable of detecting most ionic species. However, as powerful as ESI-MS is in the positive mode, it can suffer from lower sensitivity in the negative mode. One cause for the decrease in sensitivity in the negative mode is the prevalence of corona discharge sometimes leading to arcing events. This phenomenon results in an unstable Taylor cone and higher background noise leading to poorer LODs. Studies have shown that corona discharge in the negative mode can be suppressed by using halogenated solvents or alcohols with longer alkyl chains such as propanol, 2-propanol, and butanol. However, more commonly used solvents such as water, methanol, and acetonitrile are still preferred especially when ESI-MS is coupled with reversed phase LC or ion chromatography. Consequently, it would be highly beneficial to develop methods for sensitive anion detection by ESI-MS using typical LC operating conditions.

[0087] In another embodiment, ESI-MS may be used alone or coupled with a separation method. Examples of such separation techniques include, without limitation, LC, high performance liquid chromatography ("HPLC"), ion chromatography, ion-exchange chromatography, solid phase extraction ("SPE"), solid phase microextraction ("SPME"), task-specific SPME ("TS-SPME") and SPME Matrix-Assisted Laser Desorption/Ionization ("MALDI"). In a particular aspect, the TILS is added to a carrier flow solvent following the separation technique.

[0088] In another embodiment, one or more TILSs in accordance with the present invention can be used in a detection technique such as, but not limited to, Direct Analysis in Real Time ("DART") and / or Desorption Electrospray Ionization ("DESI"). In another embodiment, DART and DESI may be used alone, together, or coupled with a

separation method. Examples of such separation techniques include, without limitation, LC, HPLC, ion chromatography, ion-exchange chromatography, SPE, SPME, TS-SPME and SPME MALDI.

[0089] In another particular embodiment, the method includes selecting a tetraionic species that has a desired composition and structure, *e.g.*, a desired charged group structure and a desired mass, or a combination thereof. The charged groups in the tetraionic species can be selected based on the composition and structure of the charged molecule to be detected. In a particular aspect, the tetraionic species is specific for the charged molecule to be detected. Thus, it is preferable that the charged group of the tetraionic species is such that it binds strongly with the charged molecule to be detected. More preferably, the charged groups of the tetraionic species is such that it does not bind strongly with other charged molecules in the sample. Using a tetraionic species that is specific for a charged molecule of interest allows high selectivity in detecting the charged molecule.

[0090] In other embodiments, the detection of dianions through complexation with tricationic pairing agents is provided. It has been determined that benzyliimidazolium and tripropylphosphonium are better cationic moieties and the reagents of flexible linear structure generally work better than rigid trigonal trications.

I. Devices / Stationary Phases / Mixed Stationary Phases

[0091] There is also provided herein a device useful in chemical separation or analysis comprising: a solid support and at least one tetraionic species adsorbed, absorbed or immobilized thereon corresponding in structure to Formula I or Formula II as defined herein. Any tetraionic species described herein, such as the tetraionic species shown in Figures 2 and 3, is suitable for use in chemical separation. Such a device is particularly useful for chemical separations.

[0092] In another embodiment, there is provided an immobilized TILS including one or more TILSs (with or without monoionic materials) as stationary phases, particularly in gas chromatography ("GC"). These stationary phases are highly selective, highly stable, and highly resistant to temperature degradation. These materials can be non-cross-linked (which often means that they are absorbed or adsorbed on a solid support or column), can be "partially" cross-linked or "more highly" cross-linked (which often means that they

are “immobilized” on a solid support or column) and can be composed of a mixture of TILSs and tetraionic material and/or dicationic, tricationic, or monocationic materials or can be made completely of TILSs in accordance with the present invention. The presence of unsaturated groups facilitates cross-linking and/or immobilization.

[0093] In the case of non-cross-linked stationary phases, the TILS(s) used may be saturated, unsaturated or a mixture of both. It should be understood, however, particularly if some amount of unsaturated TILS(s) is used, and especially where heat is used to fix the stationary phase, or the stationary phase is heated during use, as in GC, some degree of cross-linking is possible.

[0094] In a particular embodiment, the stationary phases are made from a tetraionic species which is chiral and optically enhanced. Moreover, cross-linking and/or immobilization of the TILS in a column as a stationary phase, or to a solid support for SPE, SPME, TS-SPME, SPME/MALDI, ion chromatography, ion exchange chromatography, headspace analysis or other analytical or separation technique, may not affect the selectivity of the stationary phase, thereby preserving its dual nature retention behavior.

[0095] And while stationary phases for GC and, in particular, capillary GC are one particular aspect of the present invention, the TILS(s), either alone or in combination with monoionic, diionic, and/or triionic liquid salt(s) can be used as a stationary phase in other forms of chromatography including, for example, LC and HPLC. Not only are the methods of creating stationary phases, solid supports and/or columns containing same contemplated, the stationary phases, solid supports and columns themselves and the use of columns and solid supports containing these stationary phases in chromatography, and other analytical or separation techniques are contemplated as specific aspects of the invention.

[0096] A TILS can be coated on a capillary (or solid support) and optionally, subsequently polymerized and/or cross-linked by, for example, two general methods. In the first method, the ionic liquid is coated via the static coating method at 40°C using coating solution concentrations ranging from 0.15-0.45% (w/w) using solutions of methylene chloride, acetone, ethyl acetate, pentane, chloroform, methanol, or mixtures thereof. After coating of the ionic liquid is complete, the column is purged with helium

and baked up to 100°C. The efficiency of naphthalene (other molecules such as n-hydrocarbons or Grob Test Mixture can also be used for this purpose) is then evaluated to examine the coating efficiency of the monomer ionic liquid stationary phase. If efficiency is deemed sufficient, the column is then flushed with vapors of azo-*tert*-butane, a free radical initiator, at room temperature. After flushing with the vapors, the column is then fused at both ends and heated in an oven using a temperature gradient up to 200°C for 5 hours. The column is gradually cooled and then re-opened at both ends, and purged with helium gas. After purging with helium gas overnight, the column is then heated and conditioned up to 200°C. After conditioning, the column efficiency is then examined using naphthalene at 100°C and the stationary phase coated layer examined under a microscope. Note that the cross-linking process can, and often does, also cause immobilization. "Immobilized" in the context of the invention means covalently or ionically bound to a support or to another ionic liquid (including TILSs) or both. This is to be compared with ionic liquids which may be absorbed or adsorbed on a solid support. Solid supports in these particular instances are intended to include columns (*e.g.*, the walls of the columns).

[0097] It is not necessary, however, to cross-link these materials prior to their use in GC. They may be adsorbed or absorbed in a column, or indeed on any solid support. However, at higher temperatures, their viscosity may decrease and they can, in some instances, flow and collect as droplets which can change the characteristics of the column. Immobilization or partial cross-linking also reduces the vapor pressure of the stationary phase film which translates into lower column bleed thereby increasing the useful upper temperature limit of the phase and column.

[0098] The second method involves adding a percentage of the TILS monomer weight of 2,2'-azobisisobutyronitrile ("AIBN") free radical initiator to the coating solution of the monomer. The capillary column is then filled with this solution and coated via the static coating method. After coating, the capillary column is then sealed at both ends and placed in an oven and conditioned up to 200°C for 5 hours. The column is gradually cooled and then re-opened at both ends, and purged with helium gas. After purging with helium gas overnight, the column is then heated and conditioned up to

200°C. After conditioning, the column efficiency is then examined using naphthalene at 100°C and the stationary phase coated layer examined under a microscope.

[0099] In another embodiment, there is provided a process which includes the free radical reaction of ionic liquid monomers to provide a more durable and robust stationary phase, as well as the cross-linked and/or immobilized stationary phases and the columns that include same. By partially cross-linking the ionic liquid stationary phase using a small percentage of free radical initiator, high efficiency capillary columns are produced that are able to endure high temperatures with little column bleed. It was found that low to moderate temperature separations (30°C-280°C) can be carried out with high selectivity and efficiency using special partially cross-linked ionic liquid stationary phase mixtures. These stationary phases retain their “gelatinous”, “semi liquid”, or “amorphous” state. For separations conducted at higher temperatures (300°C-400°C), more highly cross-linked/immobilized stationary phases are well-suited to provide high selectivity and efficient separations with low column bleed. The effect of different functionalized ionic liquid salt mixtures and initiator concentrations is studied for these two types of stationary phases. The goal is to maximize their separation efficiency, thermal stability, and column lifetime, without sacrificing the unique selectivity of the stationary phase.

[00100] In another embodiment a mixed stationary phase (“MSP”) is provided. The MSP comprises at least one TILS of the invention and stationary phase material such as, but not limited to, polysiloxanes, polyethylene glycols (“PEGs”), methylpolysiloxanes, phenyl substituted methylpolysiloxane, nitrile substituted methylpolysiloxane and carbowax. Such MSPs can be used as a stationary phase in chromatography such as GC, LC and HPLC as well as in SPE and SPME. The MSPs can be non-cross-linked (e.g., absorbed or adsorbed on a solid support or column), can be “partially” cross-linked or “more highly” cross-linked (*i.e.*, immobilized on a solid support or column). The TILS may also be cross-linked or otherwise reacted with the stationary phase material or merely mixed therewith.

[00101] Appropriate combinations of the TILS(s) and the stationary phase material(s) for producing a MSP is based on the particular application as are the proportions of the TILS(s) and the stationary phase material(s) in the MSP.

[00102] In a particular embodiment, the ratio of the TILS and the stationary phase material in the MSP is from about 1:9 (*i.e.*, about 10% of TILS and 90% of traditional stationary phase material) to about 9:1 (*i.e.*, about 90% of TILS and about 10% of stationary phase material), about 1:3 (*i.e.*, about 25% of TILS and about 75% of stationary phase material) to about 3:1 (*i.e.*, about 75% of TILS and about 25% of stationary phase material), about 1:2 (*i.e.*, about 33% of TILS and about 67% of stationary phase material) to about 2:1 (*i.e.*, about 67% of TILS and about 33% of stationary phase material), or about 1:1 (*i.e.*, about 50% of TILS and about 50% of stationary phase material) (w/w). Chromatography employing a MSP may perform better, *e.g.*, having higher selectivity, than chromatography employing TILS(s) or the stationary phase material alone.

[00103] In addition, the invention also provides methods of preparing MSPs, solid supports and/or columns containing same, the MSPs, solid supports, syringes, tubes, pipettes tips, needles, vials, and columns themselves, and the use of columns and solid supports containing such MSPs in chromatography and other analytical or separation techniques such as those described elsewhere herein.

[00104] The invention includes not only the use of TILSs, but also solid supports to which the TILSs are absorbed, adsorbed or immobilized as well as sampling devices such as, for example, pipettes, automatic pipettes, syringes, microsyringes and the like incorporating TILSs, which can be used in such analytical and separation techniques. Solid supports include, without limitation, mixed beds of particles coated with TILSs. These may be used as chromatographic media or for SPE, SPME, SPME/MALDI and ion exchange analysis. Particles may be composed of, for example, silica, carbons, composite particles, metal particles (zirconia, titania, *etc.*), as well as functionalized particles, *etc.*, contained in, for example, tubes, pipettes tips, needles, vials, and other common containers.

[00105] In a particular embodiment, the device comprises a syringe, a hollow needle, a plunger, and the solid support being attached to the syringe.

[00106] Another embodiment is a device useful in chemical separation or analysis comprising: a solid support and one or more TILSs, of, for example, Figures 2 and 3, adsorbed, absorbed or immobilized thereon. The device may be a column used in HPLC,

GC or supercritical fluid chromatography (“SFC”) wherein the solid support is either packed in a chromatographic column or a capillary column useful within GC.

[00107] The device may also be a syringe having a hollow needle defining an inner space, the needle being disposed at an end of a barrel and a plunger disposed within the barrel, the solid support being attached, mounted, affixed, irremovable or removably attached (collectively “attached”), to the syringe such that it may be retracted into the inner space of the needle when the plunger is retracted from the barrel and exposed from within the needle when the plunger is inserted into the barrel. In one embodiment, the syringe is a microsyringe. In some embodiments, the one or more TILSs used in these devices also include monoionic materials which may be simply mixed therewith or which may be cross-linked to the TILSs of the invention. These may be absorbed, adsorbed or immobilized on the solid support. When immobilized, it is preferred that these ionic species include unsaturated groups.

J. Methods of Separating

[00108] A method of separating one chemical from a mixture of chemicals comprising the steps of: providing a mixture of at least one first and at least one second chemical, exposing said mixture to at least one solid support including at least one tetraionic species adsorbed, absorbed or immobilized thereon of Formula I or Formula II as defined herein. Any tetraionic species described herein, such as the tetraionic species shown in Figures 2 and 3, is suitable for use in separating one chemical from a mixture of chemicals.

[00109] In a further embodiment, one or more TILSs in accordance with the present invention can be used in analytical and separation technologies such as, but not limited to, LC, HPLC, SPE, SPME, TS-SPME, and mass spectrometry known as SPME/MALDI, as well as ion exchange and headspace analysis.

[00110] “Retaining” in this context does not mean permanently. Separation can occur in a syringe device by removal of the device from the sample or ejection of the second chemical. In the case of a chromatography column, the first chemical will be absorbed or adsorbed at a different rate than the second chemical, which may be at a greater rate or a lower rate, thus resulting in separation. Both are moved through the column by a mobile phase, which can be a liquid or a gas and their interaction with the stationary phase (the ionic liquid materials on the solid support) at different rates causes separation. This is

what is meant by "retention" in the context of chromatography. However, in certain types of chromatography, it is also possible that the first chemical is bound to the stationary phase while the second chemical is not and is carried through the column by the mobile phase until it elutes. The first chemical can be eluted or removed separately and this is also embraced by the word "retained."

[00111] In another embodiment, one or more TILSs can be used in SPE. In SPE, a sample contains an impurity or some other compound or analyte to be separated, identified and/or quantified. This sample can be placed into a container in which one or more TILSs of the present invention can be present, and more broadly, TILSs in an immobilized form. Ionic liquid materials can be bound (immobilized) to the walls of the container, adsorbed, or absorbed onto a bead or other structure so as to form a bead or other structure which may rest at the bottom of the container or be packed throughout the container much as a liquid chromatography column can be packed with stationary phase. Alternatively, the TILS can be immobilized by cross-linking or an analogous immobilization reaction as described herein on some sort of other solid support such as a bead, particles and/or other chromatographic media used in chromatography as described previously. These beads can also be placed at the bottom of, or can fill a container, much as is a packed column used for liquid chromatography. Of course, the solid support can be any structure placed anywhere within the container.

[00112] In a particular embodiment, the container is actually a syringe where the TILS is affixed or disposed in one fashion or another at the base of the syringe, much as a filter. When the needle of the syringe is placed in a sample and the plunger is withdrawn, vacuum is formed drawing the sample up into the barrel of the syringe. This material would pass through at least one layer of TILS, which would bind at least one of the components of the liquid. The sample liquid could then be spilled out or the plunger depressed to eject it, the latter forcing the sample back through the TIL positioned at the bottom of the barrel.

[00113] The sample liquid can be analyzed either for the presence of certain materials or the absence of the material retained by the TILS. Alternatively, the retained materials can be removed (such as by placing the materials in a different solvent) or not removed,

and analyzed by other means. The same technique may be used in a preparative fashion and/or as a means of bulk purification as well.

[00114] In another embodiment, one or more TILSs may be used in SPME. In these techniques, a separation material (in this case an ionic liquid or in particular a TILS in accordance with the present invention or ionic liquids mixed with adsorbents, particles and other chromatographic media) is absorbed, adsorbed or immobilized in one way or another on a fiber (e.g., polydimethylsiloxane/ divinylbenzene (“PDMS/DVB”) fiber) or some other solid support which is applied to the plunger as a coating or as a sheet generally attached to a plunger in a microsyringe such as usually used in GC. A TILS of the invention can also be immobilized and attached directly without any separate solid support other than the plunger. This can be done using, for example, a film directly. The plunger is depressed, exposing the fiber and the fiber is then dipped into the sample of interest. The plunger can then be withdrawn to pull the fiber back into the barrel of the syringe, or at least the barrel of the needle for protection and transport. The syringe can then be injected through the septum of a gas chromatograph or some other device and the fiber thereby inserted into the column by redepressing the plunger of the microsyringe. The heat used in GC then volatilizes or otherwise drives the bound sample off where it is carried by the mobile phase through the GC column, allowing for separation and/or identification. It can also be eluted by a liquid mobile phase in an HPLC injector or unbuffered capillary electrophoresis. Immobilized TILS may also be used in conjunction with the coated stir bar technology, which is a higher capacity version of SPME. Some embodiments of this coated stir bar technology are sold under the trademark TWISTER™.

[00115] More specifically, SPME is a technique in which a small amount of extracting phase (in this case an ionic liquid and preferably a TILS in accordance with the present invention) is disposed on a solid support, which is then exposed to a sample for a period of time. In situations where the sample is not stirred, a partitioning equilibrium between a sample matrix and the extraction phase is reached. In cases where convection is constant, a short time pre-equilibrium extraction is realized and the amount of analyte extracted is related to time. Quantification can then be performed based on the timed accumulation of analysis in the coating. These techniques are usually performed using

open bed extraction concepts such as by using coated fibers (*e.g.*, fused silica similar to that used in capillary GC or capillary electrophoresis, glass fibers, wires, metal or alloy fibers, beads, *etc.*), vessels, agitation mechanism discs and the like. However, in-tube approaches have also been demonstrated. In-tube approaches require the extracting phase to be coated on the inner wall of the capillary and the sample containing the analyte of interest is subject to the capillary and the analytes undergo partitioning to the extracting phase. Thus, material can be coated on the inner wall of a needle, for example, and the needle injected without the need for a separate solid support.

[00116] In addition, one or more TILSs can be immobilized by being bound or cross-linked to themselves and/or to a solid support as previously discussed in connection with manufacturing capillary GC columns. To do so, however, the species used should have at least one unsaturated group disposed to allow reaction resulting in immobilization.

[00117] Another type of SPME technique is known as task-specific SPME or TS-SPME. TS-SPME allows for the separation or removal, and therefore the detection of particular species. These can include, for example, mercury and cadmium, although the technique is equally applicable to other materials. The concept is exactly the same as previously described with regard to SPME. However, in this instance, the TILS(s) used are further modified such that they will specifically interact with a particular species. The first monocationic material can be coated, absorbed or adsorbed onto a fiber as previously discussed. A TILS can also be absorbed or adsorbed in known fashion.

[00118] Finally, a particular sample can be suspended in a matrix that includes TILS(s). This matrix can be loaded or immobilized on the fiber of an SPME syringe as described above and then injected into a mass spectrometer to practice a technique known as SPME/MALDI mass spectrometry. The matrix is exposed to a UV laser. This causes the volatilization or release of the sample much as heat does in a GC. This allows the sample to enter mass spectrometer where it can be analyzed.

[00119] Examples

[00120] The following examples are merely illustrative, and not limiting to this disclosure in any way.

[00121] The work described more fully herein advanced the technique for anion detection. Eighteen tetraionic reagents constructed with different cationic moieties

connected by different linkages were synthesized. These reagents were evaluated for their ability to complex 19 trivalent anions for detection in positive mode ESI-MS. SRM experimentation was performed in an attempt to further lower LODs. The best results were compared with the LODs obtained in the negative mode. The four best tricationic reagents identified in previous studies also were tested and compared.

[00122] Chemicals

[00123] Water and methanol were of HPLC grade and were obtained from Burdick and Jackson (Morristown, NJ, USA). Amberlite IRA-400 ion exchange resin, sodium hydroxide (reagent grade) and sodium fluoride (reagent grade) for the ion exchange were obtained from Sigma-Aldrich (St Louis, MO, USA). The anions listed in Figure 1 were purchased as the sodium/potassium salt or in the acid form from Sigma-Aldrich (St Louis, MO, USA) and all were of reagent grade or better.

[00124] Ion pairing agents

[00125] The structures of the tetraionic species are in Figures 2 and 3. The four tricationic reagents synthesized and used are in Figure 4. All reagents were synthesized in the bromide salt form and exchanged to its fluoride salt form prior to the analysis. The anion exchange was performed with a 10 mL syringe filled with 4 mL of ion exchange resin in the same manner as described in earlier papers.

[00126] ESI-MS Analysis

[00127] A Finnigan LXQ (Thermo Fisher Scientific, San Jose, CA) ESI-MS was used for all of the analyses in this study. An ion pairing reagent aqueous solution (40 μ M) was pumped at 100 μ L/min using a Shimadzu LC-6A pump (Shimadzu, Columbia, MD) and mixed with 300 μ L/min carrier flow (Water/MeOH = 2/1, v/v) pumped by a Finnigan Surveyor MS pump. The positive mode ESI-MS conditions were as follows: spray voltage, 3 kV; sheath gas flow, 37 arbitrary units ("AU"); auxiliary gas flow rate, 6 AU; capillary voltage, 11 V; capillary temperature, 350°C; tube lens voltage, 105 V. When detecting the complex in the positive selective ion monitoring ("SIM") mode, the SIM width was set to 5 so as to include the isotope peaks. For the detection in SRM mode, the isolation widths were between 1 and 5, the normalized collision energy was 30, and the activation time was 30 ms. Xcalibur and Tune Plus software were used to analyze data. The initial concentrations of anion stock solutions were 1 mg/mL. Serial dilutions were

made from the stock solutions, and the anions were directly injected using the six port injector. New stock solutions were prepared every week, and the major error source for this experiment was from the injector ($\pm 5\%$). The limits of detection were determined to be when a series of five injections at a given concentration resulted in peaks giving a signal to noise ratio of 3.

[00128] Results and discussion

[00129] Tested anions

[00130] The structures of the 19 trivalent anions used in this study are listed in Figures 1 and 2. Both inorganic and organic species are included. Many of the inorganic trivalent anions are metal complexes, such as hexanitrocobaltate, hexachlororhodate, chromium oxalate, and hexacyanocobaltate. There are two phosphorous based anions: trimetaphosphate and phosphate. Orthovanadate is a protein-phosphotyrosine phosphatase inhibitor. The organic anions contained either carboxylic and/or sulfonate groups as the anionic moieties. Sodium citrate has three carboxylate groups and is a very common flavor additive in soft drinks. Sulfanilic acid, azochromotrop, tartrazine, indigotrisulfonate, 8-methoxypyrene-1,3,6-trisulfonate, 8-octanoyloxypyrene-1,3,6-trisulfonate, pyranine and 8-nonanoyloxypyrene-1,3,6-trisulfonate are dyes. Among them, tartrazine is a commonly used food pigment and is also found to be associated with a variety of children's behavioral changes when ingested.

[00131] Tetraionic ion pairing agents

[00132] The tetracations synthesized for this study are shown in Figures 2 and 3. Seventeen of them have the same general linear motif, while two are cyclic tetracations, which are much more rigid. In previous studies, it was found that linear tricationic ion pairing reagents generally produced better results than trications with a more rigid trigonal geometry. Although it remains interesting to compare the linear tetracations with at least one rigid tetraionic pairing agent, attempts to synthesis more compact rigid tetracations failed due to the repulsion between closely placed cationic moieties. As tetracations have one more charged moiety and one more carbon linkage chain than the linear trications, more variations in the structures can be made, such as the length of the middle and side carbon chain linkages, as well as, the arrangement of different cationic moieties at the middle and end. All these linear tetracations can be divided to three

groups: pure imidazolium based, pure phosphonium based, and imidazolium and phosphonium mixed tetracations. They differ in the center carbon chain length (C_4 , C_6 , and C_{10}), side carbon chain length (C_3 , C_6 , and C_{10}), center cation moieties (imidazolium, diisopropyl phosphonium, diphenyl phosphonium), and terminal groups (methyl imidazolium, benzyl imidazolium, triphenylphosphonium and tripropylphosphonium).

[00133] LODs in the negative mode

[00134] The LODs for the trivalent anions in the negative mode were determined and listed in Table 1. It should be noted that most trivalent anions do not exist in their -3 charged state in aqueous solution. They can either be singly protonated to become a divalent anion or doubly protonated to a singly charged ion. Therefore, the LODs in the negative mode were determined from the base peak. For example, all the three charged states (-1, -2, -3) of trimetaphosphate can be seen in the negative mode, and the LOD was obtained by monitoring only the -3 peak as it had the best signal to noise ratio. Three anions (X, XIV, XVI) are not detectable at a concentration of 10 $\mu\text{g/ml}$ (50 ng) which was the highest concentration injected. Signal peaks of anions XIII, VI, and VII can be seen at concentrations of 10 $\mu\text{g/ml}$ (50 ng) but the signal-to-noise-ratios were less than 3, therefore the LODs for these three anions were determined to be greater than 50 ng. The poor LODs are the result of the unstable spray conditions in the negative mode leading to the low ionization efficiency and the fact that some -3 anions (V, XIV) have mass to charge ratios which fall below the low-mass-cut off of the ion trap mass spectrometer. The LODs for the rest of the anions range from 250 pg (XI) to 20ng (V). Anions containing sulfonate groups generally had lower LODs while metal containing anions had relatively high LODs. The LODs for eight anions (II, VIII, IX, XI, XV, XVII, XVII, XIX) were determined based on their singly protonated form, four anions (I, IV, V, XII) were determined as doubly protonated (-2) species, and only one anion (III) from the unprotonated (-3) species.

[00135] Table 1. LODs for trivalent anions in the negative mode

Anion	Mass	LOD(ng)	Base peak*
XI	583.0	0.25	291.9/-2
XVII	491.0	1.5	245.87/-2
XIX	595.5	1.5	297.7/-2
VIII	454.9	2.5	227.9/-2
XVIII	581.0	2.5	291.0/-2
II	500.9	5.0	251.0/-2
I	189.0	5.0	191.0/-1
III	236.9	5.0	79.0/-3
IV	188.0	5.0	190.0/-1
IX	498.9	10.0	249.9/-2
XII	418	15.0	420.0/-1
XV	114.9	15.0	117.0/-2
V	95.0	20.0	97.0/-1
XIII	203.0	>50	205.0/-1
VI	465	>50	155.0/-3
VII	334.9	>50	111.7/-3
X	314.7	>50	not detected
XIV	123	>50	not detected
XVI	215.0	>50	not detected

* Base peak indicates the detected mass and charge state of the anion

[00136] LODs in the positive mode (SIM)

[00137] Tables 2 through 8 list the LODs for the 18 trivalent anions in the positive mode when complexing with the 19 tetracations. The detected complexes and mass to charge ratios are also listed. The best LODs for the trivalent anions ranged from 7.5 pg to 18 ng. As the anions may exist in three different charge states in solution, it is not surprising that each anion can form three possible complexes (+1, +2, +3) with tetraionic reagents. However, different tetracations pair preferentially with different anionic species. For example, for the detection of phosphate, tetraionic pairing reagents C1 and B4 gave the best LODs (380 pg and 400 pg) when the +3 complex was used for detection. Conversely, with other reagents, +1 or +2 complexes gave better signal-to-noise ratios. For some anions, +1 complexes generally gave the best signal to noise ratio compared to +2 and +3 complexes, such as hexacyanocobalte, 8-octanoyloxypyrene-1,3,6-trisulfonate, 8-nonanoyloxypyrene-1,3,6-trisulfonate, tris(2,4-dimethyl-5-sulfophenyl)-phosphine and pyranine. Anions typically giving the best LODs for +2 charged complexes were phosphate, 8-methoxypyrene-1,3,6-trisulfonate and chromium oxalate. The prevalence of +2 complexes or +1 complexes can be related to the pKa of the conjugate acid of the trivalent anion. For example, as the pKa of HPO_4^{2-} is 12.76, thus

the protonated dianionic form of phosphate will be most abundant in the aqueous solution. This could be the reason why the +2 complexes (tetracation plus HPO_4^{2-}) produce a stronger signal than the +1 complex (tetracation with PO_4^{3-}). However, it should be noted that not all of the complexes are detectable. For example, the complexes of A3, B3, B4, B5 and D2 with hexanitrocobaltate were not observed.

[00138] Among the anions studied, tris(2,4-dimethyl-5-sulfophenyl)-phosphine and hexacyanocobaltate gave the lowest LODs overall (7.5pg with A2 or B5). Compared to the LODs in the negative mode, the greatest improvement was achieved with hexacyanocobaltate when pairing with A2 or B5, The sensitivity was more than 6600 times better in positive mode (7.5pg), as it was undetectable in the negative mode (at 50ng). In general, sensitivity improvements in the positive mode were in the range of 10-1000 times those in the negative mode. Hexachlororhodate had the highest LOD (18ng), which is still more than 10 times better than the negative mode (also undetectable). Except for hexacyanocobaltate, metal containing trivalent anions generally have higher LODs than other anions. On the other hand, sulfonate based anions typically had lower LODs than all the other anions. Although 8-octanoyloxypyrene-1,3,6-trisulfonate and 8-nonanoyloxypyrene-1,3,6-trisulfonate have very similar structures, it is interesting to see that their LODs and best pairing reagents are different. This indicates that even a small change in structure can affect ion pairing. The difference may also be due to the different background noise at the mass to charge ratios of the complexes. For carboxylate based anions, oxalomalic tricarboxylate had the highest LOD (2.5 ng) and nitrilotriacetic tricarboxylate gave the lowest LOD (125 pg). Among the phosphate based anions, trimetaphosphate had the lowest LOD (37 pg) and phosphate (380 pg) had the highest.

[00139] Among the 18 cationic pairing agents tested, phosphonium-based tetracations generally produced better results than pure imidazolium-based tetracations in the SIM mode. Unsurprisingly, the imidazolium and phosphonium mixed tetracations showed moderate performance. For example, the best eight pairing agents for citrate are all phosphonium-based, while the four worst reagents were imidazolium tetracations. Also, it was found that pairing agents with more aromatic group substituents worked better for many aromatic anions while alkyl substituted phosphonium agents paired better with alkyl group containing anions. For example, B1 and B4 worked generally better than C1

for anions with aromatic groups. This indicates that π - π interactions can be important for effective ion pairing agents. However, C1 worked better for nonaromatic anions than did B1 and B4. One possible reason is because C1 has relatively less steric bulk about its cationic moieties than do B1 and B4 resulting in stronger cation-anion interactions as the ionic moieties are closer to one another.

[00140] B1, B4 and C1 were selected, which are all phosphonium-based tetracations, as the ion pairing reagents that outperformed all others for the detection of trivalent anions. These are the first recommended cations to use for the detection of -3 anions. The cyclic phosphonium tetracation worked fairly well, but not as good as the best linear tetracations. This indicates that flexibility also may be an important feature for tetraionic pairing agents. This is analogous to what was found for trication ESI-MS pairing agents.

[00141] In addition, since some of the analytes exist mainly in the -2 charge state in solution, it should be possible for them to form +1 complexes with trivalent cations. Consequently, the four best tricationic agents previously found for the detection of -2 anions (Table 1c) were used. The results are also listed in Table 3. It is obvious that tetraionic reagents are typically superior to tricationic ones in detecting these anions (except for oxalomalic tricarboxylate, for which trication 2 worked best). In many cases, the tricationic reagents performed worst, thus these agents should not be among the first tested for the detection of -3 anion.

[00142] Tetraionic pairing agents not only complex trivalent anions but also form cation-anion complexes when paired with singly charged and doubly charged anions. Therefore, two tetracations (B1 and C1) for the detection of four singly charged and four doubly charged anions were tested. The results are shown in Table 9. For monoanions, the results (*i.e.*, sensitivities) found when using tetracations B1 and C1 were not as good as those that found for the less charged pairing agents studied in earlier papers. For example, the best LOD for perfluorooctanate obtained by using a dicationic agent was 0.12 pg while B1 and C1 only gave 150 pg and 90 pg LODs, respectively. For trifluoromethanesulfonimide, the LOD achieved by B1 (4.5 pg) was close to the best LOD achieved by a dicationic ion pairing agent (2.3 pg). B1 and C1 performed well for the detection of dianions. For example, the LODs of *m*-benzenedisulfonate obtained by B1 (12.5 pg) and C1 (12.5 pg) are two times lower than the best LODs obtained with

tricationic agents (32 pg). It has been shown that tetracations may be used as universal ion pairing agents for detecting mono-, di-, and trivalent anions.

[00143] Table 2. LODs for trivalent anions I, II and III

I citrate			II sulfanilic acid azochromotrop			III trimetaphosphate		
cation	LOD(ng)	Base peak*	cation	LOD(ng)	Base peak	cation	LOD(ng)	Base peak
C1	1.50E-01	456.4/+2	B1	5.00E-02	782.3/+2	C1	3.68E-02	959.6/+1
B1	3.00E-01	626.5/+2	E2	7.00E-02	706.33/+2	B4	4.38E-02	1095.5/+1
B4	3.75E-01	524.5/+2	B4	8.75E-02	680.33/+2	B1	7.50E-02	1299.42/+1
tri2	4.00E-01	721.3/+1	D2	1.00E-01	1512/+1	F1	8.75E-02	1230.1/+1
D1	5.00E-01	516.5/+2	C1	1.25E-01	612.35 /+2	D1	1.25E-01	1080/+1
D2	7.50E-01	600.42/+2	B2	1.50E-01	810.33/+2	B2	1.50E-01	1355.3/+1
F1	1.00E+00	591.3/+2	D1	1.75E-01	1344/+1	D2	2.50E-01	1248/+1
B5	1.25E+00	552.33/+2	F1	2.00E-01	747.6/+2	B5	3.15E-01	1151.5/+1
D3	1.25E+00	474.3/+2	A3	2.20E-01	1219.7/+1	A6	6.25E-01	1107.7/+1
E2	1.25E+00	550.33/+2	E1	2.25E-01	604.4/+2	A3	7.50E-01	955.6/+1
tri4	1.50E+00	857.8/+1	B3	2.50E-01	1732.7/+1	D3	7.50E-01	498.25/+2
A1	2.00E+00	655.38/+1	D3	2.50E-01	1259.6/+1	A1	1.00E+00	703.28/+1
A3	2.00E+00	907.7/+1	tri1	2.50E-01	1099.5/+1	A4	1.00E+00	855.3/+1
B2	2.00E+00	654.5/+2	A4	2.75E-01	560.2/+2	B3	1.00E+00	1468.6/+1
B3	2.50E+00	710.3/+2	A6	3.00E-01	1371.6/+1	A2	1.25E+00	843.4/+1
E1	2.50E+00	448.4/+2	A1	3.75E-01	1169.8/+1	tri2	1.50E+00	769.3/+1
tri3	2.50E+00	741.4/+1	A5	4.25E-01	1259.7/+1	E1	2.50E+00	472.35/+2
A6	3.00E+00	1059.8/+1	B5	5.00E-01	1415.75/+1	E2	2.50E+00	575.45/+2
A2	3.50E+00	398.3/+2	A2	5.75E-01	1107.5/+1	tri3	2.50E+00	789.4/+1
A4	3.75E+00	404.3/+2	tri2	1.00E+00	1033.3/+1	tri1	4.50E+00	835.4/+1
tri1	5.00E+00	787.3/+1	tri3	2.50E+00	1053.4/+1	tri4	5.00E+00	905.6/+1
A5	>50	No complex	tri4	3.75E+00	1169.8/+1	A5	>50	No complex

* Base peak indicates the mass/charge of the highest signal given by the complexes.

[00144] Table 3. LODs for trivalent anions IV, V and VI

IV nitrilotriacetic tricarboxylate			V phosphate			VI tartrazine		
cation	LOD(ng)	Base peak	cation	LOD(ng)	Base peak	cation	LOD(ng)	Base peak
C1	1.25E-01	455.85/+2	C1	3.75E-01	409.35/+2	E2	1.50E-01	688.5/+2
tri2	3.00E-01	720.3/+1	B4	4.00E-01	477.33/+2	B1	1.75E-01	764.33/+2
B4	3.50E-01	524/+2	D1	5.60E-01	469.3/+2	A2	3.10E-01	536.3/+2
B1	5.00E-01	625.8/+2	B1	2.00E+00	386.6/+3	A5	3.60E-01	612.4/+2
F1	6.00E-01	590.8/+2	B5	2.00E+00	505.33/+2	D2	3.75E-01	1476/+1
B5	7.50E-01	552.83/+2	D3	2.25E+00	427.3/+2	A3	5.00E-01	1183.6/+1
D3	7.50E-01	473.8/+2	F1	2.50E+00	544.3/+2	A4	5.00E-01	542.2/+2
D1	8.75E-01	515.8/+2	tri4	2.50E+00	763.8/+2	tri1	5.00E-01	1063.5/+1
E2	8.75E-01	550/+2	D2	3.00E+00	553.4/+2	B4	6.00E-01	662.5/+2
A4	1.00E+00	855.3/+1	E2	3.00E+00	503.25/+2	A1	6.25E-01	931.3/+1
D2	1.00E+00	600/+2	A1	3.75E+00	561.3/+1	A6	6.25E-01	1335.8/+1
A1	1.50E+00	654.3/+1	B3	5.00E+00	442.7/+3	B2	7.50E-01	1584/+1
A3	1.50E+00	453.8/+2	tri2	5.00E+00	627.3/+1	C1	7.50E-01	1187.7/+1
tri1	1.50E+00	786.3/+1	A2	6.00E+00	351.3/+2	D1	7.50E-01	1308/+1
tri4	1.50E+00	856.8/+1	A3	6.00E+00	407.4/+2	D3	7.50E-01	1223.6/+1
tri3	1.75E+00	740.3/+1	A4	6.00E+00	357.2/+2	B3	1.00E+00	1696.5/+1
A6	2.50E+00	529.9/+2	tri1	2.50E+01	693.4/+2	B5	1.00E+00	1380.6/+1
B2	2.50E+00	653.83/+2	E1	3.50E+01	404.4/+2	E1	1.00E+00	586.4/+2
B3	2.50E+00	710/+2	A5	5.00E+01	427.35/+2	F1	1.00E+00	1458.2/+1
E1	2.50E+00	447.9/+2	A6	5.00E+01	483.4/+2	tri2	2.50E+00	499.15/+2
A2	3.00E+00	397.8/+2	B2	5.00E+01	405.3/+3	tri3	2.50E+00	590.2/+2
A5	5.00E+00	473.5/+2	tri3	>50	No complex	tri4	5.00E+00	1133.8/+1

[00145] Table 4. LODs for trivalent anions VII, VIII, and IX

VII hexanitrocobaltate			VIII pyranine			IX indigotrisulfonate		
cation	LOD(ng)	Base peak	cation	LOD(ng)	Base peak	cation	LOD(ng)	Base peak
D3	1.00E+01	365.2/+3	B1	7.50E-02	1517.5/+1	B1	1.50E-01	781.25/+2
E2	1.80E+01	613.8/+2	D1	7.50E-02	1297.6/+1	D1	2.50E-01	671.33/+1
B1	2.00E+01	1397.5/+1	D2	1.25E-01	1465.5/+1	D2	2.50E-01	1511/+1
tri2	2.00E+01	867/+2	tri1	1.25E-01	1053.5/+1	A1	5.00E-01	965.4/+1
tri3	2.50E+01	434.5/+2	B4	1.50E-01	1313.5/+1	A3	5.00E-01	1217.7/+1
B2	3.75E+01	1454.5/+1	D3	1.75E-01	1213.4/+1	B2	5.00E-01	809.3/+2
A5	5.00E+01	1093.7/+1	B2	2.00E-01	1574.5/+1	A6	6.25E-01	1370.7/+1
A6	5.00E+01	603.4/+2	B5	2.00E-01	1369.7/+1	A4	7.00E-01	559.7/+2
C1	5.00E+01	1057.7/+1	A1	2.50E-01	921.3/+1	E2	7.50E-01	706/+2
D1	5.00E+01	589.5/+2	A5	2.50E-01	1236.2/+1	F1	7.50E-01	1493.5/+1
F1	5.00E+01	1309.5/+1	C1	2.50E-01	1177.6/+1	A2	1.00E+00	1106.5/+1
A1	>5.00E+01	401.2/+2	E2	2.50E-01	1366/+1	A5	1.00E+00	1258.7/+1
A2	>5.00E+01	471.3/+2	A2	3.00E-01	531.3/+2	D3	1.00E+00	1258.6/+1
A3	>5.00E+01	351.9/+3	B3	3.00E-01	1686.5/+1	B4	1.13E+00	680/+2
A4	>5.00E+01	No complex	F1	3.75E-01	1448.5/+1	tri1	1.50E+00	1097.4/+1
B3	>5.00E+01	No complex	A3	5.00E-01	1173.7/+1	B3	2.50E+00	1730.7/+1
B4	>5.00E+01	No complex	A4	5.00E-01	1073.4/+1	B5	2.50E+00	1415/+1
B5	>5.00E+01	No complex	A6	6.25E-01	1325.63/+1	C1	2.50E+00	611.45/+2
D2	>5.00E+01	No complex	E1	6.25E-01	1161.8/+1	E1	2.50E+00	603.9/+1
E1	>5.00E+01	No complex	tri2	2.50E+00	987.38/+1	tri2	5.00E+00	1031.4/+1
tri1	>5.00E+01	No complex	tri3	3.50E+00	1007.4/+1	tri3	2.00E+01	1052.4/+1
tri4	>5.00E+01	No complex	tri4	5.00E+01	1153.8/+1	tri4	5.00E+01	1168.8/+1

[00146] Table 5. LODs for trivalent anions X and XI

X hexachlororhodate			XI tris(2,4-dimethyl-5-sulfo-phenyl)phosphine		
cation	LOD(ng)	Base peak	cation	LOD(ng)	Base peak
E2	1.80E+01	613.8/+2	C1	7.50E-03	1305.8/+1
tri3	2.50E+01	434.5/+2	B4	1.23E-02	1441.67/+1
B1	3.00E+01	688.72/+2	B5	1.25E-02	1498.75/+1
E1	3.00E+01	341.5/+3	B2	1.50E-02	1701.75/+1
A6	4.25E+01	395.85/+3	B1	2.00E-02	1646.5/+1
A1	5.00E+01	391.5/+2	B3	2.50E-02	1814.75/+1
B2	5.00E+01	1434.2/+1	F1	2.50E-02	1576.7/+1
C1	5.00E+01	1038.7/+1	D1	3.00E-02	1425.67/+1
D1	5.00E+01	579.8/+2	D2	3.50E-02	1594/+1
D3	5.00E+01	537.6/+2	E2	3.75E-02	747.75/+1
F1	5.00E+01	1309.5/+1	D3	5.00E-02	1342.5/+1
A3	>5.00E+01	1033.3/+1	A1	7.50E-02	1049.55/+1
B4	>5.00E+01	1174.6/+1	A2	7.50E-02	1189.5/+1
B3	>5.00E+01	1546.6/+1	A3	7.50E-02	1301.7/+1
A4	>5.00E+01	467.5/+2	A4	1.25E-01	1201.4/+1
D2	>5.00E+01	663.8/+2	A6	1.25E-01	1454.3/+1
tri2	>5.00E+01	847.9/+1	E1	1.50E-01	645.4/+2
A2	>5.00E+01	No complex	tri1	1.50E-01	1181.6/+1
A5	>5.00E+01	No complex	A5	1.75E-01	1342.7 /+1
B5	>5.00E+01	No complex	tri2	2.50E-01	1115.4/+1
tri1	>5.00E+01	No complex	tri3	5.00E-01	1135.9/+1
tri4	>5.00E+01	No complex	tri4	1.50E+00	1049.55/+1

[00147] Table 6. LODs for trivalent anions XIII, XIV, and XV

XIII oxalomalic tricarboxylate			XIV phosphoformate			XV orthovanadate		
cation	LOD(ng)	Base peak	cation	LOD(ng)	Base peak	cation	LOD(ng)	Base peak
tri2	2.50E+00	735/+1	C1	2.50E-01	423.35/ +2	F1	4.25E-01	554/+2
A1	5.00E+00	669.2/+1	B4	3.00E-01	491.67/ +2	B1	5.00E-01	589.3/+2
C1	1.50E+01	925.5/+1	B5	5.00E-01	519.33/ +2	B2	1.00E+00	1233.3/+1
D1	1.50E+01	925.5/+1	tri2	7.50E-01	655.22/ +1	B4	1.25E+00	487.5/+2
tri3	1.50E+01	755.4/+1	B2	1.00E+00	621.25/ +2	B5	2.50E+00	515.6/+2
F1	2.00E+01	1196.2/+2	tri4	1.00E+00	791.55/ +2	C1	2.50E+00	419.35/+2
B2	4.00E+01	441.3/+3	D1	1.25E+00	966/+1	B3	3.00E+00	673.7/+2
A4	5.00E+01	821.4/+1	B1	1.50E+00	593.3/+ 2	E2	5.00E+00	1025.3/+1
A5	5.00E+01	481.3/+2	D2	1.50E+00	1133.6/ +1	tri2	5.00E+00	647.3/+1
B1	5.00E+01	1266/+1	E2	2.00E+00	517.5/+ 2	tri4	7.00E+00	392.4/+2
B3	5.00E+01	717.5/+2	A1	2.50E+00	589.3/+ 1	A4	2.10E+01	245.1/+3
B4	5.00E+01	531.5/+2	B3	2.50E+00	1354/+ 1	tri1	3.00E+01	713.3/+1
B5	5.00E+01	559.5/+3	tri3	3.00E+00	675.4/+ 1	A6	5.00E+01	329.3/+3
D3	5.00E+01	481.3/+2	D3	3.20E+00	441.3/+ 2	D1	5.00E+01	479.5/+2
E2	5.00E+01	557.5/+2	A4	4.00E+00	371.2/+ 2	A1	>5.00E+0 1	No complex
E1	>5.00E+0 1	909.9/+1	F1	5.25E+00	558.6/+ 2	A2	>5.00E+0 1	No complex
A2	>5.00E+0 1	No complex	A6	6.25E+00	497.4/+ 2	A3	>5.00E+0 1	No complex
A3	>5.00E+0 1	No complex	A3	1.00E+01	841.7/+ 1	A5	>5.00E+0 1	No complex
A6	>5.00E+0 1	No complex	E1	1.00E+01	415.4/+ 2	D2	>5.00E+0 1	No complex
D2	>5.00E+0 1	No complex	A5	1.05E+01	441.3/+ 2	D3	>5.00E+0 1	No complex
tri1	>5.00E+0 1	No complex	tri1	2.50E+01	721.3/+ 1	E1	>5.00E+0 1	No complex
tri4	>5.00E+0 1	No complex	A2	3.00E+01	365.25/ +2	tri3	>5.00E+0 1	No complex

[00148] Table 7. LODs for trivalent anions XVI, XVII and XVIII

XVI hexacyanocobaltate			XVII 8-methoxypyrene-1,3,6- trisulfonate			XVIII 8-octanoyloxypyrene-1,3,6- trisulfonate		
cation	LOD(ng)	Base peak	cation	LOD(ng)	Base peak	cation	LOD(n g)	Base peak
A2	7.50E-03	821.5 /+1	B5	5.00E-02	777.3/+2	B1	5.00E-02	1496.6/+1
B5	7.50E-03	1329. 5/+1	B3	8.75E-02	675.33/+2	B4	8.75E-02	1812.67/+1
D1	1.25E-02	1057. 55/+1	B1	1.00E-01	667.3/+2	D1	1.00E-01	1644.5/+1
B1	1.75E-02	1278. 3/+1	A4	1.85E-01	625.3/+2	A5	1.85E-01	1199.9/+1
B4	2.10E-02	1073. 55/+1	B2	2.50E-01	549.3/+2	A2	2.50E-01	1700.7/+1
C1	2.50E-02	938/+1	C1	2.50E-01	703.3/+2	B5	2.50E-01	1303.8/+1
D3	2.50E-02	973.5 /+1	D1	2.50E-01	701.5/+2	E2	2.50E-01	1424.7/+1
F1	3.75E-02	1207. 4/+1	E2	2.50E-01	1023.4/+1	tri2	2.50E-01	746.8/+1
A1	5.00E-02	681.3 /+1	B4	2.75E-01	625.2/+2	D3	2.75E-01	1440.67/+1
A6	5.00E-02	1085. 7/+1	D2	3.75E-01	805.3/+2	B2	3.75E-01	1592.5/+1
B2	5.00E-02	1334. 5/+1	D3	5.00E-01	751.7/+2	D2	5.00E-01	1339.6/+1
D2	5.00E-02	1226. 5/+1	A1	5.00E-01	1089.5/+1	tri1	5.00E-01	1047.5/+1
E1	6.25E-02	921.6 8/+1	A6	6.50E-01	555.2/+2	A4	6.50E-01	1452.3/+1
A3	7.50E-02	933.5 /+1	F1	7.50E-01	607.4/+2	C1	7.50E-01	1574.5/+1
A4	7.50E-02	833.7 /+1	E1	7.50E-01	742.5/+2	F1	7.50E-01	644.4/+2
E2	7.50E-02	1126. 3/+1	A5	1.00E+00	861.3/+2	B3	1.00E+00	1342.7/+1
B3	1.00E-01	1445. 5/+1	A3	1.25E+00	957.3/+1	A1	1.25E+00	1299.7/+1
A5	1.25E-01	973.6 /+1	A2	1.25E+00	605.4/+2	A3	1.25E+00	1188.0/+1
tri4	5.00E-01	1159. 8/+1	tri1	1.25E+00	681.4/+2	A6	1.25E+00	1180.5/+1
tri1	1.25E+00	813.3 /+1	tri3	2.50E+00	1197.8/+1	E1	2.50E+00	1133.9/+1
tri3	2.00E+00	767.2 /+1	tri2	2.75E+00	1133.9/+1	tri3	2.75E+00	1113.5/+1
tri2	5.00E+00	747.3 /+1	tri4	5.00E+00	1250.3/+1	tri4	5.00E+00	1250.3/+1

[00149] Table 8. LODs for trivalent anions XIX

XIX 8-nonanoyloxy pyrene-1,3,6- trisulfonate		
cation	LOD(ng)	Base peak
B5	3.50E-02	821.5/+1
D2	5.00E-02	1329.5/+1
D3	5.00E-02	1057.6/+1
A5	7.50E-02	1278.3/+1
B1	7.50E-02	1073.6/+1
B4	7.50E-02	938.0/+1
A2	1.00E-01	973.5/+1
D1	1.00E-01	1207.4/+1
F1	1.05E-01	681.3/+1
A1	1.25E-01	1085.7/+1
A6	1.25E-01	1334.5/+1
C1	1.25E-01	1226.5/+1
A3	1.50E-01	921.7/+1
B2	1.50E-01	933.5/+1
E2	1.50E-01	833.7/+1
A4	2.50E-01	1126.3/+1
B3	2.50E-01	1445.5/+1
tri1	3.00E-01	973.6/+1
E1	5.00E-01	1159.8/+1
tri2	2.50E+00	813.3/+1
tri3	2.50E+00	767.2/+1
tri4	5.00E+00	747.3/+1

[00150] LODs in the positive mode (SRM)

[00151] SRM mode may further reduce the detection limits of anions. In the SRM mode, anion-cation complexes are first selected, and then disassociated into fragments. The LODs were obtained by monitoring the strongest fragment peak. In this study, the three best tetracations (B1, B4 and C1) for the detection of trianions in the positive SRM mode were tested. The SRM results are listed in Table 5. Typically 3 to 10 times better (lower) LODs were achieved. However, the metal containing anions did not show immense improvements in the SRM mode. For example, the LOD of hexachlororhodate in the SRM mode (10 ng) was only slightly better than the LOD in the SIM mode (18 ng). The LODs of some anions were lowered to the 100 fg range, for example hexacyanocobalte, 8-methoxypyrene-1,3,6-trisulfonate and tris(2,4-dimethyl-5-sulfophenyl)-phosphine. When compared to the LODs in the negative mode, the biggest

improvements found by using the tetraionic agents are more than four orders of magnitude (as for hexacyanocobaltate).

[00152] Eighteen newly synthesized tetraionic ion pairing agents with diverse structures have been evaluated for the detection of trivalent anions in both positive SIM and SRM modes of ESI-MS. The best LODs obtained in the positive mode were compared with the LODs for the negative mode. Improvements from 10 to greater than 6600 times were found in the SIM positive mode. It has been determined that the phosphonium based reagents generally gave lower LODs than the imidazolium-based tetracations. The pairing agents overall geometry plays as an important role as the nature of the cationic moieties in the effectiveness. The three best tetravalent reagents were selected for SRM mode experiments. Furthermore, the utility of these tetracations was demonstrated by also using them to successfully complex mono- and dianions. The LODs of most anions were lower in the SRM mode and up to four orders of magnitude of improvement was seen for the SRM mode as compared to the negative mode.

[00153] Table 9. LODs for monovalent and divalent anions pairing with tetracations B1 and C1 in positive mode:

Anions	Mass	B1		C1	
		LOD(pg)	Base peak	LOD(pg)	Base peak
perfluorooctanate (-1)	413.06	150	491.8/+3	90	424.02/+3
benzenesulfonate (-1)	157.16	15	406.6/+3	15	338.55/+3
monochloroacetate (-1)	93.5	1000	625/+2	2500	523/+2
trifluoromethanesulfonimide (-1)	280	4.5	447.5/+3	15	379.8/+3
hexachloroplatinate (-2)	407.9	25	735.17/+2	50	633.45/+2
<i>m</i> -benzenedisulfonate (-2)	236.2	12.5	649.35/+2	12.5	547.35/+2
fluorophosphate (-2)	98	500	387.33/+3	20	477.33/+2
nitroprusside (-2)	216	10	639.25/+2	25	537.55/+2

[00154] Table 10. LODs for trivalent anions in the SRM positive mode:

Anion	Precursor ion	Tetracation B1	
		Base fragment peak	LOD(ng) ^b
I	626.5/+2	530.3/+2	6.25E-02^a
II	782.3/+2	773.33/+2	1.50E-02
III	1299.42/+1	1037.38/+1	1.50E-02
IV	625.8/+2	530.3/+2	1.50E-01
V	386.3/+3	353.88/+3	5.00E+01
VI	764.33/+2	742.3/+2	1.88E-02
VII	1397.5/+1	1185.3/+1	1.00E+01
VIII	1518.5/+1	1255.42/+1	1.25E-02
IX	781.5/+2	819.2/+1	5.00E-01
X	688.72/+2	652.3/+2	2.50E+02
XI	1646.5/+1	1385.3/+1	2.50E-03
XII	1481/+1	1460/+1	5.00E+00
XIII	1266/+1	1133.48/+1	7.50E+01
XIV	593.3/+2	571.3/+2	5.00E-01
XV	589.3/+2	500.3/+2	1.50E-02
XVI	1278.3/+1	503.3/+1	1.25E-02
XVII	777.3/+2	769.8/+2	1.13E-03
XVIII	1644./+1	1381.5/+1	1.25E-02
XIX	1658.5/+1	1395.5/+1	2.00E-02

^a: Complex is not detected.^b: Numbers in bold indicate the best LODs.

[00155] Table 11. LODs for trivalent anions in the SRM positive mode:

Anion	Precursor ion	Tetracation B4	
		Base fragment peak	LOD(ng) ^b
I	524.5/+2	428.3/+2	6.25E-02
II	782.3/+2	655.8/+2	1.50E-02
III	1095.5/+1	401.3/+1	2.00E-02
IV	524/+2	215.22/+1	6.50E-02
V	477.33/+2	428.3/+2	2.50E-01
VI	662.5/+2	640.3/+2	1.50E-02
VII	N ^a	N	N
VIII	1313.5/+1	401.3/+1	1.25E-01
IX	680/+2	241.12/+1	1.00E+00
X	N	N	N
XI	1441.67/+1	1281.5/+1	2.50E-02
XII	1277.4/+1	1175.5/+1	2.25E+00
XIII	531.5/+2	295.2/+1	7.50E-01
XIV	491.67/+2	469.3/+2	1.75E-02
XV	487.5/+2	448.3/+2	1.25E-02
XVI	1073.55/+1	401.3/+1	2.00E-03
XVII	675.33/+2	595.3/+2	7.50E-02
XVIII	1440.67/+1	1279.6/+1	1.25E-01
XIX	1454.5/+1	1293.6/+1	2.00E-01

^a: Complex is not detected.^b: Numbers in bold indicate the best LODs.

[00156] Table 12. LODs for trivalent anions in the SRM positive mode:

Anion	Precursor ion	Tetracation C1	
		Base fragment peak	LOD(ng) ^b
I	456.4/+2	425.4/+2	2.50E-02
II	612.35/+2	485.8/+2	2.50E-02
III	959.6/+1	917.58/+1	3.75E-03
IV	455.85/+2	215.3/+2	5.00E-02
V	409.35/+2	280.3/+2	2.50E-01
VI	1187./+1	1143.8/+1	1.25E-01
VII	1057.7/+1	845.63/+1	5.00E+00
VIII	1177.6/+1	1135.6/+1	1.25E-02
IX	611.45/+2	590.3/+2	5.00E-01
X	1037.8/+1	541.4/+2	2.50E+01
XI	1305.8/+1	1263.8/+1	6.00E-04
XII	570.8/+2	503.7/+2	1.25E+01
XIII	925.5/+1	792.55/+2	2.50E+01
XIV	423.35/+2	397.3/+2	2.50E-01
XV	419.35/+2	621.4/+2	1.88E-02
XVI	938/+1	333.3/+2	2.20E-03
XVII	607.35/+2	546.32/+2	3.75E-03
XVIII	1303.8/+1	1261.7/+1	2.50E-02
XIX	1317.8/+1	1275.8/+1	2.50E-02

^b: Numbers in bold indicate the best LODs.

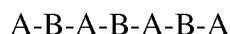
[00157] One of ordinary skill in the art would appreciate that all examples and embodiments of this disclosure are exemplary and are not meant to limit the scope of this disclosure, but are provided for the purpose of illustration and description. It is not intended to be exhaustive or to limit the invention. Individual elements of features of a particular embodiment are generally not limited to that particular embodiment, but, where applicable, are interchangeable and can be used in a selected embodiment, even if not specifically shown or described. The same may also be varied in many ways. Such variations are not to be regarded as a departure from invention, and all such modifications are intended to be included within the scope of the invention.

[00158] The terminology used herein is for the purpose of describing particular example embodiments only and is not intended to be limiting. As used herein, the singular forms “a”, “an”, and “the” may be intended to include the plural forms as well, unless the context clearly indicates otherwise. The terms “comprises,” “comprising,” “including,” and “having” are inclusive and therefore specify the presence of stated features, integers, steps, operations, elements, components, groups, or combinations thereof, but do not preclude the presence or addition of one or more other features,

integers, steps, operations, elements, components, or groups thereof. The method steps, processes, and operations described herein are not to be construed as necessarily requiring their performance in the particular order discussed or illustrated, unless specifically identified as an order of performance. It is also to be understood that additional or alternative steps may be employed.

WHAT IS CLAIMED IS:

1. A tetraionic liquid salt comprising a tetraionic species corresponding in structure to Formula I:

**Formula I**

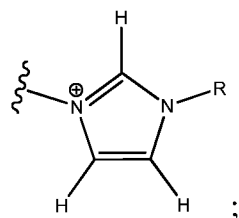
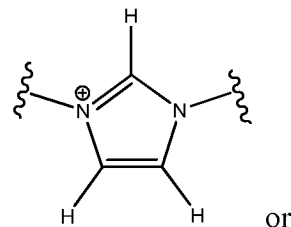
and at least one counter-anion,

wherein:

A is selected from the group consisting of optionally substituted protonated

tertiary amine of formula $\text{--}\overset{\text{~}}{\text{~}}\text{--NRH}^+\text{--}\overset{\text{~}}{\text{~}}\text{--}$ or $\text{--}\overset{\text{~}}{\text{~}}\text{--NR}_2\text{H}^+\text{--}$, optionally substituted phosphonium

of formula $\text{--}\overset{\text{~}}{\text{~}}\text{--PR}_2^+\text{--}\overset{\text{~}}{\text{~}}\text{--}$ or $\text{--}\overset{\text{~}}{\text{~}}\text{--PR}_3^+\text{--}$, and imidazolium of formula



wherein each R is independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, alkoxy, carbocyclyl, carbocyclylalkyl, heterocyclyl, heterocyclylalkyl and hydroxyalkyl;

wherein each R group of protonated tertiary amine or phosphonium is optionally substituted with one or more substituents selected from the group consisting of C₁-C₁₅-alkyl, alkenyl, alkynyl, alkoxy, carbocyclyl, carbocyclylalkyl, heterocyclyl, heterocyclylalkyl and hydroxyalkyl;

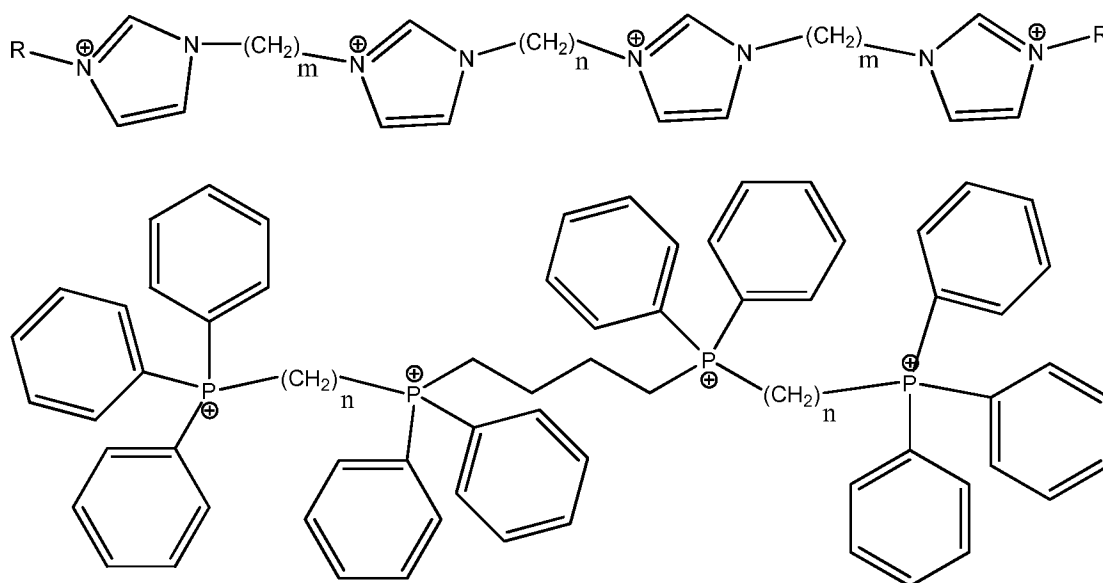
B is a divalent fragment composed of a chain of one or more moieties selected from the group consisting of C₃-C₂₀-alkylene, C₂-C₂₀-alkenylene, and C₂-C₂₀-alkynylene;

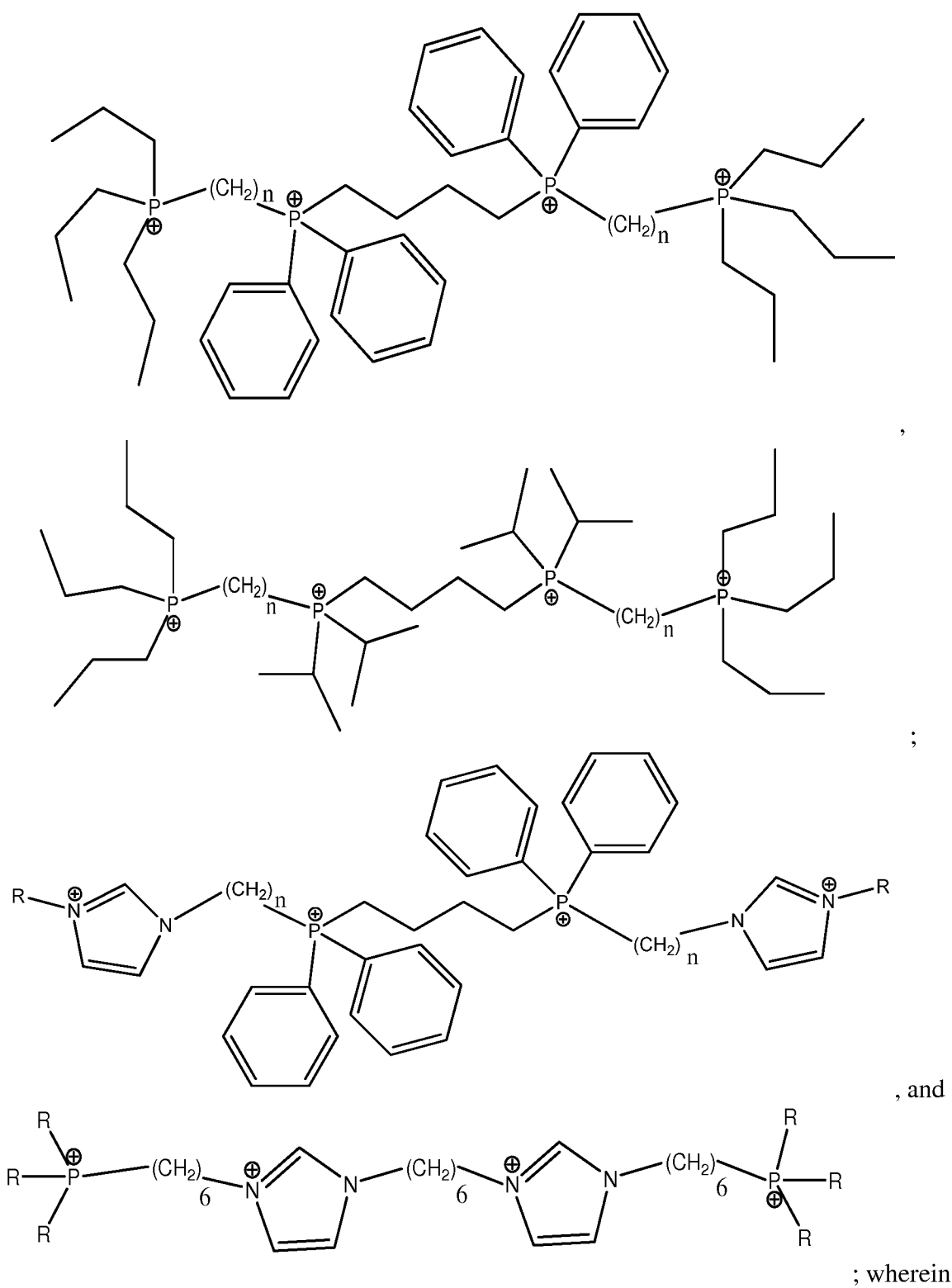
wherein C₃-C₂₀-alkylene, C₂-C₂₀-alkenylene, and C₂-C₂₀-alkynylene optionally contain in the chain one or more heteroatoms selected from the group consisting of O, N, S and Si;

wherein **B** is optionally substituted with one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, and halo.

2. The tetraionic liquid salt of Claim 1, wherein the at least one counter-anion is independently selected from the group consisting of citrate, sulfanilic acid azochromotrop, trimetaphosphate, nitrilotriacetic tricarboxylate, phosphate, tartrazine, hexanitrocobaltate, pyranine, indigotrisulfonate, hexachlororhodate, tris(2,4-dimethyl-5-sulfophenyl)-phosphine, chromium oxalate, oxalomalic tricarboxylate, phosphoformate, orthovanadate, hexacyanocobaltate, 8-methoxypyrene-1,3,6-trisulfonate, 8-octanoyloxypyrene-1,3,6-trisulfonate, and 8-nonanoyloxypyrene-1,3,6-trisulfonate.
3. The tetraionic liquid salt of Claim 1, wherein
A is imidazolium, optionally substituted phosphonium, or optionally substituted protonated tertiary amine; and
B is C₃-C₂₀-alkylene;
wherein **B** optionally contains in the chain one or more heteroatoms selected from the group consisting of O, N, S and Si; and
wherein **B** is optionally substituted with one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, and halo.
4. The tetraionic liquid salt of Claim 3, wherein each R is independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, alkoxy, and carbocyclyl.
5. The tetraionic liquid salt of Claim 4, wherein each R is independently selected from the group consisting of propyl, isopropyl, and phenyl.
6. The tetraionic liquid salt of Claim 4, wherein each R is independently selected from the group consisting of methyl, *n*-butyl, phenyl, and benzyl.

7. The tetraionic liquid salt of Claim 3, wherein
A is optionally substituted phosphonium; and
B is C₃-C₂₀-alkylene.
8. The tetraionic liquid salt of Claim 3, wherein
A is imidazolium; and
B is C₃-C₂₀-alkylene.
9. The tetraionic liquid salt of Claim 3, wherein
A is optionally substituted protonated tertiary amine; and
B is C₃-C₂₀-alkylene.
10. The tetraionic liquid salt of Claim 1, wherein the tetraionic species is selected from the group consisting of:



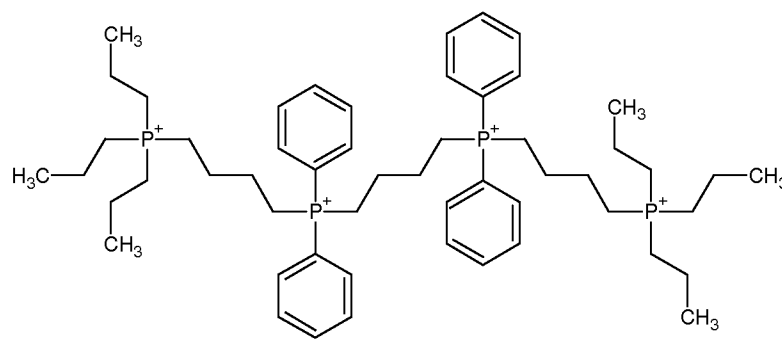
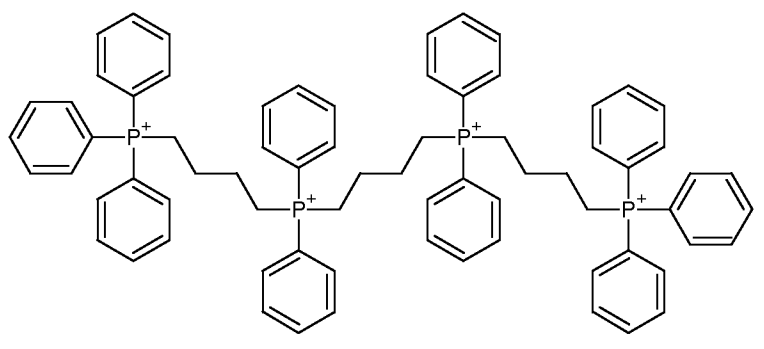
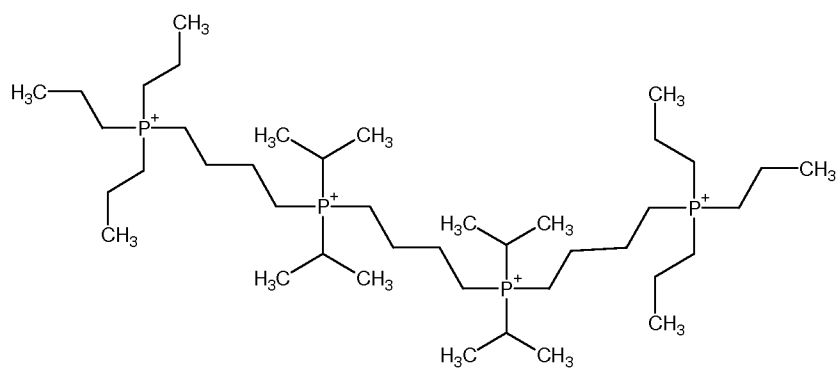


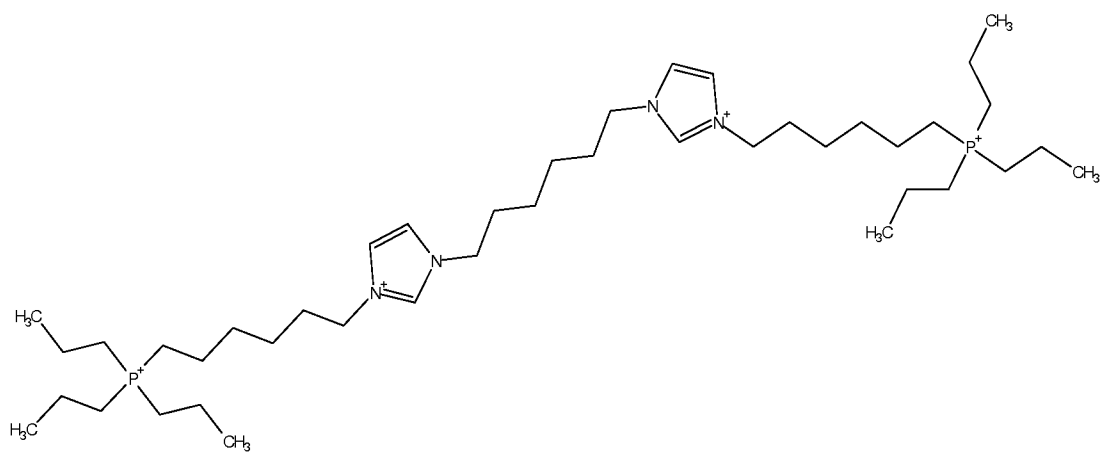
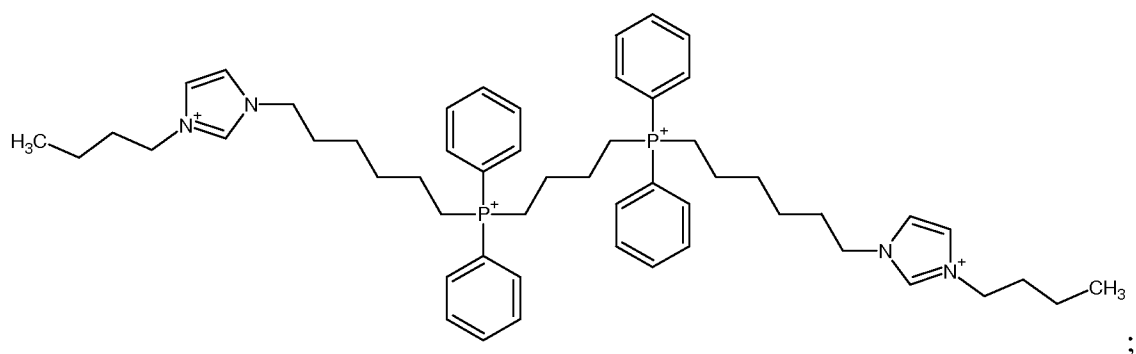
each R is independently selected from a group consisting of methyl, phenyl, n-butyl, isopropyl and propyl;

n is 6, 10, or 12; and

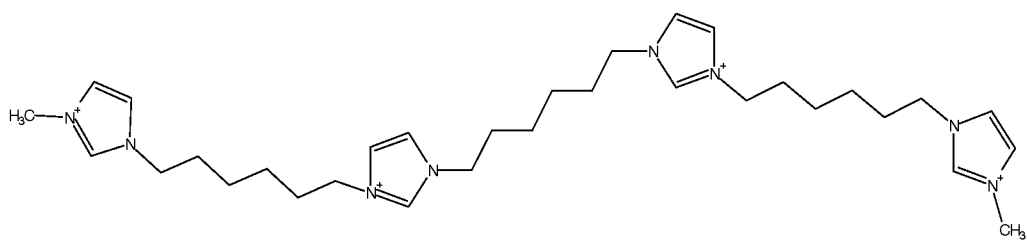
m is 3, 6, or 10.

11. The tetraionic liquid salt of Claim 1, wherein the tetraionic species is selected from the group consisting of:





and

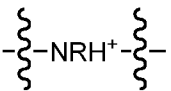
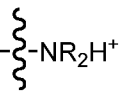


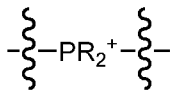
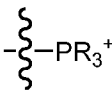
12. A method of detecting at least one anion, the method comprising using at least one tetraionic liquid salt comprising a tetraionic species corresponding in structure to Formula I:

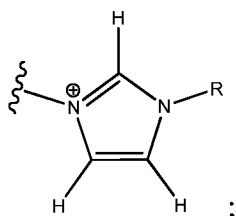
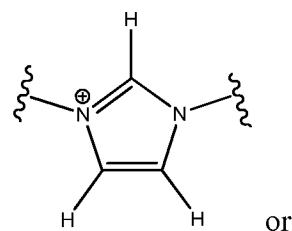
A-B-A-B-A-B-A

Formula I

and at least one counter-anion,
wherein:

A is selected from the group consisting of optionally substituted protonated tertiary amine of formula  or , optionally substituted phosphonium

of formula  or , and imidazolium of formula



wherein each **R** is independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, alkoxy, carbocyclyl, carbocyclylalkyl, heterocyclyl, heterocyclylalkyl and hydroxyalkyl;

wherein each R group of protonated tertiary amine or phosphonium is optionally substituted with one or more substituents selected from the group consisting of C₁-C₁₅-alkyl, alkenyl, alkynyl, alkoxy, carbocyclyl, carbocyclylalkyl, heterocyclyl, heterocyclylalkyl and hydroxyalkyl;

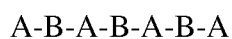
B is a divalent fragment composed of a chain of one or more moieties selected from the group consisting of C₁-C₂₀-alkylene, C₂-C₂₀-alkenylene, and C₂-C₂₀-alkynylene;

wherein C₁-C₂₀-alkylene, C₂-C₂₀-alkenylene, and C₂-C₂₀-alkynylene optionally contain in the chain one or more heteroatoms selected from the group consisting of O, N, S and Si;

wherein **B** is optionally substituted with one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, and halo.

13. The method of Claim 12, wherein ESI-MS is used to detect the at least one anion.
14. The method of Claim 12, wherein the tetraionic liquid salt is added to a carrier flow solvent.

15. The method of Claim 13, further comprising coupling ESI-MS with at least one separation technique selected from the group consisting of LC, HPLC, ion chromatography, ion-exchange chromatography, SPE, SPME, TS-SPME and SPME/MALDI.
16. The method of Claim 12, further comprising using a detection technique selected from the group consisting of DESI and DART.
17. The method of Claim 12, wherein
 A is imidazolium, optionally substituted phosphonium, or optionally substituted protonated tertiary amine; and
 B is C₃-C₂₀-alkylene;
 wherein **B** optionally contains in the chain one or more heteroatoms selected from the group consisting of O, N, S and Si; and
 wherein **B** is optionally substituted with one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, and halo.
18. The method of Claim 12, wherein each R is independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, alkoxy, and carbocyclyl.
19. The method of Claim 18, wherein each R is independently selected from the group consisting of methyl, *n*-butyl, phenyl, benzyl, isopropyl and propyl.
20. A solvent comprising at least one tetraionic liquid salt comprising a tetraionic species of Claim 1.
21. A device useful in chemical separation or analysis comprising: a solid support and at least one tetraionic species adsorbed, absorbed or immobilized thereon corresponding in structure to Formula I:



Formula I

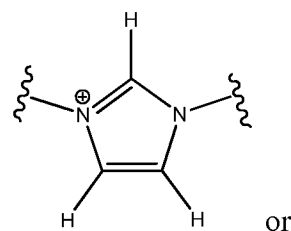
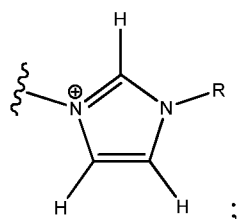
and at least one counter-anion,

wherein:

A is selected from the group consisting of optionally substituted protonated

tertiary amine of formula $\text{---}\text{N}^+\text{R}_2\text{H---}$ or $\text{---}\text{N}^+\text{R}_2\text{H---}$, optionally substituted phosphonium

of formula $\text{---}\text{P}^+\text{R}_3\text{---}$ or $\text{---}\text{P}^+\text{R}_3\text{---}$, and imidazolium of formula



wherein each **R** is independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, alkoxy, carbocyclyl, carbocyclylalkyl, heterocyclyl, heterocyclylalkyl and hydroxyalkyl;

wherein each R group of protonated tertiary amine or phosphonium is optionally substituted with one or more substituents selected from the group consisting of C₁-C₁₅-alkyl, alkenyl, alkynyl, alkoxy, carbocyclyl, carbocyclylalkyl, heterocyclyl, heterocyclylalkyl and hydroxyalkyl;

B is a divalent fragment composed of a chain of one or more moieties selected from the group consisting of C₁-C₂₀-alkylene, C₂-C₂₀-alkenylene, and C₂-C₂₀-alkynylene;

wherein C₁-C₂₀-alkylene, C₂-C₂₀-alkenylene, and C₂-C₂₀-alkynylene optionally contain in the chain one or more heteroatoms selected from the group consisting of O, N, S and Si;

wherein **B** is optionally substituted with one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, and halo and at least one counter anion.

22. The device of Claim 21, wherein

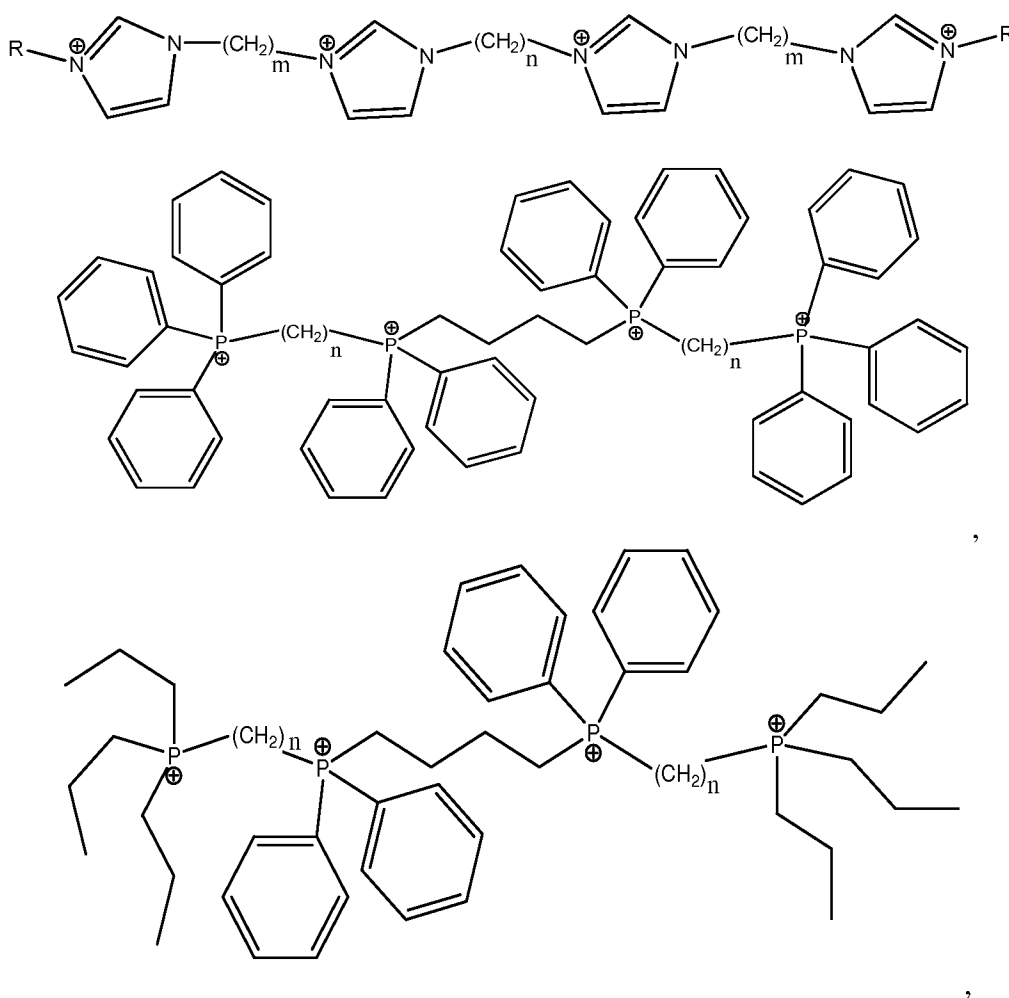
A is imidazolium, optionally substituted phosphonium, or optionally substituted protonated tertiary amine; and

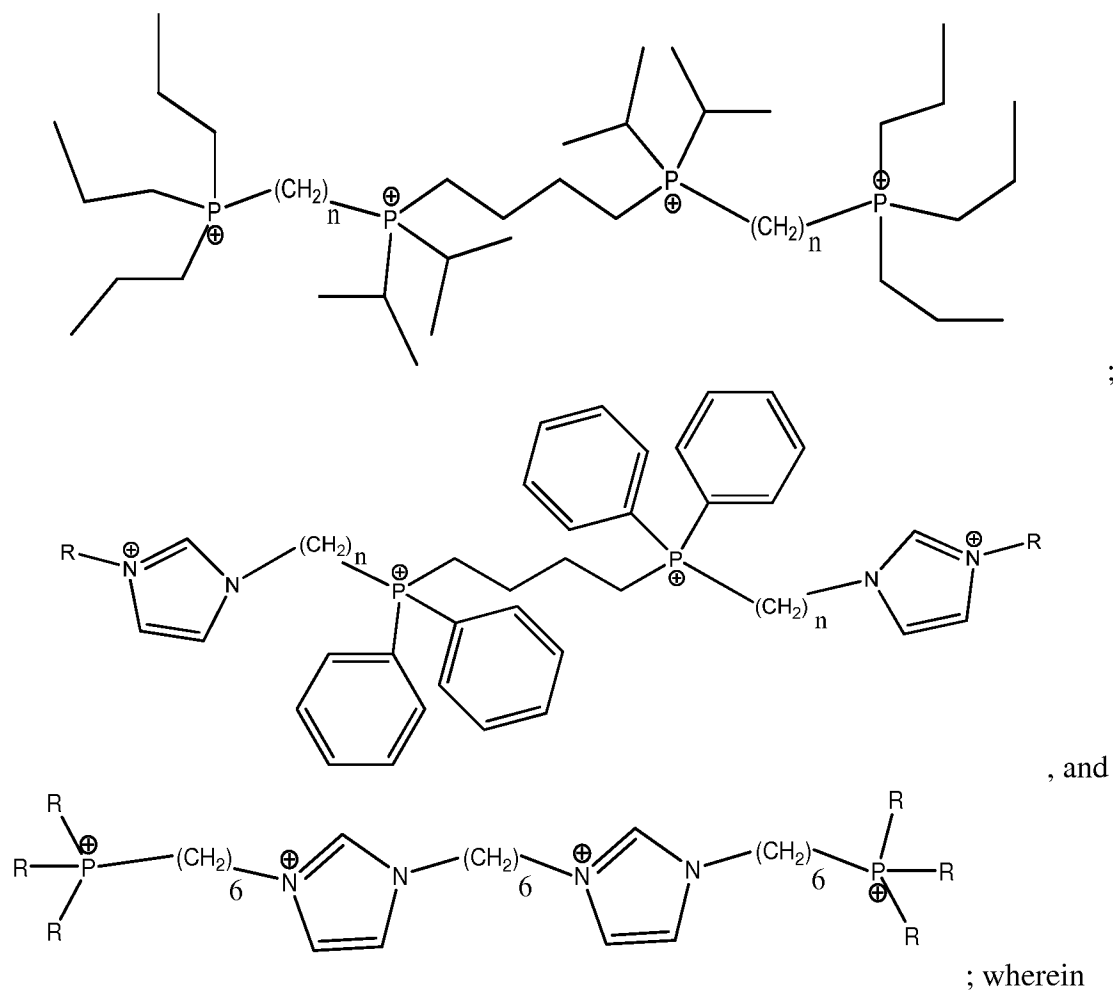
B is C₃-C₂₀-alkylene.

23. The device of Claim 21, wherein each R is independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, alkoxy, and carbocyclyl.

24. The device of Claim 23, wherein each R is independently selected from the group consisting of methyl, *n*-butyl, phenyl, benzyl, isopropyl and propyl.

25. The device of Claim 21, wherein the tetraionic species is selected from the group consisting of:



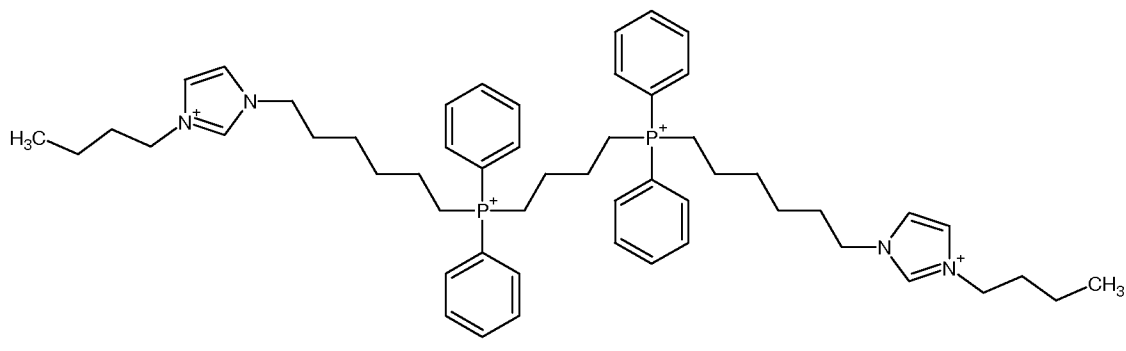
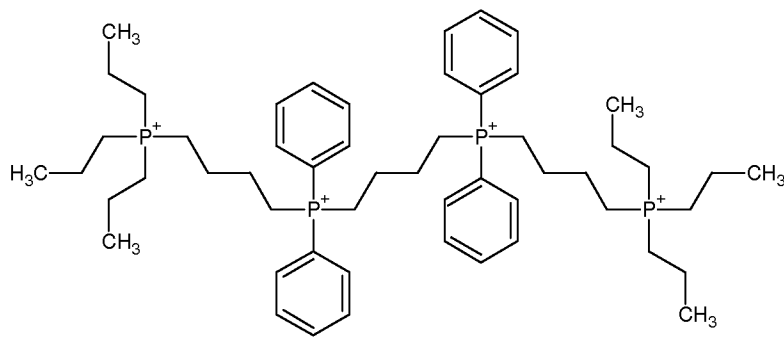
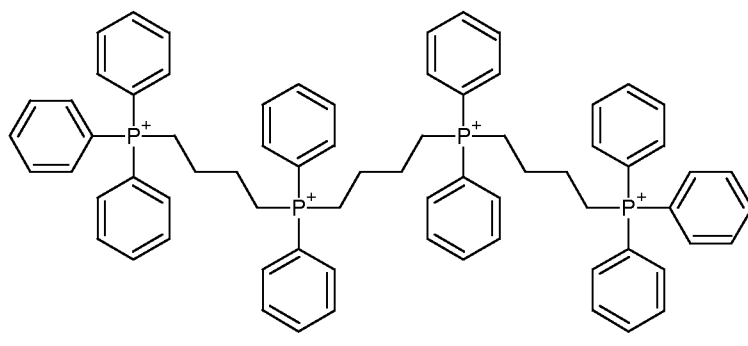
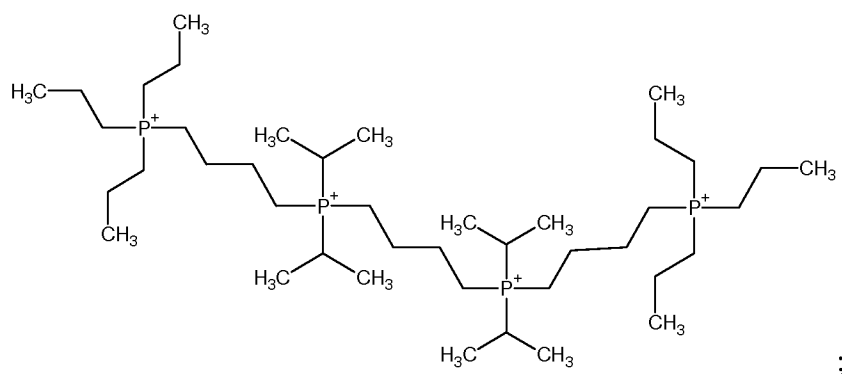


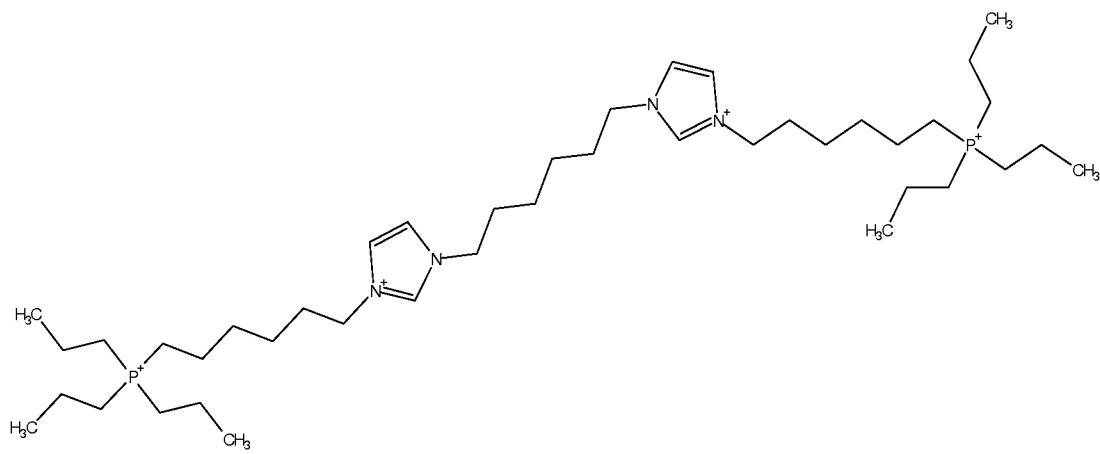
each R is independently selected from a group consisting of methyl, phenyl, n-butyl, and propyl;

n is 6, 10, or 12; and

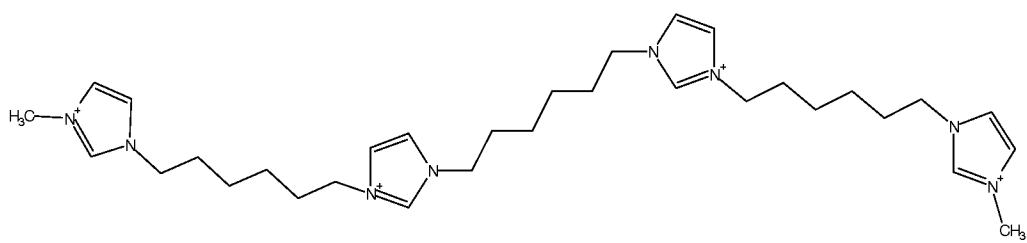
m is 3, 6, or 10.

26. The device of Claim 21, wherein the tetraionic species is selected from the group consisting of:

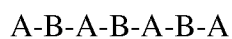




and



27. A method of separating one chemical from a mixture of chemicals comprising the steps of: providing a mixture of at least one first and at least one second chemical, exposing said mixture to at least one solid support including at least one tetraionic species adsorbed, absorbed or immobilized thereon of Formula I:

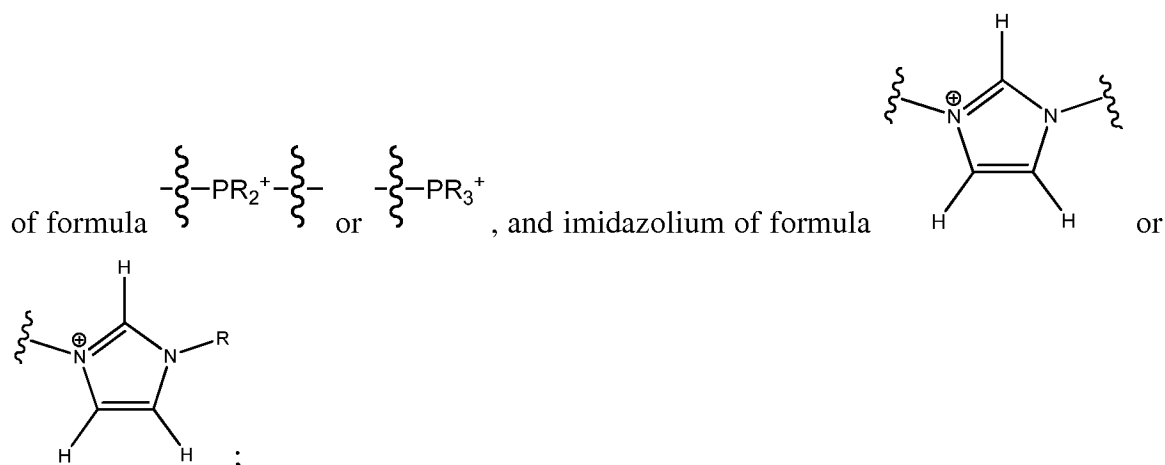
**Formula I**

and at least one counter-anion,

wherein:

A is selected from the group consisting of optionally substituted protonated

tertiary amine of formula $\text{--}\overset{\text{~}}{\underset{\text{~}}{\text{N}}}\text{RH}^+\text{--}$ or $\text{--}\overset{\text{~}}{\underset{\text{~}}{\text{N}}}\text{R}_2\text{H}^+$, optionally substituted phosphonium



wherein each **R** is independently selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, carbocyclyl, carbocyclylalkyl, heterocyclyl, heterocyclylalkyl and hydroxyalkyl;

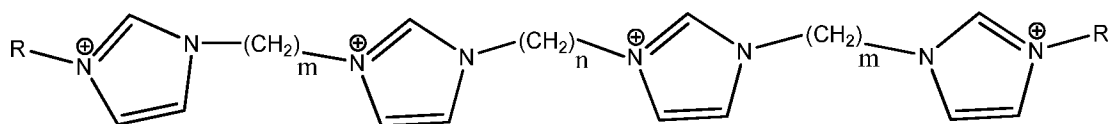
wherein each R group of protonated tertiary amine or phosphonium is optionally substituted with one or more substituents selected from the group consisting of C₁-C₁₅-alkyl, alkenyl, alkynyl, alkoxy, carbocyclyl, carbocyclylalkyl, heterocyclyl, heterocyclylalkyl and hydroxyalkyl;

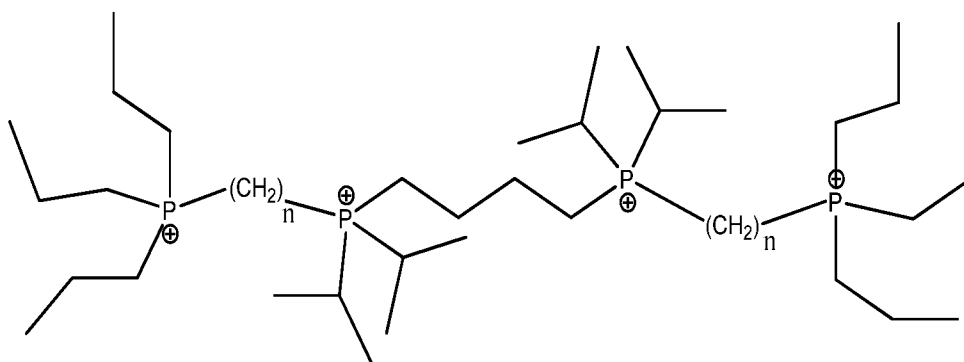
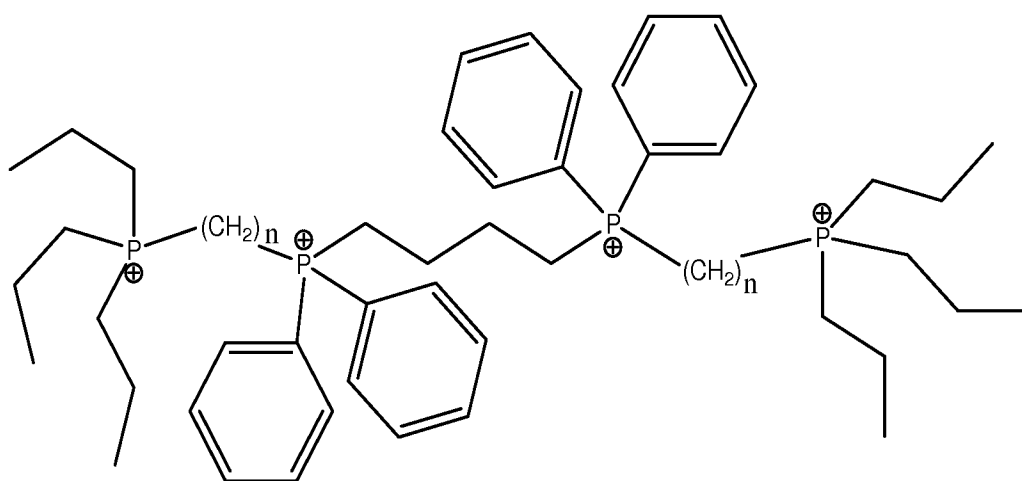
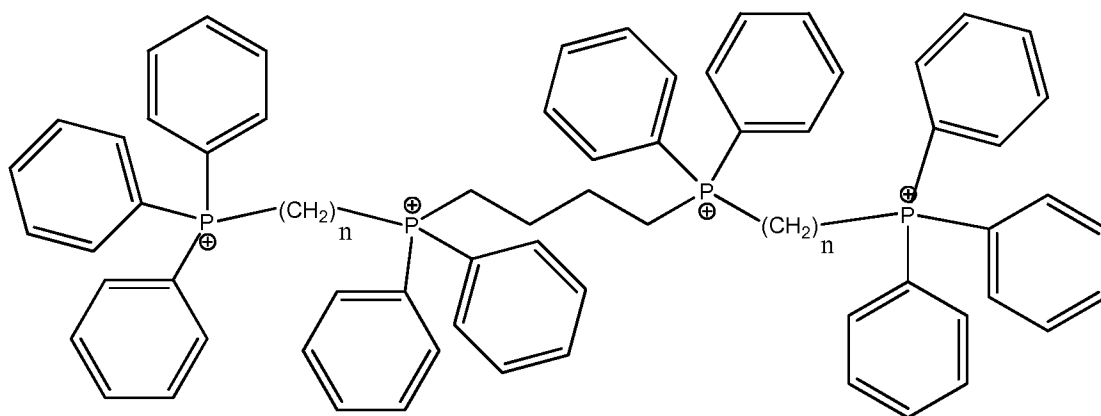
B is a divalent fragment composed of a chain of one or more moieties selected from the group consisting of C₁-C₂₀-alkylene, C₂-C₂₀-alkenylene, and C₂-C₂₀-alkynylene;

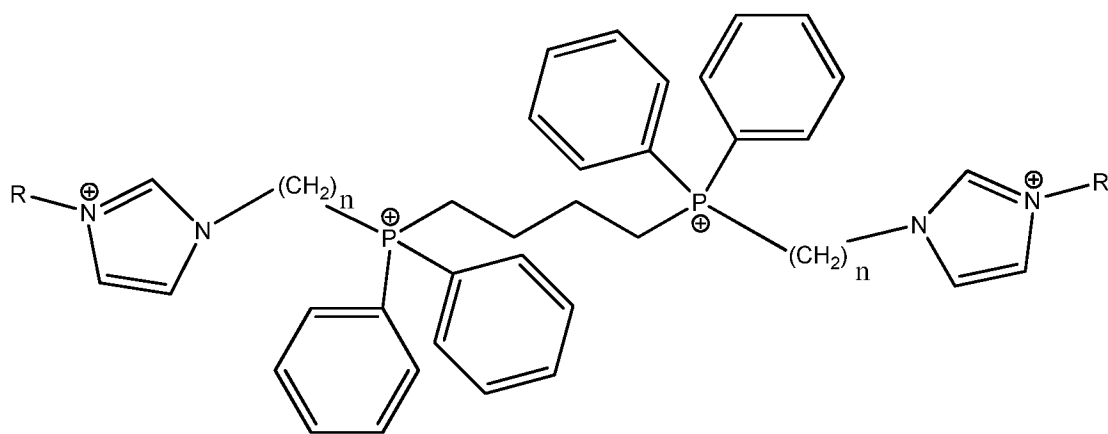
wherein C₁-C₂₀-alkylene, C₂-C₂₀-alkenylene, and C₂-C₂₀-alkynylene optionally contain in the chain one or more heteroatoms selected from the group consisting of O, N, S and Si;

wherein **B** is optionally substituted with one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, and halo and at least one counter anion.

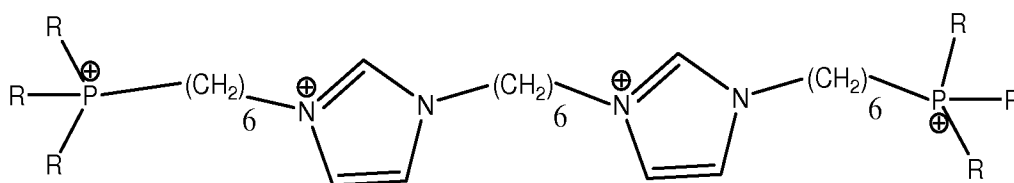
28. The method of Claim 27, wherein the tetraionic species is selected from the group consisting of:







and



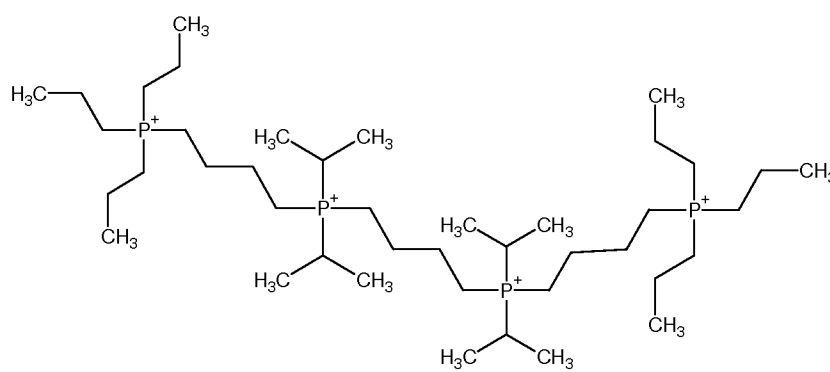
; wherein

each R is independently selected from a group consisting of methyl, phenyl, n-butyl, and propyl;

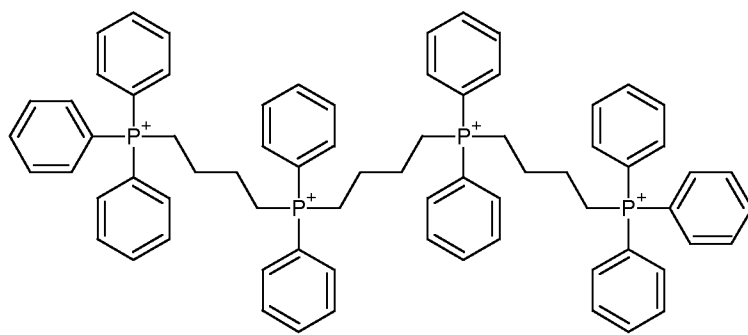
n is 6, 10, or 12; and

m is 3, 6, or 10.

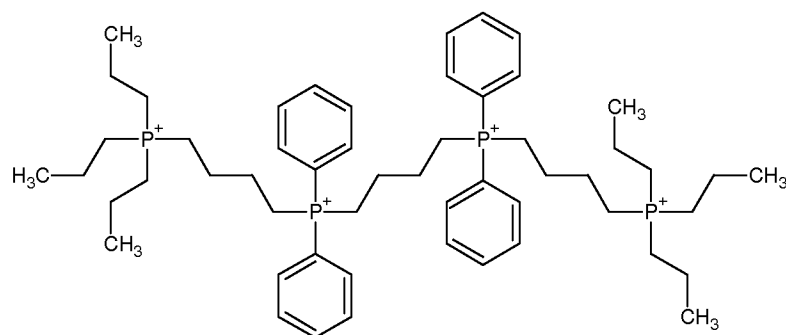
29. The method of Claim 27, wherein the tetraionic species is selected from the group consisting of:



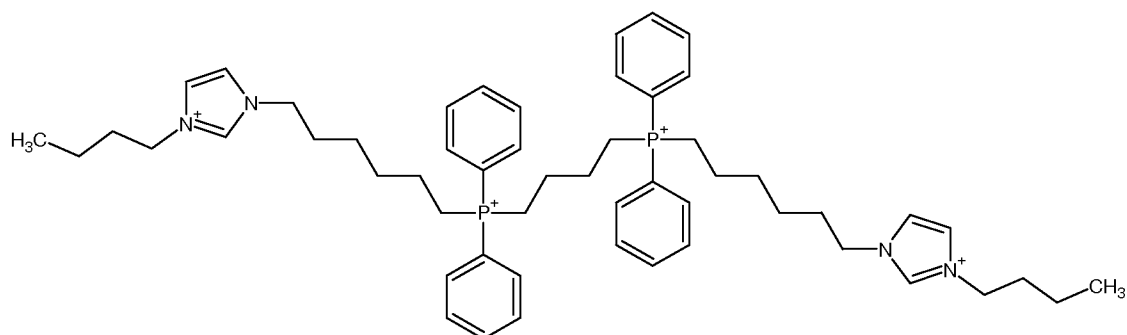
;



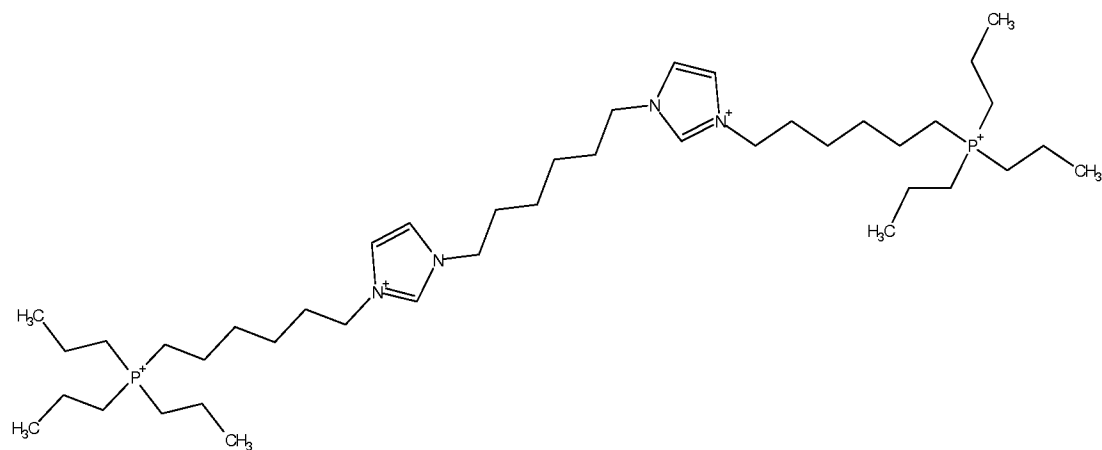
;



;

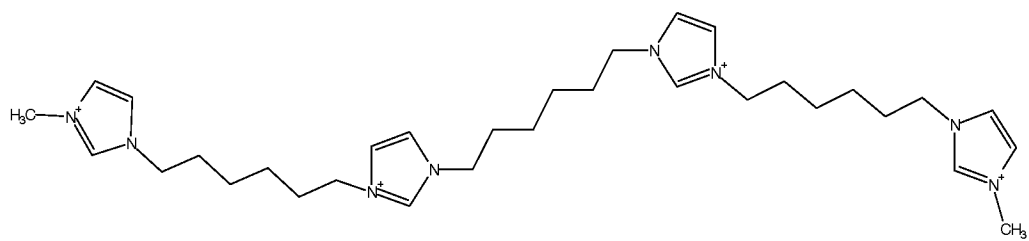


;



;

and



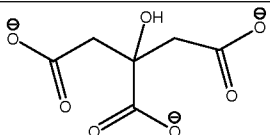
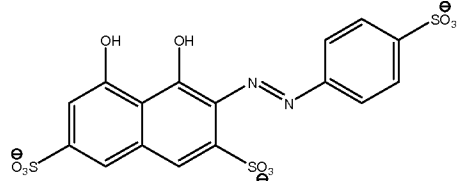
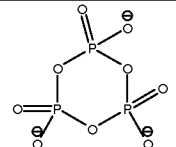
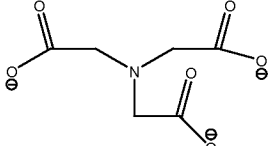
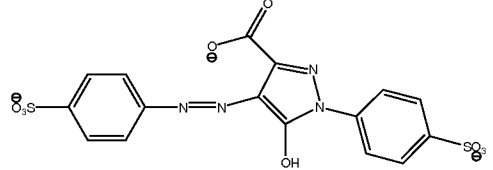
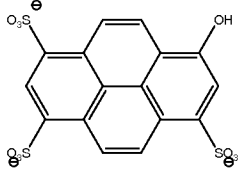
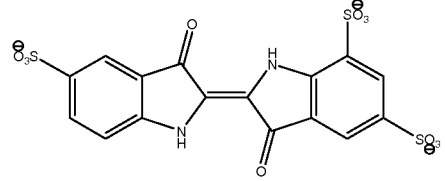
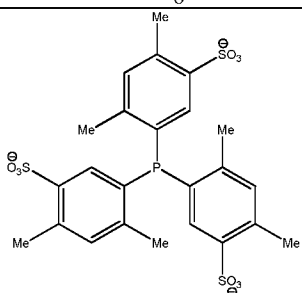
No.	Name	Mass	Structure
I	citrate	189.0	
II	sulfanilic acid azochromotrop	500.9	
III	trimetaphosphate	236.9	
IV	nitrilotriacetic tricarboxylate	188.0	
V	phosphate	95.0	PO_4^{3-}
VI	tartrazine	465.0	
VII	hexanitrocobaltate	334.9	$\text{Co}(\text{NO}_2)_6^{3-}$
VIII	pyranine	454.9	
IX	indigotrisulfonate	498.9	
X	hexachlororhodate	315.6	RhCl_6^{3-}
XI	tris(2,4-dimethyl-5-sulfophenyl)-phosphine	583.0	

Figure 1

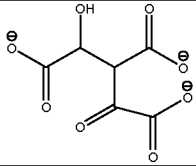
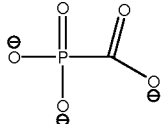
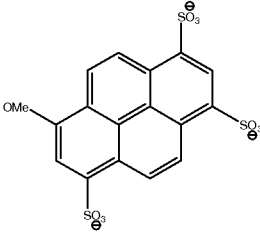
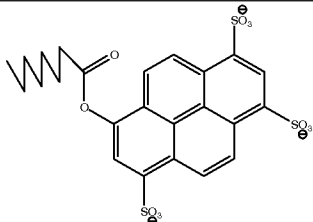
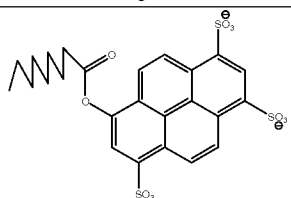
No.	Name	Mass	Structure
XII	chromium oxalate	418	$\text{Cr}(\text{C}_2\text{O}_4)_3^{3-}$
XIII	oxalomalic tricarboxylate	203.0	
XIV	phosphoformate	123.0	
XV	orthovanadate	114.9	VO_4^{3-}
XVI	hexacyanocobaltate	215.0	$\text{Co}(\text{CN})_6^{3-}$
XVII	8-methoxypyrene-1,3,6-trisulfonate	468.9	
XVIII	8-octanoyloxypyrene-1,3,6-trisulfonate	581.0	
XIX	8-nonanoyloxypyrene-1,3,6-trisulfonate	595.0	

Figure 1, cont.

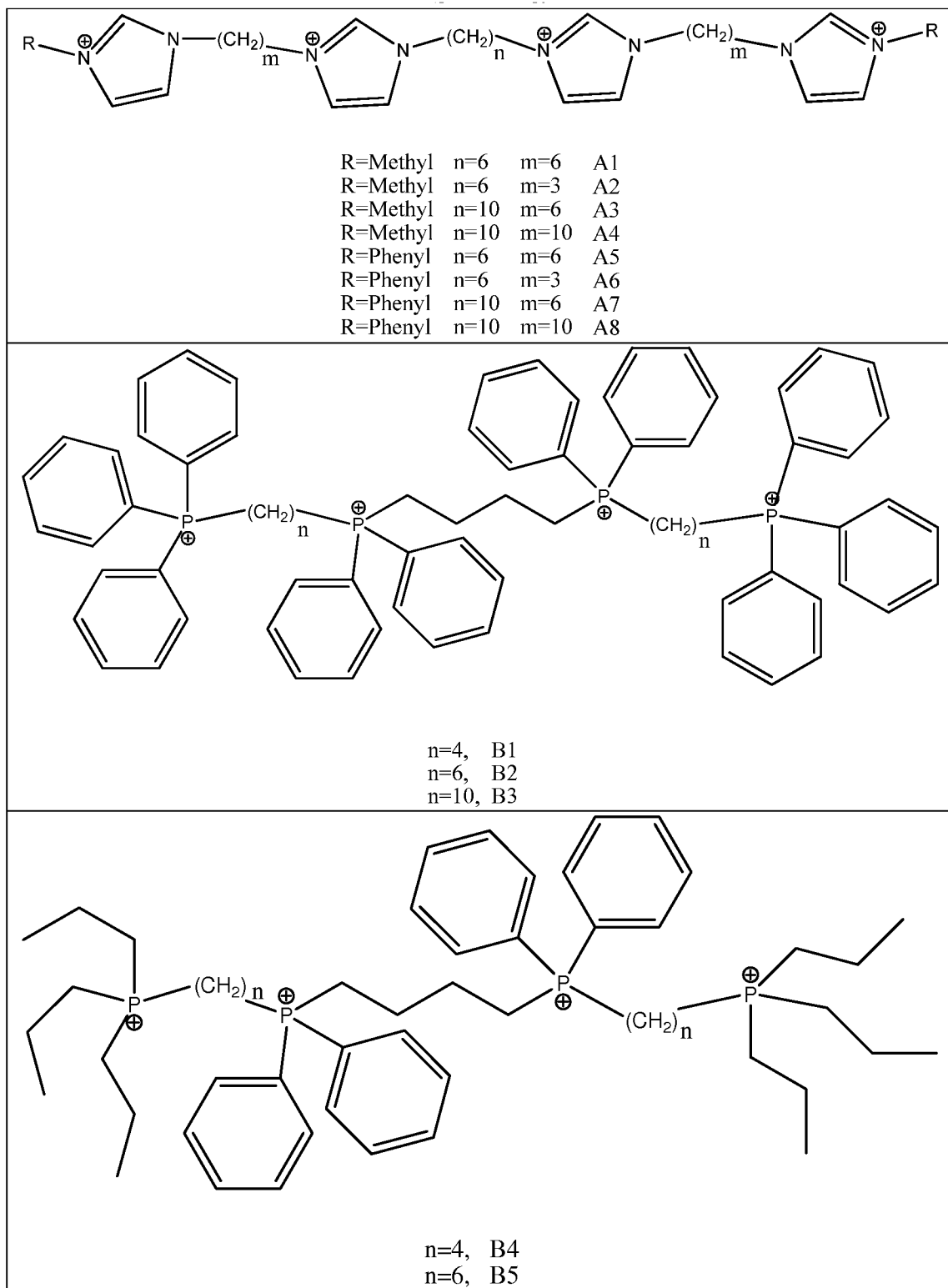


Figure 2

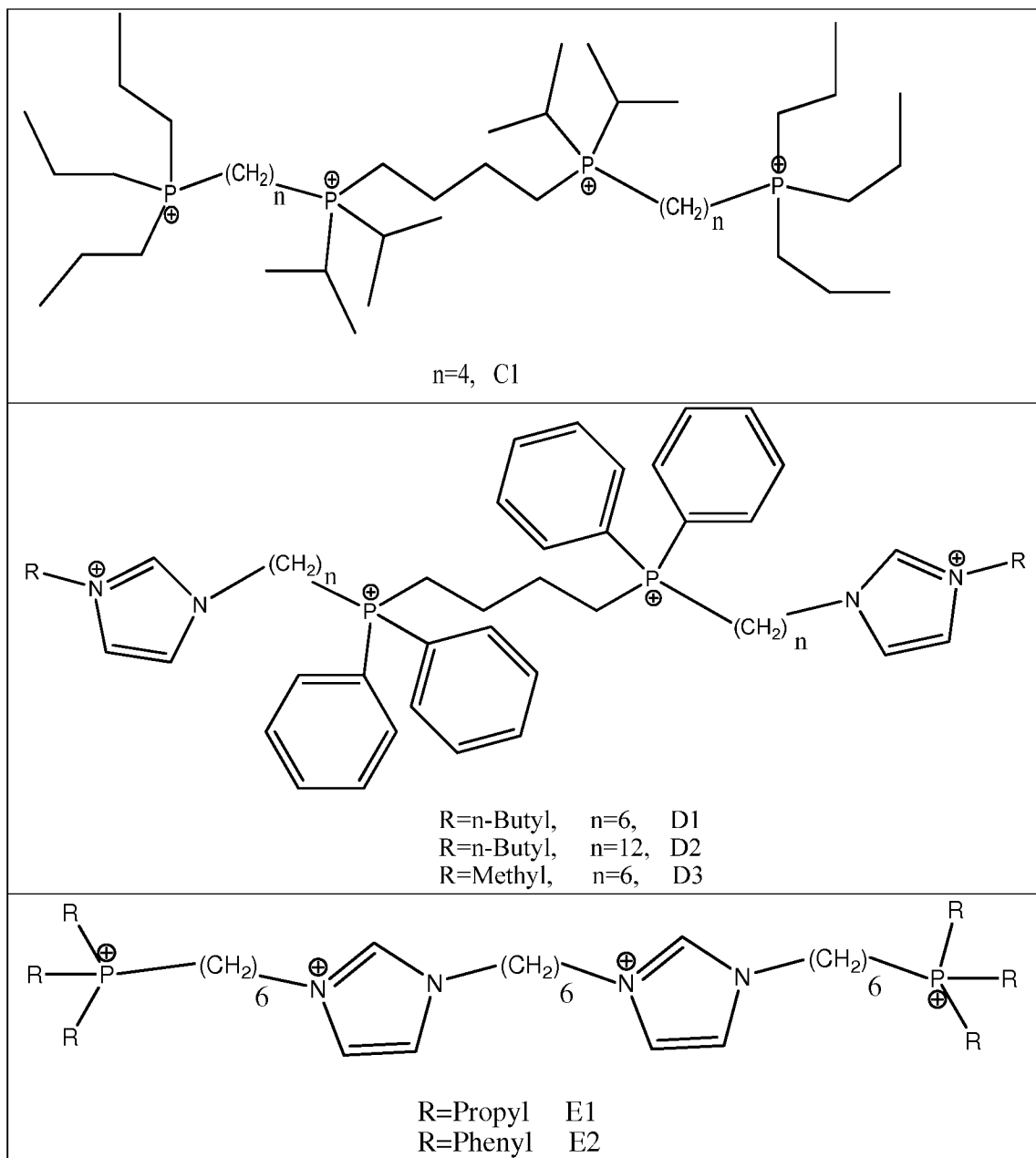
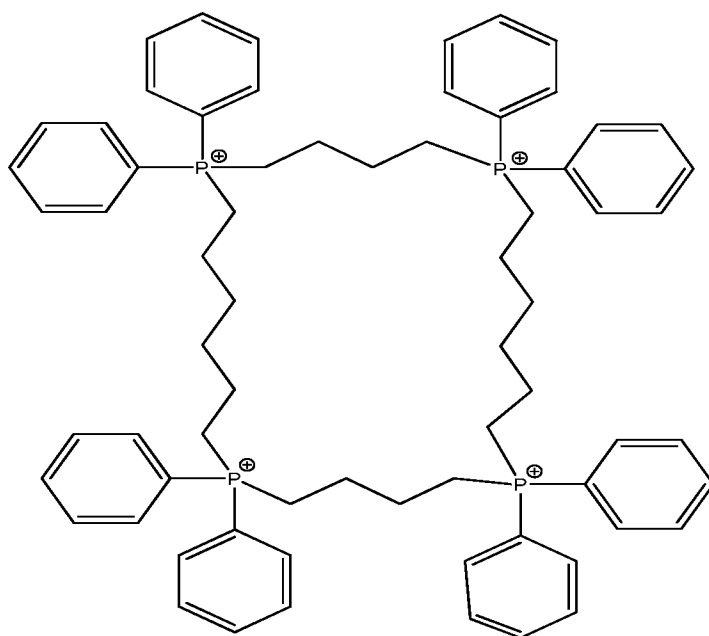
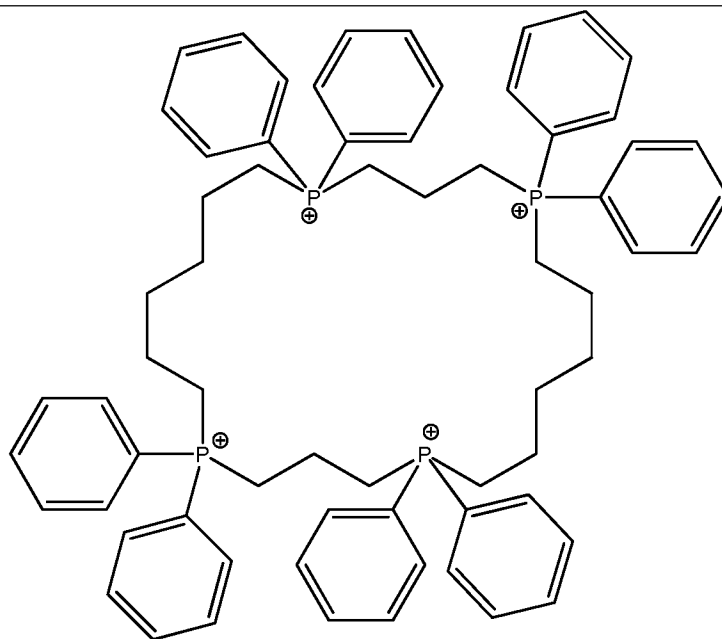


Figure 2, cont.

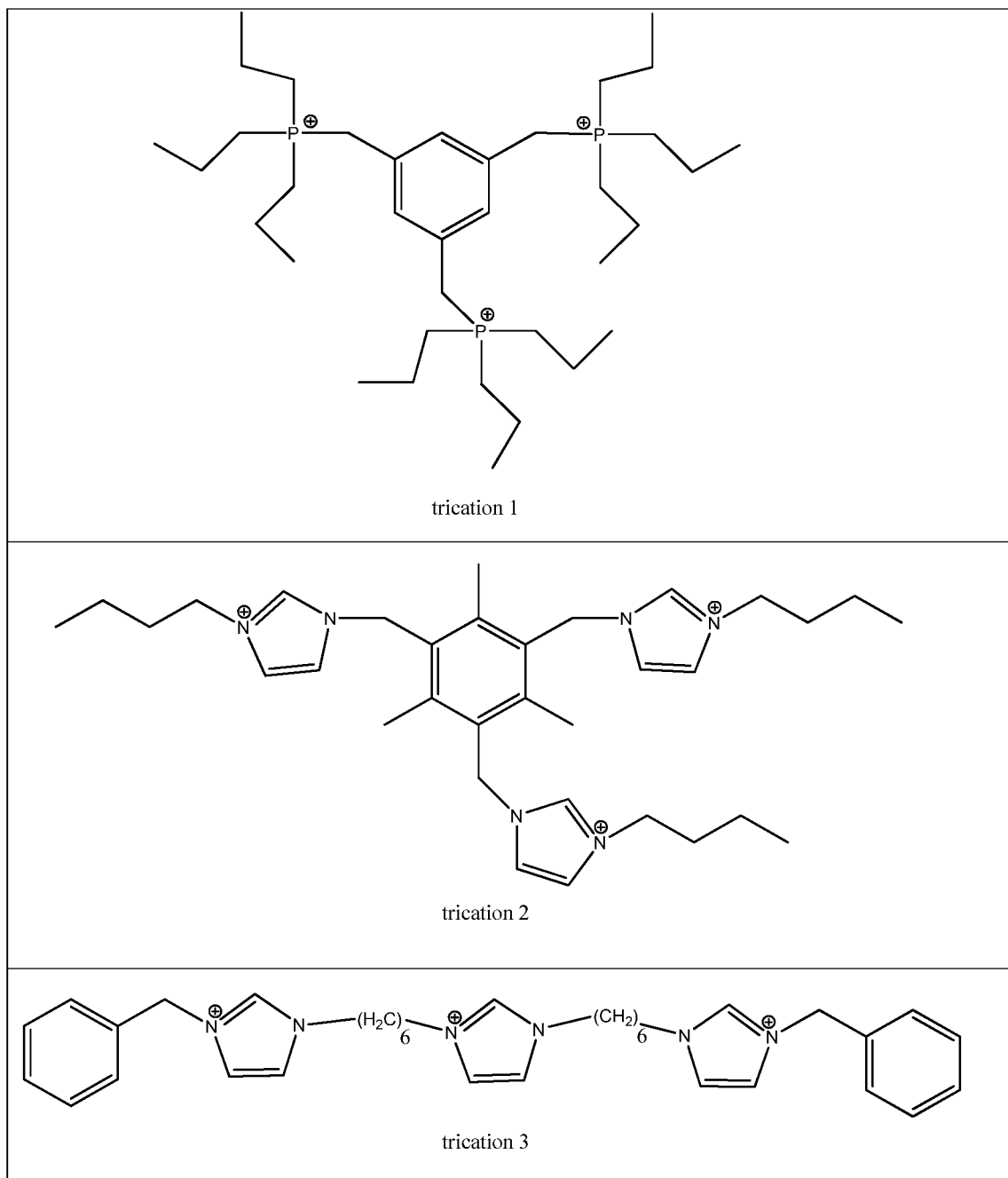


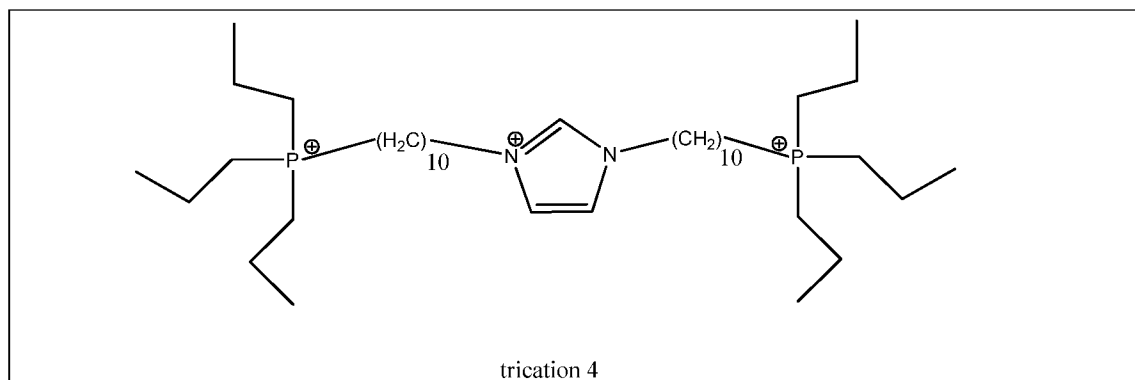
F1



F2

Figure 3

**Figure 4**

**Figure 4, cont.**

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2010/058679

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D233/61 H01J49/16
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07D H01J

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2008/110007 A1 (UNIV MCGILL [CA]; UNIV HONG KONG POLYTECHNIC [CN]; CHAN TAK-HANG [CA];) 18 September 2008 (2008-09-18) page 17 - page 22; example 16 -----	1-29
Y	WO 2008/095064 A2 (SIGMA ALDRICH CO [US]; ARMSTRONG DANIEL W [US]; ANDERSON JARED [US]) 7 August 2008 (2008-08-07) examples -----	1-29
Y	WO 2008/095069 A2 (SIGMA ALDRICH CO [US]; ARMSTRONG DANIEL W [US]; HUANG JUNMIN [US]) 7 August 2008 (2008-08-07) cited in the application tables 1-7, 9, 11 -----	1-29
X	WO 91/04668 A1 (FABRICOM AIR CONDITIONING SA [BE]) 18 April 1991 (1991-04-18) examples P19, A9, P36 -----	1-8,10



Further documents are listed in the continuation of Box C.



See patent family annex.

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"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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"&" document member of the same patent family

Date of the actual completion of the international search

15 April 2011

Date of mailing of the international search report

26/04/2011

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2010/058679

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