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(54) **Title**: NOVEL LIPIDS AND NOVEL PHOSPHOLIPIDS STRUCTURES

(57) **Abstract**: The invention relates to a lipids comprising or consisting of 1,3-diamidolipids or/and 1,2-diamidolipids or/and 2,3-diamidolipids or/and 1,3-diurealipids or/and 1,2-diurealipids or/and 2,3-diurealipids or/and 1,3 -dithiourealipids or/and 1,2-dithiourealipids or/and 2,3-dithiourealipids or/and 1,3-diacylurealipids or/and 1,2-diacylurealipids or/and 2,3-diacylurealipids or/and 1 -amidolipids or/and 1-urealipids or/and 1-thiourealipids or/and 1-acylurealipids or/and cyclic-amidolipids or/and cyclic urealipids or/and cyclic thiourealipids or/and cyclic acylurealipids, and their medical and non-medical use.

# NOVEL LIPIDS AND NOVEL PHOSPHOLIPIDS STRUCTURES

## FIELD OF THE INVENTION

The invention relates to new lipid and phospholipid compounds, mixtures of such compounds alone or in combination with additional compounds, three-dimensional structures comprising same, methods for making same and their non-medical as well as medical use.

## BACKGROUND OF THE INVENTION

Phospholipids are a class of lipids and are a major component of all cell membranes as they can form lipid bilayers. Phospholipids may contain a diglyceride, a phosphate group, and a simple organic molecule such as choline. Sphingomyelin is another type of phospholipid, which is derived from sphingosine instead of glycerol. One of the first phospholipids identified as such in biological tissues was lecithin, or phosphatidylcholine, in the egg yolk.

Phospholipids are composed of a hydrophilic "head" and a hydrophobic "tail". The hydrophilic head contains the negatively charged phosphate group, and may contain other polar groups. The hydrophobic tail usually consists of long fatty acid hydrocarbon chains. Their specific properties allow phospholipids to play an important role in phospholipid bilayers or cell membranes. In biological systems, the phospholipids often occur with other molecules (e.g. proteins, glycolipids and cholesterol) in a bilayer such as a cell membrane.

Phospholipids may also play an important role as second messengers or in signal transduction. In the cellular context phospholipids are synthesized adjacent to the endoplasmatic reticulum (ER).

Lipids in contrast to phospholipids do not carry a phosphate group and are often defined as substances such as fat, oil or wax that dissolve in a non-polar solvent (e.g. alcohol) but not in a polar solvent (e.g. water). Cholesterol and triglycerides also belong to the class of lipids.

WO2009/056955 A2 describes amine bearing phospholipids and their use as a drug delivery system. Particular compositions, their synthesis and their use according to the present invention are not disclosed neither suggested in this patent application.

Fedotenko I.A. et al., Tetrahedron Letters 51, 2010, 5382-5384 describe 1,3-diamidophospholipids and a method of making same. The particular compounds of the invention, their mixtures and use in nanoparticles as well as their use according to the invention are neither disclosed nor suggested therein.

It is one object of the present invention to provide new compounds and mixtures of compounds which may form 3-dimensional structures and preferably which structures are useful for non-medical and medical applications in a system or a patient, or to improve the disadvantages of the state of the art.

Another object of the invention is to provide for methods of making compounds, compositions and means useful in the above object.

## SUMMARY OF THE INVENTION

In one aspect the invention relates to lipids comprising or consisting of 1,3-diamidolipids or/and 1,2-diamidolipids or/and 2,3-diamidolipids or/and 1,3-diurealipids or/and 1,2-diurealipids or/and 2,3-diurealipids or/and 1,3-dithiourealipids or/and 1,2-dithiourealipids or/and 2,3-dithiourealipids or/and 1,3-diacylurealipids or/and 1,2-diacylurealipids or/and 2,3-diacylurealipids or/and 1-amidolipids or/and 1-urealipids or/and 1-thiourealipids or/and 1-acylurealipids or/and cyclic-amidolipids or/and cyclic urealipids or/and cyclic thiourealipids or/and cyclic acylurealipids.

In another aspect the invention is a composition wherein the composition is provided in the form of functional 3-dimensional structures.

Another aspect of the invention relates to a method of making the novel lipids of the invention.

In a further aspect the invention relates to a method of making a composition according to the invention and to a method of making 3-dimensional structures.

In yet another aspect the invention relates to a pharmaceutical or cosmetic composition according to the invention, and preferably comprising further useful carriers or/and additives.

In yet another aspect the invention relates to a composition according to the invention for use in a pharmaceutical or cosmetic application.

In yet another aspect the invention relates to a composition or functional 3-dimensional structure according to the invention for use in the prophylaxis or treatment of a dermatological disorder or disease, or for use as cosmetic.

In another aspect the invention relates to the provision of compounds capable of forming 3-dimensional structures useful in non-medical and/or medical applications and uses as well as methods.

## BRIEF DESCRIPTION OF THE FIGURES

FIGS. 1 – 4 are depicting the characterization of preferred embodiments of the phospholipids according to the invention.

FIG. 5 A to D

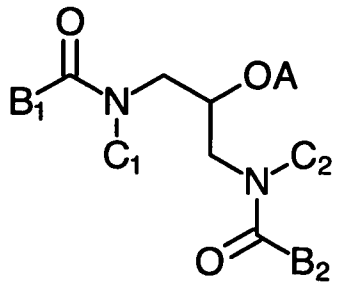
The Figure shows structures prepared from 50 mol% Sad-PC-Sad and 50 mol% Pad-PC-Pad (A and B), Mad-PC-Mad (C), and Pur-PC-Pur (D). All preparations contain 1 mol% of DOPE Rhodamine. Scale bars = 5 μm.

## DETAILED DESCRIPTION

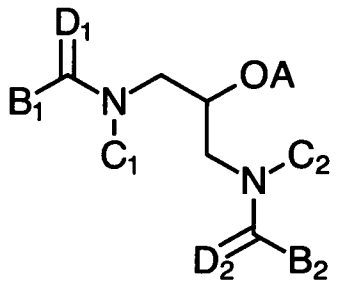
The invention provides novel phospholipids and lipids. In particular the invention relates to lipids comprising or consisting of 1,3-diamidolipids or/and 1,2-diamidolipids or/and 2,3-diamidolipids or/and 1,3-diurealipids or/and 1,2-diurealipids or/and 2,3-diurealipids or/and 1,3-dithiourealipids or/and 1,2-dithiourealipids or/and 2,3-dithiourealipids or/and 1,3-diacylurealipids or/and 1,2-diacylurealipids or/and 2,3-diacylurealipids or/and 1-amidolipids or/and 1-urealipids or/and 1-thiourealipids or/and 1-acylurealipids or/and cyclic-amidolipids or/and cyclic urealipids or/and cyclic thiourealipids or/and cyclic acylurealipids.

The inventors have developed novel phospholipids and lipids, and compositions comprising same useful in non-medical as well as medical applications. In particular the novel compositions are useful in medical and cosmetic applications. The invention may also be used in the targeted delivery of an active compound or composition.

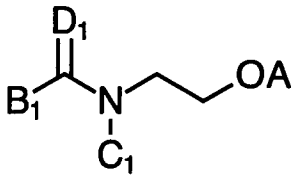
The lipids of the invention are depicted in the following formulae Ia, Ib, Ic and Id:



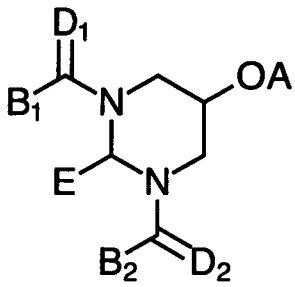

Formula Ia




Formula Ib



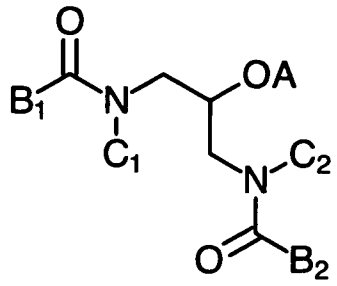

Formula Ic




Formula Id

wherein the residues "A", "B", "C" and "D" are as defined below in the preferred embodiments of the invention.

In a preferred embodiment a composition as described above is provided wherein the 1,3-diamidophospholipid or 1, 3-diaminolipid has the following Formula Ia:



Formula Ia

and wherein

i. "$B_1$" is equal or different from "$B_2$", and "$B_1$" and "$B_2$" is selected from:

ii. H;

iii. alkyl-, such as methyl-, ethyl-, propyl-, isopropyl-, butyl-, pentyl-, hexyl-, heptyl-, octyl-, nonyl-, decyl-, undecyl-, dodecyl-, tridecyl-, tetradecyl-, pentadecyl-, hexadecyl-, heptadecyl-, nonadecyl-, eicosyl-, heneicosyl-, docosyl-, tricosyl-, or tetracosyl-;

iv. preferably, undecyl-, tridecyl-, pentadecyl-, heptadecyl-;

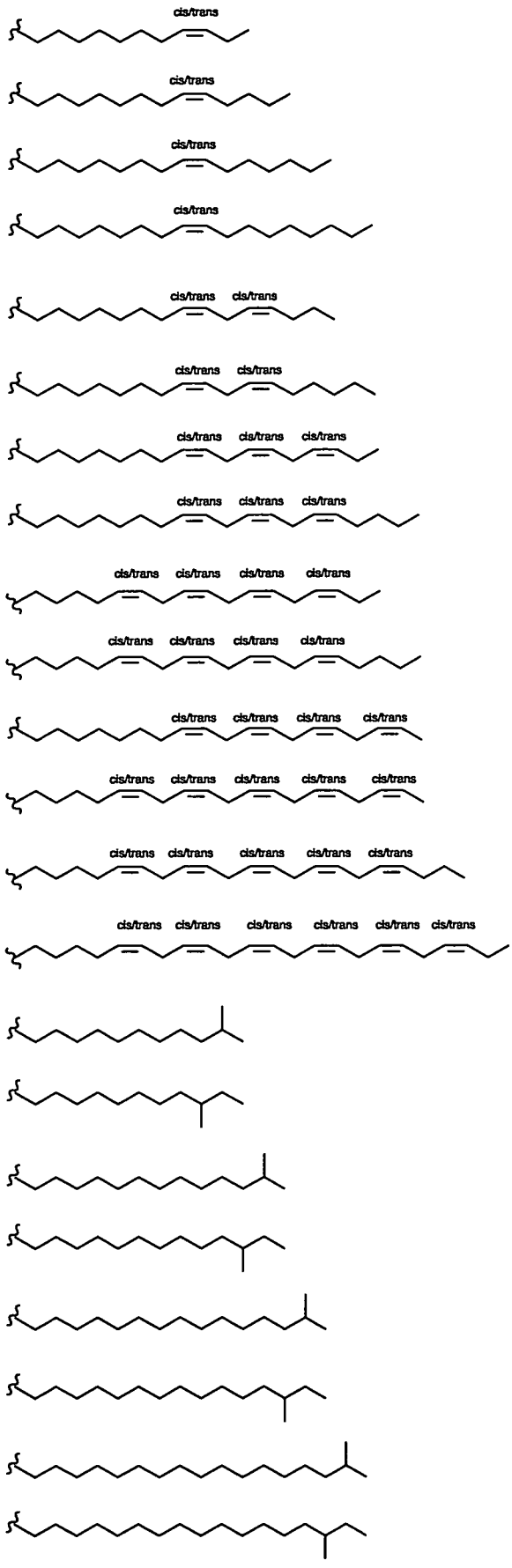
v. an optionally substituted $C_1$-$C_{10}$ alkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

vi. an optionally substituted $C_{11}$-$C_{17}$ alkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

vii. an optionally substituted $C_{18}$-$C_{24}$ alkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

viii. wherein 11, 13, 15, and 17 C-atoms are preferred;

ix. a group listed in the figures below: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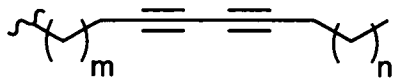



where m and n can be different or the same and

m = 0-7

preferably m=7

n=0-11

preferably n=8, 10, or 11

or "$B_1$" and "$B_2$" are the same or different and are selected from:

i. primary amines such as methyl-, ethyl-, propyl-, isopropyl-, butyl-, pentyl-, hexyl-, heptyl-, octyl-, nonyl-, decyl-, undecyl-, dodecyl-, tridecyl-, tetradecyl-, pentadecyl-, hexadecyl-, heptadecyl-, nonadecyl-, eicosyl-, heneicosyl-, docosyl-, tricosyl-, or tetracosyl-amine

ii. preferably, decyl-, dodecyl-, tetradecyl-, hexadecyl-amine;

iii. an optionally substituted C1-C8 aminoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

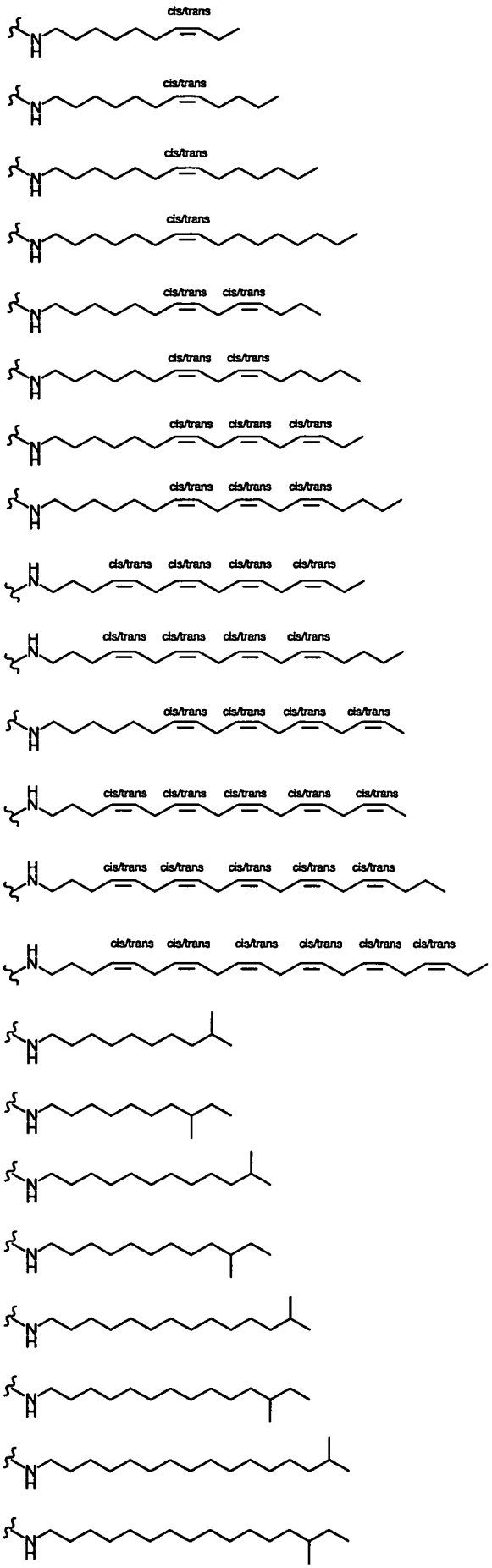
iv. an optionally substituted C9-C15 aminoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

v. an optionally substituted C16-C22 aminoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

vi. wherein 9, 11, 13, and 15 C-atoms are preferred;

vii. a group listed in the figures below:

viii.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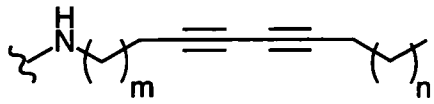


where m=0-6, and preferably m=6

n=0-11, preferably n=8, 10, or 11

or

ix. primary amides (to give acylureas) such as methyl-, ethyl-, propyl-, isopropyl-, butyl-, pentyl-, hexyl-, heptyl-, octyl-, nonyl-, decyl-, undecyl-, dodecyl-, tridecyl-, tetradecyl-, pentadecyl-, hexadecyl-, heptadecyl-, nonadecyl-, eicosyl-, heneicosyl-, docosyl-, tricosyl-, or tetracosyl-amide;

x. preferably, decyl-, dodecyl-, tetradecyl-, hexadecyl-amide;

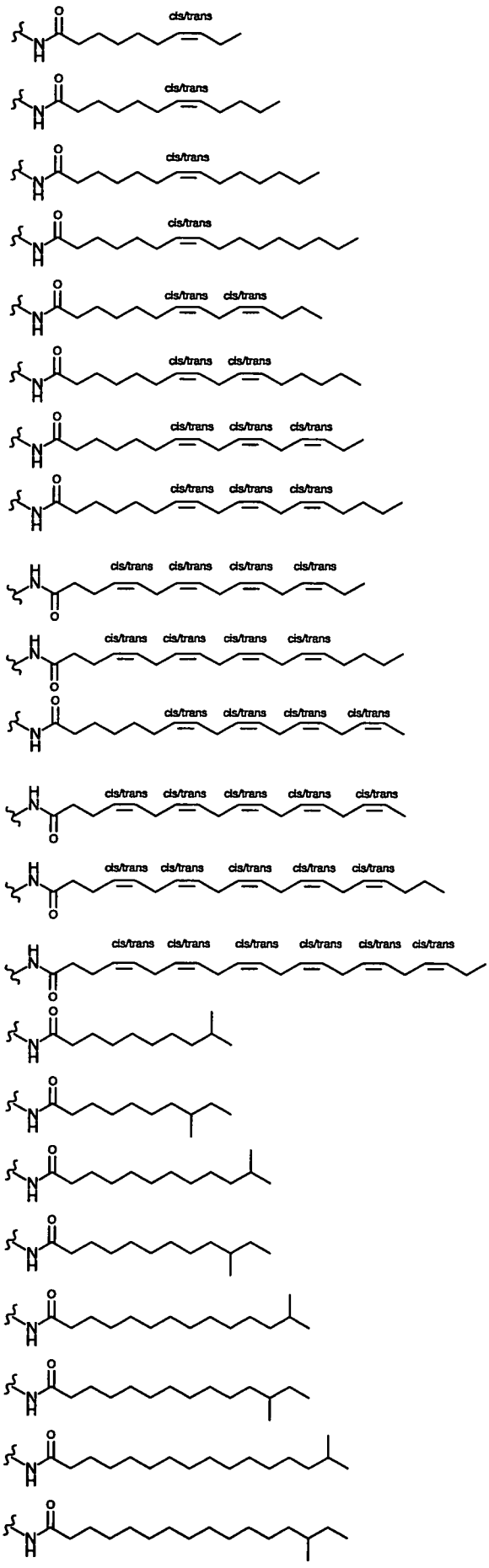
xi. an optionally substituted C1-C8 amidoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

xii. an optionally substituted C9-C15 amidoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

xiii. an optionally substituted C16-C22 amidoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

xiv. wherein 9, 11, 13, and 15 C-atoms are preferred;

xv. a group listed in the figures below: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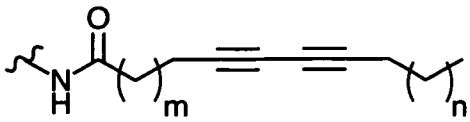


where m=0-5, and preferably m=5;

n=0-11, preferably n=8, 10, or 11;

wherein said lipid may be fully or partially deuterated, or radioactively labeled; and

wherein "A" is selected from:

a proton (H), a phosphatic acid or a phosphate ester substituted group such as phosphocholine, phosphoethanolamine, phosphoglycerol, phosphoserine, phosphoinositol, phosphoinositol 4,5-bisphosphate, a phosphate ester substituted sugar, a phosphate ester substituted polyethyleneglycol, a phosphate ester substituted electrophile, such as an activated ester including N-hydroxysuccinimic ester, or an acid chloride or an halogenide, a phosphate ester substituted nucleophile such as a thiol or an amine, a phosphate ester substituted fluorescent group such as fluoresceine, a phosphate ester substituted radioactively labeled group, a phosphate ester substituted alkyne and a phosphate substituted azide, and wherein "$C_1$" and "$C_2$" may be H or a methyl.

In yet another preferred embodiment the 1, 3-diamidophospholipids of the invention of Formula Ia are defined as follows:

i. "$B_1$" is equal or different from "$B_2$", and "$B_1$" and "$B_2$" is selected from:

ii.H;

iii.alkyl-, such as methyl-, ethyl-, propyl-, isopropyl-, butyl-, pentyl-, hexyl-, heptyl-, octyl-, nonyl-, decyl-, undecyl-, dodecyl-, tridecyl-, tetradecyl-, pentadecyl-, hexadecyl-, heptadecyl-, nonadecyl-, eicosyl-, heneicosyl-, docosyl-, tricosyl-, or tetracosyl-;

iv.preferably, undecyl-, tridecyl-, pentadecyl-, heptadecyl-;

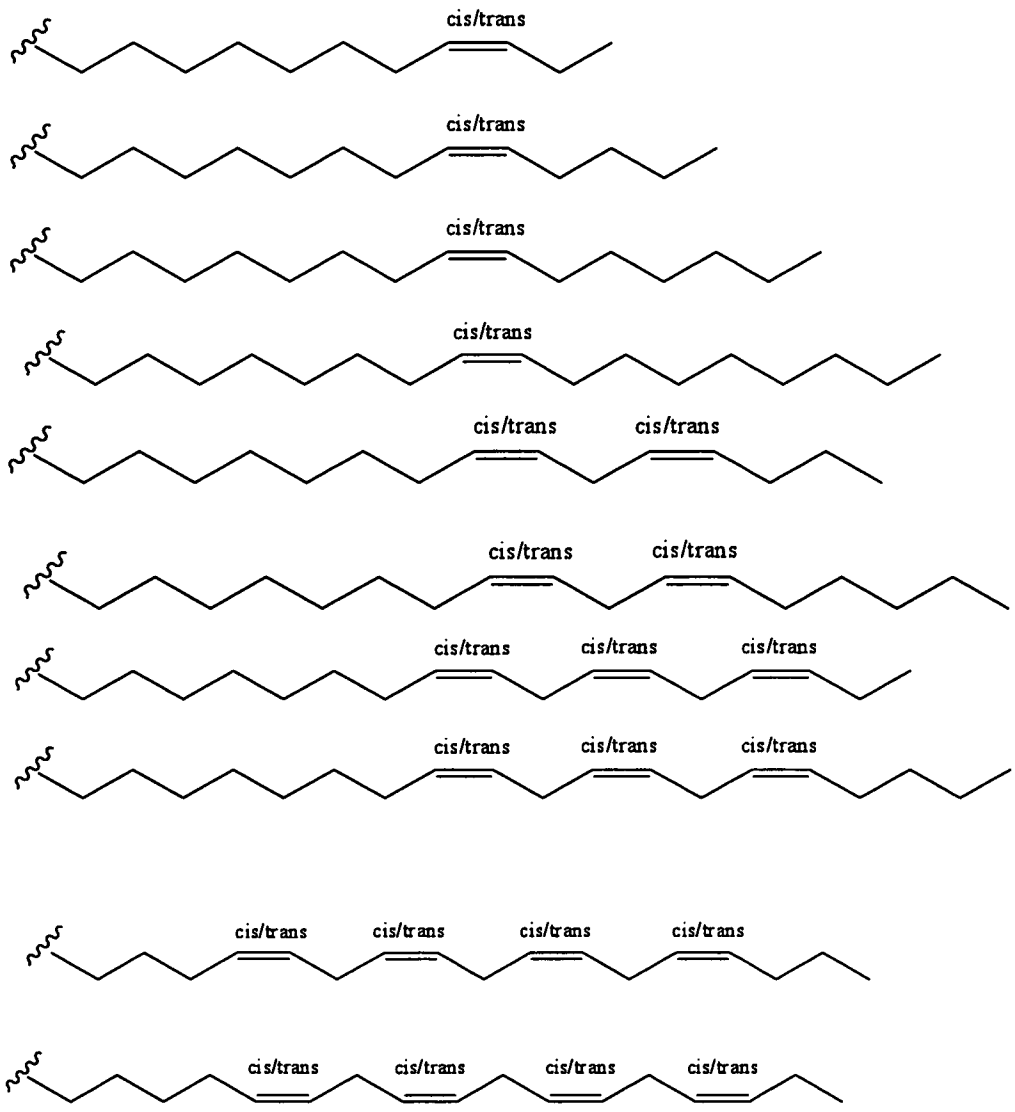
v.an optionally substituted $C_1$-$C_{10}$ alkyl group with 1, 2, 3, 4, or 5 cis- or trans-double bonds;

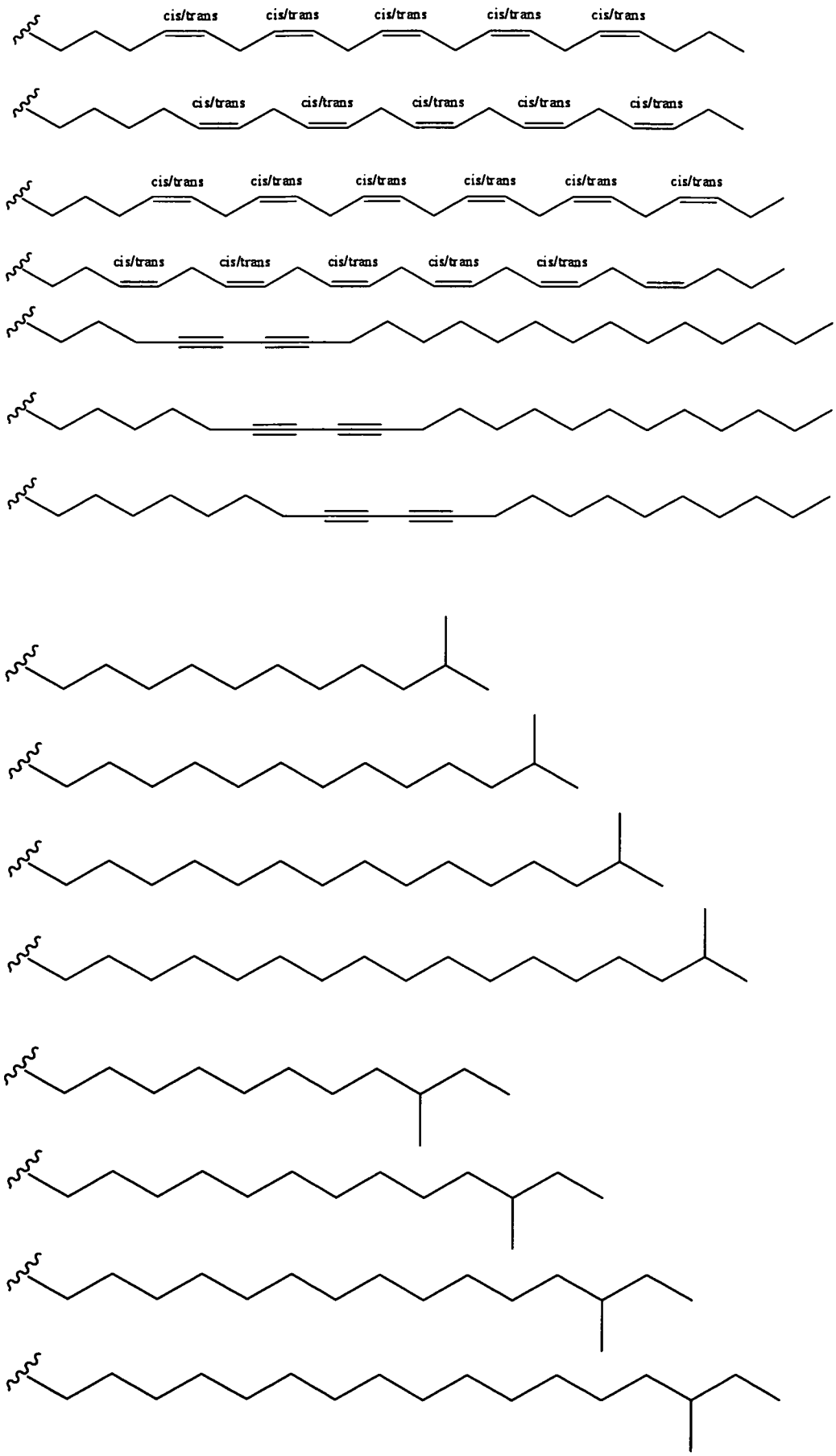
vi.an optionally substituted $C_{11}$-$C_{17}$ alkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

vii.an optionally substituted $C_{18}$-$C_{24}$ alkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

viii.wherein 11, 13, 15, and 17 C-atoms are preferred;

ixa group listed in the figures below:

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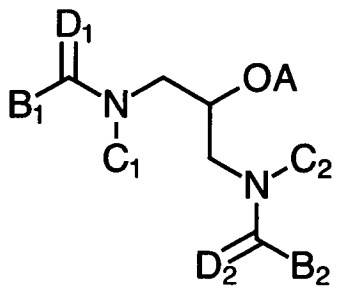
wherein said lipid may be fully or partially deuterated, or radioactively labeled;

wherein "A" is selected from:
a phosphatic acid or a phosphate ester substituted group such as phosphocholine, phosphoethanolamine, phosphoglycerol, phosphoserine, phosphoinositol, phosphoinositol 4,5-bisphosphate, a phosphate ester substituted sugar, a phosphate ester substituted polyethyleneglycol, a phosphate ester substituted electrophile, such as an activated ester including N-hydroxysuccinimic ester, or an acid chloride or an halogenide, a phosphate ester substituted nucleophile such as a thiol or an amine, a phosphate ester substituted fluorescent group such as fluoresceine, a phosphate ester substituted radioactively labeled group, a phosphate ester substituted alkyne and a phosphate substituted azide; and

wherein "$C_1$" and "$C_2$" is selected from H or methyl.

In another preferred embodiment of the invention the lipids are defined according to formula Ib:




Formula Ib

and wherein

i. "$B_1$" is equal or different from "$B_2$", and "$B_1$" and "$B_2$" is selected from:

ii. H;

iii. alkyl-, such as methyl-, ethyl-, propyl-, isopropyl-, butyl-, pentyl-, hexyl-, heptyl-, octyl-, nonyl-, decyl-, undecyl-, dodecyl-, tridecyl-, tetradecyl-, pentadecyl-, hexadecyl-, heptadecyl-, nonadecyl-, eicosyl-, heneicosyl-, docosyl-, tricosyl-, or tetracosyl-;

iv. preferably, undecyl-, tridecyl-, pentadecyl-, heptadecyl-;

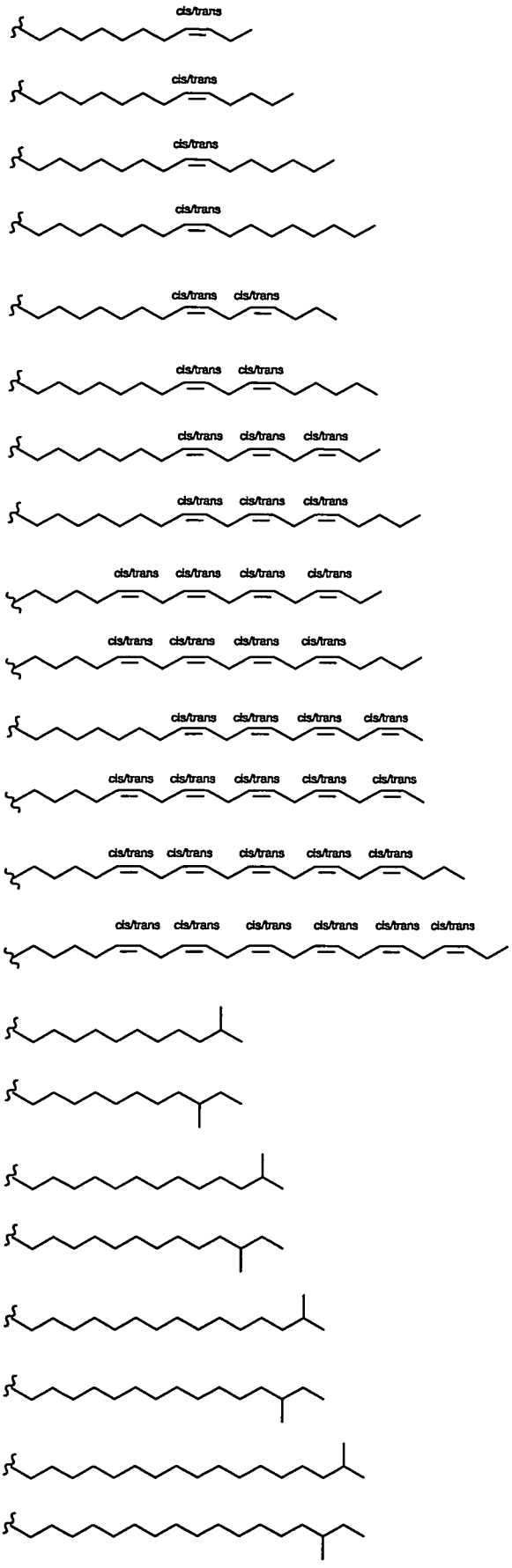
v. an optionally substituted $C_1$-$C_{10}$ alkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

vi. an optionally substituted $C_{11}$-$C_{17}$ alkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

vii. an optionally substituted $C_{18}$-$C_{24}$ alkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

viii. wherein 11, 13, 15, and 17 C-atoms are preferred;

ix. a group listed in the figures below: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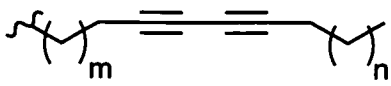



where m and n can be different or the same and

m = 0-7, preferably m=7

n=0-11, preferably n=8, 10, or 11

or "$B_1$" and "$B_2$" are the same or different and are selected from:

i. primary amines such as methyl-, ethyl-, propyl-, isopropyl-, butyl-, pentyl-, hexyl-, heptyl-, octyl-, nonyl-, decyl-, undecyl-, dodecyl-, tridecyl-, tetradecyl-, pentadecyl-, hexadecyl-, heptadecyl-, nonadecyl-, eicosyl-, heneicosyl-, docosyl-, tricosyl-, or tetracosyl-amine;

ii. preferably, decyl-, dodecyl-, tetradecyl, hexadecyl-amine;

iii. an optionally substituted C1-C8 aminoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

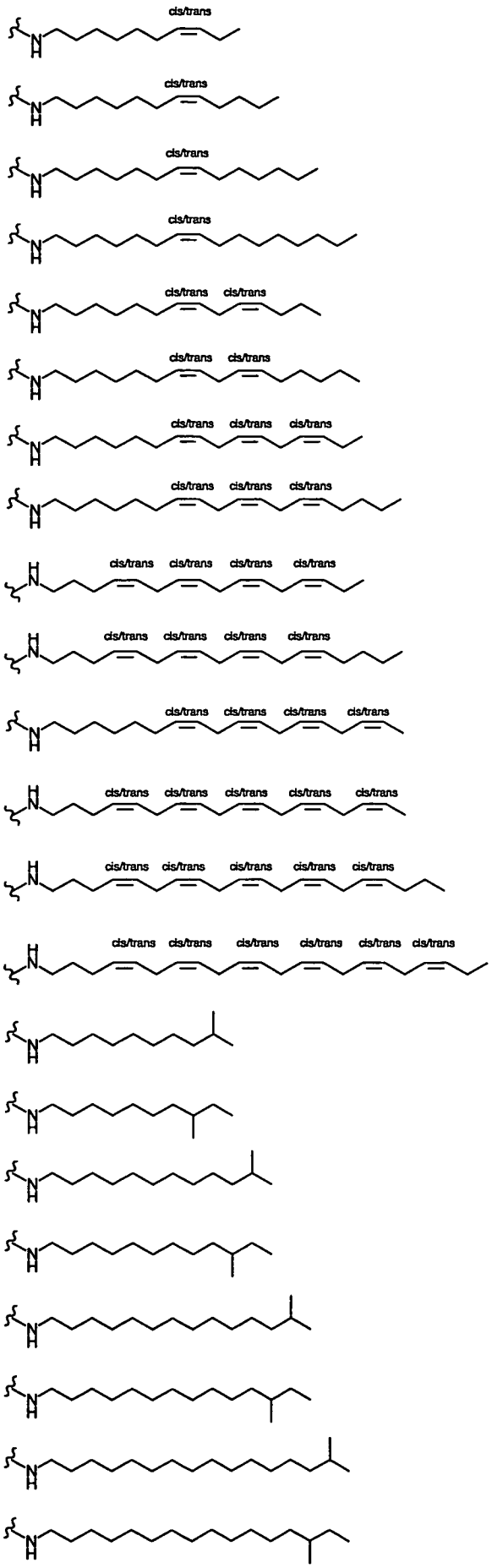
iv. an optionally substituted C9-C15 aminoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

v. an optionally substituted C16-C22 aminoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

vi. wherein 9, 11, 13, and 15 C-atoms are preferred;

vii. a group listed in the figures below:

viii.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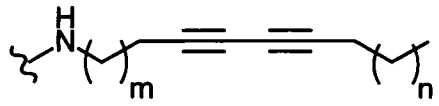


where m=0-6, and preferably m=6

n=0-11, preferably n=8, 10, or 11

or

ix. primary amides (to give acylurea) such as methyl-, ethyl-, propyl-, isopropyl-, butyl-, pentyl-, hexyl-, heptyl-, octyl-, nonyl-, decyl-, undecyl-, dodecyl-, tridecyl-, tetradecyl-, pentadecyl-, hexadecyl-, heptadecyl-, nonadecyl-, eicosyl-, heneicosyl-, docosyl-, tricosyl-, or tetracosyl-amide;

x. preferably, decyl-, dodecyl-, tetradecyl, hexadecyl-amide;

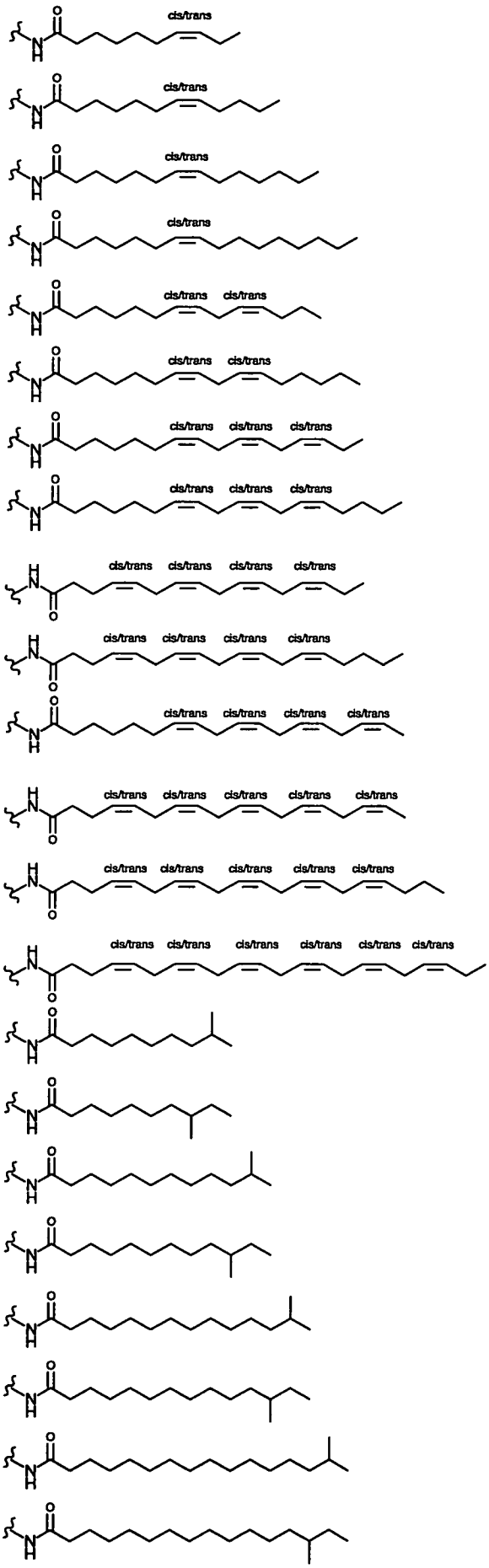
xi. an optionally substituted C1-C8 amidoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

xii. an optionally substituted C9-C15 amidoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

xiii. an optionally substituted C16-C22 amidoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

xiv. wherein 9, 11, 13, and 15 C-atoms are preferred;

xv. a group listed in the figures below: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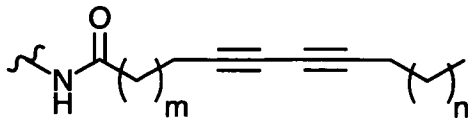


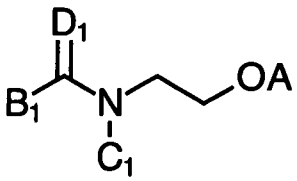
where m=0-5, and preferably m=5;

n=0-11, preferably n=8, 10, or 11;

"$D_1$" and "$D_2$" can be the same or can be different and are either O (oxygen) or S (sulfur),

wherein said lipid preferably may be fully or partially deuterated, or radioactively labeled; and wherein "A" is selected from: a proton (H), a phosphatic acid or a phosphate ester substituted group such as phosphocholine, phosphoethanolamine, phosphoglycerol, phosphoserine, phosphoinositol, phosphoinositol 4,5-bisphosphate, a phosphate ester substituted sugar, a phosphate ester substituted polyethyleneglycol, a phosphate ester substituted electrophile, such as an activated ester including N-hydroxysuccinimic ester, or an acid chloride or an halogenide, a phosphate ester substituted nucleophile such as a thiol or an amine, a phosphate ester substituted fluorescent group such as fluoresceine, a phosphate ester substituted radioactively labeled group, a phosphate ester substituted alkyne and a phosphate substituted azide; and wherein "C1" and "C2" may be H or a methyl.

In another preferred embodiment of the invention the lipids are defined according to formula Ic:



Formula Ic

and wherein

i. "$B_1$" is selected from:

ii. H;

iii. alkyl-, such as methyl-, ethyl-, propyl-, isopropyl-, butyl-, pentyl-, hexyl-, heptyl-, octyl-, nonyl-, decyl-, undecyl-, dodecyl-, tridecyl-, tetradecyl, pentadecyl-, hexadecyl-, heptadecyl-, nonadecyl-, eicosyl-, heneicosyl-, docosyl-, tricosyl-, or tetracosyl-;

iv. preferably, undecyl-, tridecyl-, pentadecyl-, heptadecyl-;

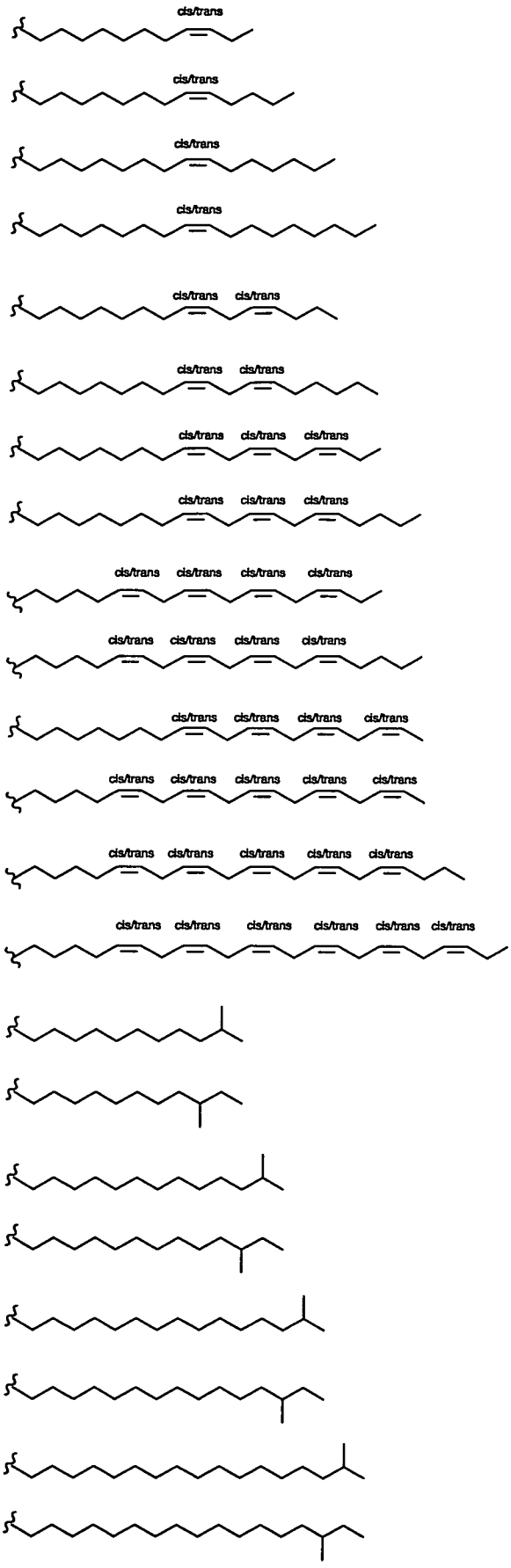
v. an optionally substituted $C_1$-$C_{10}$ alkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

vi. an optionally substituted $C_{11}$-$C_{17}$ alkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

vii. an optionally substituted $C_{18}$-$C_{24}$ alkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

viii. wherein 11, 13, 15, and 17 C-atoms are preferred;

ix. a group listed in the figures below: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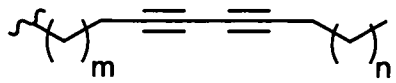
or




where m and n can be different or the same and

m = 0-7, preferably m=7;

n=0-11, preferably n=8, 10, or 11;

or is selected from

x. primary amines such as methyl-, ethyl-, propyl-, isopropyl-, butyl-, pentyl-, hexyl-, heptyl-, octyl-, nonyl-, decyl-, undecyl-, dodecyl-, tridecyl-, tetradecyl-, pentadecyl-, hexadecyl-, heptadecyl-, nonadecyl-, eicosyl-, heneicosyl-, docosyl-, tricosyl-, or tetracosyl-amine;

xi. preferably, decyl-, dodecyl-, tetradecyl, hexadecyl-amine;

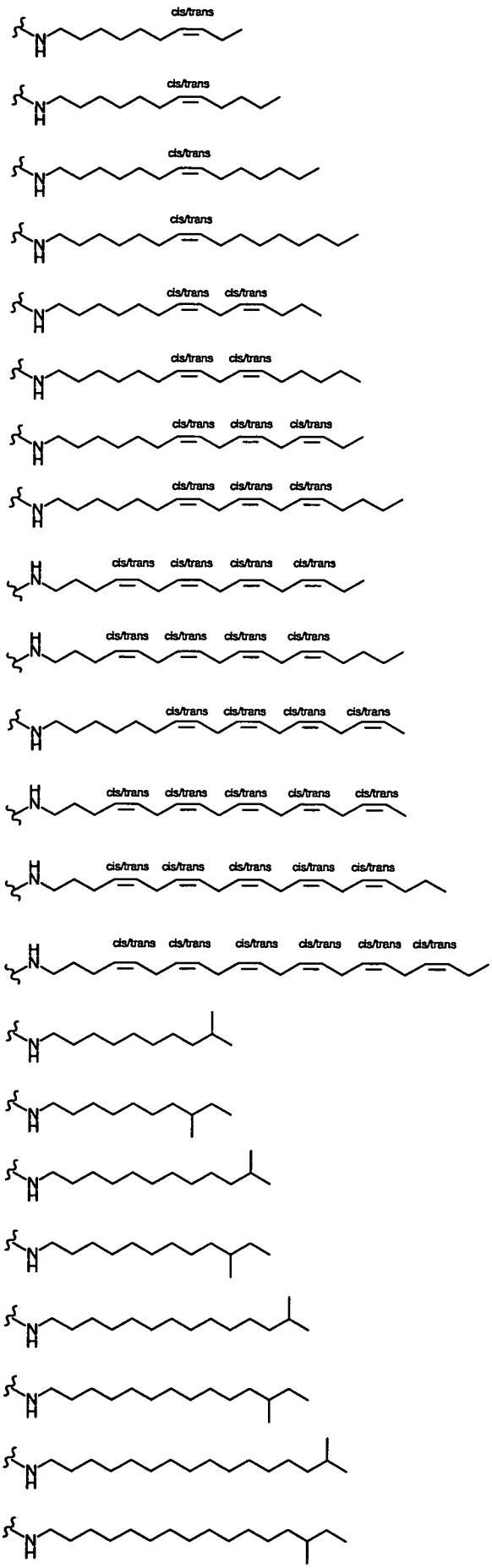
xii. an optionally substituted C1-C8 aminoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

xiii. an optionally substituted C9-C15 aminoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

xiv. an optionally substituted C16-C22 aminoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

xv. wherein 9, 11, 13, and 15 C-atoms are preferred;

xvi. a group listed in the figures below: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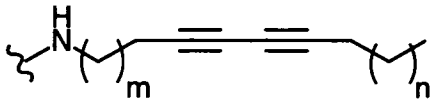


where m=0-6, and preferably m=6;

n=0-11, and preferably n=8, 10, or 11;

or

xvii. primary amides (to give acylureas) such as methyl-, ethyl-, propyl-, isopropyl-, butyl-, pentyl-, hexyl-, heptyl-, octyl-, nonyl-, decyl-, undecyl-, dodecyl-, tridecyl-, tetradecyl-, pentadecyl-, hexadecyl-, heptadecyl-, nonadecyl-, eicosyl-, heneicosyl-, docosyl-, tricosyl-, or tetracosyl-amide;

xviii. preferably, decyl-, dodecyl-, tetradecyl, hexadecyl-amide;

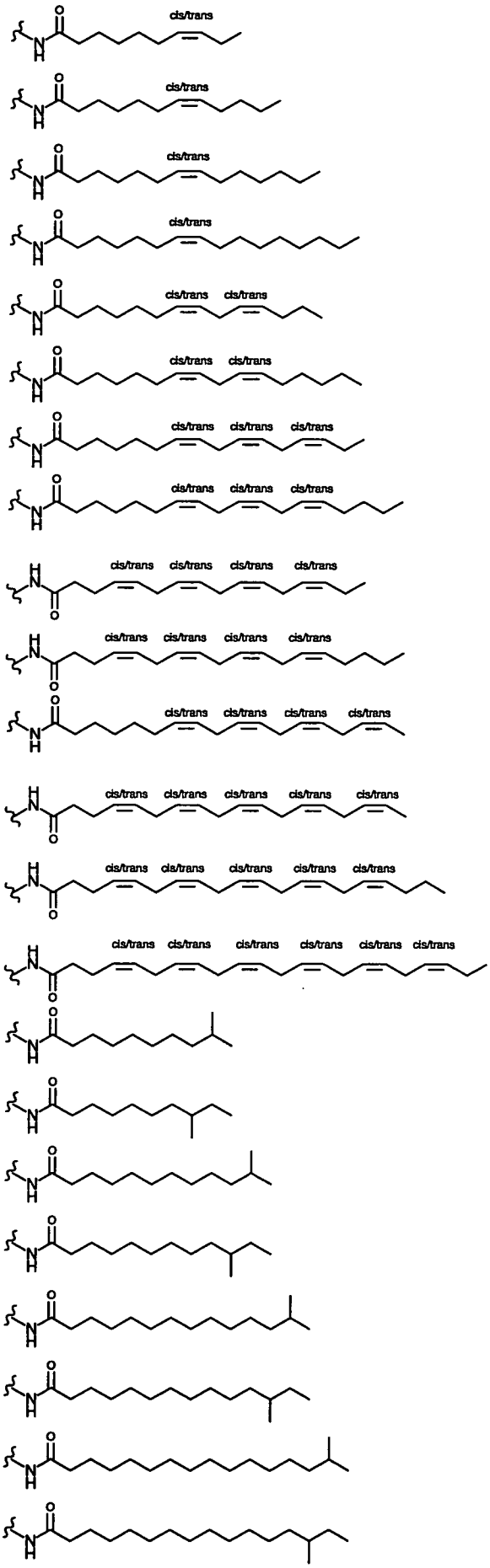
xix. an optionally substituted C1-C8 amidoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

xx. an optionally substituted C9-C15 amidoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

xxi. an optionally substituted C16-C22 amidoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

xxii. wherein 9, 11, 13, and 15 C-atoms are preferred;

xxiii. a group listed in the figures below: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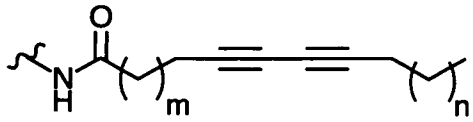
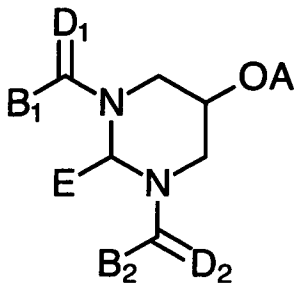


where m=0-5, and preferably m=5;

n=0-11, preferably n=8, 10, or 11;

"$D_1$" is either O (oxygen) or S (sulfur),
wherein said lipid preferably may be fully or partially deuterated, or radioactively labeled; and wherein "A" is selected from: a proton (H), a phosphatic acid or a phosphate ester substituted group such as phosphocholine, phosphoethanolamine, phosphoglycerol, phosphoserine, phosphoinositol, phosphoinositol 4,5-bisphosphate, a phosphate ester substituted sugar, a phosphate ester substituted polyethyleneglycol, a phosphate ester substituted electrophile, such as an activated ester including N-hydroxysuccinimic ester, or an acid chloride or an halogenide, a phosphate ester substituted nucleophile such as a thiol or an amine, a phosphate ester substituted fluorescent group such as fluoresceine, a phosphate ester substituted radioactively labeled group, a phosphate ester substituted alkyne and a phosphate substituted azide; and wherein "C1" may be H or a methyl.

In another preferred embodiment of the invention the lipids are defined according to formula Id:



Formula Id

wherein

i. "$B_1$" is equal or different from "$B_2$" or "E", and "$B_1$", "$B_2$" and "E" are selected from:

ii. H;

iii. alkyl-, such as methyl-, ethyl-, propyl-, isopropyl-, butyl-, pentyl-, hexyl-, heptyl-, octyl-, nonyl-, decyl-, undecyl-, dodecyl-, tridecyl-, tetradecyl-, pentadecyl-, hexadecyl-, heptadecyl-, nonadecyl-, eicosyl-, heneicosyl-, docosyl-, tricosyl-, or tetracosyl-;

iv. preferably, undecyl-, tridecyl-, pentadecyl-, heptadecyl-;

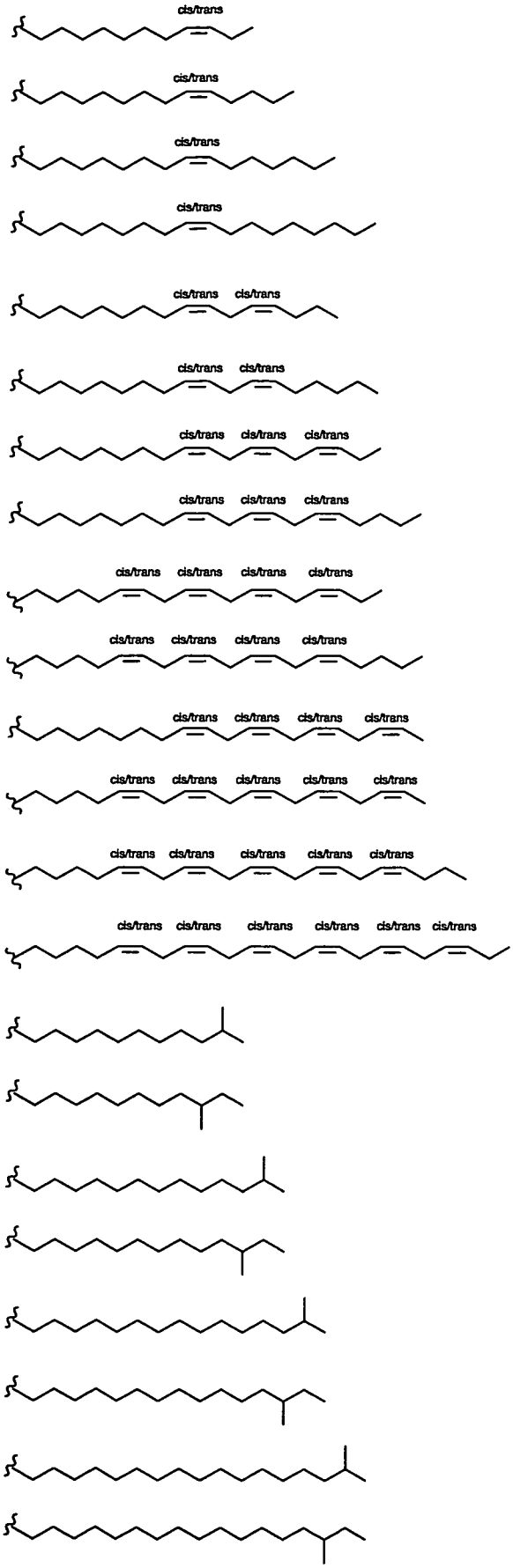
v. an optionally substituted $C_1$-$C_{10}$ alkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

vi. an optionally substituted $C_{11}$-$C_{17}$ alkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

vii. an optionally substituted $C_{18}$-$C_{24}$ alkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

viii. wherein 11, 13, 15, and 17 C-atoms are preferred;

ix. a group listed in the figures below: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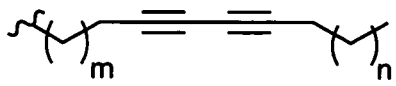



where m and n can be different or the same and

m = 0-7, preferably m=7;

n=0-11; preferably n=8, 10, or 11;

or "$B_1$" and "$B_2$" are equal or the same and are selected from:

i. primary amines such as methyl-, ethyl-, propyl-, isopropyl-, butyl-, pentyl-, hexyl-, heptyl-, octyl-, nonyl-, decyl-, undecyl-, dodecyl-, tridecyl-, tetradecyl-, pentadecyl-, hexadecyl-, heptadecyl-, nonadecyl-, eicosyl-, heneicosyl-, docosyl-, tricosyl-, or tetracosyl-amine;

ii. preferably, decyl-, dodecyl-, tetradecyl, hexadecyl-amine;

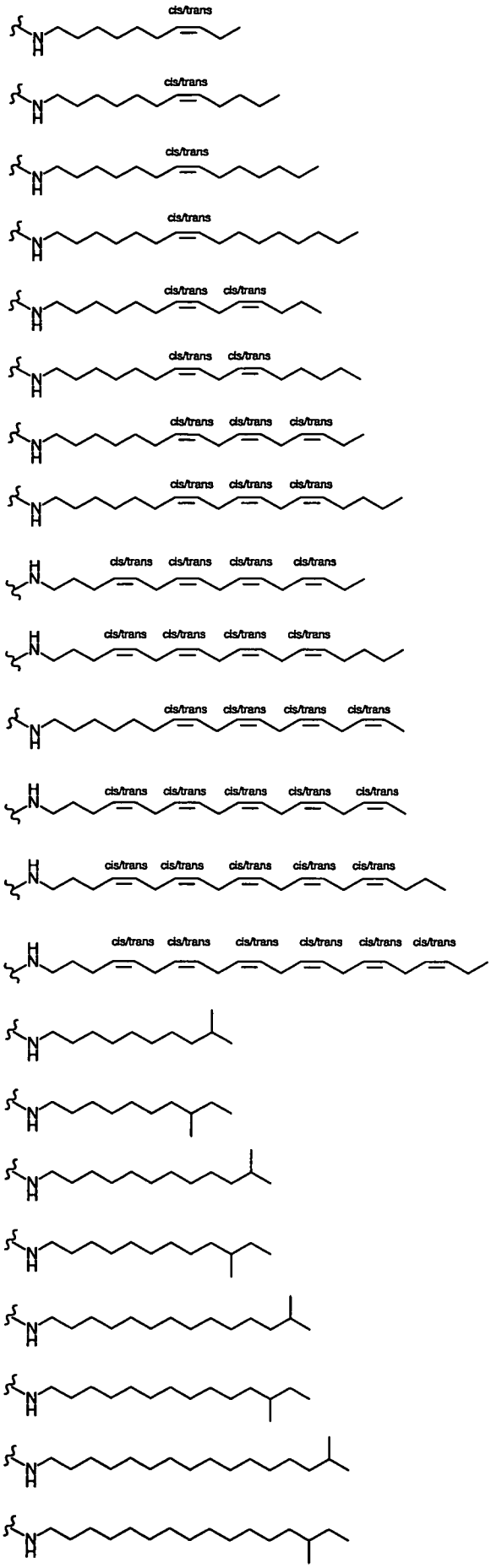
iii. an optionally substituted C1-C8 aminoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

iv. an optionally substituted C9-C15 aminoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

v. an optionally substituted C16-C22 aminoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

vi. wherein 9, 11, 13, and 15 C-atoms are preferred;

vii. a group listed in the figures below: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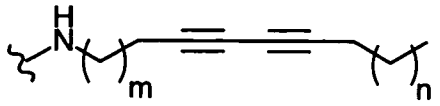


where m=0-6, and preferably m=6;

n=0-11, preferably n=8, 10, or 11;

or "$B_1$" and "$B_2$" are the same or different and are selected from:

viii. primary amides (to give acylureas) such as methyl-, ethyl-, propyl-, isopropyl-, butyl-, pentyl-, hexyl-, heptyl-, octyl-, nonyl-, decyl-, undecyl-, dodecyl-, tridecyl-, tetradecyl-, pentadecyl-, hexadecyl-, heptadecyl-, nonadecyl-, eicosyl-, heneicosyl-, docosyl-, tricosyl-, or tetracosyl-amide;

ix. preferably, decyl,- dodecyl-, tetradecyl, hexadecyl-amide;

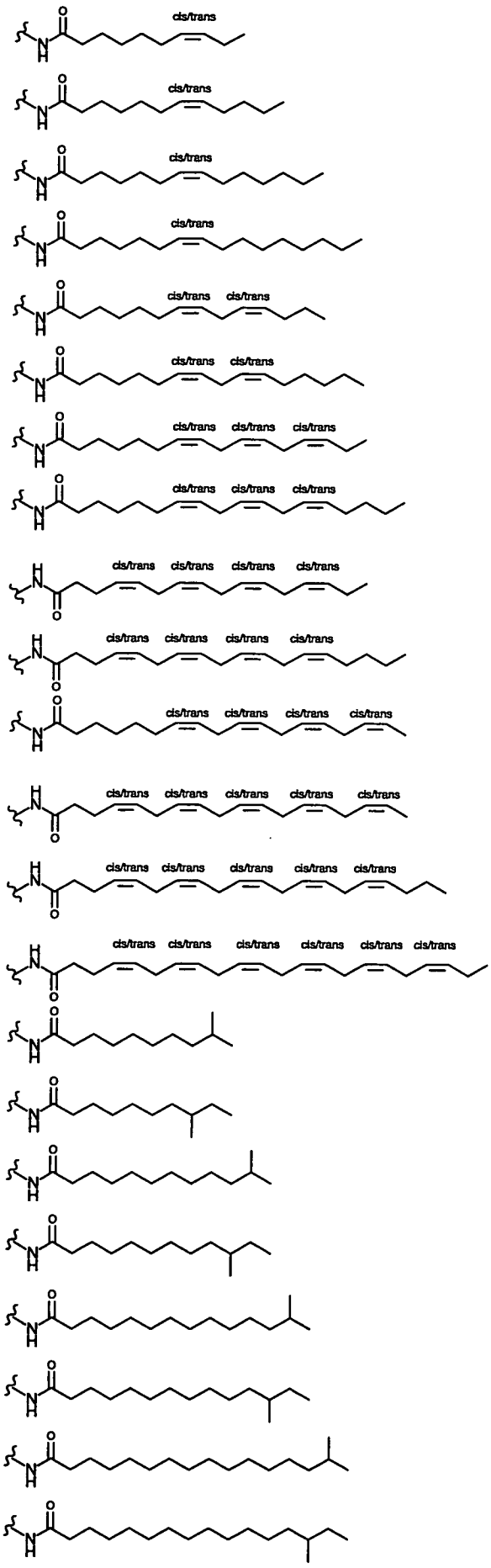
x. an optionally substituted C1-C8 amidoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

xi. an optionally substituted C9-C15 amidoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

xii. an optionally substituted C16-C22 amidoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

xiii. wherein 9, 11, 13, and 15 C-atoms are preferred;

xiv. a group listed in the figures below: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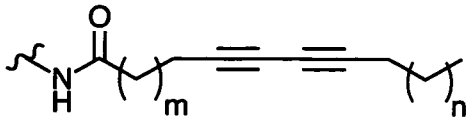


where m=0-5, preferably m=5;

n=0-11, preferably n=8, 10, or 11;

"$D_1$" and "$D_2$" can be the same or can be different and are either O (oxygen) or S (sulfur),

wherein said lipid preferably may be fully or partially deuterated, or radioactively labeled; and wherein "A" is selected from: a proton (H), a phosphatic acid or a phosphate ester substituted group such as phosphocholine, phosphoethanolamine, phosphoglycerol, phosphoserine, phosphoinositol, phosphoinositol 4,5-bisphosphate, a phosphate ester substituted sugar, a phosphate ester substituted polyethyleneglycol, a phosphate ester substituted electrophile, such as an activated ester including N-hydroxysuccinimic ester, or an acid chloride or an halogenide, a phosphate ester substituted nucleophile such as a thiol or an amine, a phosphate ester substituted fluorescent group such as fluoresceine, a phosphate ester substituted radioactively labeled group, a phosphate ester substituted alkyne and a phosphate substituted azide.

In the context of the invention "alkyl" is to be understood as any chain of C-atoms being linear or branched, "optionally substituted" is to be understood as having no substitutions or being substituted with residues being compatible with the remaining molecule without interfering with its structure and providing optional functionality in the context of the invention.

In further preferred embodiments the non-natural phospholipids may be defined to have the form Xn-HG-Ym wherein HG (head group) may be selected from the group consisting of phosphatidylethanolamine (PE), phosphatidylcholine (PC), phosphatidic acid (PA) and phosphatidylglycerol (PG) and X, Y are saturated or/and unsaturated aliphatic chains of 10, 12, 14, 16 and 18 carbons, wherein n, m may comprise an ester (es), amide (ad), amine (an), and ether (et) linkers.

Throughout the description of the invention various chemical residues or compounds may be abbreviated. Examples of such abbreviation are "HG" for "head group" which may include "phosphoethanolamine" denoted as "PE", "phosphocholine" as "PC", "phosphatidic acid" as "PA", "polyethylene glycol" as "PEG", "phosphoglycerol" as "PG", "EYPC" as "egg yolk phosphocholine". Furthermore "ester" may be denoted "es", "amide" as "ad", "amine" as "an", and "ether" as "et".

The term acylurea is to be understood as generally known by the skilled person in the field of the invention and is a urea moiety containing an additional carbonyl group alpha to the amine.

Lipids according to the invention are not restricted to 1,3- or 1,2- or 2,3-phospholipids and comprise non-phospholipids according to any of the formulae Ia, Ib, Ic and Id as defined above. Lipids represented by any of these formulae can be used in individual form, as mixtures of lipids covered by either of these formulae or as a combination of one or several compounds originating from either of these formulae with one another.

Advantageous compounds are Pad-PC-Pad and Sad-PC-Sad which have been shown to exhibit the capacity to form advantageous and unexpected 3-dimensional structures. A particularly preferred embodiment comprises or consists of a 50:50 mixture of these compounds. In a more preferred embodiment the mixture Pad-PC-Pad to Sad-PC-Sad can vary from 10:90 to 90:10 ratio. Sad-PC-Sad and Pad-PC-Pad can e.g. be combined with any of the other compounds of the invention or described herein.

The skilled person will adapt the particular compounds and compounds mixtures of the invention with regard to their combination, ratios, etc. depending on the particular need of the application. He thus will easily find the best suitable mixtures and the specific ratios, way of mixing etc. for the particular application and use by way of simple experimentation as described herein.

These lipids can be combined with each other in any useful manner including but not restricted with regard to the number of compounds, their ratios of mixtures etc.

In another embodiment the lipids according to the invention can also be combined with any natural lipid as described below.

The natural lipid may be any known natural lipid useful in the invention. Preferably the natural lipid chosen for the composition according to the invention is selected from the group consisting of egg yolk phosphatidylcholine (EYPC), a phosphatidylethanolamine (PE), a phosphatidylcholine (PC), a phosphatic acid (PA), a phosphatidylglycerol (PG), preferably 1,2-dioleoyl-sn-glycero-3-phosphocholine (DOPC), 1-palmitoyl-2-oleoyl-*sn*-glycero-3-phosphocholine (POPC), 1,2-phosphatidylcholine, 1,2-dipalmitoyl-*sn*-glycero-3-phosphocholine (DPPC), 1,2-dilauroyl-*sn*-glycero-3-phosphocholine (DLPC), 1,2-dimyristoyl-*sn*-glycero-3-phosphocholine (DMPC), 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), *N*-palmitoylsphingomyelin, miltefosine.

The composition of the invention may comprise a synthetic lipid selected from any synthetic lipid known in the art. It will be appreciated by the skilled person that preferably the synthetic lipid is chosen according to the particular requirements of the further application and use of the composition according to the invention. Particularly preferred are the synthetic lipids and the phospholipids described above. In particular the synthetic lipids and phospholipids according to any of formula Ia, Ib, Ic and Id are preferred.

In a preferred embodiment the lipids may be modified and in particular double bonds may be replaced by methylation. The lipids may be bolaamphiphile lipids and they may contain iso and anteiso chains. Examples of such modified lipids can be found in archaebacteria. Examples of such lipids are described in Zhang Y.M. and Rock C.O., Nature Vol. 6, March 2008, p. 222 – 233 which disclosure is herewith incorporated by reference.

The composition may contain any useful number of compounds as described above and also the ratios of single compounds and compound groups may vary. The ratios can be modified and adapted according to the particular application of the composition of the invention. In a preferred embodiment the first and second

compounds are present in a ratio of from 99.9 : 0.1 to 1 : 99 mol-%, preferably from 90 : 10 to 40 : 60 mol-%, more preferably from 70 : 30 to 50 : 50 mol-%, even more preferably wherein the first compound is present in either 50 mol-%, 60 mol-%, 70 mol-%, 75 mol-%, 80 mol-%, 85 mol-%, 90 mol-%, 95 mol-%, or 98 mol-%.

Other compositions of the invention according to any of formulae Ia, Ib, Ic and Id may comprise natural phospholipids (e.g. EYPC, DOPC, POPC, DPPC, sphingomyelin) with cholesterol, miltefosine and octadecanol in various concentrations up to 50 mol%, preferably 10 – 40 mol%, 20 – 30 mol%, or 30 – 50 mol%.

The skilled person will appreciate that various combinations of lipids according to any of the formulae Ia, Ib, Ic or/and Id may be combined as described above or in an advantageous manner in order to adapt to the requirements of the desired medical or non-medical application and use.

One achievement of the inventors is to a great extent that they found that the synthetic phospholipids, and in another embodiment the lipids of the invention in combination with natural lipids and eventually additional compounds can be tailored to form special 3-dimensional structures such as faceted vesicles, sheets, and tubular structures. These structures can be applied and used advantageously in various medical and non-medical uses.

The compositions according to invention may further comprise an active compound or selected compound. In the context of the invention the term "active compound" is preferably used for compounds which are applied in a medical context and preferably relate to drugs or any compounds which are used for the purpose to achieve an effect in a system, e.g. an animal or human body.

This active or selected compound may be chosen from any known class of chemical compounds and have different properties. It may have pharmaceutical, diagnostic, biomarker or other properties as may be required for the particular application of the composition of the invention. The active or selected compound may also be denoted as a "payload". In the context of the invention this payload will be incorporated by

known techniques with the composition of the invention and may be produced as vesicles, sheets or tubules. In particular applications of the invention the structure will applied to a particular target site where the payload is released, or the structure will be transported in a medium or a system like the circulation of a patient to a particular target site where the payload is released. The amount and timing of the release can be engineered according to the circumstances and the particular mixture of chemical compounds in the composition to arrive at a desired release profile.

In a further preferred embodiment the active compound may exert its effect whilst in situ in or on the structure.

In a further preferred embodiment the active compound is selected from the group consisting of anabolic agents, antacids, anti-asthmatic agents, anti-cholesterolemic and anti-lipid agents, anti-coagulants, anti-convulsants, anti-diarrheals, anti-emetics, anti-infective agents including antibacterial, anitviral and antimicrobial agents, anti-inflammatory agents, anti-manic agents, antimetabolite agents, anti-nauseants, anti-neoplastic agents, anti-obesity agents, anti-pyretic and analgesic agents, anti-spasmodic agents, anti-thrombotic agents, anti-tussive agents, anti-uricemic agents, anti-anginal agents, antihistamines, appetite suppressants, biologicals, cerebral dilators, coronary dilators, bronchiodilators, cytotoxic agents, decongestants, diuretics, diagnostic agents, erythropoietic agents, expectorants, gastrointestinal sedatives, hyperglycemic agents, hypnotics, hypoglycemic agents, immunomodulating agents, ion exchange resins, laxatives, mineral supplements, mucolytic agents, neuromuscular drugs, peripheral vasodilators, psychotropics, sedatives, stimulants, thyroid and anti-thyroid agents, tissue growth agents, uterine relaxants, vitamins, or antigenic materials.

Other active compounds include androgen inhibitors, polysaccharides, growth factors, hormones, anti-angiogenesis factors, dextromethorphan, dextromethorphan hydrobromide, noscapine, carbetapentane citrate, chlophedianol hydrochloride, chlorpheniramine maleate, phenindamine tartrate, pyrilamine maleate, doxylamine succinate, phenyltoloxamine citrate, phenylephrine hydrochloride, phenylpropanolamine hydrochloride, pseudoephedrine hydrochloride, ephedrine, codeine phosphate, codeine sulfate, morphine, mineral supplements, cholestryramine,

N-acetylprocainamide, acetaminophen, acetylsalicylic acid, ibuprofen, phenyl propanolamine hydrochloride, caffeine, guaifenesin, aluminum hydroxide, magnesium hydroxide, peptides, polypeptides, proteins, amino acids, hormones, interferons, cytokines, and vaccines.

Representative drugs that can be used as active compounds in the compositions include, but are not limited to, peptide drugs, protein drugs, therapeutic antibodies, desensitizing materials, antigens, anti-infective agents such as antibiotics, antimicrobial agents, antiviral, antibacterial, antiparasitic, antifungal substances and combinations thereof, antiallergenics, androgenic steroids, decongestants, hypnotics, steroidal anti-inflammatory agents, anti-cholinergics, sympathomimetics, sedatives, miotics, psychic energizers, tranquilizers, vaccines, estrogens, progestational agents, humoral agents, prostaglandins, analgesics, antispasmodics, antimalarials, antihistamines, cardioactive agents, nonsteroidal anti-inflammatory agents, antiparkinsonian agents, antihypertensive agents, β-adrenergic blocking agents, nutritional agents, and the benzophenanthridine alkaloids. The agent can further be a substance capable of acting as a stimulant, sedative, hypnotic, analgesic, anticonvulsant, and the like.

Other active compounds include but are not limited to analgesics such as acetaminophen, acetylsalicylic acid, and the like; anesthetics such as lidocaine, xylocaine, and the like; anorexics such as dexadrine, phendimetrazine tartrate, and the like; antiarthritics such as methylprednisolone, ibuprofen, and the like; antiasthmatics such as terbutaline sulfate, theophylline, ephedrine, and the like; antibiotics such as sulfisoxazole, penicillin G, ampicillin, cephalosporins, amikacin, gentamicin, tetracyclines, chloramphenicol, erythromycin, clindamycin, isoniazid, rifampicin, and the like; antifungals such as amphotericin B, nystatin, ketoconazole, and the like; antivirals such as acyclovir, amantadine, and the like; anticancer agents such as cyclophosphamide, methotrexate, etretinate, and the like; anticoagulants such as heparin, warfarin, and the like; anticonvulsants such as phenytoin sodium, diazepam, and the like; antidepressants such as isocarboxazid, amoxapine, and the like; antihistamines such as diphenhydramine HCl, chlorpheniramine maleate, loratadine and the like; hormones such as insulin, progestins, estrogens, corticoids, glucocorticoids, androgens, and the like; tranquilizers such as thorazine, diazepam,

chlorpromazine HCl, reserpine, chlordiazepoxide HCl, and the like; antispasmodics such as belladonna alkaloids, dicyclomine hydrochloride, and the like; anti-psychotics such as haloperidol, risperidone, and the like; vitamins and minerals such as essential amino acids, calcium, iron, potassium, zinc, vitamin $B_{12}$, and the like; cardiovascular agents such as prazosin HCl, nitroglycerin, propranolol HCl, hydralazine HCl, pancrelipase, succinic acid dehydrogenase, and the like; peptides and proteins such as LHRH, somatostatin, calcitonin, growth hormone, glucagon-like peptides, growth hormone releasing factor, angiotensin, FSH, EGF, bone morphogenic protein (BMP), erythropoeitin (EPO), interferon, interleukin, collagen, fibrinogen, insulin, Factor VIII, Factor IX, Enbrel®, Rituxan®, Herceptin®, alpha-glucosidase, Cerazyme/Ceredose®, vasopressin, ACTH, human serum albumin, gamma globulin, structural proteins, blood product proteins, complex proteins, enzymes, antibodies, monoclonal antibodies, and the like; prostaglandins; nucleic acids; carbohydrates; fats; narcotics such as morphine, codeine, and the like, psychotherapeutics; anti-malarials, L-dopa, diuretics such as furosemide, spironolactone, and the like; antiulcer drugs such as ranitidine HCl, cimetidine HCl, and the like.

The active compound can also be an immunomodulator, including, for example, cytokines, interleukins, interferon, colony stimulating factor, tumor necrosis factor, and the like; allergens such as cat dander, birch pollen, house dust mite, grass pollen, and the like; antigens of bacterial organisms such as *Streptococcus pneumoniae, Haemophilus influenzae, Staphylococcus aureus, Streptococcus pyrogenes, Corynebacterium diphteriae, Listeria monocytogenes, Bacillus anthracis, Clostridium tetani, Clostridium botulinum, Clostridium perfringens, Neisseria meningitides, Neisseria gonorrhoeae, Streptococcus mutans, Pseudomonas aeruginosa, Salmonella typhi, Haemophilus parainfluenzae, Bordetella pertussis, Francisella tularensis, Yersinia pestis, Vibrio cholerae, Legionella pneumophila, Mycobacterium tuberculosis, Mycobacterium leprae, Treponema pallidum, Leptspirosis interrogans, Borrelia burgdorferi, Campylobacter jejuni,* and the like; antigens of such viruses as smallpox, influenza A and B, respiratory syncytial, parainfluenza, measles, HIV, SARS, varicella-zoster, herpes simplex 1 and 2, cytomegalovirus, Epstein-Barr, rotavirus, rhinovirus, adenovirus, papillomavirus, poliovirus, mumps, rabies, rubella, coxsackieviruses, equine encephalitis, Japanese encephalitis, yellow fever, Rift Valley fever, lymphocytic choriomeningitis, hepatitis B, and the like; antigens of such

fungal, protozoan, and parasitic organisms such as *Cryptococcus neoformans, Histoplasma capsulatum, Candida albicans, Candida tropicalis, Nocardia asteroids, Rickettsia ricketsii, Rickettsia typhi, Mycoplasma pneumoniae, Chlamyda psittaci, Chlamydia trachomatis, Plasmodium falciparum, Trypanasoma brucei, Entamoeba histolytica, Toxoplasma gondii, Trichomonas vaginalis, Schistosoma mansoni,* and the like. These antigens may be in the form of whole killed, or attenuated, organisms, peptides, proteins, glycoproteins, carbohydrates, or combinations thereof.

In a further specific aspect, the active compound comprises an antibiotic. The antibiotic can be, for example, one or more of Amikacin, Gentamicin, Kanamycin, Neomycin, Netilmicin, Streptomycin, Tobramycin, Paromomycin, Ansamycins, Geldanamycin, Herbimycin, Carbacephem, Loracarbef, Carbapenems, Ertapenem, Doripenem, Imipenem/Cilastatin, Meropenem, Cephalosporins (First generation), Cefadroxil, Cefazolin, Cefalotin or Cefalothin, Cefalexin, Cephalosporins (Second generation), Cefaclor, Cefamandole, Cefoxitin, Cefprozil, Cefuroxime, Cephalosporins (Third generation), Cefixime, Cefdinir, Cefditoren, Cefoperazone, Cefotaxime, Cefpodoxime, Ceftazidime, Ceftibuten, Ceftizoxime, Ceftriaxone, Cephalosporins (Fourth generation), Cefepime, Cephalosporins (Fifth generation), Ceftobiprole, Glycopeptides, Teicoplanin, Vancomycin, Macrolides, Azithromycin, Clarithromycin, Dirithromycin, Erythromycin, Roxithromycin, Troleandomycin, Telithromycin, Spectinomycin, Monobactams, Aztreonam, Penicillins, Amoxicillin, Ampicillin, Azlocillin, Carbenicillin, Cloxacillin, Dicloxacillin, Flucloxacillin, Mezlocillin, Meticillin, Nafcillin, Oxacillin, Penicillin, Piperacillin, Ticarcillin, Polypeptides, Bacitracin, Colistin, Polymyxin B, Quinolones, Ciprofloxacin, Enoxacin, Gatifloxacin, Levofloxacin, Lomefloxacin, Moxifloxacin, Norfloxacin, Ofloxacin, Trovafloxacin, Sulfonamides, Mafenide, Prontosil (archaic), Sulfacetamide, Sulfamethizole, Sulfanilimide (archaic), Sulfasalazine, Sulfisoxazole, Trimethoprim, Trimethoprim-Sulfamethoxazole (Co-trimoxazole) (TMP-SMX), Tetracyclines, including Demeclocycline, Doxycycline, Minocycline, Oxytetracycline, Tetracycline, and others; Arsphenamine, Chloramphenicol, Clindamycin, Lincomycin, Ethambutol, Fosfomycin, Fusidic acid, Furazolidone, Isoniazid, Linezolid, Metronidazole, Mupirocin, Nitrofurantoin, Platensimycin, Pyrazinamide, Quinupristin/Dalfopristin, Rifampicin (Rifampin in U.S.), Tinidazole, Ropinerole, Ivermectin, Moxidectin, Afamelanotide, Cilengitide, or a combination

thereof. In one aspect, the bioactive agent can be a combination of Rifampicin (Rifampin in U.S.) and Minocycline.

The composition according to the invention preferably may be provided in the form of 3-dimensional structures wherein the structure is preferably composed of a monolayer, biilayer or multilayers, and/or a vesicle and/or a sheet and/or a tubule.

The 3-dimensional structures according to the invention may be designed in any useful size and amount. Preferably the structure has an average dimension of about 10 to 1000 nm, preferably of about 50 to 500 nm, more preferably of about 50 to 200 nm.

In a further aspect the invention related to a method of making a 1,3-diamidophospholipid wherein a phosphoethanolamine is alkylated under appropriate conditions, preferably with the use of dimethyl sulfoxide. Other methods of alkylation with alternative alkylating agents may be used such as alkylation with the corresponding alkylhalide, preferably methyliodide (Lu, X.; Bittman, R. The Journal of Organic Chemistry 2005, 70, 4746-4750)

The inventors thus could provide for a simple and economically advantageous method of making the compounds according to the invention.

In a further aspect the invention relates to a method of making a composition according to the invention as described above.

In another aspect the invention relates to a method of making 3-dimensional structures comprising a composition and preferably a payload as described above.

Another aspect of the invention relates to a pharmaceutical or cosmetic composition comprising a composition according to the invention as described above or a 3-dimensional structure as described above, and preferably further useful carriers or/and additives.

Yet another aspect of the invention is a composition according to the invention and the functional 3-dimensional structure according to the invention for use in a pharmaceutical or cosmetic application.

The pharmaceutical and cosmetic compositions of the invention will be prepared using known methods and useful auxiliary compounds as known in the art and applicable in the context of the invention.

Another aspect of the invention relates to a composition according to the invention or 3-dimensional structures according to the invention for use in the prophylaxis or treatment of a dermatological disorder or disease, or for use as cosmetic.

Alternatively, the invention relates to a method for the prophylaxis or treating a patient in need thereof by administering compositions or functional 3-dimensional structures according to the invention with an active compound as describe above to a patient in an effective dosage to a patient.

The treatment or prophylaxis may be for a dermatological disorder or disease, wound or lesion coverage, delivery of an active or antiseptic compound to a wound or tissue surface. In general the wound or lesion to be treated may be situated at a tissue surface or interface. The invention also covers systemic delivery. The method may be as well a cosmetic method wherein preferably the cosmetic method comprises topical applications.

The invention may be applied in a method of treatment or prophylaxis or use for treatment or prophylaxis in any disease or disorder wherein a local delivery of an active compound is advantageous. One advantage of the invention is that the dosage delivered to a patient may be reduced due to the use of the inventive compositions or 3-dimensional structures. Another or additional advantage that may be achieved by the invention is the reduction of undesired side effects due to the site specific or targeted delivery of the active compound.

One particular aspect of the invention is the provision of 3-dimensional structures or geometrical structures comprising also sheet like structures due to the selection and combination of one or more of the compounds of the invention.

Possible structures moreover comprise preferably flattened, faceted, platonic, or tubular and lengthy geometrical structures. These structures may advantageously be used as a delivery vehicle or to form a 3-dimensional scaffold. These structures may be used as such or in combination with other compounds or active compounds. Examples of such structures are depicted in Fig. 5.

The 3-dimensional structures according to the invention will exhibit different forms. The invention makes advantageously use thereof for the medical and non-medical applications and methods of the invention. The selection of the particular lipid according to the invention or a mixture thereof will result in particular structures which may be useful for particular applications.

In a preferred embodiment the use or method of treatment can be applied to a dermatological disease or disorder wherein the dermatological disease or disorder is preferably selected from the group consisting of acne, napkin dermatitis, atopic dermatitis, seborrhoeic dermatitis, psoriasis, warts, tinia pedis, seborrhoeic keratosis, hives, rosacea, dermatological viral infection and dermatological bacterial infection.

Another preferred application is the use of the compounds of the invention in wound or lesion healing, or wound or lesion dressing, preferably antiseptic coating, or wound, lesion, skin or tissue surface protection.

In another preferred embodiment the composition according to the invention can be used as complexation agent, preferably as delivery compound for a second compound, more preferably of ions, preferably Ag or Fe, preferably in a patient's circulation

Non-medical applications may comprise coating of a surface with preferably a sheet comprising the compounds or compound mixtures of the invention and more preferably another active compound or compound useful in surface coating or in uses for lubrication.

The compounds of the invention may be advantageous as food additives for purposes such as providing structural integrity to fragile or short-lived physical characteristics. An example is foaming of milk or milk like substances used in the food industry.

Also of use may be their application in the context of cleaning polluted areas or surfaces, through characteristics such as surfactant properties and large surface area, and by performance as efficient carriers of active molecules useful for pollution control such as detergents, enzymes, neutralizing agents, etc.
In a preferred embodiment the selected compound is selected from the group consisting of a medium, a small molecule, a protein, peptide, nucleic acid, nucleotide or an antibody.

In the use and methods according to the invention the selected compound is preferably released at a therapeutically effective amount.

The term "therapeutically effective amount" or "effective amount" of an active compound as understood in the context of the invention is meant as the amount released from the structures of the invention at the target site or in the vicinity of the target site and reaching the medical target producing the desired effect or response in the treatment or prophylaxis of the disease or disorder in question. It will be appreciated by the skilled person, that depending on the particular circumstances the amount loaded onto the 3-dimensional structure of the invention and the finally effective amount released to achieve a particular effect at the target site will vary significantly.

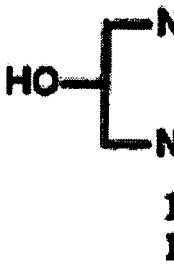
The "target site" as understood in the context of the invention is the area of the system or in the animal or human body whereto the active or selected compound is to be delivered.

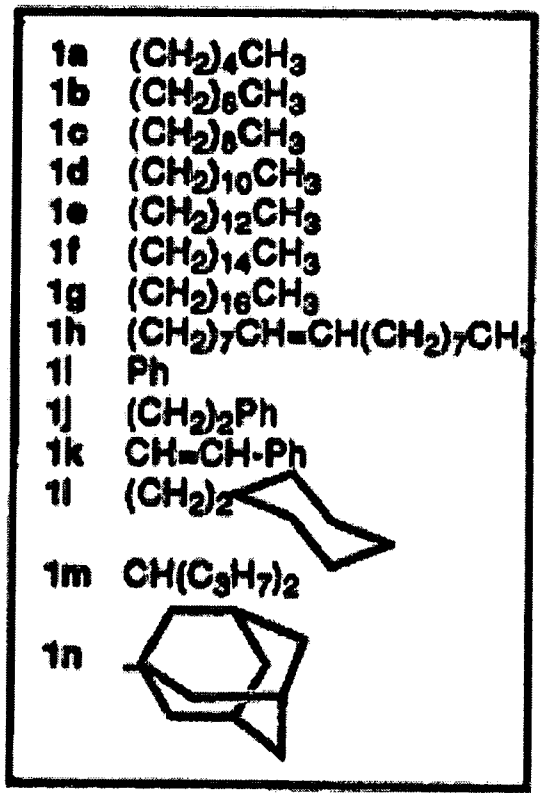
The following examples will further illustrate the invention without being understood as limiting or restricting the invention. The examples represent preferred embodiments of the invention or serve simply to explain and illustrate the mechanisms underlying the invention.

In a preferred embodiment, the following compounds cited in the below cited literature are disclaimed from the scope of the compounds as described above. The literature and compounds disclosed therein are:

Mergen, F.; Lambert, D. M.; Poupaert, J. H.; Bidaine, A.; Dumont, P. Chem. Phys Lipids 1991, 59, 267-272.

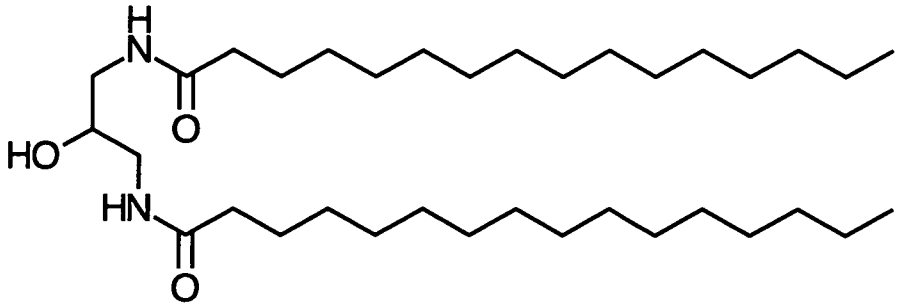
Compounds of the invention as above defined relating to A=H; several amide linear tails and double bonded tails are herewith disclaimed.



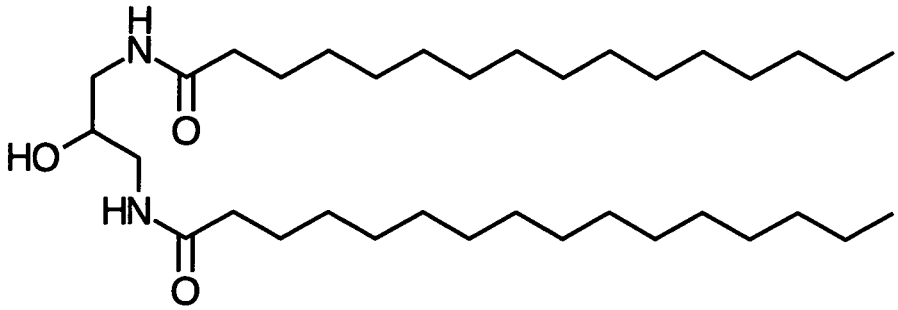




ElKhihel, L.; Loiseau, P. M.; Bourass, J.; Gayral, P.; Letourneux, Y. *Arzneim. Forsch/Drug. Res.* **1994**, *11*, 1259-1264.

Compounds of the invention as above defined relating to A=H and C1 and C2 =C15:

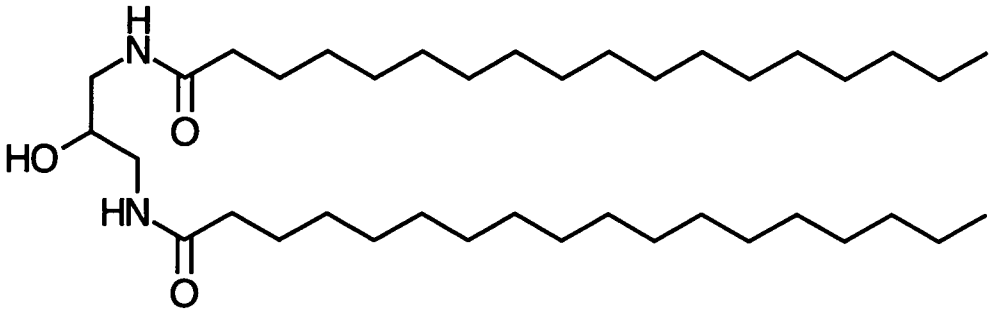


and in:
Morris, A. D.; Atassi, G.; Guilbaud, N.; Cordi, A. A. *Eur. J. Med. Chem.* **1997**, *32*, 343-349.

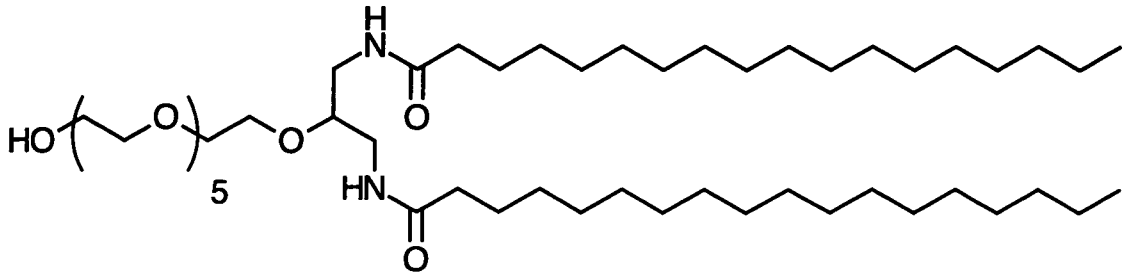


Compounds of the invention as above defined with C1=C2=17:

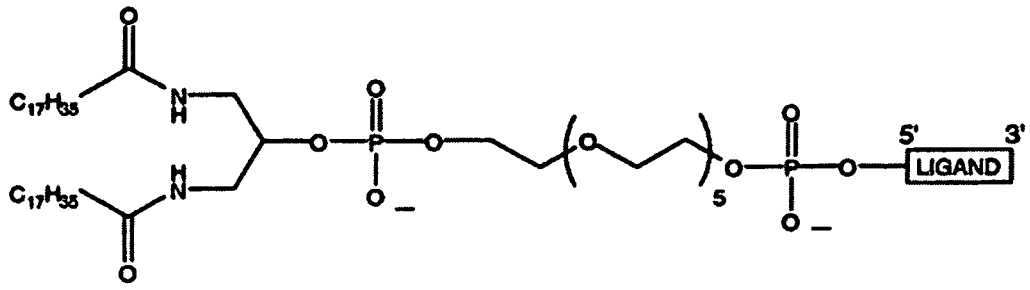
in US 6,168,778 B1



and with a PEG headgroup:

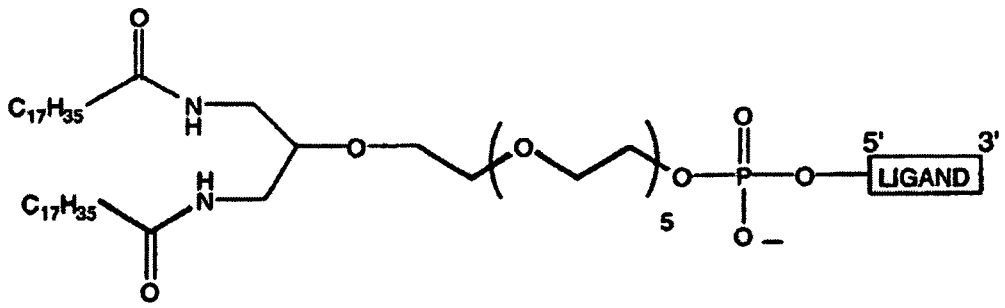


and other groups in the patent:



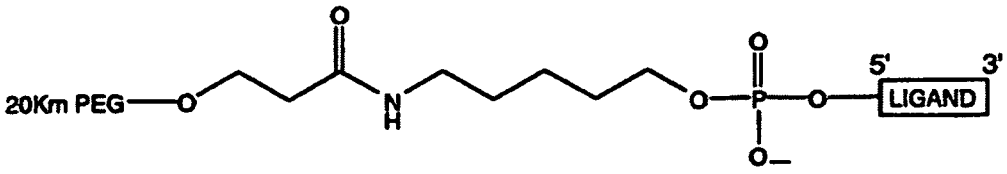

NX31838 Lipid-amide 1

Ligand Component =
fCmGmGrArAfUfCmAmGfUmGmAmAfUmGfCfUfUmAfUmAfCmAfUfCfCmG-3'3'-dT
(VEGF ligand) SEQ ID NO:6



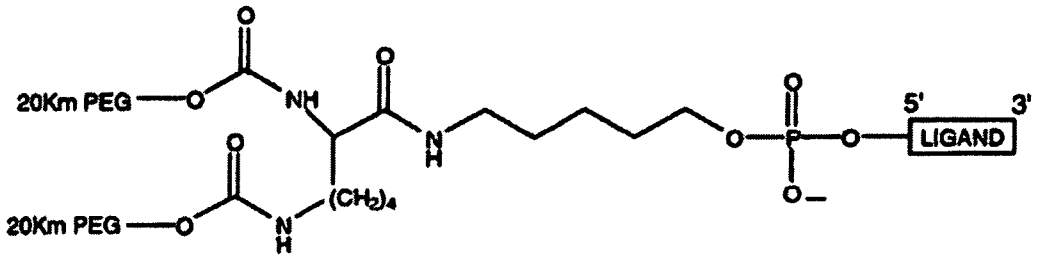

NX31838 Lipid-amide 2

Ligand Component =
fCmGmGrArAfUfCmAmGfUmGmAmAfUmGfCfUfUmAfUmAfCmAfUfCfCmG-3'3'-dT
(VEGF ligand) SEQ ID NO:7




**NX31838 20Km PEG**

**Ligand Component =**
**fCmGmGrArAfUfCmAmGfUmGmAmAfUmGfCfUfUmAfUmAfCmAfUfCfCmG-3'3'-dT**
**(VEGF ligand)** **SEQ ID NO:9**

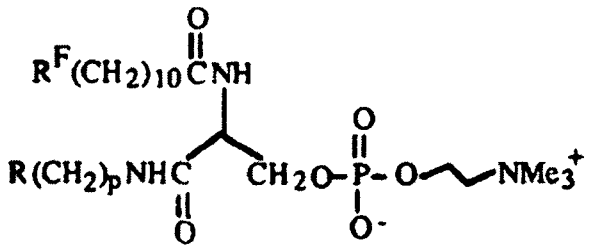



**NX31838 40K mPEG**

**Ligand Component =**
**fCmGmGrArAfUfCmAmGfUmGmAmAfUmGfCfUfUmAfUmAfCmAfUfCfCmG-3'3'-dT**
**(VEGF ligand)** **SEQ ID NO:8**

Clary, L.; Santaella, C.; Vierling, P. *Tetrahedron Lett.* **1995**, *51*, 13073-13088.

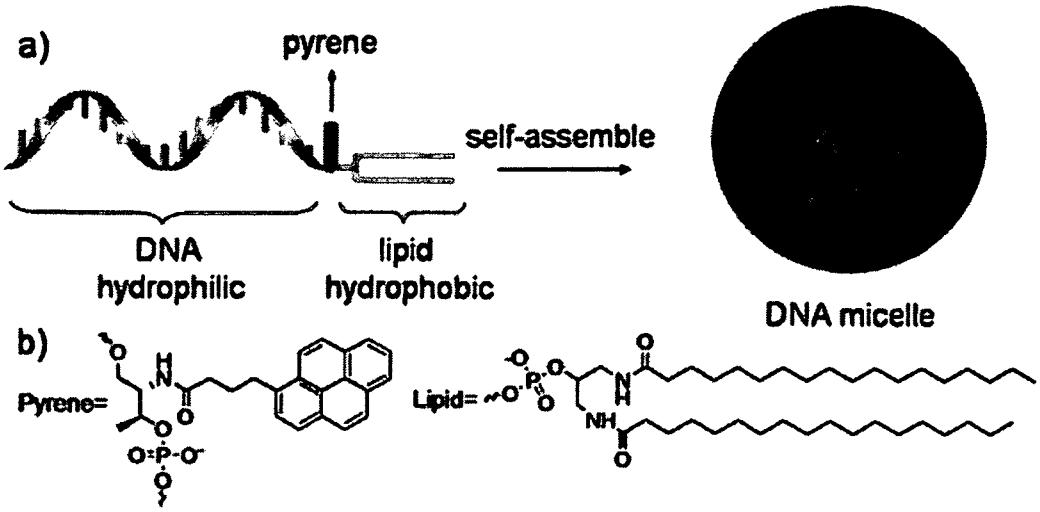
The phospholipids with one CH tail and one fluorinated CH tail:




**IIIa:** $p = 15, R = CH_3$ $R^F = C_6F_{13}$
**IIIb:** $p = 11, R = C_4F_9$ $R^F = C_4F_9$
**IIIc:** $p = 11, R = C_4F_9$ $R^F = C_6F_{13}$
**IIId:** $p = 11, R = C_6F_{13}$ $R^F = C_6F_{13}$

Liu, H.; Kang, H.; Wu, Y.; Sefan, K.; Tan, W. *Chem. Eur. J.* **2010**, *16*, 3791-3797.

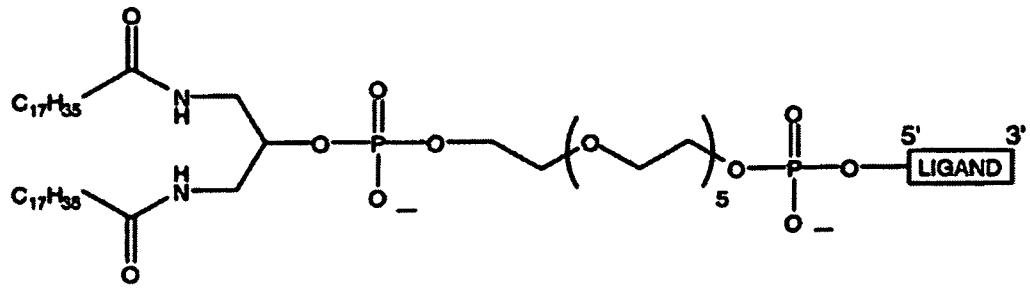
Phospholipids with one fluorescent head group and 1,3-diamide:




Compounds that are disclaimed from the scope of the application are also listed and depicted below:

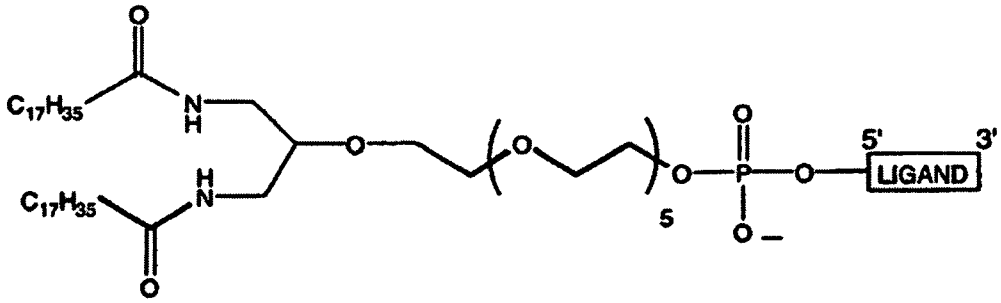
*N,N'*-(2-hydroxypropane-1,3-diyl)dihexanamide
*N,N'*-(2-hydroxypropane-1,3-diyl)dioctanamide
*N,N'*-(2-hydroxypropane-1,3-diyl)bis(decanamide)
*N,N'*-(2-hydroxypropane-1,3-diyl)didodecanamide
*N,N'*-(2-hydroxypropane-1,3-diyl)ditetradecanamide
*N,N'*-(2-hydroxypropane-1,3-diyl)dipalmitamide
*N,N'*-(2-hydroxypropane-1,3-diyl)distearamide
(*E or Z*)-*N,N'*-(2-hydroxypropane-1,3-diyl)dioleamide
*N,N'*-(2-hydroxypropane-1,3-diyl)dibenzamide
*N,N'*-(2-hydroxypropane-1,3-diyl)bis(3-phenylpropanamide)
(*2E or Z,2'E or Z*)-*N,N'*-(2-hydroxypropane-1,3-diyl)bis(3-phenylacrylamide)
*N,N'*-(2-hydroxypropane-1,3-diyl)bis(3-cyclohexylpropanamide)
*N,N'*-(2-hydroxypropane-1,3-diyl)bis(2-isopropyl-3-methylbutanamide)
(3*r*,3'*r*,5*r*,5'*r*,7*r*,7'*r*)-*N,N'*-(2-hydroxypropane-1,3-diyl)bis(adamantane-1-carboxamide)
*N,N'*-(2-hydroxypropane-1,3-diyl)dipalmitamide
*N,N'*-(2-hydroxypropane-1,3-diyl)dipalmitamide
*N,N'*-(2-hydroxypropane-1,3-diyl)distearamide

*N,N'*-(2-((17-hydroxy-3,6,9,12,15-pentaoxaheptadecyl)oxy)propane-1,3-diyl)distearamide



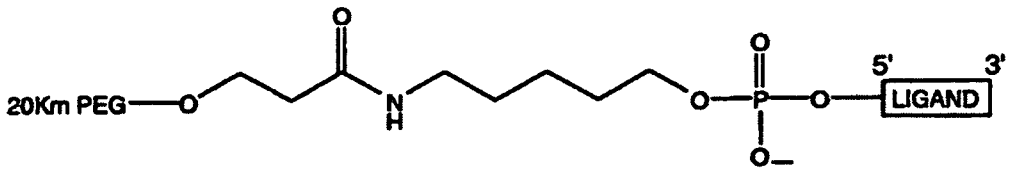

**NX31838 Lipid-amide 1**

**Ligand Component =**
**fCmGmGrArAfUfCmAmGfUmGmAmAfUmGfCfUfUmAfUmAfCmAfUfCfCmG-3'3'-dT**
**(VEGF ligand)** **SEQ ID NO:6**



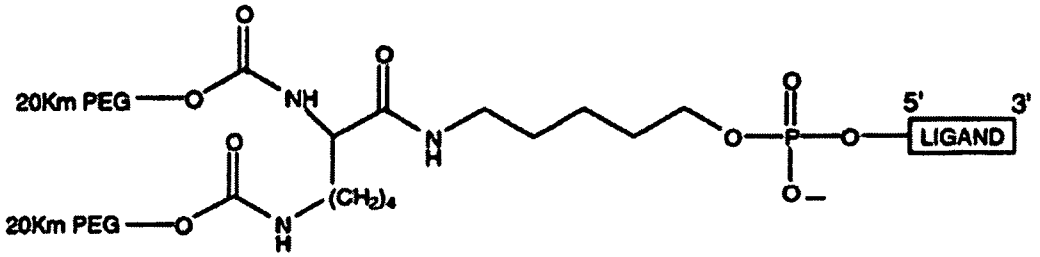

**NX31838 Lipid-amide 2**

**Ligand Component =**
**fCmGmGrArAfUfCmAmGfUmGmAmAfUmGfCfUfUmAfUmAfCmAfUfCfCmG-3'3'-dT**
**(VEGF ligand)** **SEQ ID NO:7**




**NX31838 20Km PEG**

**Ligand Component =**
**fCmGmGrArAfUfCmAmGfUmGmAmAfUmGfCfUfUmAfUmAfCmAfUfCfCmG-3'3'-dT**
**(VEGF ligand)** **SEQ ID NO:9**




**NX31838 40K mPEG**

**Ligand Component =**
**fCmGmGrArAfUfCmAmGfUmGmAmAfUmGfCfUfUmAfUmAfCmAfUfCfCmG-3'3'-dT**
**(VEGF ligand)** **SEQ ID NO:8**

3-(hexadecylamino)-3-oxo-2-(12,12,13,13,14,14,15,15,16,16,17,17,17-tridecafluoroheptadecanamido)propyl (2-(trimethylammonio)ethyl) phosphate

2-(12,12,13,13,14,14,15,15,15-nonafluoropentadecanamido)-3-((12,12,13,13,14,14,15,15,15-nonafluoropentadecyl)amino)-3-oxopropyl (2-(trimethylammonio)ethyl) phosphate

3-((12,12,13,13,14,14,15,15,15-nonafluoropentadecyl)amino)-3-oxo-2-(12,12,13,13,14,14,15,15,16,16,17,17,17-tridecafluoroheptadecanamido)propyl (2-(trimethylammonio)ethyl) phosphate

3-oxo-2-(12,12,13,13,14,14,15,15,16,16,17,17,17-tridecafluoroheptadecanamido)-3-((12,12,13,13,14,14,15,15,16,16,17,17,17-tridecafluoroheptadecyl)amino)propyl (2-(trimethylammonio)ethyl) phosphate

The above disclaimed compounds do however not relate to the gist of the invention in respect to their applications and uses. The inventors were the first to find the advantageous properties and useful applications of the compounds as described in this patent application. Accordingly, all described compounds, within the scope of the embodiments and the preferred embodiments are applicable in the uses and methods as defined herein throughout the specification, examples and claims.

## EXAMPLES

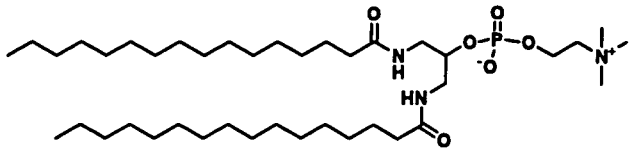
### 1. Synthesis of lipids of the invention and their characterization

Starting compounds and solvents were purchased from Sigma-Aldrich/Fluka or Acros and were used without further purification. Pad-PE-Pad and its homologues were synthesized using the procedures from Fedotenko et al.

Column chromatographic separation was carried out using 230-400 mesh silica gel. TLC plates were developed either with potassium permanganate mixture (1 g of $KMnO_4$, 2 g of $Na_2CO_3$, 100 mL of $H_2O$) or ethanolic solution of phosphomolybdic acid. $^1H$,$^{13}C$ and $^{31}P$ NMR spectra were recorded (as indicated) on either a Bruker 300 MHz or 400 MHz spectrometer and are reported as chemical shifts ($\delta$) in ppm relative to TMS ($\delta$ = 0). Spin multiplicities are reported as a singlet (s) or triplet (t) with coupling constants (J) given in Hz, or multiplet (m). ESI-MS for the characterization of new compounds was performed on an ESI API 150EX and are reported as mass-per-charge ratio *m/z*. IR spectra were recorded on a Perkin Elmer Spectrum One FT-IR spectrometer (ATR, Golden Gate). Melting point is uncorrected. For the experiments with vortex was used a device IKA Vortex Genius 3.

### 1.1 Synthesis of compounds of the invention

**Synthesis of 1,3-dipalmitamidopropan-2-yl 2-(trimethylammonio)ethyl phosphate (Pad-PC-Pad).**



1 g (1.45 mmol) of Pad-PE-Pad (non-methylated phosphoethanolamine) was solubilized in 100 mL of methanol. 1 mL (1.33 g, 10.5 mmol) of dimethylsulfate was added, the mixture was warmed up to 40 °C and then a solution of 1.45 g (10.5 mmol) of potassium carbonate in 20 mL water was added in one minute, while the mixture was being strongly stirred for 30 min and then cooled down to 20 °C. The solvent was removed under reduced pressure. Then the solid was purified on a silica gel column (75% $CH_2Cl_2$, 22% MeOH, 3% aq. $NH_4OH$ (25%)). Obtained were 0.56 g of the product (0.81 mmol, 53%) .

Compounds with the aliphatic chains containing 12, 14 and 18 carbon atoms were synthesized in the same way starting from the corresponding phosphoethanolamine.

**R*f*** = 0.32 (75% $CH_2Cl_2$, 22% MeOH, 3% aq. $NH_4OH$ (25%)).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.58 (s, 2H), 4.39 (s, 2H), 4.12 (s, 1H), 3.89 (s, 2H), 3.48 (s, 2H), 3.36 (s, 9H), 3.25 – 3.02 (m, 2H), 2.18 (t, $J$ = 7.3 Hz, 4H), 1.56 (s, 4H), 1.24 (s, 48H), 0.87 (t, $J$ = 6.7 Hz, 6H).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 174.7 (C=O), 72.2 (CH), 66.7, 59.6, 54.7(CH3s at the headgroup), 41.0, 36.9, 32.1, 29.89, 29.84, 29.72, 29.70, 29.59, 26.2, 22.9, 14.3 (CH3s of the tails).

**$^{31}$P NMR** (121 MHz, $CDCl_3$) δ 2.97.

**LRMS (ESI+)** *m/z* calcd for $C_{40}H_{83}N_3O_6P$ $[M+H]^+$ 732.6, found 732.7.

**FTIR** ($cm^{-1}$): 3285, 2917, 2850, 1651, 1545, 1468, 1239, 1088, 1058, 967, 720.

**mp** 203°C.

**Synthesis of 1,3-lauramidopropan-2-yl 2-(trimethylammonio)ethyl phosphate (Lad-PC-Lad, 1)**

0.80 g (1.38 mmol) of Lad-PE-Lad (non-methylated phosphoethanolamine) was mixed with 100 mL of methanol. 1.30 mL (1.74 g, 18.5 mmol) of dimethylsulfate was added shortly after that. The mixture was warmed up to 40 °C and then a solution of 1.91 g (18.5 mmol) of potassium carbonate in 20 mL water was added in one minute, while the mixture was strongly stirring. It was then stirred further 30 min at 40 °C and then cooled down to 20 °C. Methanol-water was removed under reduced pressure. To the solid residue was added methanol and the solvent was again removed under reduced pressure. Then the solid was mixed with 10 mL of a solution containing by volume 75% $CH_2Cl_2$, 22% MeOH, 3% aq. $NH_4OH$ (25%) and purified on a silica gel

column using the mobile phase of the same composition. Obtained was 0.26 g of the product (0.42 mmol, 30%).

***Rf***= 0.47 (75% $CH_2Cl_2$, 22% MeOH, 3% aq. $NH_4OH$ (25%))

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.44 (s, 2H), 4.40 (s, 2H), 4.14 (s, 1H), 3.88 (s, 2H), 3.37 (s, 9H), 3.12 (s, 2H), 2.17 (t, $J$ = 7.7 Hz, 4H), 1.57 (s, 4H), 1.24 (s, 31.3H), 0.87 (t, $J$ = 6.8 Hz, 6H).

**$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 174.62, 72.10, 66.37, 59.47, 54.36, 40.53, 36.64, 31.93, 29.72, 29.67, 29.62, 29.51, 29.49, 29.38, 25.92, 22.69, 14.12.

**$^{31}$P NMR** (121 MHz, $CDCl_3$) δ -0.6.

**HRMS (ESI+)** *m/z* calcd $[M+H]^+$ 620.4762, obs. 620.4775

**FTIR** ($cm^{-1}$): 3280, 2919, 2851, 1648, 1551, 1468, 1219, 1084, 1058, 966, 798.

**mp**=145-150°C

**Synthesis of 1,3-dimyristamidopropan-2-yl 2-(trimethylammonio)ethyl phosphate (Mad-PC-Mad, 2)**

0.82 g (1.29 mmol) of Mad-PE-Mad (non-methylated phosphoethanolamine) was mixed with 100 mL of methanol. 2 mL (2.66 g, 21.1 mmol) of dimethylsulfate was added shortly after that. The mixture was warmed up to 40 °C and then a solution of 2.92 g (21.1 mmol) of potassium carbonate in 20 mL water was added in one minute, while the mixture was strongly stirring. It was then stirred further 30 min at 40 °C and then cooled down to 20 °C. Methanol-water was removed under reduced pressure. To the solid residue was added methanol and the solvent was again removed under reduced pressure. Then the solid was partially mixed with 10 mL of a solution containing by volume 75% $CH_2Cl_2$, 22% MeOH, 3% aq. $NH_4OH$ (25%) and purified over a silica gel column using the mobile phase of the same composition. Obtained was 0.56 g of the product (0.83 mmol, 63%).

**Rf=0.51** (75% $CH_2Cl_2$, 22% MeOH, 3% aq. $NH_4OH$ (25%)).

$^1$H NMR (400 MHz, $CDCl_3$) δ 7.52 (s, 2H), 4.37 (s, 2H), 4.19 – 4.05 (m, 1H), 3.85 (s, 2H), 3.55 (s, 2H), 3.35 (s, 9H), 3.20 – 2.98 (m, 2H), 2.17 (t, $J$ = 7.3 Hz, 4H), 1.57 (s, 4H), 1.24 (s, 39H), 0.87 (t, $J$ = 6.8 Hz, 6H).

$^{13}$C NMR (126 MHz, $CDCl_3$) δ 174.61, 72.10, 66.36, 66.31, 59.47, 54.34, 40.52, 36.64, 31.94, 31.80, 29.74, 29.69, 29.64, 29.53, 29.50, 29.39, 25.92, 22.83, 22.70, 22.55, 14.12.

**$^{31}$P NMR** (121 MHz, $CDCl_3$) δ -2.9.

**HRMS (ESI+)** *m/z calc.* $[M+H]^+$ 676.5388, obs. 676.5385.

**FTIR** ($cm^{-1}$): 3287, 2918, 2851, 1651, 1547, 1468, 1235, 1058, 969, 788.

**mp**=189-193°C

**Improved synthesis of 1,3-distearamidopropan-2-yl 2-(trimethylammonio)ethyl phosphate (Pad-PC-Pad 3)**

1 g (1.45 mmol) of Pad-PE-Pad (non-methylated phosphoethanolamine) was mixed with 100 mL of methanol. 1 mL (1.33 g, 10.5 mmol) of dimethylsulfate was added shortly after that. The mixture was warmed up to 40 °C and then a solution of 1.45 g (10.5 mmol) of potassium carbonate in 20 mL water was added in one minute, while the mixture was strongly stirring. It was then stirred further 30 min at 40 °C and then cooled down to 20 °C. Methanol-water was removed under reduced pressure. To the solid residue was added methanol and the solvent was again removed under reduced pressure. Then the solid was partially mixed with 10 mL of a solution containing by volume 75% $CH_2Cl_2$, 22% MeOH, 3% aq. $NH_4OH$ (25%) and purified on an alumina column using the mobile phase of the same composition. The second time it was purified over a silica gel column. Obtained were 0.56 g of the product (0.81 mmol, 53%).

**R*f*** = 0.56 (75% $CH_2Cl_2$, 22% MeOH, 3% aq. $NH_4OH$ (25%)).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.58 (s, 2H), 4.39 (s, 2H), 4.12 (s, 1H), 3.89 (s, 2H), 3.36 (s, 9H), 3.12 (s, 2H), 3.25 – 3.02 (m, 2H), 2.18 (t, $J$ = 7.3 Hz, 4H), 1.56 (s, 4H), 1.24 (s, 48H), 0.87 (t, $J$ = 6.7 Hz, 6H).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 174.7 (C=O), 72.2 (CH), 66.7, 59.6, 54.7(CH3s at the headgroup), 41.0, 36.9, 32.1, 29.89, 29.84, 29.72, 29.70, 29.59, 26.2, 22.9, 14.3 (CH3s of the tails).

**$^{31}$P NMR** (121 MHz, $CDCl_3$) δ 2.97.

**HRMS (ESI+)** *m/z* calcd for $C_{40}H_{83}N_3O_6P$ $[M+H]^+$ 732.6, found 732.7.

**FTIR** ($cm^{-1}$): 3285, 2917, 2850, 1651, 1545, 1468, 1239, 1088, 1058, 967, 720.

**mp** 202-204°C.

**Synthesis of 1,3-distearamidopropan-2-yl 2-(trimethylammonio)ethyl phosphate**

**(Sad-PC-Sad, 4)**

116 mg (0.155 mmol) of Sad-PE-Sad (non-methylated phosphoethanolamine) was mixed with 15 mL of methanol. 0.1 mL (133 mg , 1.05 mmol) of dimethylsulfate was added shortly after that. The mixture was warmed up to 40 °C and then a solution of 145 mg (1.05 mmol) of potassium carbonate in 2 mL water was added in one minute, while the mixture was strongly stirring. It was then stirred further 30 min at 40 °C and then cooled down to 20°C. Methanol-water was removed under reduced pressure. To the solid residue was added methanol and the solvent was again removed under reduced pressure. Then the solid was partially mixed with 2 mL of a solution containing by volume 75% $CH_2Cl_2$, 22% MeOH, 3% aq. $NH_4OH$ (25%) and run over an alumina and a silica gel column using the mobile phase of the same composition. Obtained were 60 mg of the product (0.08mmol, 49%).

**Rf= 0.64** (75% $CH_2Cl_2$, 22% MeOH, 3% aq. $NH_4OH$ (25%)).

$^1$H NMR (400 MHz, $CDCl_3$) δ 7.47 (s, 2H), 4.39 (s, 2H), 4.13 (s, 1H), 3.88 (s, 2H), 3.66 – 3.43 (m, 2H), 3.36 (s, 9H), 3.26 – 2.99 (m, 2H), 2.17 (t, $J$ = 7.3 Hz, 4H), 1.57 (s, 4H), 1.24 (s, 55H), 0.87 (t, $J$ = 6.8 Hz, 6H).

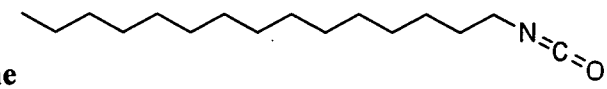
$^{13}$C NMR (101 MHz, $CDCl_3$) δ 174.71, 66.36, 59.43, 54.41, 40.37, 36.61, 31.97, 29.80, 29.72, 29.69, 29.57, 29.55, 29.41, 25.97, 22.73, 14.15.

**$^{31}$P NMR** (121 MHz, $CDCl_3$) δ 3.0.

**HRMS (ESI+)** *m/z* calcd $[M+H]^+$ 788.6616, obs. 788.6641

**FTIR** ($cm^{-1}$): 3297, 2917, 2850, 1649, 1549, 1469, 1226, 1087, 1058, 970, 720.

**mp**=222-225°C

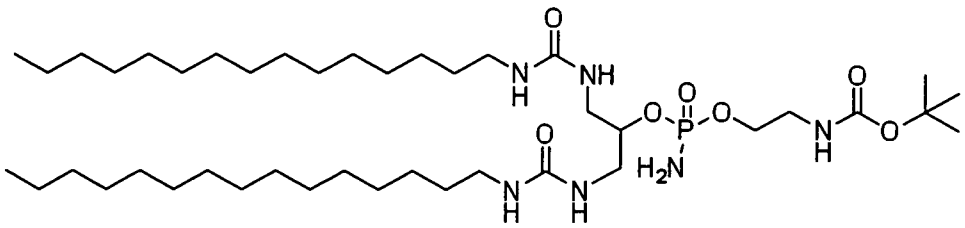



**1-isocyanatopentadecane**

Palmitoyl chloride (5.56 mL, 17.8 mmol) and sodium azide (1.5 g, 23 mmol) were mixed in 40 mL of dry toluene and the solution was refluxed for 5 h under an $N_2$ atmosphere. The product was directly used without further purification.

$^1$H NMR (300 MHz, $CDCl_3$) δ 3.29 (t, $J$ = 6.7 Hz, 2H), 1.69 – 1.52 (m, 2H), 1.26 (s, 24H), 0.88 (t, $J$ = 6.6 Hz, 3H).

**Tert-butyl (2-((amino((17,23-dioxo-16,18,22,24-tetraazanonatriacontan-20-yl)oxy)phosphoryl)oxy)ethyl)carbamate** (Pur-PEBoc-Pur)



Tert-butyl-(2-((amino((1,3-diaminopropan-2-yl)oxy)phosphoryl)oxy)ethyl)carbamate (210 mg, 0.672 mmol) and 5 mL of the solution of 1-isocyanatopentadecane (511 mg, 2.02 mmol) and triethylamine (470 µL, 3.36 mmol) were mixed with 6 mL of dry acetonitrile. The solution was heated up to 40 °C for 50 min. 100 mL of $CH_2Cl_2$ was added and the solution was extracted with saturated $NaHCO_3$ (100 mL). The aqueous phase was washed 2 times with 50 mL of $CH_2Cl_2$. The organic phases were dried over MgSO4. The organic solvents were removed under reduced pressure. After silica gel column chromatographic purification ($CH_2Cl_2$-MeOH 95:5), a white solid was obtained (148 mg, 0.18 mmol, **38 %**).

**Rf**: 0.11 ($CH_2Cl_2$-MeOH 95:5)

**$^1$H NMR** (500 MHz, Chloroform-d) δ 6.17 (br, 1H), 6.09 (br, 1H), 5.77 (br, 1H), 5.43 (br, 1H), 5.21 (br, 1H), 4.32 (s, 1H), 4.01 (d, $J$ = 34.2 Hz, 4H), 3.37 (s, 6H), 3.11 (q, $J$ = 6.4 Hz, 4H), 1.44 (s, 13H), 1.25 (s, 48H), 0.88 (t, $J$ = 7.0 Hz, 6H).

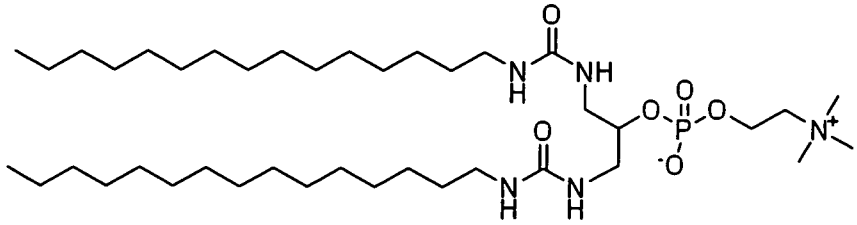
**$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 159.28, 156.42, 79.49, 76.16, 65.85, 41.05, 40.42, 31.93, 30.38, 30.33, 29.73, 29.47, 29.38, 28.43, 27.02, 22.70, 14.12.

**$^{31}$P NMR** (122 MHz, $CDCl_3$) δ 10.68.

**FTIR (cm$^{-1}$)** 3360, 3110, 2921, 2852, 1694, 1629, 1570, 1466, 1366, 1245, 1173, 992, 721.

**HRMS (ESI+)** *m/z* calcd for $C_{42}H_{88}N_6O_7P$ $[M+H]^+$ 819.6446 found 819.6448.

**17,23-dioxo-16,18,22,24-tetraazanonatriacontan-20-yl-(2-(trimethylammonio)ethyl) phosphate (Pur-PC-Pur)**



tert-butyl-(2-((amino((17,23-dioxo-16,18,22,24-tetraazanonatriacontan-20-yl)oxy)phosphoryl)oxy)ethyl)carbamate (140mg, 0.17 mmol) was dissolved in 9 mL dioxane and HCl (3 mL, 12 mmol) in dioxane was added. After 4 h the reaction was stopped. Nitrogen was bubbled through the solution over 1 h and solvent was evaporated under reduced pressure. The crude material was the dissolved in 12 mL of methanol. Dimethyl sulfate (120 μL, 1.27 mmol) was added and the solution was heated to 40 °C. 3.5 mL of a solution of potassium carbonate (210 mg, 1.5 mmol) was added and stirring was continued for 1 h at 40 °C. Then the solvents were evaporated under reduced pressure and the product was purified by silica gel column chromatography ($CH_2Cl_2$-MeOH-NH4OH 25% 75:22:3) to get a white solid (40 mg, 0.053 mmol, **30%**).

**Rf**: 0.11 ($CH_2Cl_2$-MeOH 95:5)

**$^1$H NMR** (500 MHz, Chloroform-d) δ 6.17 (br, 1H), 6.09 (br, 1H), 5.77 (br, 1H), 5.43 (br, 1H), 5.21 (br, 1H), 4.32 (s, 1H), 4.01 (d, $J$ = 34.2 Hz, 4H), 3.37 (s, 6H), 3.11 (q, $J$ = 6.4 Hz, 4H), 1.44 (s, 13H), 1.25 (s, 48H), 0.88 (t, $J$ = 7.0 Hz, 6H).

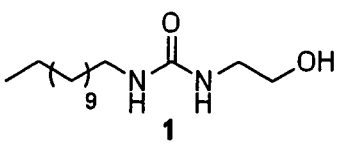
**$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 159.28, 156.42, 79.49, 76.16, 65.85, 41.05, 40.42, 31.93, 30.38, 30.33, 29.73, 29.47, 29.38, 28.43, 27.02, 22.70, 14.12.

**$^{31}$P NMR** (122 MHz, $CDCl_3$) δ 10.68.

**FTIR (cm$^{-1}$)** 3360, 3110, 2921, 2852, 1694, 1629, 1570, 1466, 1366, 1245, 1173, 992, 721.

**HRMS (ESI+)** *m/z* calcd for $C_{42}H_{88}N_6O_7P$ $[M+H]^+$ 819.6446 found 819.6448.

**Synthesis of 1-dodecyl-3-(2-hydroxyethyl)urea (1).**




**1**

Tridecanoic acid (0.86 g, 4.0 mmol), triethylamine (1.0 mL, 7.2 mmol) and diphenylphosphoryl azide (0.95 mL, 4.4 mmoL) were dissolved in dry toluene (20 mL). The solution was refluxed over 3h. The solution was kept at 0 °C and ethanolamine (0.24 mL, 4.0 mmol) was added. The mixture was stirred at 20 °C overnight and mixed with 70 mL of $CH_2Cl_2$ to be extracted with 100 mL of water mixed with 10 mL of $NH_4OH$ (25%). The water phase was washed twice with 70 mL of $CH_2Cl_2$. After drying over magnesium sulfate, the solvent were evaporated and the crude product was purified by silica gel column (95 % $CH_2Cl_2$, 5% MeOH). A white powder (440 mg, 1.62 mmol, 40.4%) was obtained.

**Rf** = 0.17 (95 % $CH_2Cl_2$, 5% MeOH).

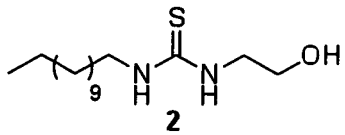
**$^1$H NMR** (500 MHz, Methanol-d4) δ 3.67 (t, $J$ = 5.3 Hz, 2H), 3.58 (s, 2H), 3.46 (s, 2H), 1.65 – 1.47 (m, 2H), 1.30 (s, 18H), 0.90 (t, $J$ = 7.0 Hz, 3H).

**$^{13}$C NMR** (126 MHz, MeOD) δ 161.47 (s), 62.66 (s), 43.46 (s), 41.06 (s), 33.09 (s), 32.15 – 29.47 (m), 27.98 (s), 14.44 (s).

**IR** ($cm^{-1}$): 3340, 3317, 3030, 2955, 2921, 2849, 1619, 1591, 1462, 1268, 1057, 620.

**HRMS** *(ESI+) m/z* calcd for $C_{15}H_{33}N_2O_2$ $[M+H]^+$ 273.2536 found 273.2532.

**Synthesis of 1-dodecyl-3-(2-hydroxyethyl)thiourea (2).**




**2**

Dodecyl isothiocyanate was first synthesized by variation of a procedure of Meijer.[1] DCC (2.9 g17 mmol) and $CS_2$ (7.2 mL, 119 mmol) were dissolved in dry diethyl ether (40 mL). Dodecyl amine (3.2 g, 17 mmol) was added at 0°C to the mixture that was stirred overnight at room temperature. The precipated solid was filtered off and washed with 60 mL of dry diethyl ether. The solvent were removed by evaporation and the isothiocyanate was used without further purification.

Ethanolamine (0.23 mL, 3.8 mmol) and triethylamine (0.61 mL, 4.37 mmol) were dissolved in dry THF (40 mL). At 0°C was added dropwise dodecyl isothiocyanate (1.0 mL, 3.8 mmol). After stirring at 20°C for 3h30, the mixture was added to $CH_2Cl_2$ (70 mL) to be extracted with 100 mL of water mixed with 10 mL of $NH_4OH$ (25%). The water phase was washed twice with 70 mL of $CH_2Cl_2$. After drying over magnesium sulfate, the solvent were evaporated and the crude product was purified by silica gel column (95 % $CH_2Cl_2$, 5% MeOH). The product was recristallised from

dioxane/pentane (1:1) at 8°C overnight. A white powder (850 mg, 2.95 mmol, **77.5%**) was obtained.

**Rf** = 0.28 (95 % $CH_2Cl_2$, 5% MeOH).

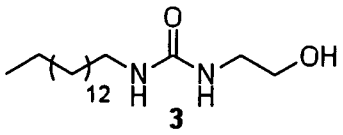
**$^1$H NMR** (500 MHz, Methanol-d4) δ 3.67 (t, *J* = 5.3 Hz, 2H), 3.58 (s, 2H), 3.46 (s, 2H), 1.65 – 1.47 (m, 2H), 1.30 (s, 18H), 0.90 (t, *J* = 7.0 Hz, 3H).

**$^{13}$C NMR** (126 MHz, MeOD) δ 183.84, 61.82, 47.43, 45.39, 33.09, 30.79, 30.79, 30.49, 30.20, 27.99, 23.75, 14.45.

**IR** ($cm^{-1}$): 3293, 3233, 3071, 2918, 2849, 1565, 1471, 1461, 1294, 1276, 1255, 1210, 1163, 1059, 1034, 728, 650.

**HRMS** *(ESI+) m/z* calcd for $C_{15}H_{33}N_2OS$ $[M+H]^+$ 289.2308 found 289.2305.

**Synthesis of 1-(2-hydroxyethyl)-3-pentadecylurea (3).**




**3**

Pentadecyl isocyanate was first synthesized by variation of a procedure of De Feyter and all.[2] Palmitoyl chloride (5.6 mL, 18 mmol) and sodium azide (1.5 g, 23 mmol) were mixed in dry toluene (40 mL). The solution was refluxed over 5h. The solution was directly used without further purification.

Ethanolamine (0.22 mL, 3.7 mmol) and dry $Et_3N$ (1.04 mL, 7.42 mmol) were dissolved in dry THF (25 mL). 4.9 mL of the toluene solution of 1-isocyanatopentadecane (0.94 g, 3.7 mmol) in dry THF (10 mL) was added dropwise (30 min) to the solution under stirring at 0 °C and still stirred 3 h at room temperature. Then the solution was treated with 10 mL $NH_4OH$ 25% in 100 mL water, and extracted with $CH_2Cl_2$ (4 x 50 mL). The solvents from the combined organic phases were dried with $MgSO_4$ and removed under reduced pressure. The crude product was purified on silica gel column (95 % $CH_2Cl_2$, 5% MeOH) to give a white powder (555 mg, 1.76 mmol, **47.7%**).

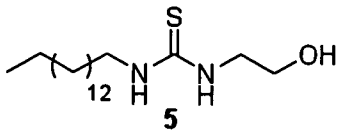
**Rf** = 0.20 (95 % $CH_2Cl_2$, 5% MeOH).

**$^1$H NMR** (500 MHz, $CDCl_3$/Methanol-d4 1:1) δ 3.56 (t, *J* = 5.4 Hz, 2H), 3.21 (t, *J* = 5.3 Hz, 2H), 3.07 (t, *J* = 7.1 Hz, 2H), 1.52 – 1.35 (m, 2H), 1.22 (s, 24H), 0.84 (t, *J* = 7.0 Hz, 3H).

**$^{13}$C NMR** (126 MHz, $CDCl_3$/Methanol-d4 1:1) δ 159.66, 61.40, 41.98, 39.68, 31.40, 29.56, 29.15, 29.13, 29.11, 29.09, 28.87, 28.82, 26.37, 22.13, 13.29.

**IR** ($cm^{-1}$): 3309, 3214, 3079, 2919, 2850, 1572, 1471, 1348, 1271, 1037, 718, 650.

**Synthesis of 1-(2-hydroxyethyl)-3-pentadecylthiourea (5).**




**5**

Pentadecyl isothiocyanate was first synthesized by variation of a procedure of Meijer.[1] DCC (3.1 g, 15 mmol) and $CS_2$ (6.3 mL, 104 mmol) were dissolved in dry diethyl ether (40 mL). Pentadecyl amine (3.4 g, 15 mmol) was added at 0°C to the mixture that was stirred overnight at room temperature. The precipated solid was filtered off and washed with 60 mL of dry diethyl ether. The solvent were removed by evaporation and the isothiocyanate was used without further purification.

Ethanolamine (0.23 mL, 3.8 mmol) and triethylamine (1.0 mL, 7.4 mmol) were dissolved in dry THF (40 mL). At 0°C was added dropwise pentadecyl isothiocyanate (1.0 mL, 3.7 mmol) in dry THF (20 mL) over 1h30. After stirring at 20°C for 4h30, the mixture was added to $CH_2Cl_2$ (70 mL) to be extracted with 100 mL of water mixed with 10 mL of $NH_4OH$ (25%). The water phase was washed twice with 70 mL of $CH_2Cl_2$. After drying over magnesium sulfate, the solvent were evaporated and the crude product was purified by silica gel column (95 % $CH_2Cl_2$, 5% MeOH). The product was recristallised from dioxane/pentane (1:4) at 8°C overnight. A white powder (700 mg, 2.12 mmol, **57.1%**) was obtained.

**Rf** = 0.36 (95 % $CH_2Cl_2$, 5% MeOH).

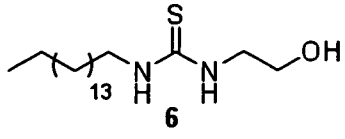
**$^1$H NMR** (300 MHz, $CDCl_3$) δ 3.92 – 3.76 (m, 2H), 3.68 (s, 2H), 3.37 (s, 2H), 1.69 – 1.49 (m, 2H), 1.25 (s, 24H), 0.88 (t, $J$ = 6.5 Hz, 3H).

**$^{13}$C NMR** (126 MHz, MeOD) δ 183.71, 61.82, 47.43, 45.39, 33.08, 30.78, 30.48, 30.20, 27.98, 23.74, 14.44.

**IR** ($cm^{-1}$): 3228, 3073, 2915, 2848, 1567, 1470, 1365, 1293, 1276, 1216, 1049, 738, 720, 665.

**HRMS** *(ESI+) m/z* calcd for $C_{18}H_{39}N_2OS$ $[M+H]^+$ 331.2777 found 331.2774.

**Synthesis of 1-(2-hydroxyethyl)-3-hexadecylthiourea (6).**



6

Hexadecyl isothiocyanate was first synthesized by variation of a procedure of Meijer.[1] DCC (2.42 g, 14.5 mmol) and $CS_2$ (6.00 mL, 100 mmol) were dissolved in dry diethyl ether (40 mL). Hexadecyl amine (3.80 g, 14.2 mmol) was added at 0°C to the mixture that was stirred overnight at room temperature. The precipated solid was filtered off and washed with 60 mL of dry diethyl ether. The solvents were removed by evaporation and the isothiocyanate was used without further purification.

Aminoethanol (0.22 mL, 3.7 mmol) and dry $Et_3N$ (1.0 mL, 7.4 mmol) were dissolved in dry THF (25 mL). 1-isothiocyanatohexadecane (1.0 mL, 3.7 mmol) in dry THF (15 mL) was added dropwise (1h15) to the solution under stirring at 0 °C and still stirred 3h30 at room temperature. Then the solution was treated with 10 mL $NH_4OH$ 25% in 100 mL water, and extracted with $CH_2Cl_2$ (4 x 50 mL). The solvents from the combined organic phases were dried with $MgSO_4$ anhyd and removed under reduced pressure. The crude product was purified on silica gel column (95 % $CH_2Cl_2$, 5% MeOH) and then by recristallisation (dioxane/pentane, 4:1) to give the product as a white powder (756 mg, 2.19 mmol, **59.1 %**).

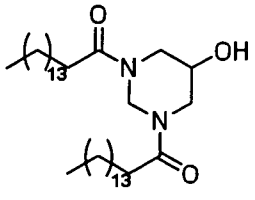
**Rf** = 0.25 (95 % $CH_2Cl_2$, 5% MeOH).

**$^1$H NMR** (500 MHz, Methanol-d4) δ 3.66 (t, *J* = 5.4 Hz, 2H), 3.57 (s, 2H), 3.43 (s, 2H), 1.64 – 1.47 (m, 2H), 1.29 (s, 26H), 0.90 (t, *J* = 7.0 Hz, 3H).

**$^{13}$C NMR** (126 MHz, MeOD) δ 183.01, 61.82, 47.45, 45.57, 33.08, 30.79, 30.73, 30.71, 30.48, 30.20, 27.98, 23.74, 14.44.

**IR** ($cm^{-1}$): 3298, 3231, 3073, 2917, 2849, 1565, 1461, 1366, 1286, 1272, 1211, 1059, 1036, 728, 651.

**Synthesis of 1,1'-(5-hydroxydihydropyrimidine-1,3(2H,4H)-diyl)bis(hexadecan-1-one) (Cyclo[6]Pad-OH-Pad)**



**Method A.** 100 mg (0.98 mmol) of 5-hydroxy-1,3-diaziridine and 0.349 mL (253 mg, 2.5 mmol) of $Et_3N$ were mixed with 10 mL of dry $CH_2Cl_2$. 0.611 mL (550 mg, 1.96 mmol) of palmitoyl chloride were added. The mixture was left stirring for 10 h.

$CH_2Cl_2$ was removed under reduced pressure. The product was purified over a silica gel column to give 142 mg of a white solid (0.24 mmol, 25%).

**Method B.** 5-hydroxy-1,3-diaziridine (402 mg, 3.94 mmol) was dissolved in a mixture of $CH_2Cl_2$ (18 mL), toluene (7 mL) and NaOH (693 mg, 17.3 mmol) in $H_2O$ (13 mL). At 20 °C, palmitoyl chloride (2.4 ml, 7.87 mmol) was added in one step. After stirring for 3 h, the solution was extracted with 50 mL of $NaHCO_3$ saturated and washed 2 times with 50 mL of $CH_2Cl_2$. (If an emulsion appears because of palmitic acid, the solution must be filtered and re-extracted) The organic phases were dried over $MgSO_4$ and the solvents were evaporated.

Purification was done with a silica gel column, eluted with $CH_2Cl_2$ then $CH_2Cl_2$/Ethyl acetate 1:1. Obtained 935 mf of white solid (1.62 mmol, 41%)

**R*f*** = 0.5 ($CH_2Cl_2$/Ethyl acetate 1:1)

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 5.69 (d, *J* = 13.1 Hz, 1H), 4.54 (d, *J* = 13.1 Hz, 1H), 4.16 (dd, *J* = 13.6, 3.4 Hz, 1H), 3.95 – 3.85 (m, 1H), 3.73 (dd, *J* = 13.8, 4.1 Hz, 1H), 3.54 (d, *J* = 13.6 Hz, 1H), 3.46 (d, *J* = 13.5 Hz, 1H), 2.67 – 2.50 (m, 2H), 2.35 (ddt, *J* = 30.7, 15.4, 7.9 Hz, 2H), 1.66 (d, *J* = 46.1 Hz, 9H), 1.26 (s, 49H), 0.89 (t, *J* = 6.8 Hz, 6H).

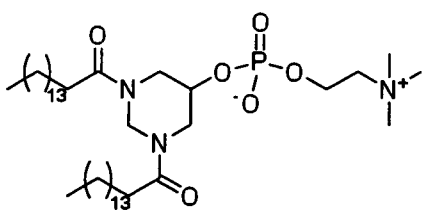
**$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 174.35, 172.91, 64.20, 55.91, 51.01, 47.83, 33.16, 32.91, 31.94, 29.71, 29.38, 25.29, 24.95, 22.71, 14.21.

**HRMS (ESI+)** *m/z* calcd for $C_{36}H_{71}N_2O_3$ $[M+H]^+$ 579.5459 obs. 579.5466

**FTIR ($cm^{-1}$)**: 3414, 2918, 2850, 1658, 1619, 1468, 1255, 1145, 885, 722

**$M_p$**= 84-86 °C

**1,3-dipalmitoylhexahydropyrimidin-5-yl (2-(trimethylammonio)ethyl) phosphate (Cyclo[6]Pad-PC-Pad)**



To a solution of 150 mg (0.259 mmol) of the cyclo[6]Pad-OH-Pad and 0.253 mL (184 mg, 1.81 mmol) of $NEt_3$ in 15 mL of $CH_2Cl_2$ was added ethylene chlorophosphite (0.099 mL, 142 mg, 1.09 mmol) at 0 °C. After that the

mixture was stirred for 24 h. Then 1 M bromine solution (1.74 mL, 1.74 mmol) was added at 0 °C. After 10 min, the solvent was removed under reduced pressure. The residue was dissolved in 9 mL of $CH_3CN$/*i*-PrOH/$CHCl_3$ (1.5:1.5:1), and 5 mL of 45% aqueous trimethylamine was added at rt. After 24 h, the solvents were removed. The product was purified first - by passing through a column chromatography on silica gel (elution with $CH_2Cl_2$-$CH_3$-OH-$H_2O$ 65:25:4). Then the small portions (30-50 mg) were purified on a SEPHADEX LH-20 column (elution with $CH_2Cl_2$-$CH_3$-OH-$H_2O$ 65:25:4). Purity was controlled by 1H- NMR for each portion. If the purity was insufficient, the separation was repeated. Yield 140 mg (0.189 mmol, 73%)

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 5.38 (d, *J* = 14.4 Hz, 1H), 4.79 (d, *J* = 13.0 Hz, 1H), 4.49 – 4.25 (m, 3H), 4.08 – 3.96 (m, 1H), 3.87 (s, 2H), 3.82 – 3.71 (m, 1H), 3.68 – 3.58 (m, 1H), 3.54 – 3.44 (m, 1H), 3.37 (s, 7H), 2.69 – 2.33 (m, 4H), 1.71 – 1.48 (m, 4H), 1.46 – 1.09 (m, 48H), 0.92 (t, *J* = 6.8 Hz, 6H).

**$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 173.30, 172.65, 66.78, 66.33, 59.45, 55.64, 54.44, 50.48, 46.46, 33.38, 32.85, 31.94, 29.75, 29.69, 29.62, 29.55, 29.46, 29.38, 25.63, 24.99, 22.70, 14.13.

**$^{31}$P NMR** (121 MHz, $CDCl_3$) δ 2.63.

**Mp**=214-218°C

**HRMS (ESI+)** *m/z* calcd for $C_{41}H_{82}N_3O_6P$ $[M+H]^+$ 744.6014 obs. 744.6003

**FTIR** ($cm^{-1}$): 3341, 2921, 2853, 1642, 1466, 1430, 1087, 1054, 970, 920, 875, 778, 722

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## 2. Preparation of 3-dimensional structures

The modularity of the liposome preparation technology allows for rapid formulation of vesicles containing mixed lipid components. Therefore, we prepared GUVs

containing equimolar fractions of Xad-PC-Xad phospholipids with various degrees of chain mismatch. A mismatch of 2 carbon units in the hydrocarbon chain (Sad-PC-Sad vs. Pad-PC-Pad) led to the formation of almost spherically shaped vesicles with two distintive curvatures separated at the vesicle's equator (Figure B). When this vesicle preparation was left in the alternating electrical field for prolonged times, larger, trigonal shaped GUVs formed, possibly after degradation of the lipid phosphatidyl choline head group (Figure A). In the general formula A=H would be expected.

**Figures 5A to 5D** depict unilamellar vesicles prepared from 50 mol% Sad-PC-Sad and 50 mol% Pad-PC-Pad (A and B), Mad-PC-Mad (C), and Pur-PC-Pur (D). All preparations contain 1 mol% of DOPE Rhoadmine. Scale bars = 5 μm.

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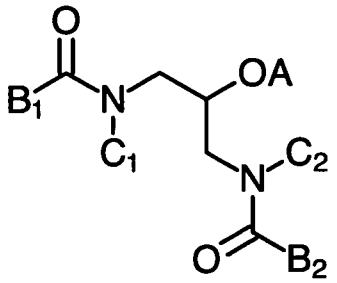
**Abbreviations**

| | |
|---|---|
| EYPC | Egg yolk phosphatidylcholine |
| DOPC | 1,2-dioleoyl-*sn*-glycero-3-phosphocholine |
| POPC | 1-palmitoyl-2-oleoyl-*sn*-glycero-3-phosphocholine |
| DPPC | 1,2-dipalmitoyl-*sn*-glycero-3-phosphocholine |
| PEG | Polyethyleneglycol |
| Brij S10 | decaethylene glycol octadecyl ether |
| Brij P4 | tetraethylene glycol hexadecyl ether |
| Brij P10 | decaethylene glycol hexadecyl ether |
| Pa, KPa | Pascal, kilopascal |

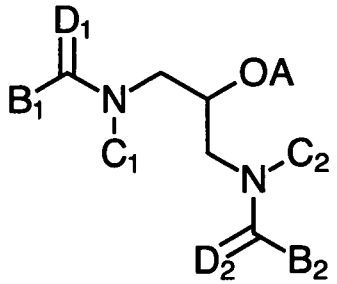
Claims

1. Composition of one or more lipids comprising or consisting of 1,3-diamidolipids or/and 1,2-diamidolipids or/and 2,3-diamidolipids or/and 1-amidolipids or/and 1,3-diurealipids or/and 1,2-diurealipids or/and 2,3-diurealipids or/and 1,3-dithiourealipids or/and 1,2-dithiourealipids or/and 2,3-dithiourealipids or/and 1,3-diacylurealipids or/and 1,2-diacylurealipids or/and 2,3-diacylurealipids or/and 1-amidolipids or/and 1-urealipids or/and 1-thiourealipids or/and 1-acylurealipids or/and cyclic-amidolipids or/and cyclic urealipids or/and cyclic thiourealipids or/and cyclic acylurealipids.

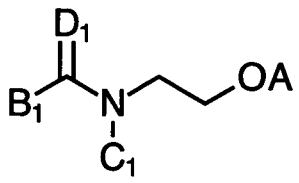
2. Composition according to claim 1 wherein the lipid has one of the following formulae:



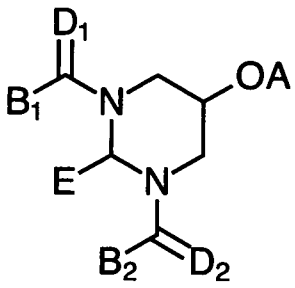

Formula Ia




Formula Ib




Formula Ic




Formula Id

wherein Formula Ia is characterized in that

i. "$B_1$" is equal or different from "$B_2$", and "$B_1$" and "$B_2$" is selected from:

ii. H;

iii. alkyl-, such as methyl-, ethyl-, propyl-, isopropyl-, butyl-, pentyl-, hexyl- heptyl-, octyl-, nonyl-, decyl-, undecyl-, dodecyl-, tridecyl-, tetradecyl-, pentadecyl-, hexadecyl-, heptadecyl-, nonadecyl-, eicosyl-, heneicosyl-, docosyl-, tricosyl-, or tetracosyl-;

iv. preferably, undecyl-, tridecyl-, pentadecyl-, heptadecyl-;

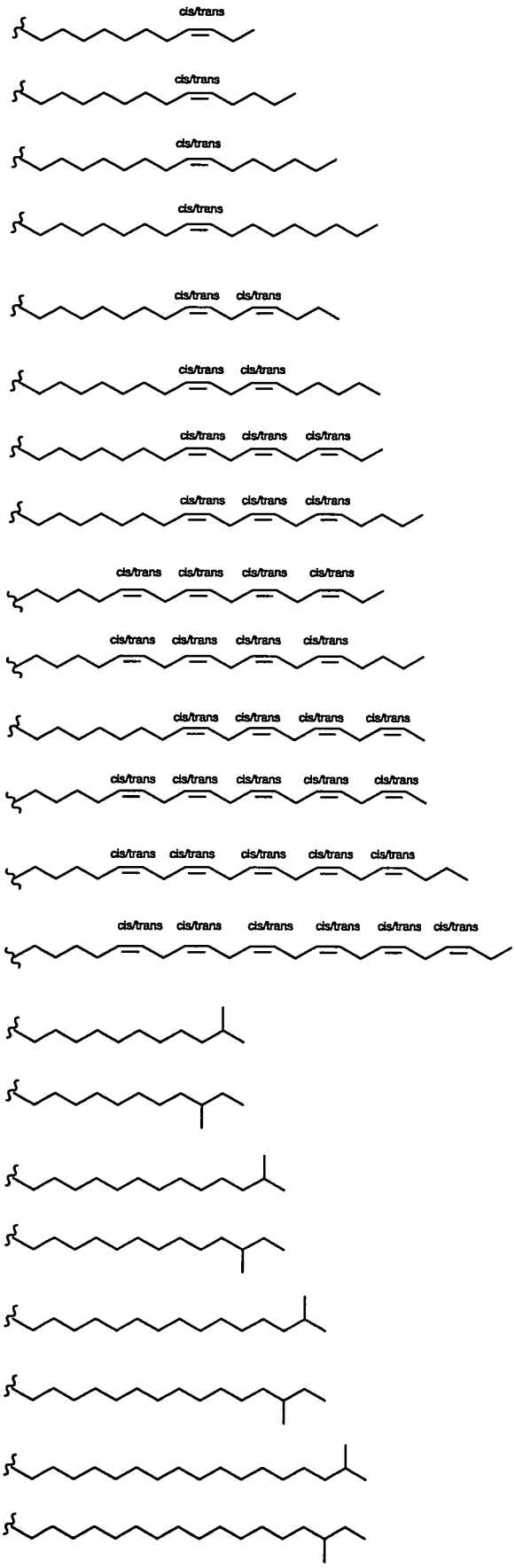
v. an optionally substituted $C_1$-$C_{10}$ alkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

vi. an optionally substituted $C_{11}$-$C_{17}$ alkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

vii. an optionally substituted $C_{18}$-$C_{24}$ alkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

viii. wherein 11, 13, 15, and 17 C-atoms are preferred;

ix. a group listed in the figures below: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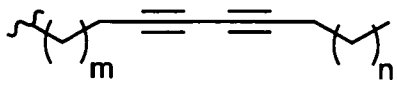
or




where m and n can be different or the same and

m = 0-7

preferably m=7

n=0-11

preferably n=8, 10, or 11

or "$B_1$" and "$B_2$" are the same or different and are selected from:

i. primary amines such as methyl-, ethyl-, propyl-, isopropyl-, butyl-, pentyl-, hexyl- heptyl-, octyl-, nonyl-, decyl-, undecyl-, dodecyl-, tridecyl-, tetradecyl-, pentadecyl-, hexadecyl-, heptadecyl-, nonadecyl-, eicosyl-, heneicosyl-, docosyl-, tricosyl-, or tetracosyl-amine;

ii. preferably, decyl-, dodecyl-, tetradecyl-, hexadecyl-amine;

iii. an optionally substituted C1-C8 aminoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

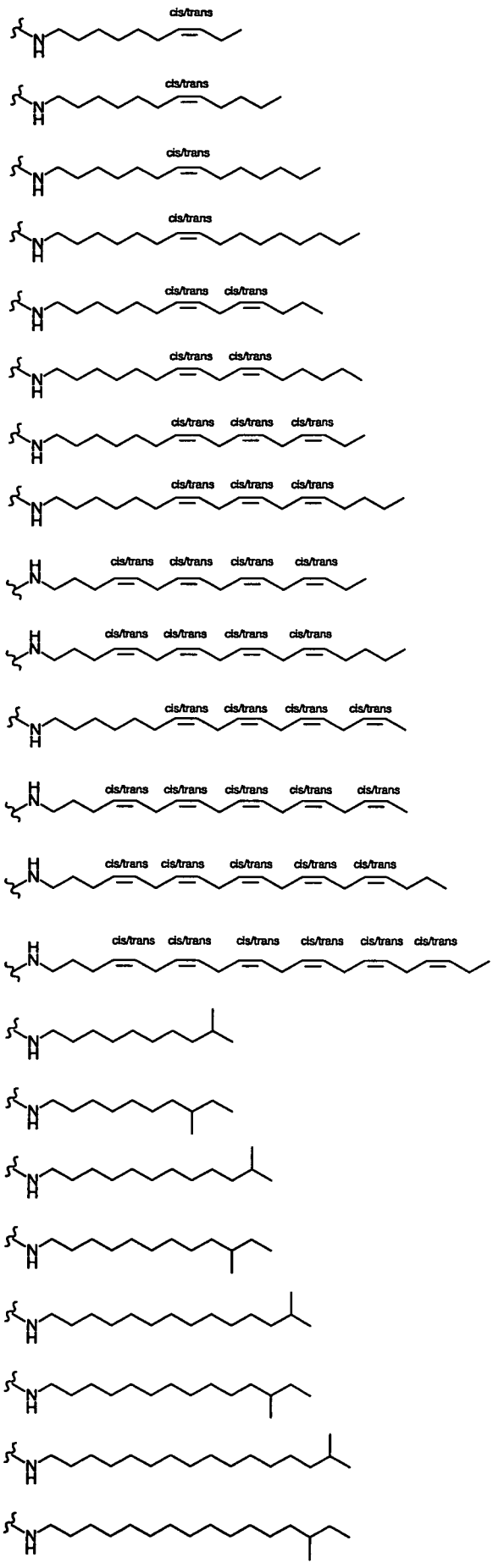
iv. an optionally substituted C9-C15 aminoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

v. an optionally substituted C16-C22 aminoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

vi. wherein 9, 11, 13, and 15 C-atoms are preferred;

vii. a group listed in the figures below:

viii.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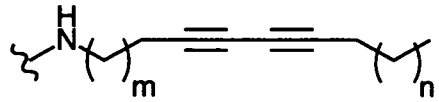


where m=0-6, and preferably m=6

n=0-11, preferably n=8, 10, or 11

or

ix. primary amides (to give acylureas) such as methyl-, ethyl-, propyl-, isopropyl-, butyl-, pentyl-, hexyl- heptyl-, octyl-, nonyl-, decyl-, undecyl-, dodecyl-, tridecyl-, tetradecyl-, pentadecyl-, hexadecyl-, heptadecyl-, nonadecyl-, eicosyl-, heneicosyl-, docosyl-, tricosyl-, or tetracosyl-amide;

x. preferably, decyl-, dodecyl-, tetradecyl-, hexadecyl-amide;

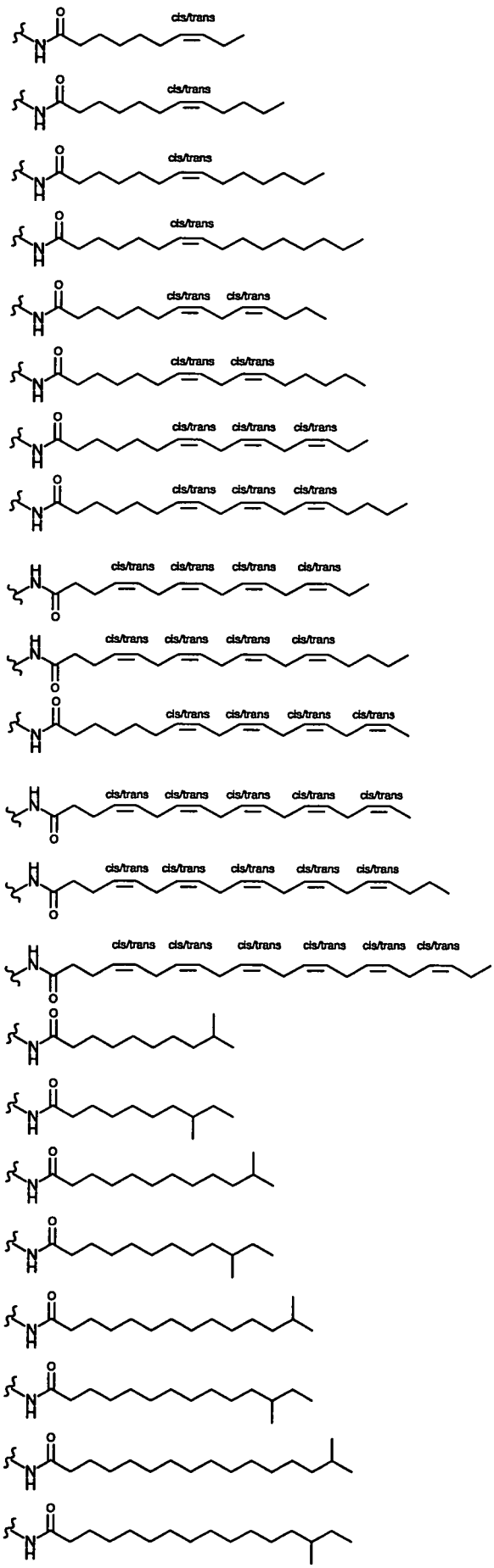
xi. an optionally substituted C1-C8 amidoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

xii. an optionally substituted C9-C15 amidoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

xiii. an optionally substituted C16-C22 amidoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

xiv. wherein 9, 11, 13, and 15 C-atoms are preferred;

xv. a group listed in the figures below: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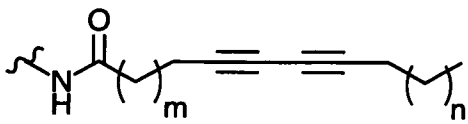


where m=0-5, and preferably m=5;

n=0-11, preferably n=8, 10, or 11;

wherein said lipid may be fully or partially deuterated, or radioactively labeled; and

wherein "A" is selected from:

a proton (H), a phosphatic acid or a phosphate ester substituted group such as phosphocholine, phosphoethanolamine, phosphoglycerol, phosphoserine, phosphoinositol, phosphoinositol 4,5-bisphosphate, a phosphate ester substituted sugar, a phosphate ester substituted polyethyleneglycol, a phosphate ester substituted electrophile, such as an activated ester including N-hydroxysuccinimic ester, or an acid chloride or an halogenide, a phosphate ester substituted nucleophile such as a thiol or an amine, a phosphate ester substituted fluorescent group such as fluoresceine, a phosphate ester substituted radioactively labeled group, a phosphate ester substituted alkyne and a phosphate substituted azide, and wherein "$C_1$" and "$C_2$" may be H or a methyl;

wherein Formula Ib is characterized in that

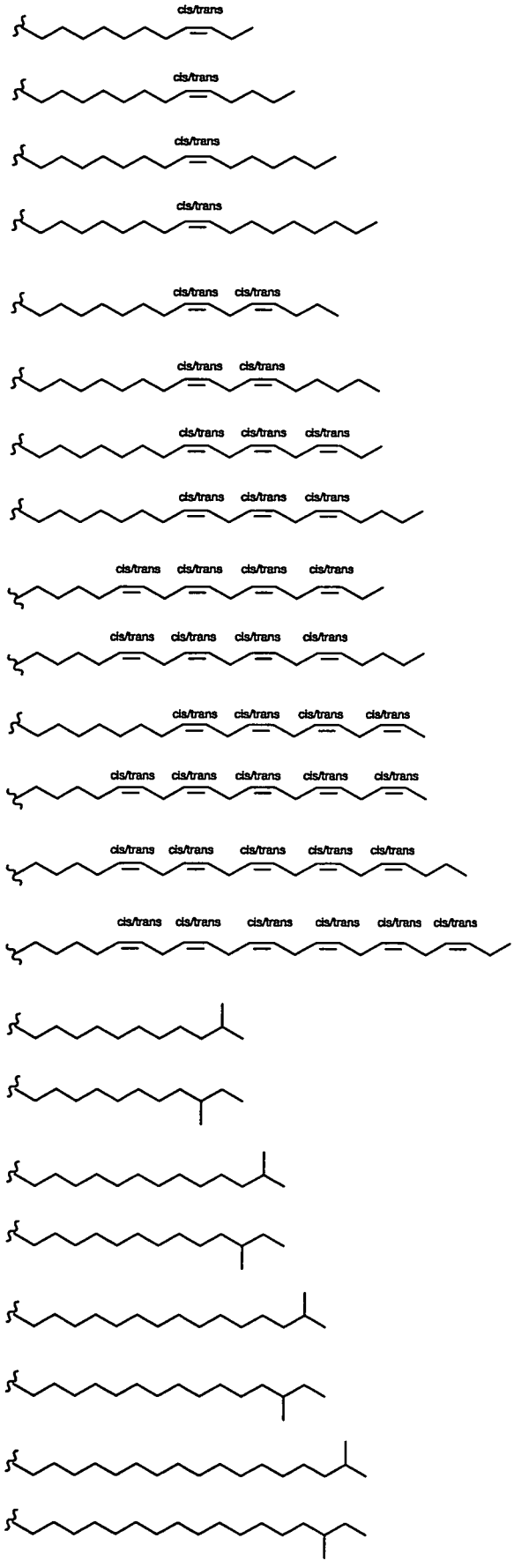
i. "$B_1$" is equal or different from "$B_2$", and "$B_1$" and "$B_2$" is selected from:
ii. H;
iii. alkyl-, such as methyl-, ethyl-, propyl-, isopropyl-, butyl-, pentyl-, hexyl-heptyl-, octyl-, nonyl-, decyl-, undecyl-, dodecyl-, tridecyl-, tetradecyl-, pentadecyl-, hexadecyl-, heptadecyl-, nonadecyl-, eicosyl-, heneicosyl-, docosyl-, tricosyl-, or tetracosyl-;
iv. preferably, undecyl-, tridecyl-, pentadecyl-, heptadecyl-;
v. an optionally substituted $C_1$-$C_{10}$ alkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

vi. an optionally substituted $C_{11}$-$C_{17}$ alkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

vii. an optionally substituted $C_{18}$-$C_{24}$ alkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

viii. wherein 11, 13, 15, and 17 C-atoms are preferred;

ix. a group listed in the figures below: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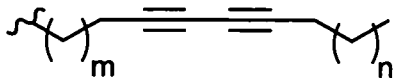



where m and n can be different or the same and

m = 0-7, preferably m=7

n=0-11, preferably n=8, 10, or 11

or "$B_1$" and "$B_2$" are the same or different and are selected from:

i. primary amines such as methyl-, ethyl-, propyl-, isopropyl-, butyl-, pentyl-, hexyl- heptyl-, octyl-, nonyl-, decyl-, undecyl-, dodecyl-, tridecyl-, tetradecyl-, pentadecyl-, hexadecyl-, heptadecyl-, nonadecyl-, eicosyl-, heneicosyl-, docosyl-, tricosyl-, or tetracosyl-amine;

ii. preferably, decyl-, dodecyl-, tetradecyl-, hexadecyl-amine;

iii. an optionally substituted C1-C8 aminoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

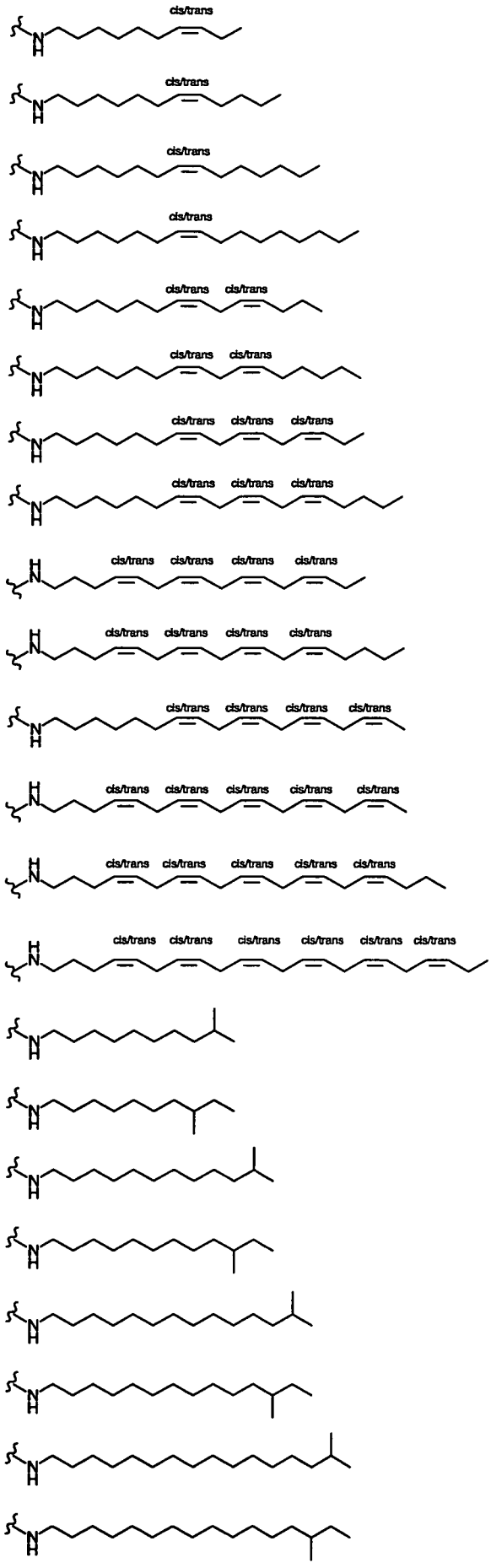
iv. an optionally substituted C9-C15 aminoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

v. an optionally substituted C16-C22 aminoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

vi. wherein 9, 11, 13, and 15 C-atoms are preferred;

vii. a group listed in the figures below:

viii.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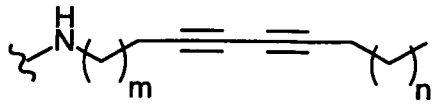


where m=0-6, and preferably m=6

n=0-11, preferably n=8, 10, or 11

or

ix. primary amides (to give acylurea) such as methyl-, ethyl-, propyl-, isopropyl-, butyl-, pentyl-, hexyl- heptyl-, octyl-, nonyl-, decyl-, undecyl-, dodecyl-, tridecyl-, tetradecyl-, pentadecyl-, hexadecyl-, heptadecyl-, nonadecyl-, eicosyl-, heneicosyl-, docosyl-, tricosyl-, or tetracosyl-amide;

x. preferably, decyl-, dodecyl-, tetradecyl-, hexadecyl-amide;

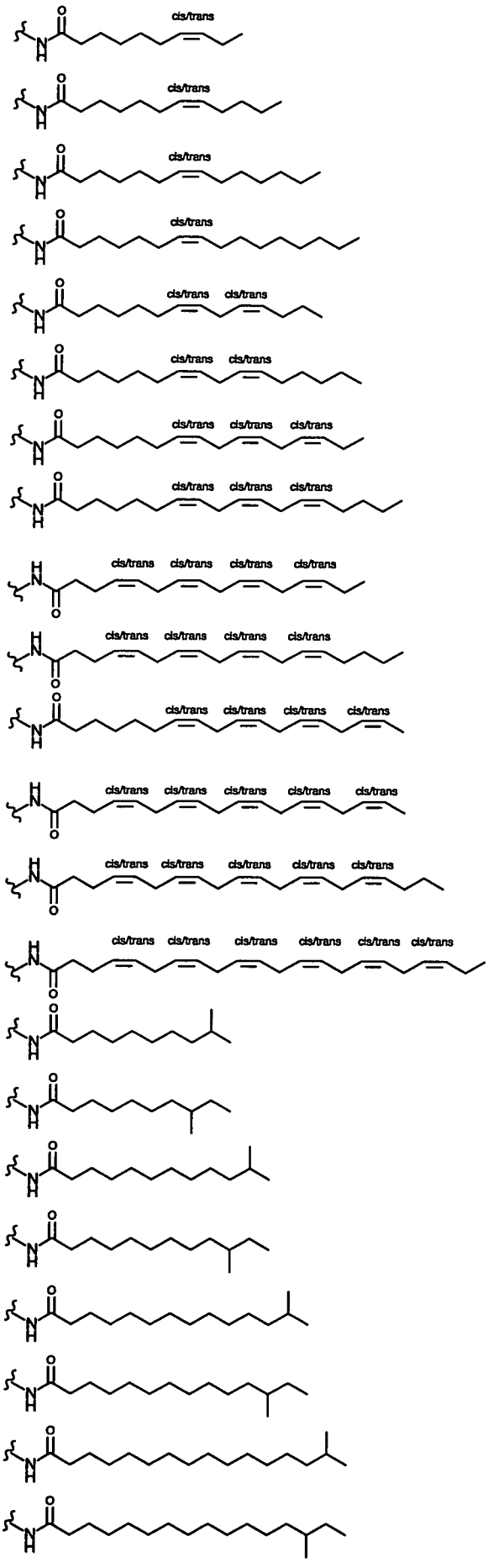
xi. an optionally substituted C1-C8 amidoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

xii. an optionally substituted C9-C15 amidoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

xiii. an optionally substituted C16-C22 amidoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

xiv. wherein 9, 11, 13, and 15 C-atoms are preferred;

xv. a group listed in the figures below: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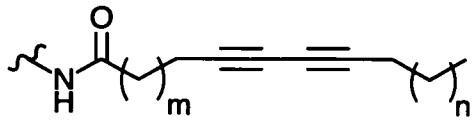


where m=0-5, and preferably m=5;

n=0-11, preferably n=8, 10, or 11;

"$D_1$" and "$D_2$" can be the same or can be different and are either O (oxygen) or S (sulfur),

wherein said lipid preferably may be fully or partially deuterated, or radioactively labeled; and wherein "A" is selected from: a proton (H), a phosphatic acid or a phosphate ester substituted group such as phosphocholine, phosphoethanolamine, phosphoglycerol, phosphoserine, phosphoinositol, phosphoinositol 4,5-bisphosphate, a phosphate ester substituted sugar, a phosphate ester substituted polyethyleneglycol, a phosphate ester substituted electrophile, such as an activated ester including N-hydroxysuccinimic ester, or an acid chloride or an halogenide, a phosphate ester substituted nucleophile such as a thiol or an amine, a phosphate ester substituted fluorescent group such as fluoresceine, a phosphate ester substituted radioactively labeled group, a phosphate ester substituted alkyne and a phosphate substituted azide; and wherein "C1" and "C2" may be H or a methyl;

wherein Formula Ic is characterized in that

i. "$B_1$" is selected from:

ii. H;

iii. alkyl-, such as methyl-, ethyl-, propyl-, isopropyl-, butyl-, pentyl-, hexyl- heptyl-, octyl-, nonyl-, decyl-, undecyl-, dodecyl-, tridecyl-, tetradecyl-, pentadecyl-, hexadecyl-, heptadecyl-, nonadecyl-, eicosyl-, heneicosyl-, docosyl-, tricosyl-, or tetracosyl-;

iv. preferably, undecyl-, tridecyl-, pentadecyl-, heptadecyl-;

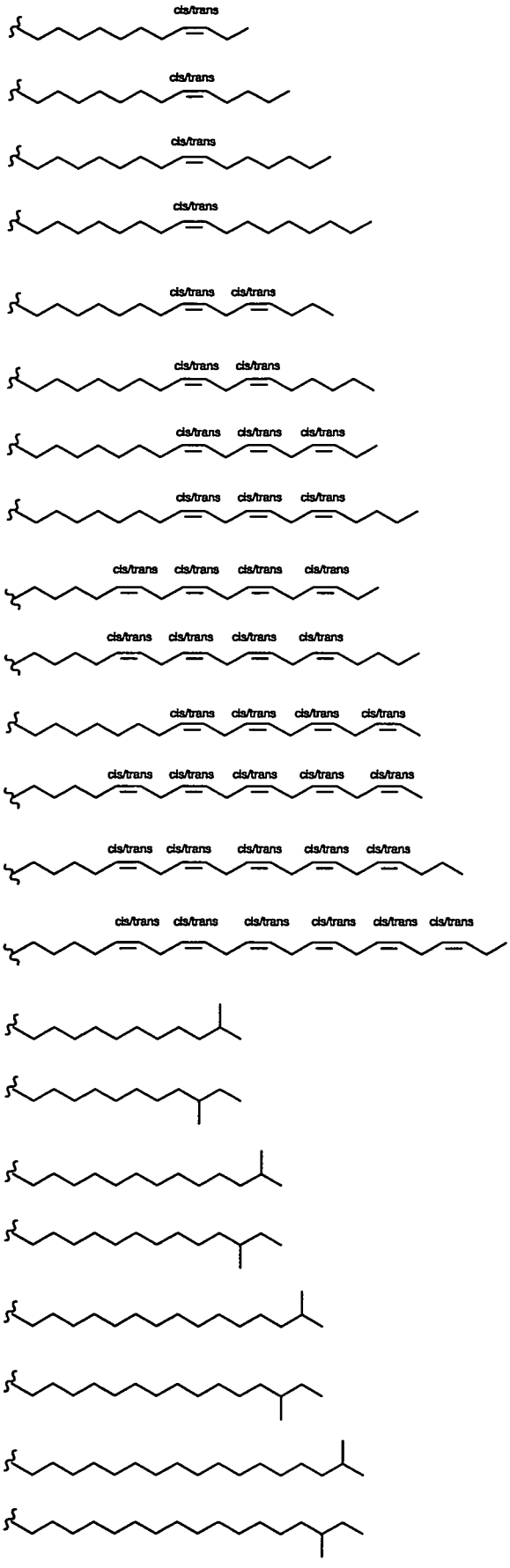
v. an optionally substituted $C_1$-$C_{10}$ alkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

vi. an optionally substituted $C_{11}$-$C_{17}$ alkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

vii. an optionally substituted $C_{18}$-$C_{24}$ alkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

viii. wherein 11, 13, 15, and 17 C-atoms are preferred;

ix. a group listed in the figures below: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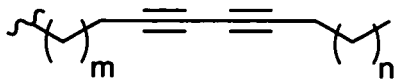


where m and n can be different or the same and

m = 0-7, preferably m=7;

n=0-11, preferably n=8, 10, or 11;

or is selected from

x. primary amines such as methyl-, ethyl-, propyl-, isopropyl-, butyl-, pentyl-, hexyl- heptyl-, octyl-, nonyl-, decyl-, undecyl-, dodecyl-, tridecyl-, tetradecyl-, pentadecyl-, hexadecyl-, heptadecyl-, nonadecyl-, eicosyl-, heneicosyl-, docosyl-, tricosyl-, or tetracosyl-amine;

xi. preferably, decyl-, dodecyl-, tetradecyl-, hexadecyl-amine;

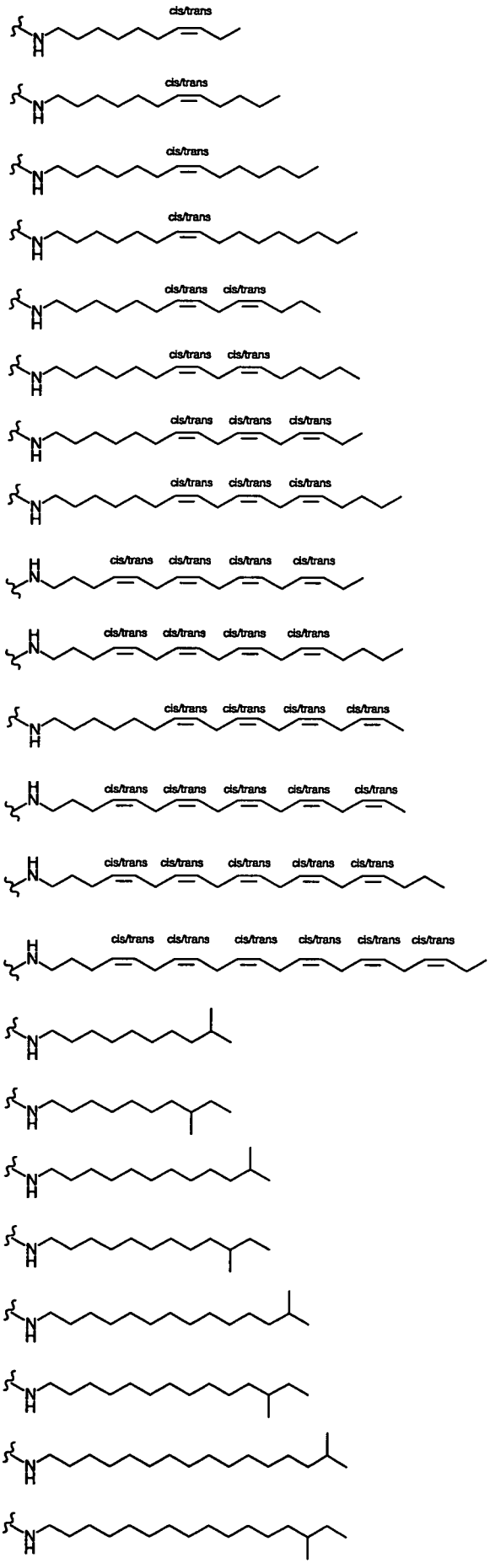
xii. an optionally substituted C1-C8 aminoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

xiii. an optionally substituted C9-C15 aminoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

xiv. an optionally substituted C16-C22 aminoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

xv. wherein 9, 11, 13, and 15 C-atoms are preferred;

xvi. a group listed in the figures below: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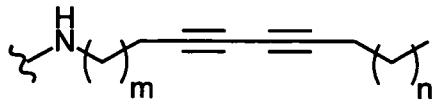


where m=0-6, and preferably m=6;

n=0-11, and preferably n=8, 10, or 11;

or

xvii. primary amides (to give acylureas) such as methyl-, ethyl-, propyl-, isopropyl-, butyl-, pentyl-, hexyl- heptyl-, octyl-, nonyl-, decyl-, undecyl, dodecyl-, tridecyl-, tetradecyl-, pentadecyl-, hexadecyl-, heptadecyl-, nonadecyl-, eicosyl-, heneicosyl-, docosyl-, tricosyl-, or tetracosyl-amide;

xviii. preferably, decyl-, dodecyl-, tetradecyl-, hexadecyl-amide;

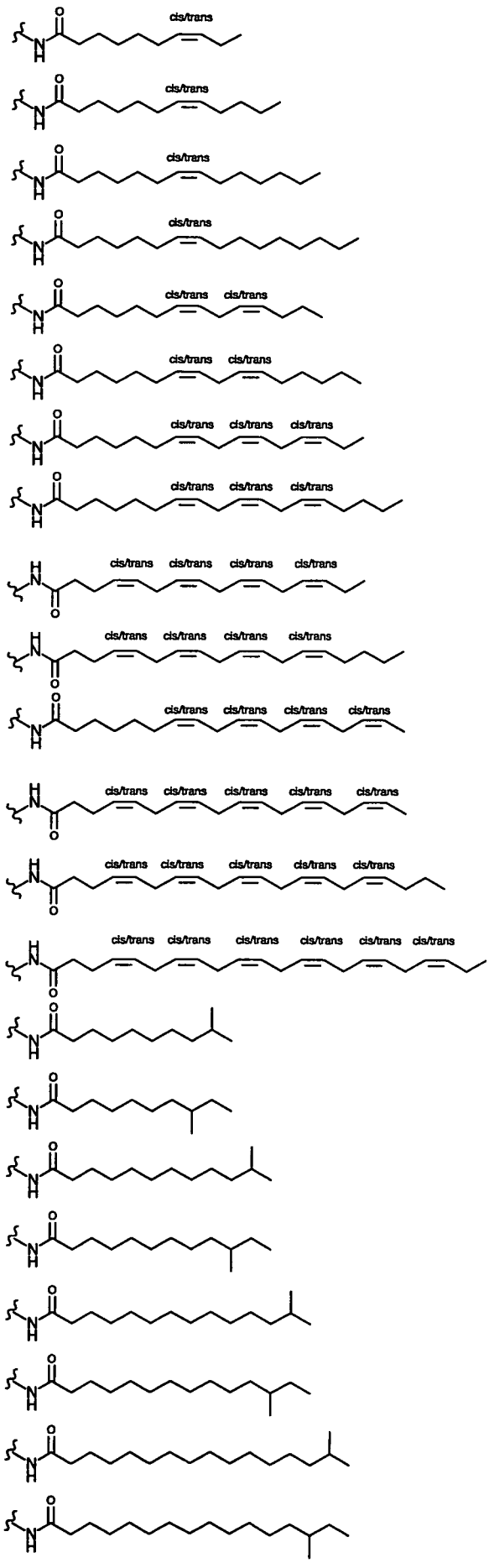
xix. an optionally substituted C1-C8 amidoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

xx. an optionally substituted C9-C15 amidoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

xxi. an optionally substituted C16-C22 amidoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

xxii. wherein 9, 11, 13, and 15 C-atoms are preferred;

xxiii. a group listed in the figures below: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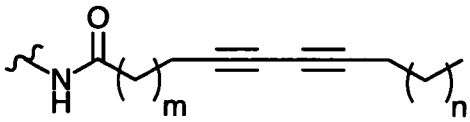


where m=0-5, and preferably m=5;

n=0-11, preferably n=8, 10, or 11;

"$D_1$" is either O (oxygen) or S (sulfur),
wherein said lipid preferably may be fully or partially deuterated, or radioactively labeled; and wherein "A" is selected from: a proton (H), a phosphatic acid or a phosphate ester substituted group such as phosphocholine, phosphoethanolamine, phosphoglycerol, phosphoserine, phosphoinositol, phosphoinositol 4,5-bisphosphate, a phosphate ester substituted sugar, a phosphate ester substituted polyethyleneglycol, a phosphate ester substituted electrophile, such as an activated ester including N-hydroxysuccinimic ester, or an acid chloride or an halogenide, a phosphate ester substituted nucleophile such as a thiol or an amine, a phosphate ester substituted fluorescent group such as fluoresceine, a phosphate ester substituted radioactively labeled group, a phosphate ester substituted alkyne and a phosphate substituted azide; and wherein "C1" may be H or a methyl;

wherein Formula Id is characterized in that

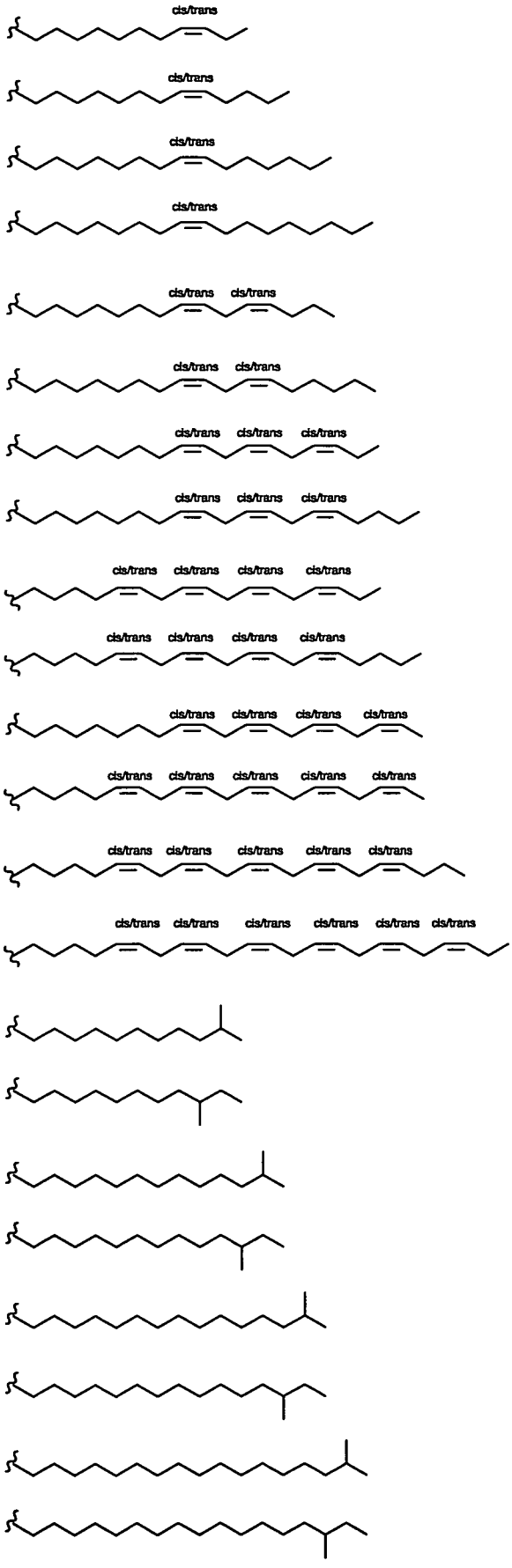
i. "$B_1$" is equal or different from "$B_2$" or "E", and "$B_1$", "$B_2$" and "E" are selected from:
ii. H;
iii. alkyl-, such as methyl-, ethyl-, propyl-, isopropyl-, butyl-, pentyl-, hexyl- heptyl-, octyl-, nonyl-, decyl-, undecyl-, dodecyl-, tridecyl-, tetradecyl-, pentadecyl-, hexadecyl-, heptadecyl-, nonadecyl-, eicosyl-, heneicosyl-, docosyl-, tricosyl-, or tetracosyl-;
iv. preferably, undecyl-, tridecyl-, pentadecyl-, heptadecyl-;
v. an optionally substituted $C_1$-$C_{10}$ alkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

vi. an optionally substituted $C_{11}$-$C_{17}$ alkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

vii. an optionally substituted $C_{18}$-$C_{24}$ alkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

viii. wherein 11, 13, 15, and 17 C-atoms are preferred;

ix. a group listed in the figures below: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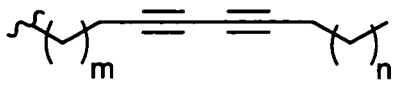


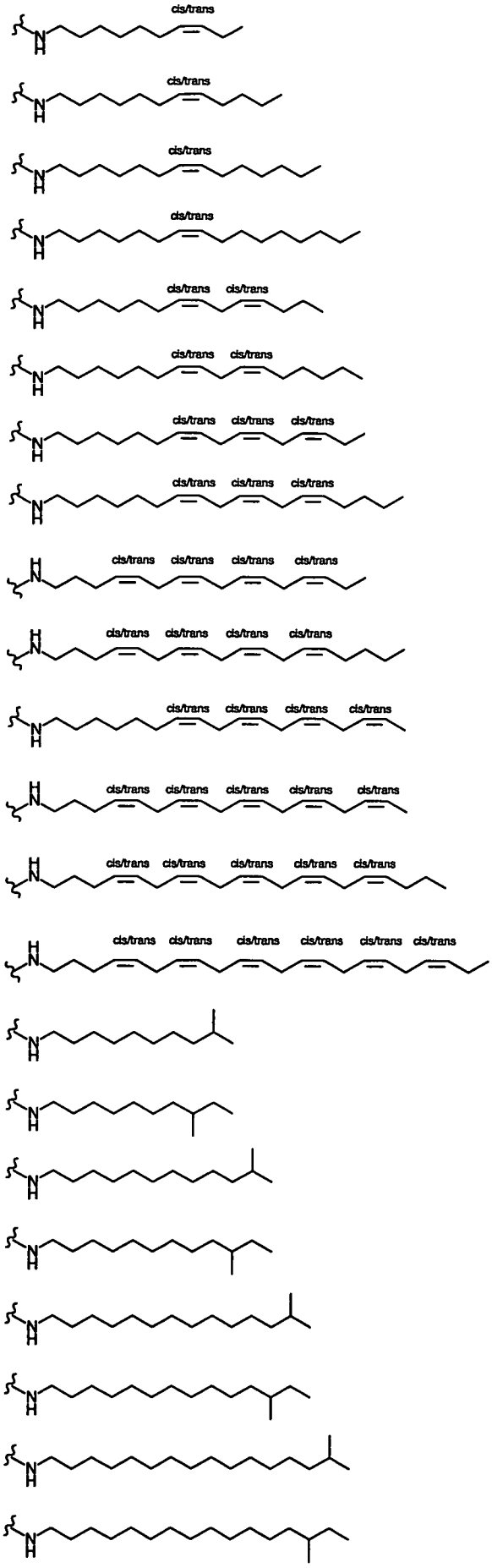
where m and n can be different or the same and

m = 0-7, preferably m=7;

n=0-11; preferably n=8, 10, or 11;

or "$B_1$" and "$B_2$" are equal or the same and are selected from:

i. primary amines such as methyl-, ethyl-, propyl-, isopropyl-, butyl-, pentyl-, hexyl- heptyl-, octyl-, nonyl-, decyl-, undecyl-, dodecyl-, tridecyl-, tetradecyl-, pentadecyl-, hexadecyl-, heptadecyl-, nonadecyl-, eicosyl-, heneicosyl-, docosyl-, tricosyl-, or tetracosyl-amine;
ii. preferably, decyl-, dodecyl-, tetradecyl-, hexadecyl-amine;
iii. an optionally substituted C1-C8 aminoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;
iv. an optionally substituted C9-C15 aminoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;
v. an optionally substituted C16-C22 aminoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;
vi. wherein 9, 11, 13, and 15 C-atoms are preferred;
vii. a group listed in the figures below: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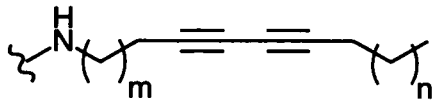


where m=0-6, and preferably m=6;

n=0-11, preferably n=8, 10, or 11;

or "$B_1$" and "$B_2$" are the same or different and are selected from:

viii. primary amides (to give acylureay) such as methyl-, ethyl-, propyl-, isopropyl-, butyl-, pentyl-, hexyl- heptyl-, octyl-, nonyl-, decyl-, undecyl-, dodecyl-, tridecyl-, tetradecyl-, pentadecyl-, hexadecyl-, heptadecyl-, nonadecyl-, eicosyl-, heneicosyl-, docosyl-, tricosyl-, or tetracosyl-amide;

ix. preferably, decyl-, dodecyl-, tetradecyl-, hexadecyl-amide;

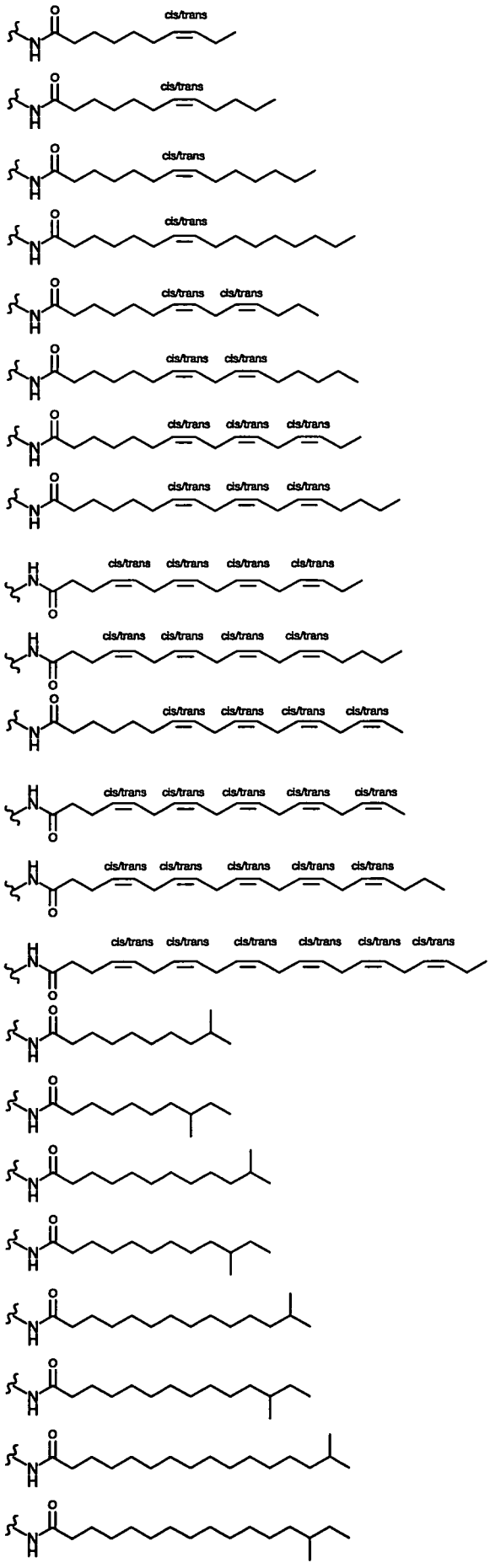
x. an optionally substituted C1-C8 amidoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

xi. an optionally substituted C9-C15 amidoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

xii. an optionally substituted C16-C22 amidoalkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

xiii. wherein 9, 11, 13, and 15 C-atoms are preferred;

xiv. a group listed in the figures below: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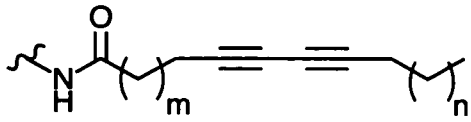


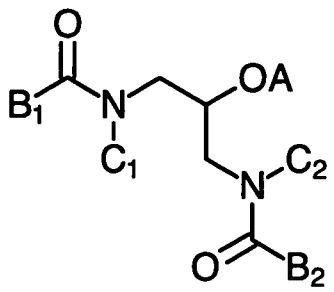
where m=0-5, preferably m=5;

n=0-11, preferably n=8, 10, or 11;

"$D_1$" and "$D_2$" can be the same or can be different and are either O (oxygen) or S (sulfur),

wherein said lipid preferably may be fully or partially deuterated, or radioactively labeled; and wherein "A" is selected from: a proton (H), a phosphatic acid or a phosphate ester substituted group such as phosphocholine, phosphoethanolamine, phosphoglycerol, phosphoserine, phosphoinositol, phosphoinositol 4,5-bisphosphate, a phosphate ester substituted sugar, a phosphate ester substituted polyethyleneglycol, a phosphate ester substituted electrophile, such as an activated ester including N-hydroxysuccinimic ester, or an acid chloride or an halogenide, a phosphate ester substituted nucleophile such as a thiol or an amine, a phosphate ester substituted fluorescent group such as fluoresceine, a phosphate ester substituted radioactively labeled group, a phosphate ester substituted alkyne and a phosphate substituted azide.

3. Composition according to claim 1 wherein the 1, 3-diamidophospholipid has the following Formula Ia:



Formula Ia

wherein

i. "$B_1$" is equal or different from "$B_2$", and "$B_1$" and "$B_2$" is selected from:

ii.H;

iii.alkyl-, such as methyl-, ethyl-, propyl-, isopropyl-, butyl-, pentyl-, hexyl-heptyl-, octyl-, nonyl-, decyl-, undecyl-, dodecyl-, tridecyl-, tetradecyl-, pentadecyl-, hexadecyl-, heptadecyl-, nonadecyl-, eicosyl-, heneicosyl-, docosyl-, tricosyl-, or tetracosyl-;

iv.preferably, undecyl-, tridecyl-, pentadecyl-, heptadecyl-;

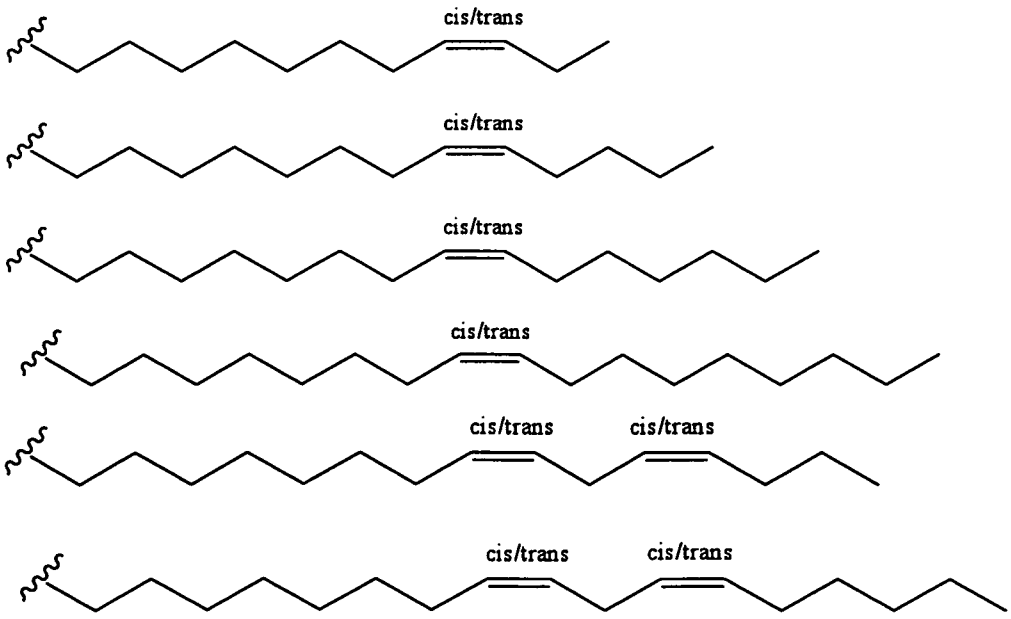
v.an optionally substituted $C_1$-$C_{10}$ alkyl group with 1, 2, 3, 4, or 5 cis- or trans-double bonds;

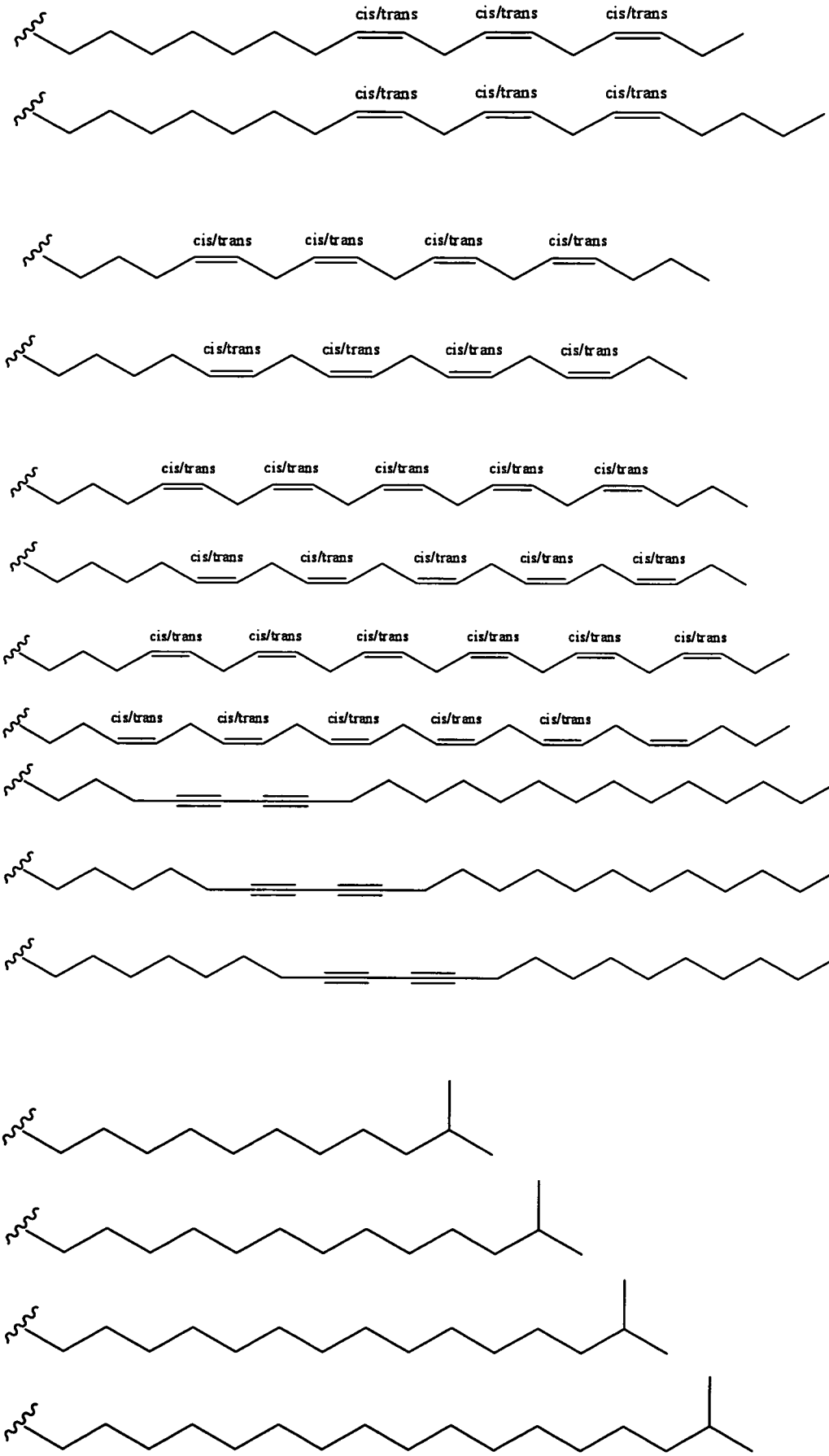
vi.an optionally substituted $C_{11}$-$C_{17}$ alkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

vii.an optionally substituted $C_{18}$-$C_{24}$ alkyl group with 1, 2, 3, 4, or 5 cis- or trans- double bonds;

viii.wherein 11, 13, 15, and 17 C-atoms are preferred;

ixa group listed in the figures below:

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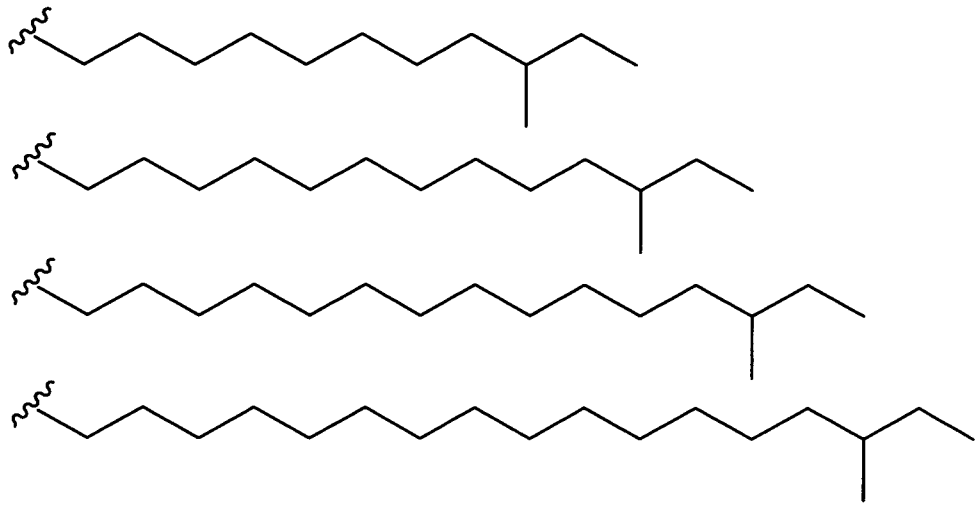

wherein said lipid may be fully or partially deuterated, or radioactively labeled;

wherein "A" is selected from:
a phosphatic acid or a phosphate ester substituted group such as phosphocholine, phosphoethanolamine, phosphoglycerol, phosphoserine, phosphoinositol, phosphoinositol 4,5-bisphosphate, a phosphate ester substituted sugar, a phosphate ester substituted polyethyleneglycol, a phosphate ester substituted electrophile, such as an activated ester including N-hydroxysuccinimic ester, or an acid chloride or an halogenide, a phosphate ester substituted nucleophile such as a thiol or an amine, a phosphate ester substituted fluorescent group such as fluoresceine, a phosphate ester substituted radioactively labeled group, a phosphate ester substituted alkyne and a phosphate substituted azide; and

wherein "$C_1$" and "$C_2$" is selected from H or methyl.

4. Composition according to any of the preceding claims wherein it further comprises an active compound.

5. Composition according to claim 4 wherein the active compound is selected from the group consisting of anabolic agents, antacids, anti-asthmatic agents, anti-cholesterolemic and anti-lipid agents, anti-coagulants, anti-convulsants, anti-diarrheals, anti-emetics, anti-infective agents including antibacterial, anitviral and antimicrobial agents, anti-inflammatory agents, anti-manic agents, antimetabolite agents, anti-nauseants, anti-neoplastic agents, anti-obesity agents, anti-pyretic and analgesic agents, anti-spasmodic agents, anti-thrombotic agents, anti-tussive agents, anti-uricemic agents, anti-anginal agents, antihistamines, appetite suppressants, biologicals, cerebral dilators, coronary dilators, bronchiodilators, cytotoxic agents, decongestants, diuretics, diagnostic agents, erythropoietic agents, expectorants, gastrointestinal sedatives, hyperglycemic agents, hypnotics, hypoglycemic agents, immunomodulating agents, ion exchange resins, laxatives, mineral supplements, mucolytic agents, neuromuscular drugs, peripheral vasodilators, psychotropics, sedatives, stimulants, thyroid and anti-thyroid agents, tissue growth agents, uterine relaxants, vitamins, antigenic materials, androgen inhibitors, polysaccharides, growth factors, hormones, anti-angiogenesis factors.

6. Composition according to any of the preceding claims wherein the composition is provided in the form of three-dimensional functional structures.

7. Structures according to claim 6 wherein the structure is a vesicle composed of a monolayer, a bilayer or multilayer.

8. Structures according to claim 6 wherein the structure is a sheet composed of a monolayer, a bilayer, or a multilayer.

9. Structures according to claim 6 wherein the structure is a tubule composed of a monolayer, a bilayer, or a multilayer.

10. Structures according to claims 7 - 9 wherein the function of the structure is provided by its three dimensional conformation.

11. Method of making a lipid wherein a phosphoethanolamine is alkylated under appropriate conditions, preferably with the use of dimethyl sulfoxide.

12. Method of making a composition according to any of claims 1 to 6.

13. Method according to claim 12 comprising mixing compounds with appropriate means.

14. Method of making structures according to any of claims 7 – 9.

15. Method according to claim 14 by thin film hydration, and/or one or more freeze-thaw cycles, sonication or/and extrusion, or by an electroformation method or by hydrating spray-dried lipids or by sonication or by repetitive freezing and thawing or by dehydration and rehydration or by the extrusion technique or by the treatment of a multilamellar vesicle suspension with a microfluidizer, or the preparation of multilamellar novasomes or the preparation of multilamellar spherulites, or the preparation of multilamellar vesicles by the "bubble method", or the preparation by the "Cochleate cylinder method", or the preparation by the "Reversed-phase evaporation technique, or the preparation from water/oil and water/oil/water emulsions, or the preparation by the "solvent-spherule (W/O/W-emulsion) method" or the "DepoFoam Technology", or the preparation from an organic aqueous two-phase system, or the preparation by the "ethanol injection method, or the preparation by the "pro-liposome method", or the preparation of multilamellar ethosomes, or the preparation by the "interdigitation-fusion method", or the preparation by the "coacervation technique", or the preparation by the "supercritical liposome method", or the preparation from an initial oil/water

emulsion, or the preparation by the "Detergent-depletion method", or the preparation by mixing bilayer-forming and micelle-forming amphiphiles, or the preparation from lipids in chaotropidc ion solutions, or the preparation of vesicles prepared from a water/oil-emulsion with the help of a detergent, or a vesicle prepared by the hydration of a multilayer of lipids on a hydrogel, or a vesicle prepared by using a microfluidics device.

16. Pharmaceutical or cosmetic composition comprising a composition according to any of claims 1 - 6 or a structure according to any of claims 7 – 10, and preferably further useful carriers or/and additives.

17. Composition according to any of claims 1 - 6 or structures according to any of claims 7 - 10 for use in a pharmaceutical or cosmetic application.

18. Composition according to any of claims 1 - 6 or structures according to any of claims 7 - 10 for use in the prophylaxis or treatment of a dermatological disorder or disease, for the use in wound or lesion healing or treatment of wounds or lesions, preferably wound or lesion dressing or antiseptic coating, for the use in the prophylaxis or treatment of anaemia, or in connection with other supportive therapies, or for use as cosmetic, or for use in a monitoring or diagnostic method.

19. Use according to claim 18 wherein the dermatological disease or disorder is selected from the group consisting of acne, napkin dermatitis, atopic dermatitis, seborrhoeic dermatitis, psoriasis, warts, tinia pedis, seborrhoeic keratosis, hives, rosacea, dermatological viral infection and dermatological bacterial infection.

20. Use according to claim 18 wherein the use as cosmetic comprises topical applications.

21. Use according to claim 18 wherein the wound or lesion is situated at a tissue surface or interface.

22. Composition according to any of the preceding claims for the application for use in wound or lesion healing, or wound or lesion dressing, preferably antiseptic coating, or wound, lesion, skin or tissue surface protection.

23. Composition according to any of claims 1 - 6 or structures according to any of claims 7 - 10 for use as complexation agent, preferably as delivery compound for a second compound, more preferably of ions, preferably Ag or Fe, preferably in a patient's circulation.

24. Composition according to any of the preceding claims for the application for use in non-medical applications, preferably coating of a surface with preferably a sheet comprising the compounds or compound mixtures of the invention and more preferably another active compound according to any of the preceding claims or a compound useful in surface coating, or for foaming purposes, or in the context of cleaning polluted areas or surfaces.

FIG 1

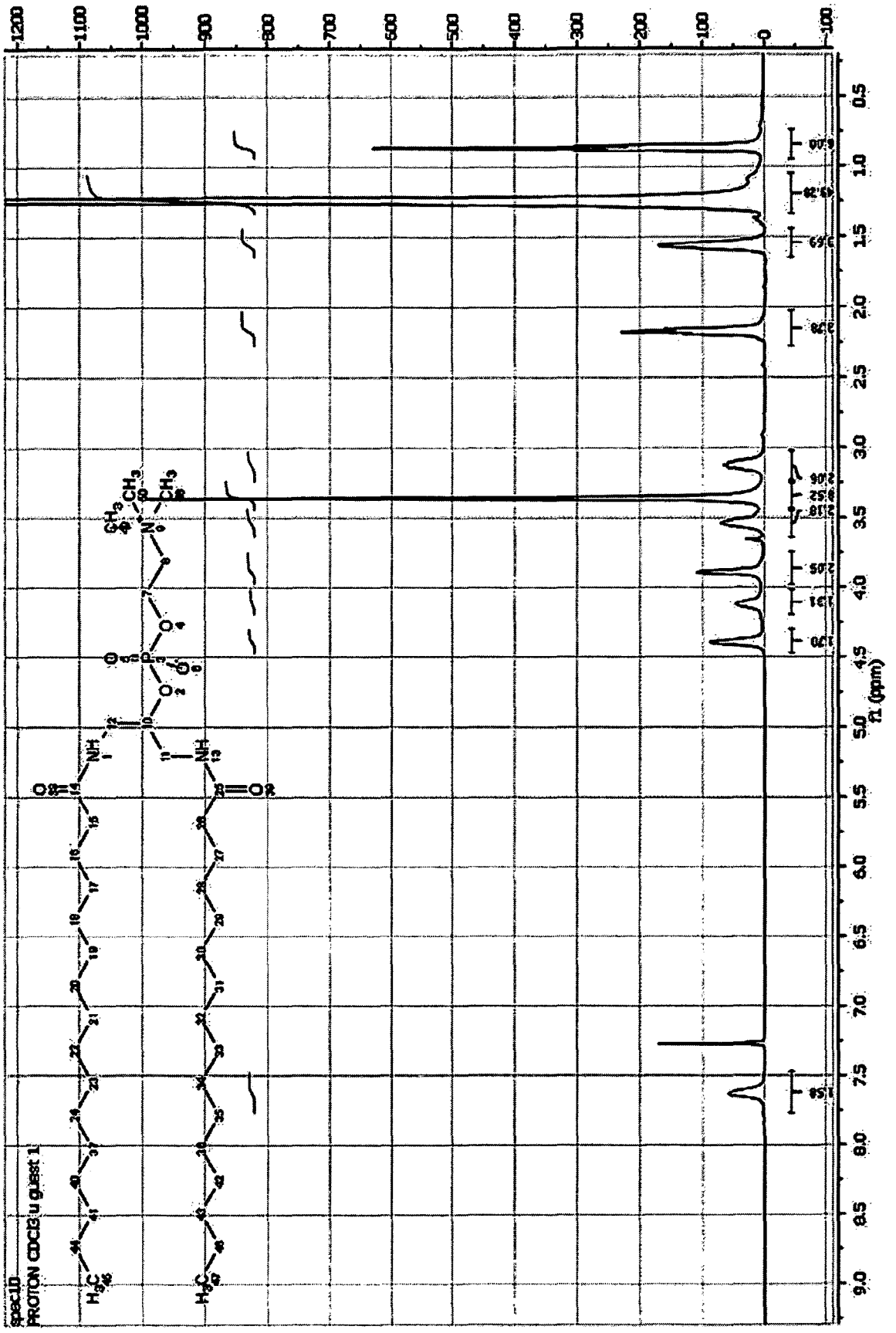

FIG 2

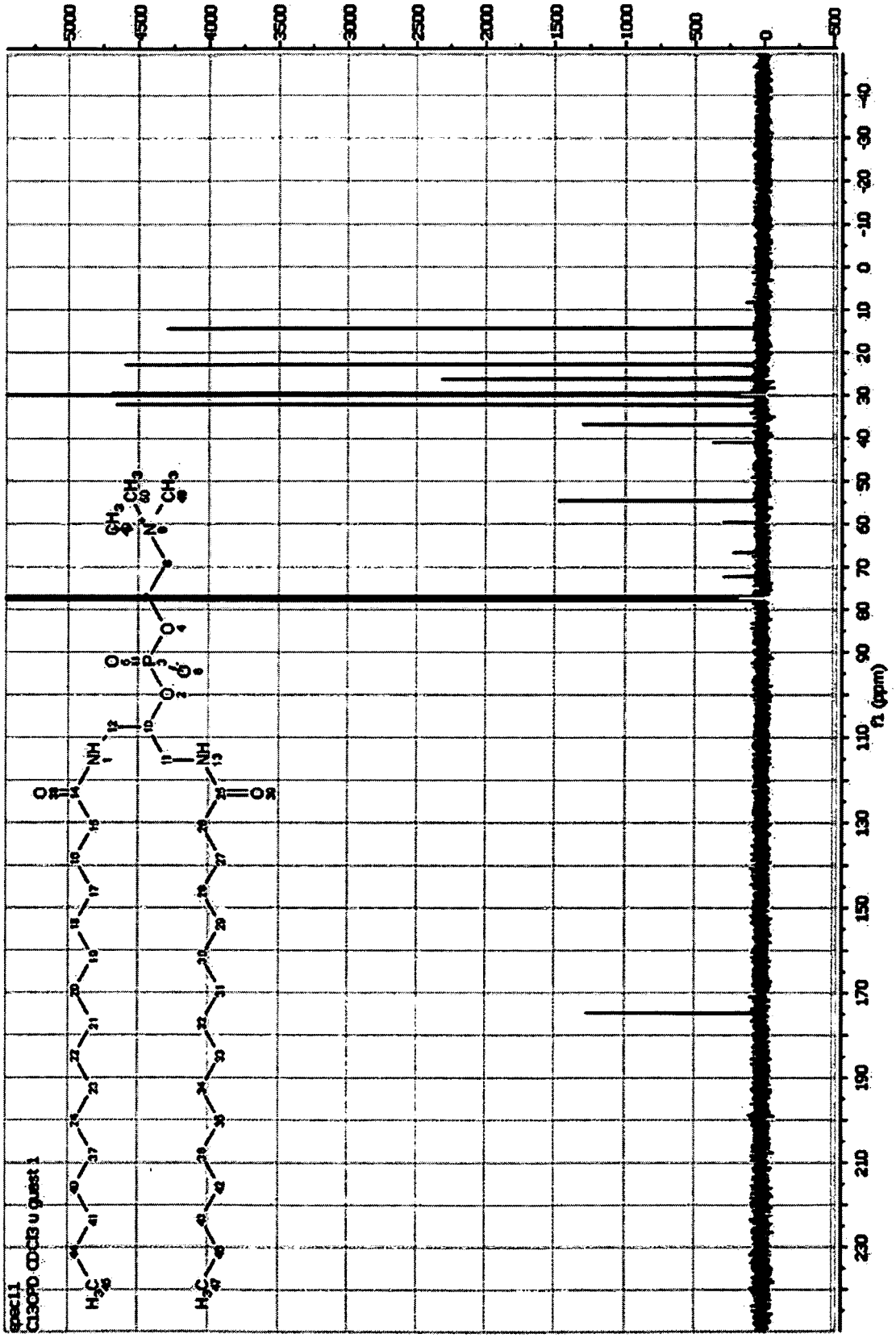
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FIG 3

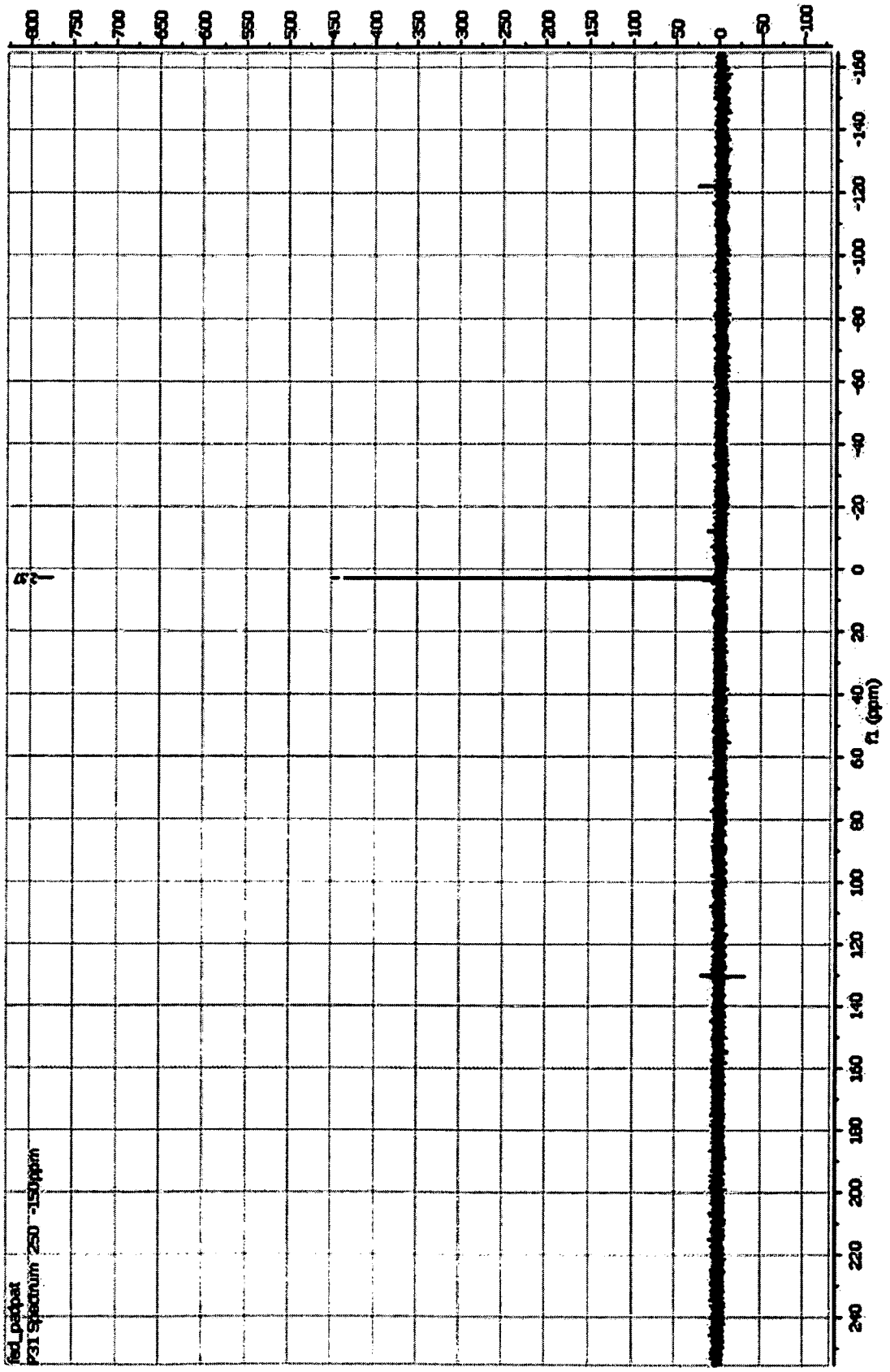
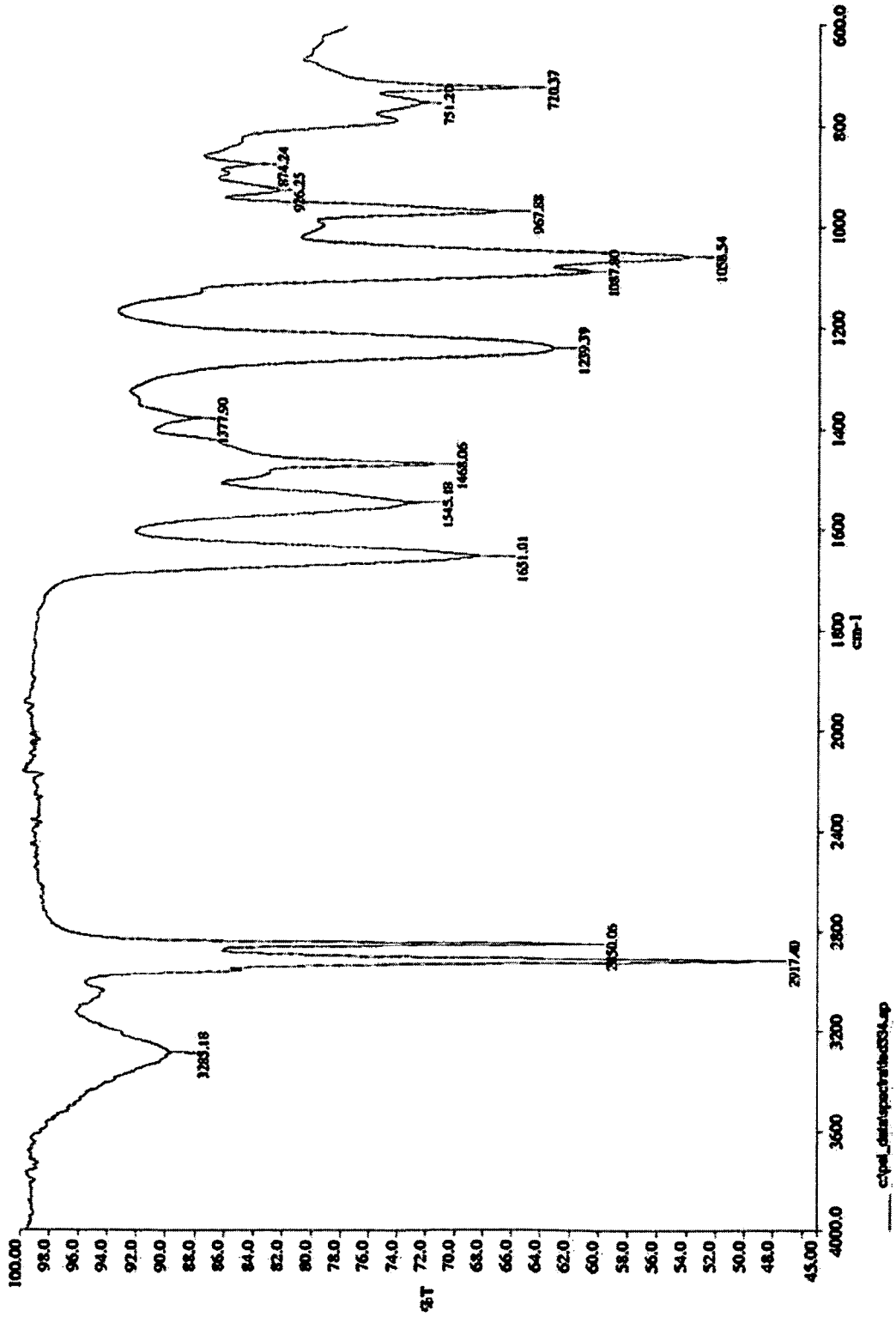


FIG 4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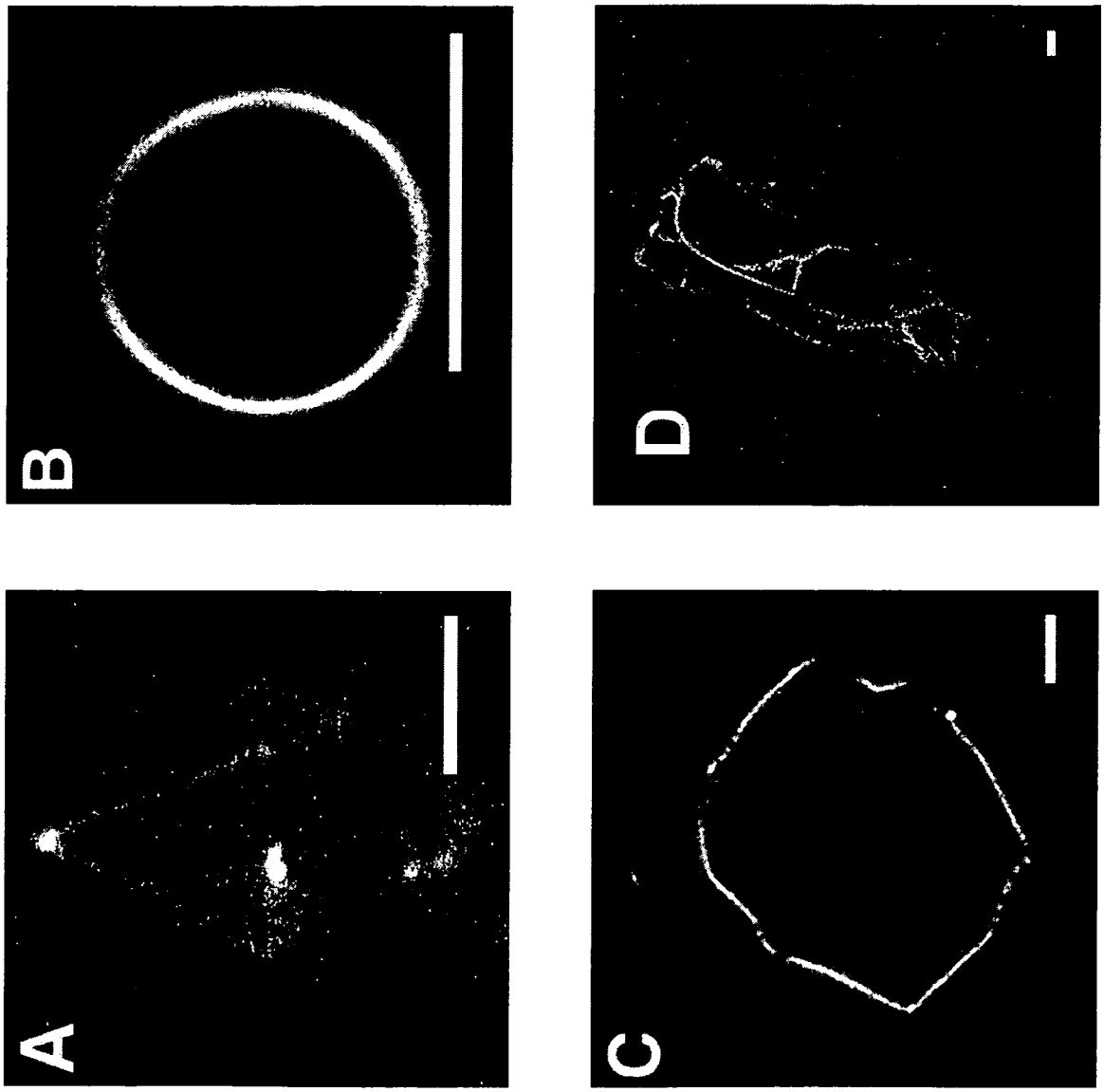


FIG 5