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(54) **Title**: DENDRITIC CORE COMPOUNDS

(57) **Abstract**: The invention relates to compounds that are useful for the preparation of dendrimer compounds, the use of these compounds for preparing dendrimers and processes for preparing the compounds.

DENDRITIC CORE COMPOUNDS

TECHNICAL FIELD

This invention relates generally to compounds that are intermediates for the preparation of dendrimer compounds, the use of these compounds for preparing dendrimers and processes for preparing the compounds.

BACKGROUND

Interest in dendritic compounds has grown in recent times, and dendrimers have found application in a wide range of areas, such as pharmaceuticals, drug delivery, gene delivery, sensor technologies (cation photodetection and fluorescence signal quenching), in the synthesis of monodisperse metallic nanoparticles, in environmental remediation, as blood substitutes usually in the oxygen-carrying sense (oxygen therapeutics) and plasma substitutes (volume expenders).

Dendritic structures tend to be complex. However, for some applications, such as pharmaceuticals, it is desirable to employ compounds that are discrete, well-characterised, single entities. This can be an issue in the dendrimer space, so it is desirable to use intermediates and processes which produce such single entities. There is therefore a need for simple dendritic cores that can be used to prepare dendritic compounds for use in certain applications.

Newkome *et al.* (*Macromolecules*, 1993, 26, 2394-2396) have described the synthesis of a dodecaacid dendritic core, starting from the tetraacid compound (structure shown in Scheme 1, below) and coupling this with a branched amine. This produced a compound with twelve terminal acids (attachment points), which was further elaborated (through five generations) to produce dendrimers having up to 972 terminal acids.

Newkome *et al.* (*J. Org. Chem.* 2002, 67, 3957-3960) have also reported the synthesis of a tetraamine (amine terminated) dendritic core, starting from the tetraacid compound. The tetraamine core was further elaborated by reaction with excess acrylonitrile to generate an octanitrile as an oily product.

Hukkamäki *et al.* (Hukkämaki, J.; Pakkanen, T.T. *Journal of Molecular Catalysis A: Chemical* **2001**, 174, 205-21) have also described the synthesis of the same amine terminated dendritic

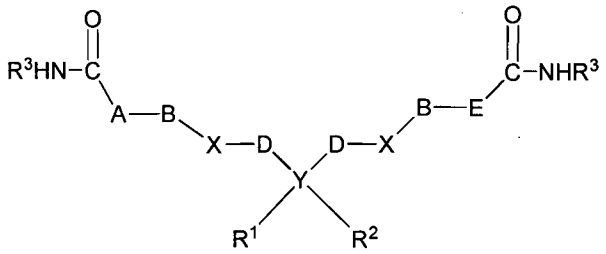
core. The tetraamine core was further elaborated by reaction with acrylonitrile to produce a (two generation) dendrimer having eight terminal amine groups.

For the synthesis of simple, well-defined dendritic molecules as single compounds, it would be desirable to employ a simple, stable dendritic core as an intermediate which could provide a route to the synthesis of, for example, dendrimers having pharmaceutical uses.

It is therefore an object of the present invention to provide intermediate compounds for the preparation of dendritic compounds, or to at least provide a useful choice.

SUMMARY OF INVENTION

In a first aspect, the invention provides a compound of formula (I)



wherein:

Y is O;

B is O;

R^1 and R^2 are absent; and

either A, E, D and X are all CH_2; or A, D and X are all CH_2 and E is $(CH_2CH_2O)_t{}^{\#}CH_2$ wherein # indicates a point of attachment of E to its adjacent carbonyl group;

t is an integer from 1 to 10;

or wherein:

Y is C;

R^1 and R^2 are both H; and

A, E, B and D are CH_2 and X is O;

or wherein:

Y is C;

A is $(CH_2)_u$

R^1 and R^2 are both H;

B, X, D and E are all absent; and

u is an integer from 1 to 10;

or wherein:

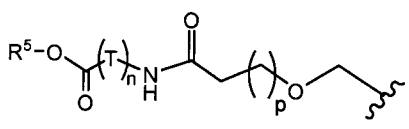
Y is C;

X is O;

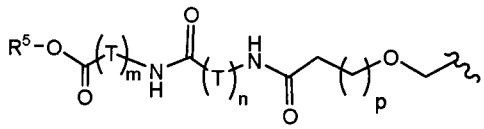
B is $(CH_2)_p$;

A, E and D are all CH_2; and

R^1 is H, NHZ or C_{1-6}alkyl and R^2 is a radical of formula (i) or a radical of formula (ii)



(i)



(ii)

;

Z is H, acyl, $C(O)(CH_2)_wN(H)G$, $*CH_3*C(O)$- where *C denotes ^{13}C or ^{14}C, 5-TAMRA (4-carboxytetramethylrhodamine), Fluorescein (resorcinolphthalein), Alexa Fluor 350 (7-amino-4-methyl-6-sulfocoumarin-3-acetic acid), BODIPY (4,4-difluoro-4-bora-3a,4a-diaza-s-indacene) or Alkyne MegaStokes dye 608 (1-{3-{[4-(2-cyclooctyn-1-ylmethyl)benzoyl]amino}propyl}-4-{2-[4-(dimethylamino)phenyl]ethenyl}pyridinium hexafluorophosphate);

w is an integer from 1 to 11;

G is H, acyl, Boc (t-butoxycarbonyl), Troc (2,2,2-trichloroethyloxycarbonyl), Fmoc (9-fluorenylmethoxycarbonyl), Cbz (benzyloxycarbonyl),$*CH_3*CO$- where *C denotes ^{13}C or ^{14}C, 5-TAMRA (4-carboxytetramethylrhodamine), Fluorescein (resorcinolphthalein), Alexa Fluor 350 (7-amino-4-methyl-6-sulfocoumarin-3-acetic acid), BODIPY (4,4-difluoro-4-bora-3a,4a-diaza-s-indacene) or Alkyne MegaStokes dye 608 (1-{3-{[4-(2-cyclooctyn-1-ylmethyl)benzoyl]amino}propyl}-4-{2-[4-(dimethylamino)phenyl]ethenyl}pyridinium hexafluorophosphate);

or wherein:

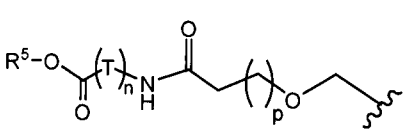
Y is C;

X is O;

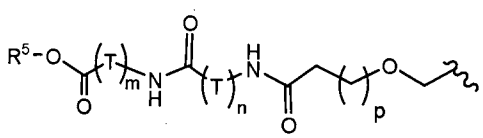
B is $(CH_2)_p$;

A, E and D are all CH_2; and

R^1 and R^2, both the same, are a radical of formula (i) or a radical of formula (ii)



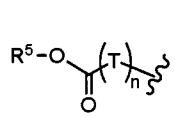
(i)



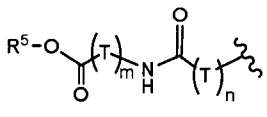
(ii)

;

R^3 is a radical of formula (iii) or a radical of formula (iv)



(iii)



(iv) ;

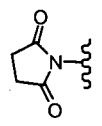
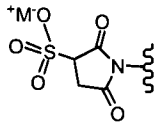
each T is independently selected from the group consisting of $(CH_2CH_2O)_xCH_2CH_2$ and CH_2;

each x is independently an integer from 1 to 12;

m is an integer from 1 to 11, provided that when T is $(CH_2CH_2O)_xCH_2CH_2$ then m is 1;

n is an integer from 1 to 11, provided that when T is $(CH_2CH_2O)_xCH_2CH_2$ then n is 1;

p is an integer from 1 to 5;

R^5 is H,  or  ; and

M is sodium or ammonium.

Preferably each T is CH_2.

Alternatively preferably at least one T is CH_2.

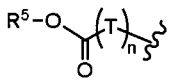
Alternatively preferably at least one T is $(CH_2CH_2O)_xCH_2CH_2$.

More preferably each T is CH_2 and m is an integer from 3 to 10, e.g. an integer from 4 to 9, e.g. an integer from 5 to 8, e.g. an integer from 6 to 7. Most preferably m is 7. Preferably each T is CH_2 and n is an integer from 3 to 10, e.g. an integer from 4 to 9, e.g. an integer from 5 to 8, e.g. an integer from 6 to 7. Most preferably n is 7.

Alternatively preferably at least one T is CH_2 and m is an integer from 3 to 10, e.g. an integer from 4 to 9, e.g. an integer from 5 to 8, e.g. an integer from 6 to 7. Most preferably m is 7. Preferably at least one T is CH_2 and n is an integer from 3 to 10, e.g. an integer from 4 to 9, e.g. an integer from 5 to 8, e.g. an integer from 6 to 7. Most preferably n is 7.

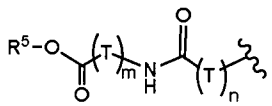
Alternatively preferably at least one T is $(CH_2CH_2O)_xCH_2CH_2$ and x is an integer from 2 to 10, e.g. an integer from 2 to 9, e.g. an integer from 2 to 8, e.g. an integer from 2 to 7, e.g. an integer from 2 to 6, e.g. an integer from 2 to 5, e.g. an integer from 2 to 4. Most preferably x is 3.

Preferably Y is O. Alternatively, it is preferred that Y is C.



(iii)

Preferably R^3 is a radical of formula (iii) .



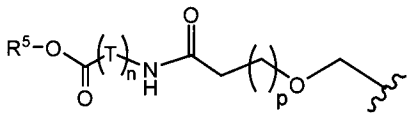
(iv)

Alternatively it is preferred that R^3 is a radical of formula (iv) .

It is further preferred that, in R^3, one T is $(CH_2CH_2O)_xCH_2CH_2$ and one T is CH_2.

It is further preferred that, in R^3, $(T)_m$ is $(CH_2CH_2O)_xCH_2CH_2$ and $(T)_n$ is $(CH_2)_n$. Alternatively it is preferred that, in R^3, $(T)_n$ is $(CH_2CH_2O)_xCH_2CH_2$ and $(T)_m$ is $(CH_2)_m$.

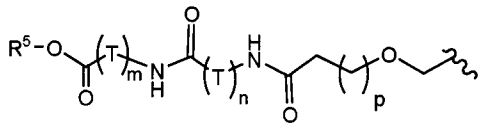
Alternatively preferably R^3 is a radical of formula (iv) wherein each T is $(CH_2CH_2O)_xCH_2CH_2$, wherein each x in each radical of formula (iv) is independently selected.



(i)

Preferably R^1 and R^2 are both a radical of formula (i) .

Alternatively it is preferred that R^1 and R^2 are both a radical of formula (ii)

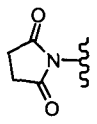
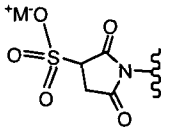


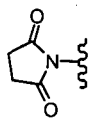
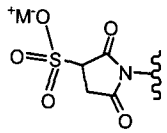
(ii)

It is further preferred that, in R^1, one T is $(CH_2CH_2O)_xCH_2CH_2$ and one T is CH_2 and, in R^2, one T is $(CH_2CH_2O)_xCH_2CH_2$ and one T is CH_2.

It is further preferred that, in both R^1 and R^2, $(T)_m$ is $(CH_2CH_2O)_xCH_2CH_2$ and $(T)_n$ is $(CH_2)_n$. Alternatively it is preferred that, in both R^1 and R^2, $(T)_n$ is $(CH_2CH_2O)_xCH_2CH_2$ and $(T)_m$ is $(CH_2)_m$. Alternatively it is preferred that, in both R^1 and R^2, each T is $(CH_2CH_2O)_xCH_2CH_2$, wherein each x in each radical of formula (ii) is independently selected.

Alternatively it is preferred that R^1 is H or C_{1-6}alkyl, e.g. CH_3 or CH_2CH_3. Alternatively it is preferred that R^1 is NH_2. Alternatively it is preferred that R^1 is NHZ, more preferably where Z is $C(O)(CH_2)_wN(H)G$, e.g. where G is Troc (2,2,2-trichloroethyloxycarbonyl), Fmoc (fluorenylmethyloxycarbonyl) or Cbz (benzyloxycarbonyl). Preferably w is 7.

Preferably R^5 is selected from the group consisting of  and  .

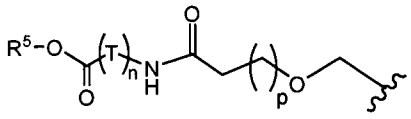
Preferably R^5 is  . Alternatively preferably R^5 is H. Alternatively preferably R^5 is  .

Preferably Y is O; B is O; R^1 and R^2 are absent; and either A, E, D and X are all CH_2 or A, D and X are all CH_2 and E is $(CH_2CH_2O)_tCH_2$; and t is an integer from 1 to 10, preferably an integer from 1 to 2.

Alternatively it is preferred that Y is C; R^1 and R^2 are both H; A, E, B and D are CH_2 and X is O.

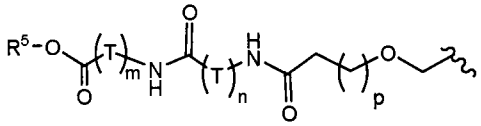
Alternatively it is preferred that Y is C; A is $(CH_2)_u$; R^1 and R^2 are both H; B, X, D and E are all absent; and u is an integer from 1 to 10.

Alternatively it is preferred that:
Y is C; X is O; A, E and D are all CH_2; B is $(CH_2)_p$;
R^1 is H, NHZ or C_{1-6}alkyl;



(i)

R^2 is a radical of formula (i) or a radical of formula (ii)



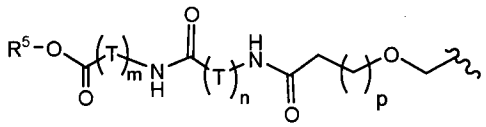
(ii)

; and

Z is H, acyl, $C(O)(CH_2)_wN(H)G$, $*CH_3*CO$- where *C denotes ^{13}C or ^{14}C, 5-TAMRA (4-carboxytetramethylrhodamine), Fluorescein (resorcinolphthalein), Alexa Fluor 350 (7-amino-4-methyl-6-sulfocoumarin-3-acetic acid), BODIPY (4,4-difluoro-4-bora-3a,4a-diaza-s-indacene) or Alkyne MegaStokes dye 608 (1-{3-{[4-(2-cyclooctyn-1-ylmethyl)benzoyl]amino}propyl}-4-{2-[4-(dimethylamino)phenyl]ethenyl}pyridinium hexafluorophosphate);

w is an integer from 1 to 11;

G is H, acyl, (t-butoxycarbonyl), Troc (2,2,2-trichloroethyloxycarbonyl), Fmoc (9-fluorenylmethoxycarbonyl), Cbz (carboxybenzyl),* $*CH_3*CO$- where *C denotes ^{13}C or ^{14}C, 5-TAMRA (4-carboxytetramethylrhodamine), Fluorescein (resorcinolphthalein), Alexa Fluor 350 (7-amino-4-methyl-6-sulfocoumarin-3-acetic acid), BODIPY (4,4-difluoro-4-bora-3a,4a-diaza-s-indacene) or Alkyne MegaStokes dye 608 (1-{3-{[4-(2-cyclooctyn-1-ylmethyl)benzoyl]amino}propyl}-4-{2-[4-(dimethylamino)phenyl]ethenyl}pyridinium hexafluorophosphate).

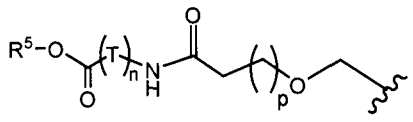


(ii)

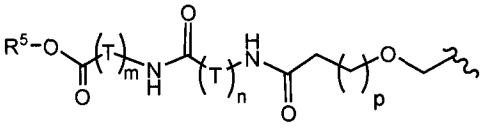
Preferably R^2 is a radical of formula (ii) and R^1 is H, NHZ or $C_{1\text{-}6}$alkyl. It is further preferred that, in R^2, one T is $(CH_2CH_2O)_xCH_2CH_2$ and one T is CH_2.

It is further preferred that, in R^2, $(T)_m$ is $(CH_2CH_2O)_xCH_2CH_2$ and $(T)_n$ is $(CH_2)_n$. Alternatively it is preferred that, in R^2, $(T)_n$ is $(CH_2CH_2O)_xCH_2CH_2$ and $(T)_m$ is $(CH_2)_m$. Alternatively it is preferred that, in R^2, each T is $(CH_2CH_2O)_xCH_2CH_2$, wherein each x in each radical of formula (ii) is independently selected.

Alternatively it is preferred that Y is C; X is O; A, E and D are all CH_2; B is $(CH_2)_p$; R^1 and R^2, both the same, are a radical of formula (i) or a radical of formula (ii)

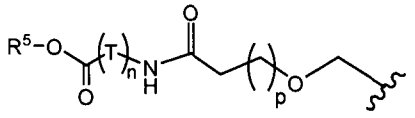


(i)



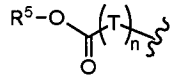
(ii)

Preferably, Y is C; X is O; A, E and D are all CH_2; B is $(CH_2)_p$; R^1 and R^2, both the same, are a



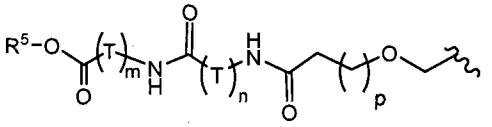
(i)

radical of formula (i) ; R^3 is a radical of formula (iii)



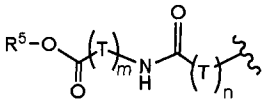
(iii) ; and p is 1.

Alternatively preferably Y is C; X is O; A, E and D are all CH_2; B is $(CH_2)_p$; R^1 and R^2, both the



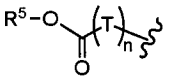
(ii)

same, are a radical of formula (ii) ; R^3 is a radical of



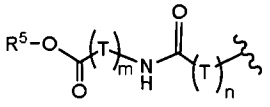
formula (iv) (iv) ; and p is 1.

Preferably Y is C; R^1 and R^2 are both H; A, E, B and D are CH_2; X is O; and R^3 is a radical of



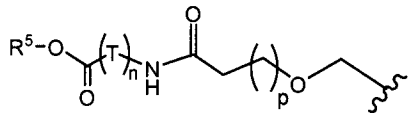
formula (iii) (iii) .

Alternatively preferably Y is C; R^1 and R^2 are both H; A, E, B and D are CH_2; X is O; and R^3 is a

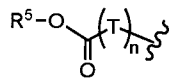


radical of formula (iv) (iv) .

Preferably Y is C; X is O; A, E and D are all CH_2; B is $(CH_2)_p$; R^1 is H; R^2 is a radical of formula (i)

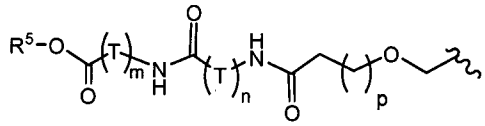


(i) ; R^3 is a radical of formula (iii)

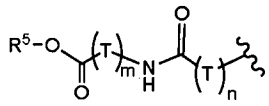


(iii) ; and p is 1.

Alternatively preferably Y is C; X is O; A, E and D are all CH_2; B is $(CH_2)_p$; R^1 is H; R^2 is a radical

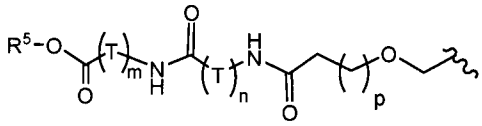


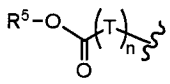
of formula (ii) (ii) ; R^3 is a radical of formula (iv)



(iv) ; and p is 1.

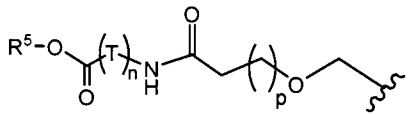
Alternatively preferably Y is C; X is O; A, E and D are all CH_2; B is $(CH_2)_p$; R^1 is H; R^2 is a radical



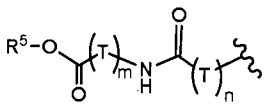


of formula (ii) (ii) ; R^3 is a radical of formula (iii) (iii) ; and p is 1.

Alternatively preferably Y is C; X is O; A, E and D are all CH_2; B is $(CH_2)_p$; R^1 is H; R^2 is a radical

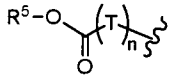


of formula (i) (i) ; and R^3 is a radical of formula (iv)



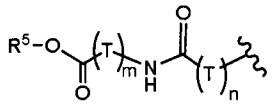
(iv) ; and p is 1.

Preferably Y is C; A is $(CH_2)_u$; R^1 and R^2 are both H; B, X, D and E are all absent; u is an integer



from 1 to 10; and R^3 is a radical of formula (iii) (iii) .

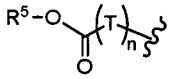
Alternatively preferably Y is C; A is $(CH_2)_u$; R^1 and R^2 are both H; B, X, D and E are all absent; u is an integer from 1 to 10; and R^3 is a radical of formula (iv)



(iv)

.

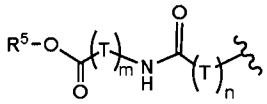
Preferably Y is O; B is O; R^1 and R^2 are absent; and either A, E, D and X are all CH_2 or A, D and X are all CH_2 and E is $(CH_2CH_2O)_tCH_2$; t is an integer from 1 to 10, preferably an integer from 1 to 2; and R^3 is a radical of formula (iii)



(iii)

.

Alternatively preferably Y is O; B is O; R^1 and R^2 are absent; and either A, E, D and X are all CH_2 or A, D and X are all CH_2 and E is $(CH_2CH_2O)_tCH_2$; t is an integer from 1 to 2; and R^3 is a radical of formula (iv)



(iv)

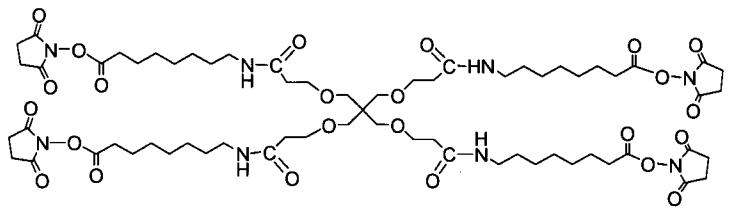
.

Preferably p is 1.

Preferably t is an integer from 1 to 2.

Preferably M is sodium.

Preferably the compound of formula (I) is selected from the group consisting of:



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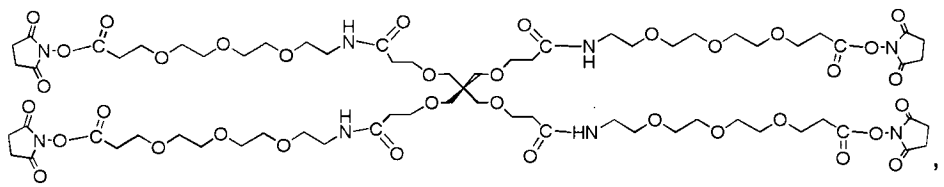

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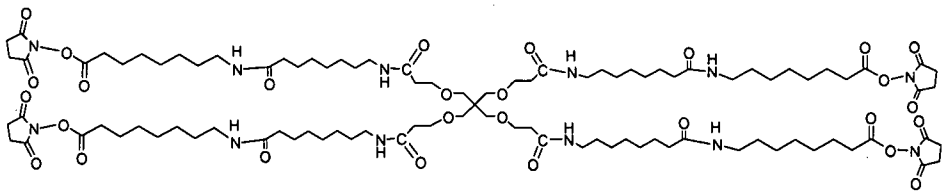

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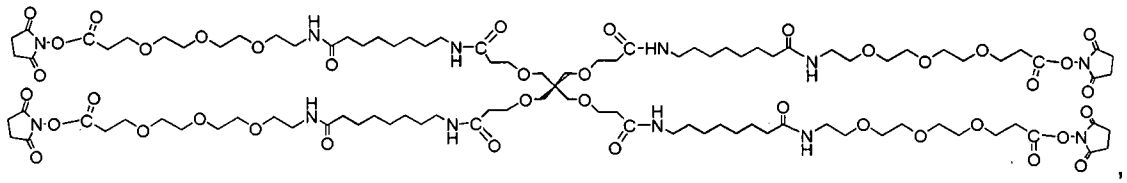

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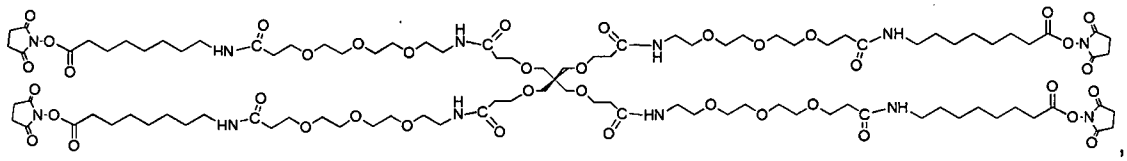

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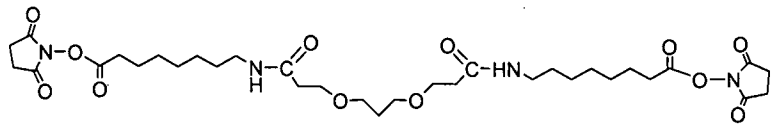

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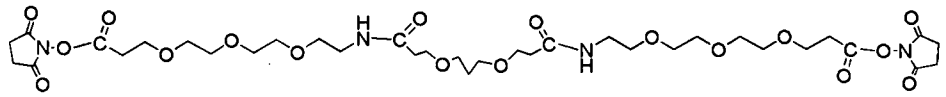

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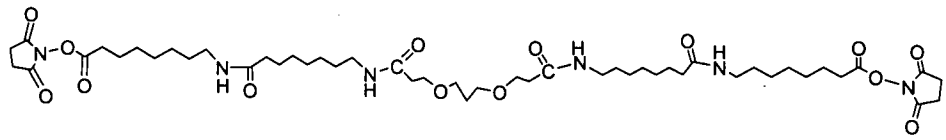

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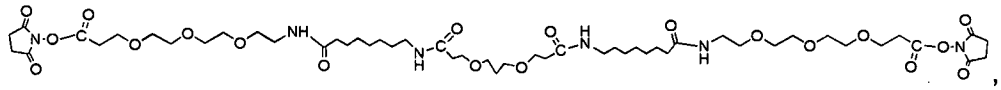

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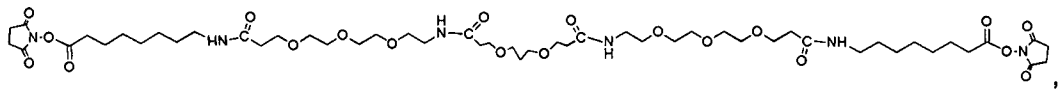

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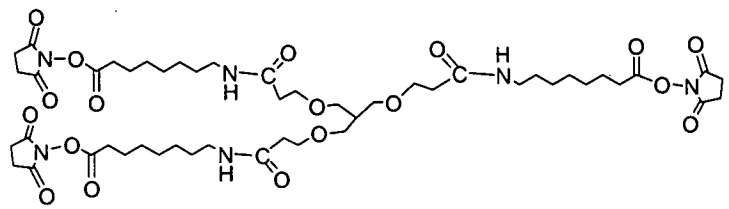

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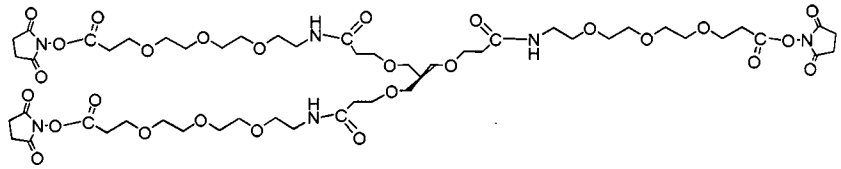

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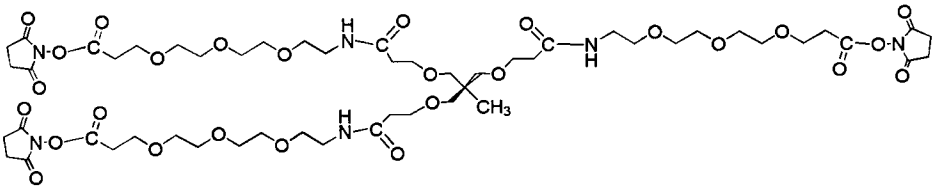

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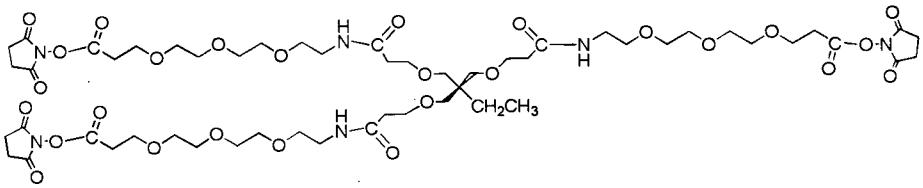

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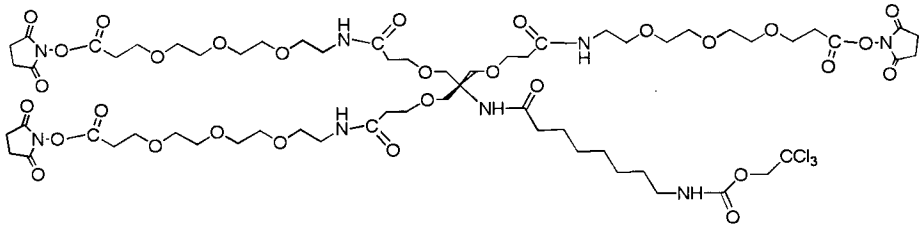

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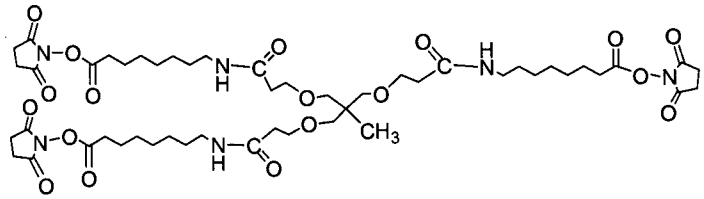

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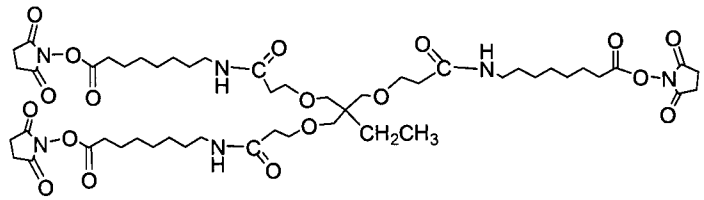

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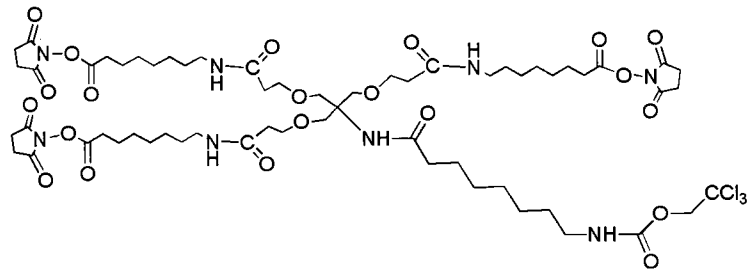

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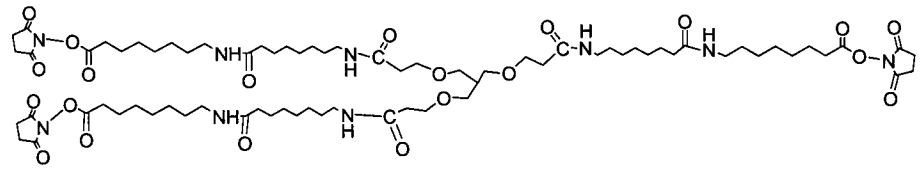

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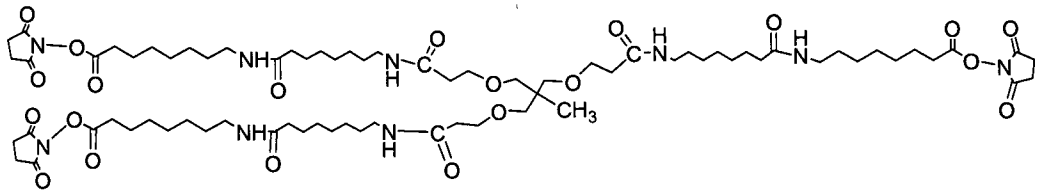

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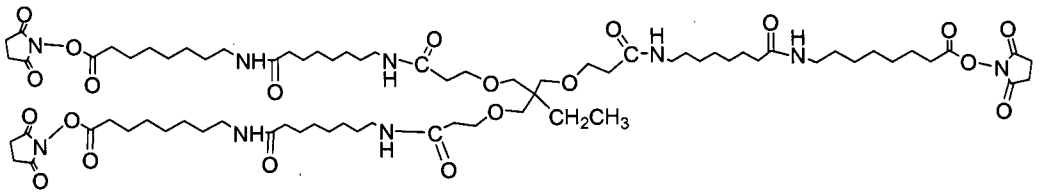

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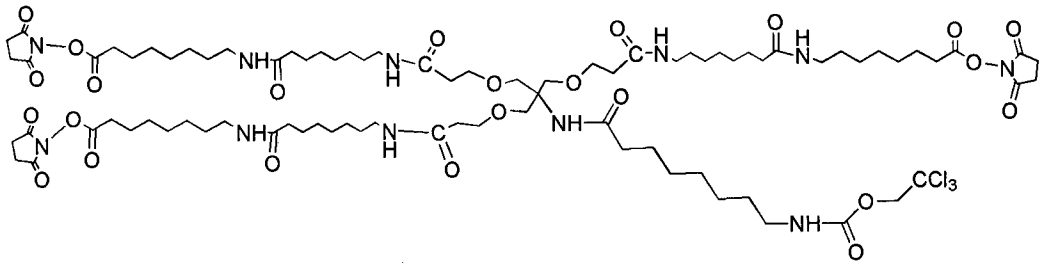

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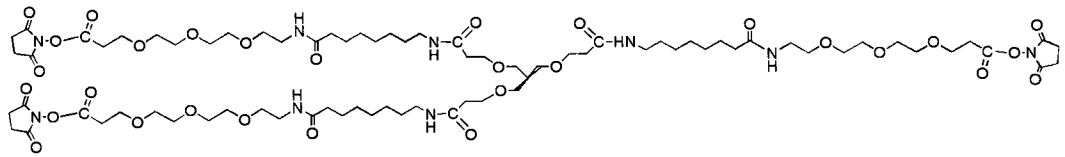

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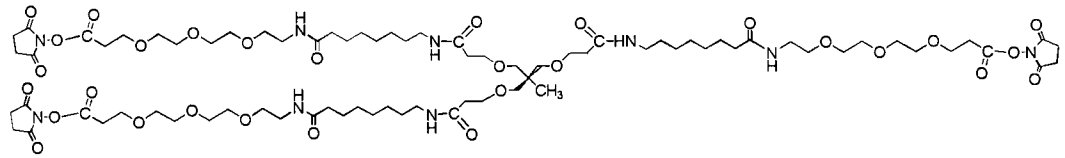

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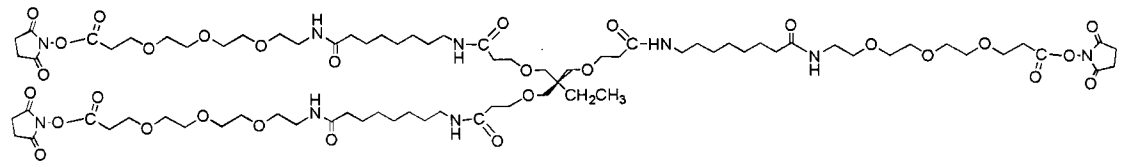

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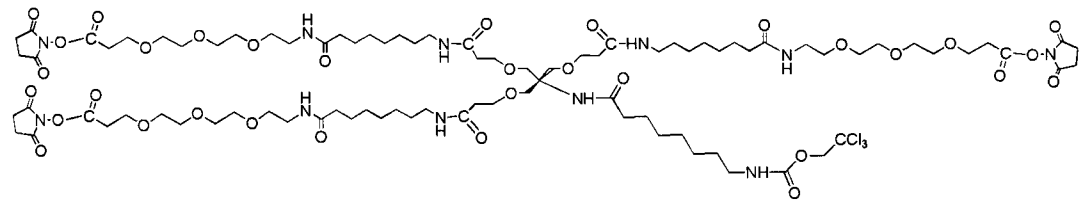

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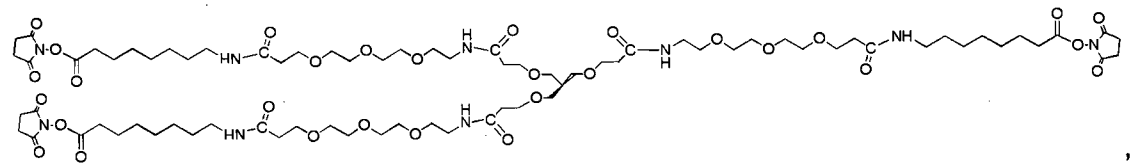

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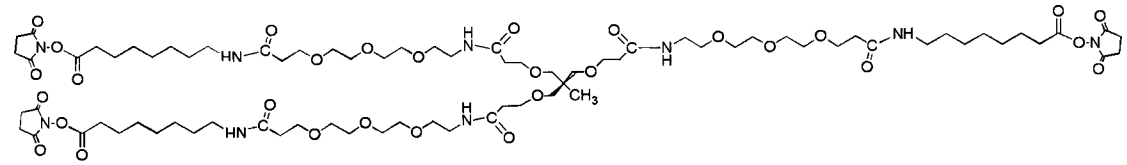

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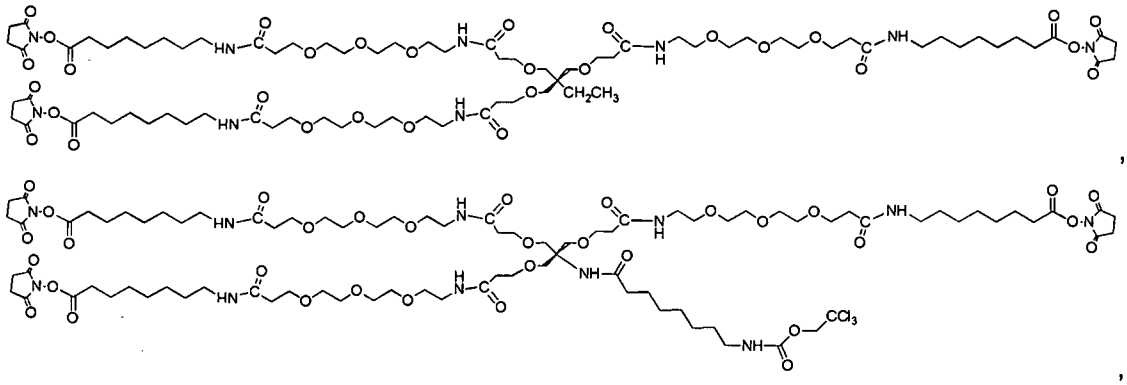

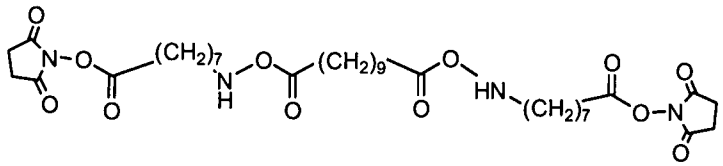

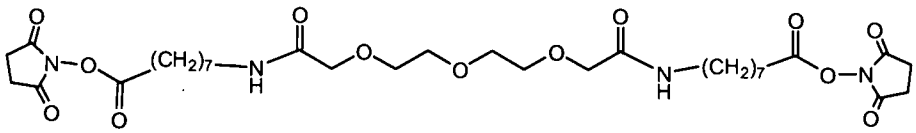

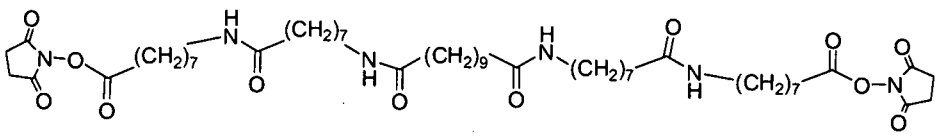

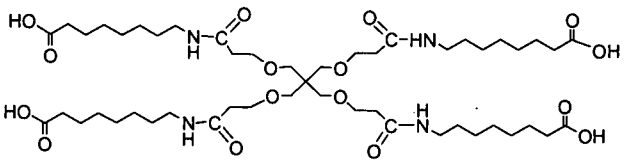

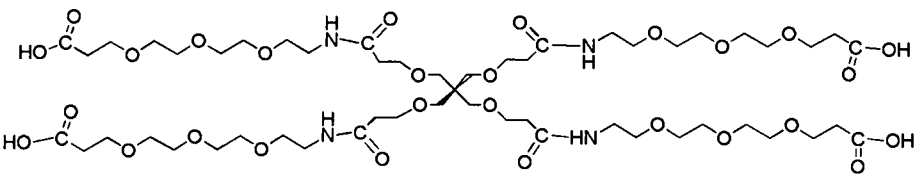

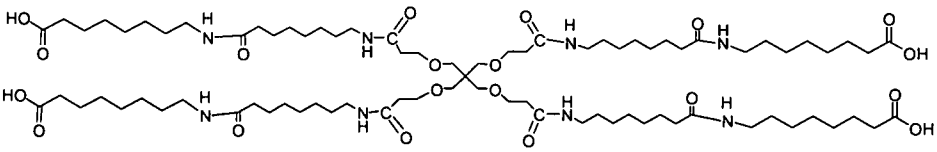

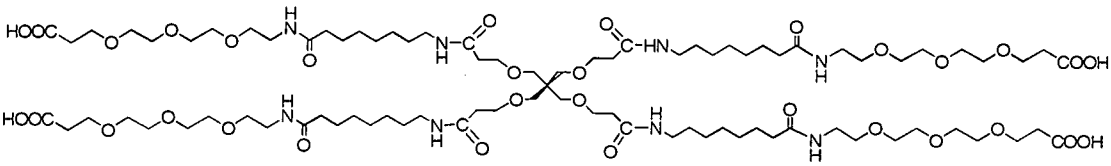

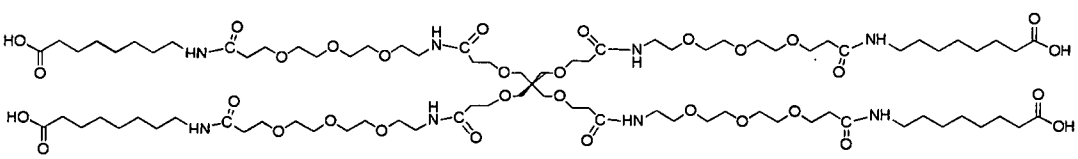

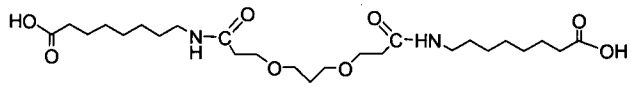

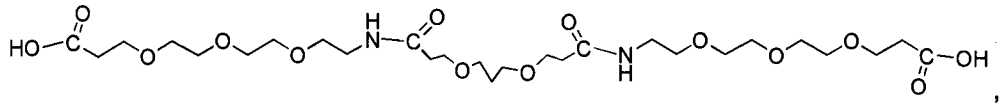

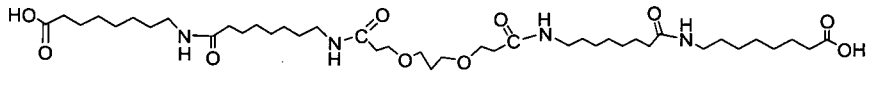

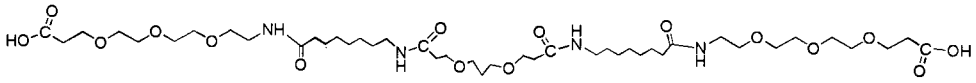

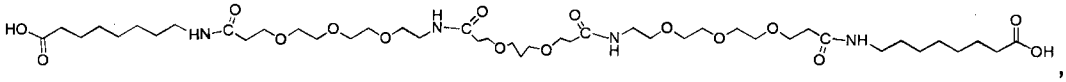

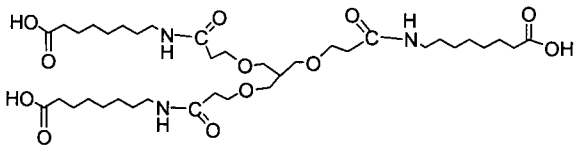

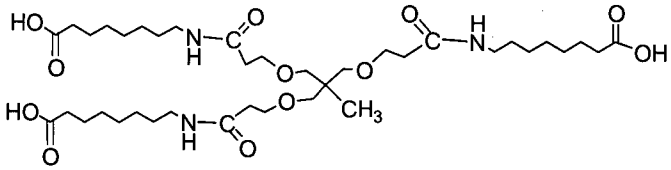

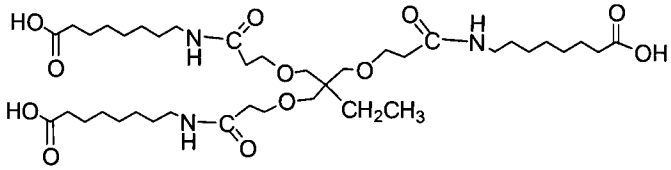

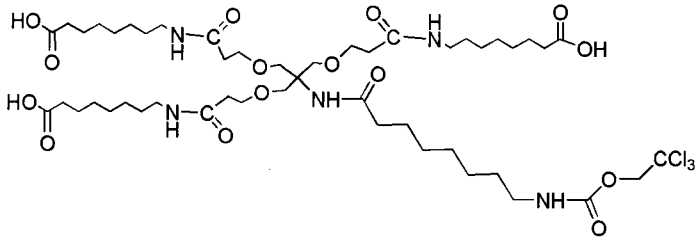

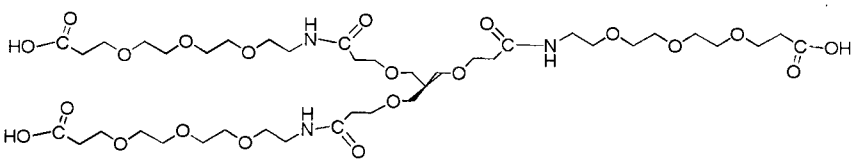

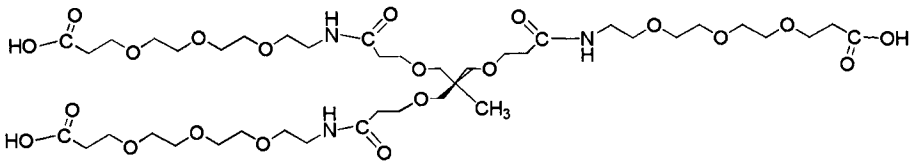

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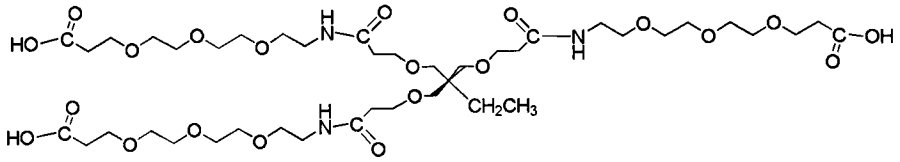

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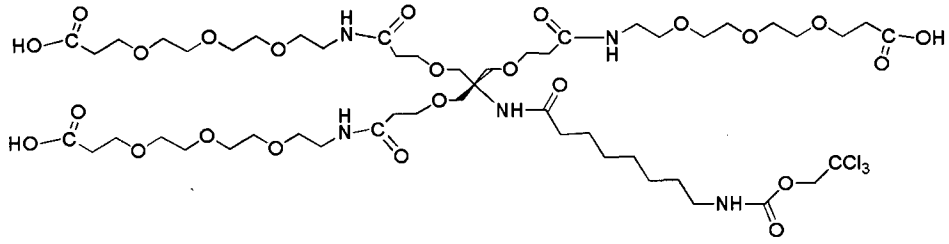

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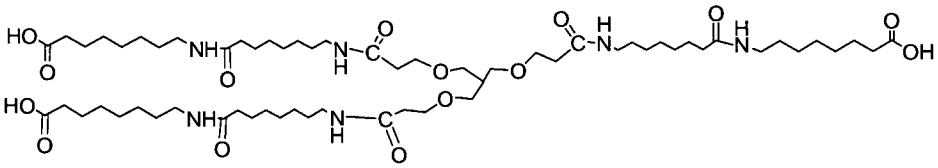

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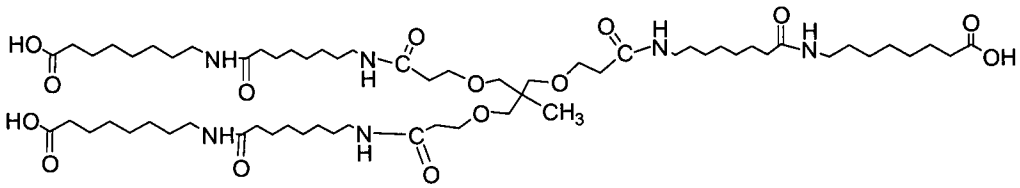

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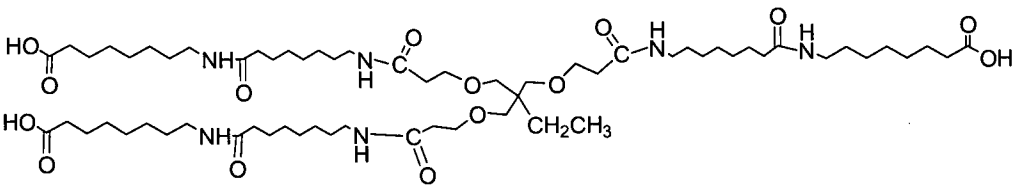

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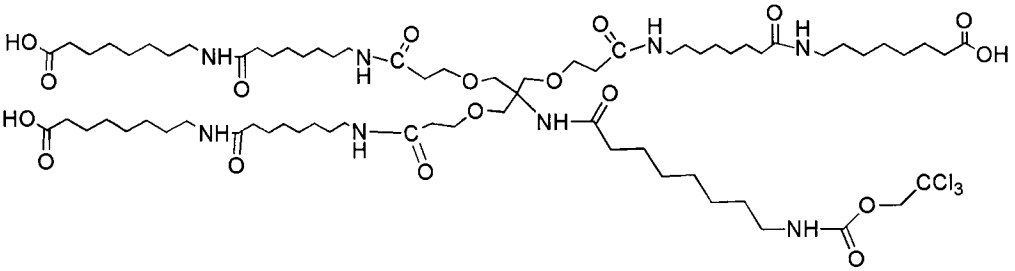

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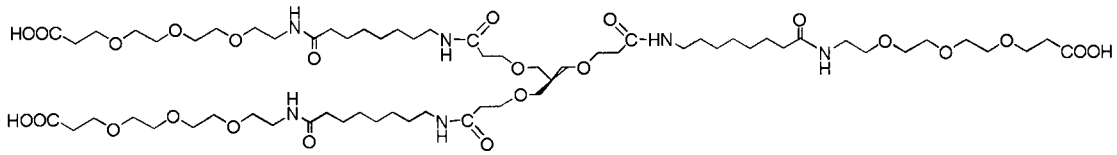

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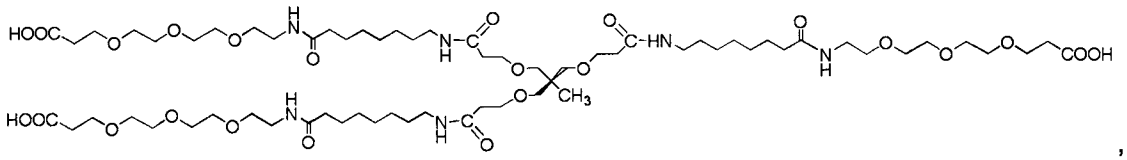
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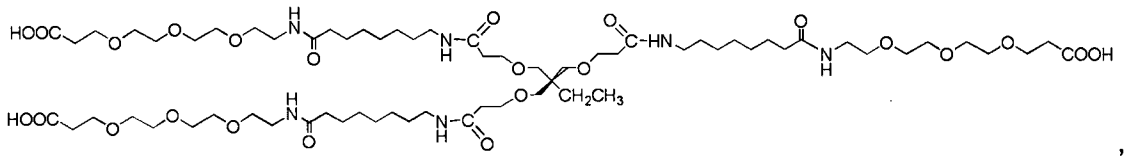
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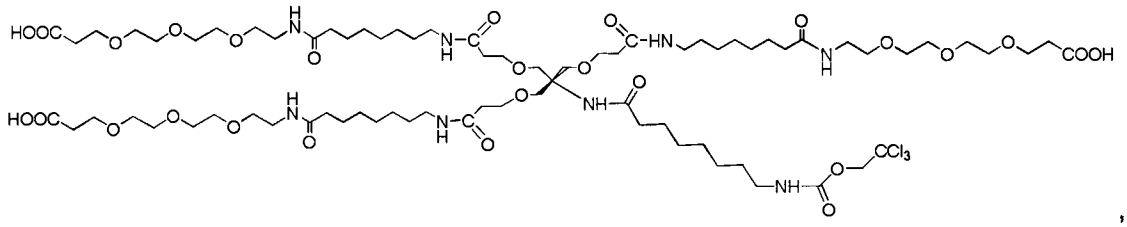
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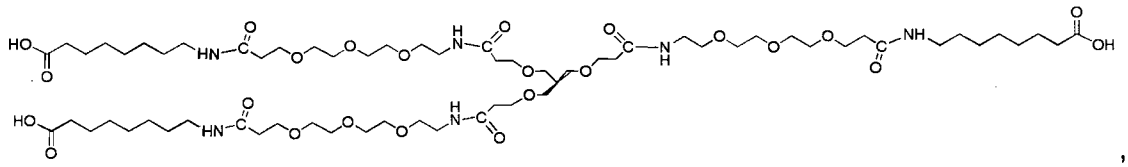
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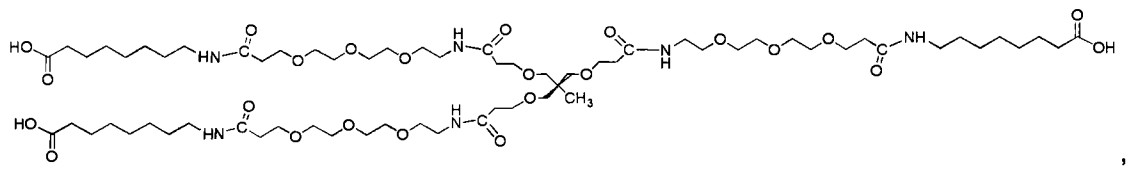
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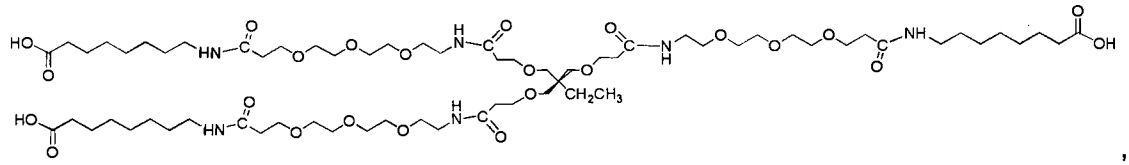
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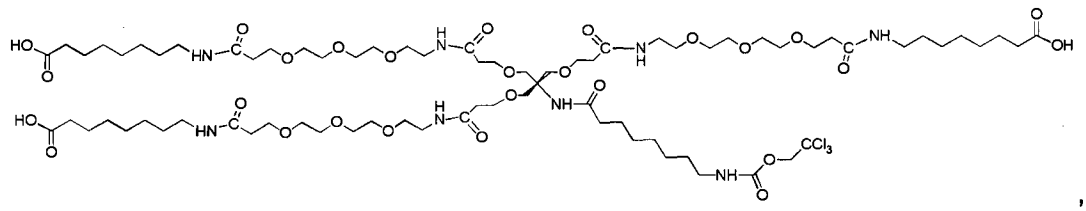
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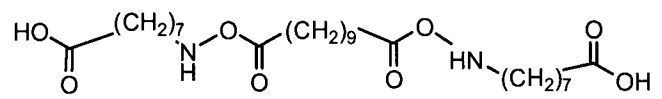
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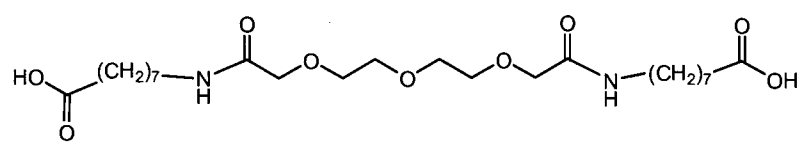
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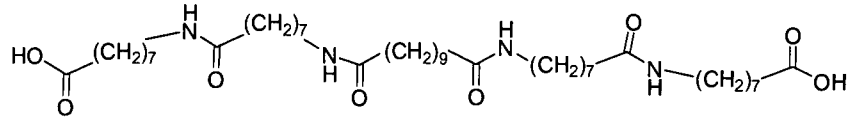
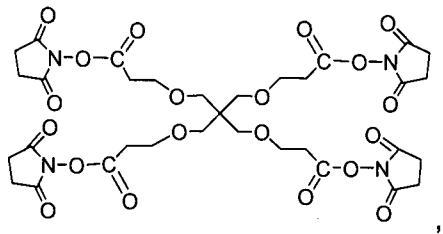


In another aspect, the invention provides a compound selected from the group consisting of:



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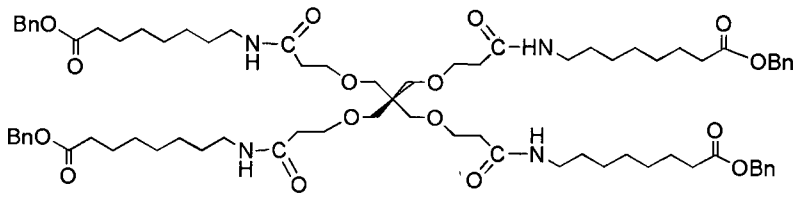

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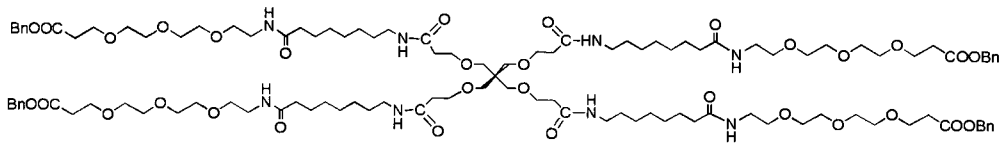
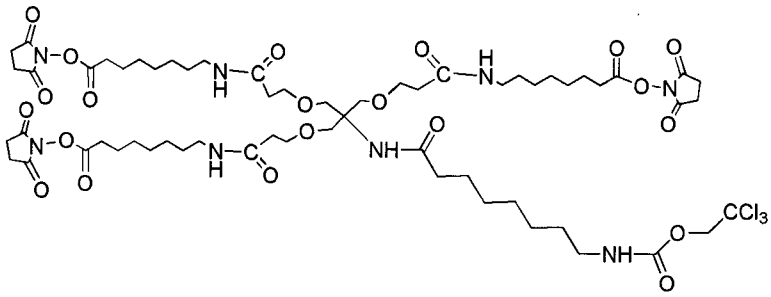


and



.

In another aspect, the invention provides the use of a compound of formula (I) as defined above for preparing a dendritic compound.

In still another aspect, the invention provides a method of preparing a dendritic compound, including the step of contacting a compound of formula (I) with a glycoside compound that contains a free amino group.

It will be appreciated that any of the sub-scopes disclosed herein, e.g. with respect to A, B, D, E, G, X, R^1, R^2, R^3, R^4, R^5, n, m, p t, u, w, x, T, Y and Z may be combined with any of the other sub-scopes disclosed herein to produce further sub-scopes.

DETAILED DESCRIPTION

Definitions

The term "C_1-C_6alkyl" means any saturated hydrocarbon radical having up to 6 carbon atoms and is intended to include both straight- and branched-chain alkyl groups. Examples of alkyl groups include: methyl group, ethyl group, *n*-propyl group, *iso*-propyl group, *n*-butyl group, *iso*-butyl group, *sec*-butyl group, *t*-butyl group, *n*-pentyl group, 1,1-dimethylpropyl group, 1,2-dimethylpropyl group, 2,2-dimethylpropyl group, 1-ethylpropyl group, 2-ethylpropyl group, *n*-hexyl group and 1-methyl-2-ethylpropyl group.

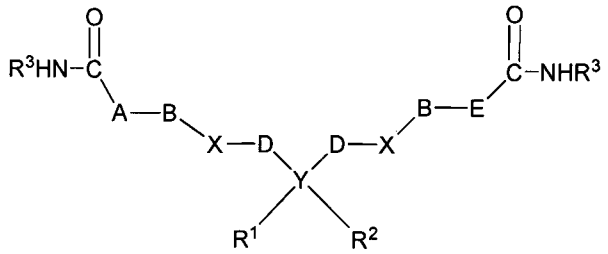
The term "acyl" means C(=O)R' group, where R' is a C_1-C_{30}alkyl group, where C_1-C_{30}alkyl means any saturated hydrocarbon radical having up to 30 carbon atoms, and is intended to include straight chain alkyl groups. Examples include acetyl group.

Compounds of the Invention

The compounds of the invention are simple, easy to use "star burst PET-PEG" dendritic cores. They are useful for the preparation of dendrimers, thereby providing a facile route to well-defined cluster molecules, e.g. pharmaceutical cluster molecules, as single compounds. The compounds of the invention are two-, three- or four-directional short-armed and long-armed dendritic cores. Some compounds of the invention are "pre-activated" (e.g. those where R^5 is a succinimidyl group) so that they can be used, without coupling reagents, for synthesising dendritic compounds. The dendritic core "arms" can be elongated in a controlled manner with suitable linkers, such as 6-8-carbon linkers or PEG linkers (one or two generations), making the "arms" shorter or longer as desired. The linkers are flexible and the tetrahedral model of the core is stable. Compounds of the invention that are succinimidyl esters are, advantageously, crystalline compounds. They are therefore stable and can be easily stored. Conveniently, the compounds of the invention can be purified by flash chromatography. Because of their simplicity of design, the compounds provide a novel approach to reaching larger sized dendrimers, but employing fewer "arms" (2-4 "arms" instead of 32-64), thus simplifying the dendrimer product. Dendritic cores with long carbon or PEG chains can be considered to be mimics of carbohydrate chains, but they avoid the costs and synthetic challenges associated with preparing linear oligosaccharides.

The invention relates to:

1. A compound of formula (I)



wherein:

Y is O;

B is O;

R^1 and R^2 are absent; and

either A, E, D and X are all CH_2; or A, D and X are all CH_2 and E is $(CH_2CH_2O)_t^{\#}CH_2$;

wherein # indicates a point of attachment of E to its adjacent carbonyl group;

t is an integer from 1 to 10;

or wherein:

Y is C;

R^1 and R^2 are both H; and

A, E, B and D are CH_2 and X is O;

or wherein:

Y is C;

A is $(CH_2)_u$

R^1 and R^2 are both H;

B, X, D and E are all absent; and

u is an integer from 1 to 10;

or wherein:

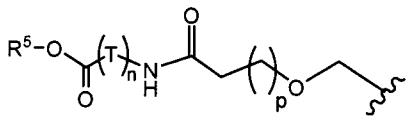
Y is C;

X is O;

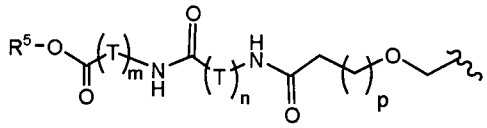
B is $(CH_2)_p$;

A, E and D are all CH_2; and

R^1 is H, NHZ or $C_{1\text{-}6}$alkyl and R^2 is a radical of formula (i) or a radical of formula (ii)



(i)



(ii)

;

Z is H, acyl, $C(O)(CH_2)_wN(H)G$, $*CH_3*C(O)$- where *C denotes ^{13}C or ^{14}C, 4-carboxytetramethylrhodamine, resorcinolphthalein, 7-amino-4-methyl-6-sulfocoumarin-3-acetic acid, 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene or 1-{3-{[4-(2-cyclooctyn-1-ylmethyl)benzoyl]amino}propyl}-4-{2-[4-(dimethylamino)phenyl]ethenyl}pyridinium hexafluorophosphate;

w is an integer from 1 to 11;

G is H, acyl, t-butoxycarbonyl, 2,2,2-trichloroethyloxycarbonyl, 9-fluorenylmethoxycarbonyl, benzyloxycarbonyl,$*CH_3*CO$- where *C denotes ^{13}C or ^{14}C, 4-carboxytetramethylrhodamine, resorcinolphthalein, 7-amino-4-methyl-6-sulfocoumarin-3-acetic acid, 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene or 1-{3-{[4-(2-cyclooctyn-1-ylmethyl)benzoyl]amino}propyl}-4-{2-[4-(dimethylamino)phenyl]ethenyl}pyridinium hexafluorophosphate;

or wherein:

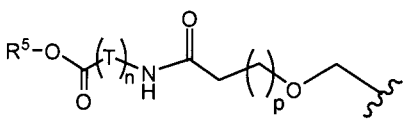
Y is C;

X is O;

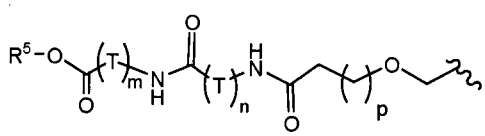
B is $(CH_2)_p$;

A, E and D are all CH_2; and

R^1 and R^2, both the same, are a radical of formula (i) or a radical of formula (ii)



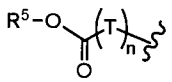
(i)



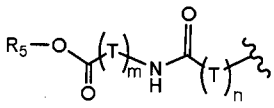
(ii)

;

R^3 is a radical of formula (iii) or a radical of formula (iv)



(iii)



(iv)

;

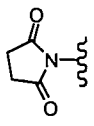
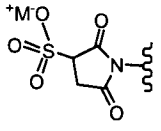
each T is independently selected from the group consisting of $(CH_2CH_2O)_xCH_2CH_2$ and CH_2;

each x is independently an integer from 1 to 12;

m is an integer from 1 to 11, provided that when T is $(CH_2CH_2O)_xCH_2CH_2$ then m is 1;

n is an integer from 1 to 11, provided that when T is $(CH_2CH_2O)_xCH_2CH_2$ then n is 1;

p is an integer from 1 to 5;

R^5 is H,  or  ; and

M is sodium or ammonium.

2. A compound as described in the above paragraph 1 wherein each T is CH_2.

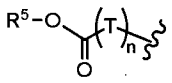
3. A compound as described in the above paragraph 1 wherein at least one T is $(CH_2CH_2O)_xCH_2CH_2$.

4. A compound as described in the above paragraph 1 wherein m is an integer from 5 to 8.

5. A compound as described in the above paragraph 1 or 2 wherein n is an integer from 5 to 8.

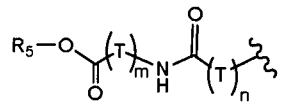
6. A compound as described in any one of the above paragraphs 1 to 5 wherein Y is C.

7. A compound as described in any one of the above paragraphs 1 to 6 wherein R^3 is a radical of formula (iii)



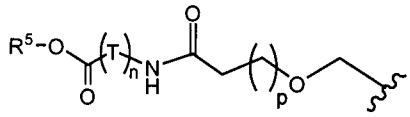
(iii)

8. A compound as described in any one of the above paragraphs 1 to 6 wherein R^3 is a radical of formula (iv)



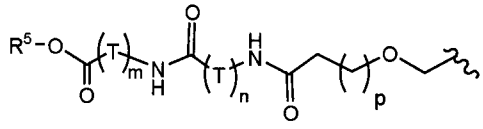
(iv)

9. A compound as described in any one of the above paragraphs 1 to 8 wherein R^1 and R^2 are both a radical of formula (i)



(i)

10. A compound as described in any one of the above paragraphs 1 to 8 wherein R^1 and R^2 are both a radical of formula (ii)

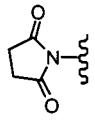


(ii)

11. A compound as described in any one of the above paragraphs 1 to 8 wherein R^1 is H or $C_{1\text{-}6}$alkyl.

12. A compound as described in any one of the above paragraphs 1 to 8 wherein R^1 is NH_2.

13. A compound as described in any one of the above paragraphs 1 to 12 wherein R^5 is



14. A compound as described in any one of the above paragraphs 1 to 5, 7 to 8 or 13 wherein Y is O; B is O; R^1 and R^2 are absent; and either A, E, D and X are all CH_2 or A, D and X are all CH_2 and E is $(CH_2CH_2O)_tCH_2$; and t is an integer from 1 to 10.

15. A compound as described in any one of the above paragraphs 1 to 8 or 13 wherein Y is C; R^1 and R^2 are both H; A, E, B and D are CH_2 and X is O.

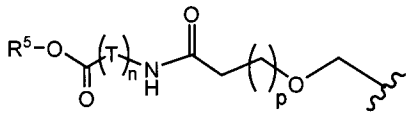
16. A compound as described in any one of the above paragraphs 1 to 8 or 13 wherein Y is C; A is $(CH_2)_u$; R^1 and R^2 are both H; B, X, D and E are all absent; and u is an integer from 1 to 10.

17. A compound as described in any one of the above paragraphs 1 to 8 or 13 wherein:

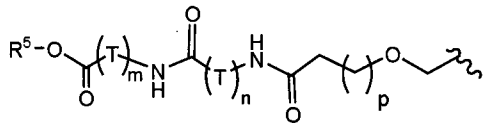
Y is C; X is O; A, E and D are all CH_2; B is $(CH_2)_p$;

R^1 is H, NHZ or $C_{1\text{-}6}$alkyl;

R^2 is a radical of formula (i) or a radical of formula (ii)



(i)



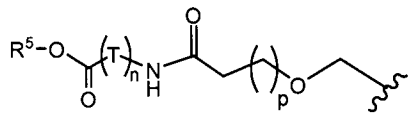
(ii) ; and

Z is H, acyl, $C(O)(CH_2)_wNH(G)$, $*CH_3*CO$- where *C denotes ^{13}C or ^{14}C, 4-carboxytetramethylrhodamine, resorcinolphthalein, 7-amino-4-methyl-6-sulfocoumarin-3-acetic acid, 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene or 1-{3-{[4-(2-cyclooctyn-1-ylmethyl)benzoyl]amino}propyl}-4-{2-[4-(dimethylamino)phenyl]ethenyl}pyridinium hexafluorophosphate;

w is an integer from 1 to 11;

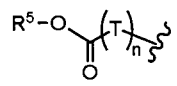
G is H, acyl, t-butoxycarbonyl, 2,2,2-trichloroethyloxycarbonyl, 9-fluorenylmethoxycarbonyl, benzyloxycarbonyl, $*CH_3*CO$- where *C denotes ^{13}C or ^{14}C, 4-carboxytetramethylrhodamine, resorcinolphthalein, 7-amino-4-methyl-6-sulfocoumarin-3-acetic acid, 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene or 1-{3-{[4-(2-cyclooctyn-1-ylmethyl)benzoyl]amino}propyl}-4-{2-[4-(dimethylamino)phenyl]ethenyl}pyridinium hexafluorophosphate.

18. A compound as described in any one of the above paragraphs 1 to 9 or 13 wherein, Y is C; X is O; A, E and D are all CH_2; B is $(CH_2)_p$; R^1 and R^2, both the same, are a radical of formula (i)



(i)

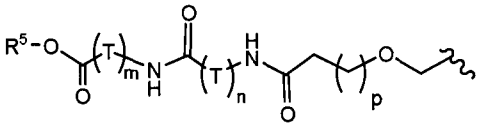
R^3 is a radical of formula (iii)



(iii) ; and

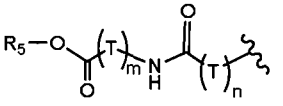
and p is 1.

19. A compound as described in any one of the above paragraphs 1 to 8 or 10 or 13 wherein Y is C; X is O; A, E and D are all CH_2; B is $(CH_2)_p$; R^1 and R^2, both the same, are a radical of formula (ii)



(ii)

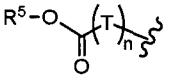
and R^3 is a radical of formula (iv)



(iv) ;

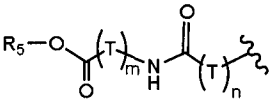
and p is 1.

20. A compound as described in any one of the above paragraphs 1 to 8 or 13 or 15 wherein Y is C; R^1 and R^2 are both H; A, E, B and D are CH_2; X is O; and R^3 is a radical of formula (iii)



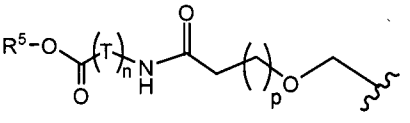
(iii) .

21. A compound as described in any one of the above paragraphs 1 to 8 or 13 or 15 wherein Y is C; R^1 and R^2 are both H; A, E, B and D are CH_2; X is O; and R^3 is a radical of formula (iv)



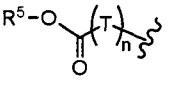
(iv) .

22. A compound as described in any one of the above paragraphs 1 to 8 or 13 or 17 wherein Y is C; X is O; A, E and D are all CH_2; B is $(CH_2)_p$; R^1 is H; R^2 is a radical of formula (i)



(i) ;

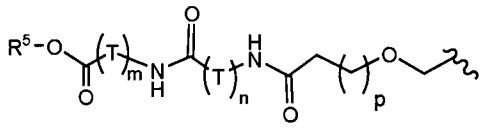
R^3 is a radical of formula (iii)



(iii) ;

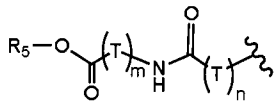
and p is 1.

23. A compound as described in any one of the above paragraphs 1 to 8 or 13 or 17 wherein Y is C; X is O; A, E and D are all CH_2; B is $(CH_2)_p$; R^1 is H; R^2 is a radical of formula (ii)



(ii) ;

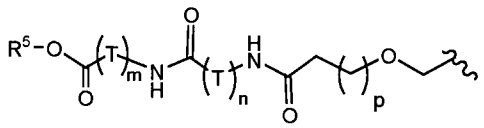
R^3 is a radical of formula (iv)



(iv) ;

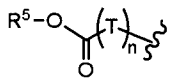
and p is 1.

24. A compound as described in any one of the above paragraphs 1 to 8 or 13 or 17 wherein Y is C; X is O; A, E and D are all CH_2; B is $(CH_2)_p$; R^1 is H; R^2 is a radical of formula (ii)



(ii) ;

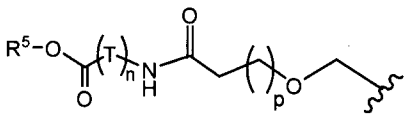
R^3 is a radical of formula (iii)



(iii) ;

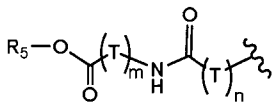
and p is 1.

25. A compound as described in any one of the above paragraphs 1 to 8 or 13 or 17 wherein Y is C; X is O; A, E and D are all CH_2; B is $(CH_2)_p$; R^1 is H; R^2 is a radical of formula (i)



(i) ;

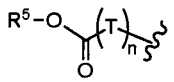
and R^3 is a radical of formula (iv)



(iv) ;

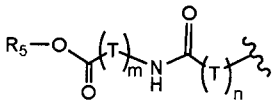
and p is 1.

26. A compound as described in any one of the above paragraphs 1 to 8 or 13 or 16 wherein Y is C; A is $(CH_2)_u$; R^1 and R^2 are both H; B, X, D and E are all absent; u is an integer from 1 to 10; and R^3 is a radical of formula (iii)



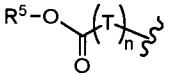
(iii)

27. A compound as described in any one of the above paragraphs 1 to 8 or 13 or 16 wherein Y is C; A is $(CH_2)_u$; R^1 and R^2 are both H; B, X, D and E are all absent; u is an integer from 1 to 10; and R^3 is a radical of formula (iv)



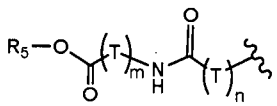
(iv)

28. A compound as described in any one of the above paragraphs 1 to 8 or 13 or 14 wherein Y is O; B is O; R^1 and R^2 are absent; and either A, E, D and X are all CH_2 or A, D and X are all CH_2 and E is $(CH_2CH_2O)_tCH_2$; t is an integer from 1 to 2; and R^3 is a radical of formula (iii)



(iii)

29. A compound as described in any one of the above paragraphs 1 to 8 or 13 or 14 wherein Y is O; B is O; R^1 and R^2 are absent; and either A, E, D and X are all CH_2 or A, D and X are all CH_2 and E is $(CH_2CH_2O)_tCH_2$; t is an integer from 1 to 2; and R^3 is a radical of formula (iv)

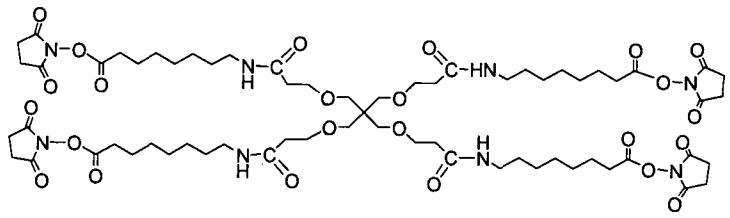


(iv)

30. A compound as described in any one of the above paragraphs 1 to 10, 17 to 19 or 22 to 25 wherein p is 1.

31. A compound as described in any one of the above paragraphs 1 to 30 wherein M is sodium.

32. A compound as described in the above paragraph 1, selected from the group consisting of:



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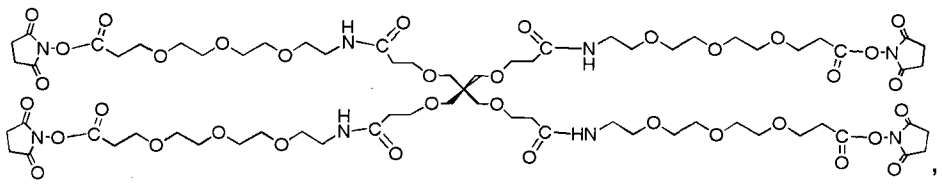

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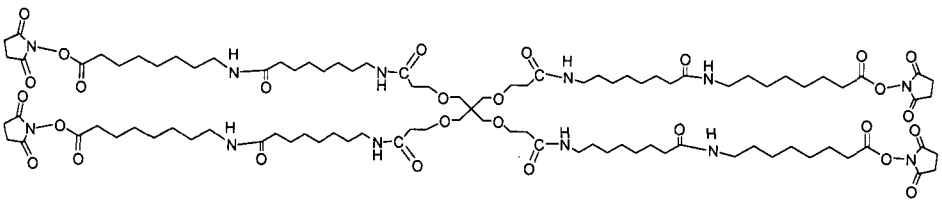

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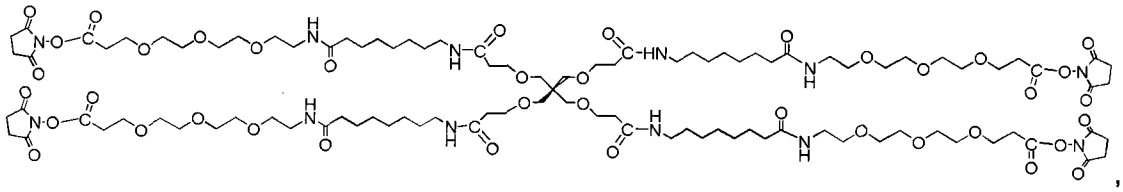

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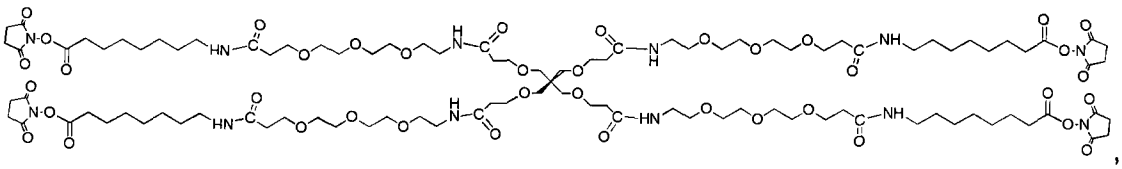

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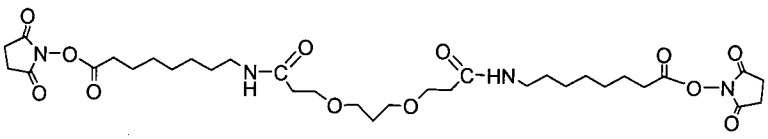

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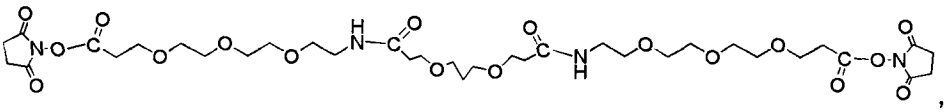

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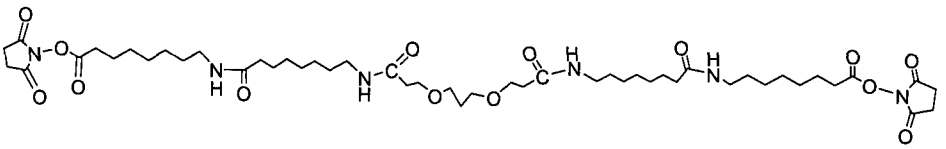

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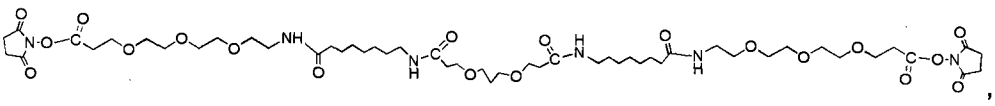

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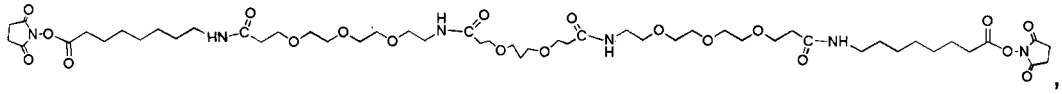

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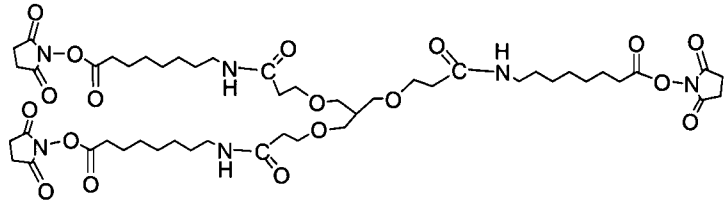

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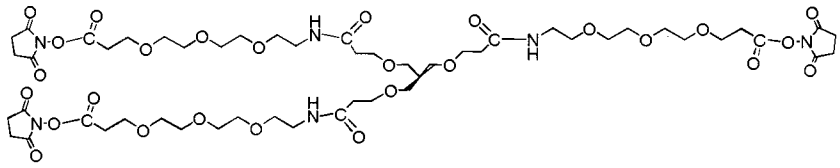

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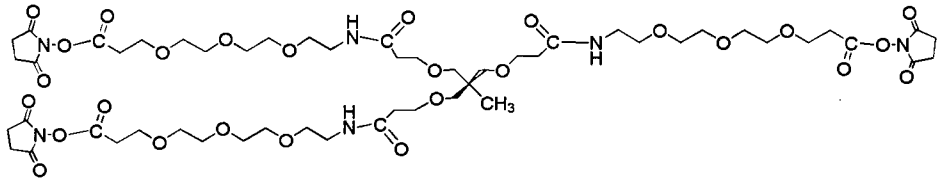

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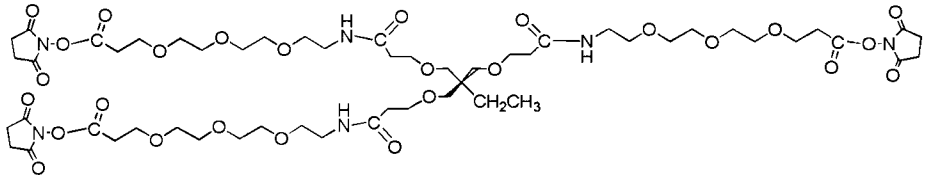

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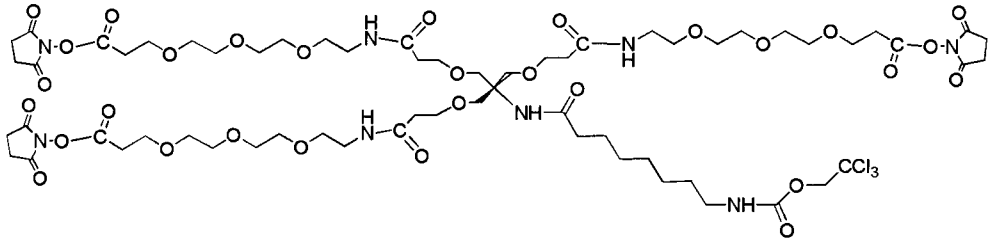

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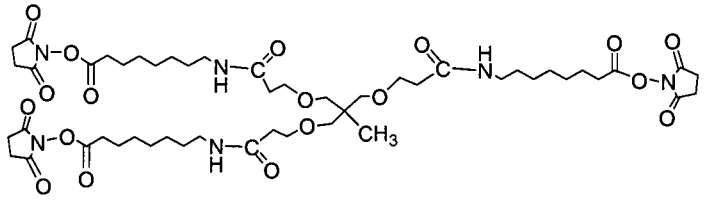

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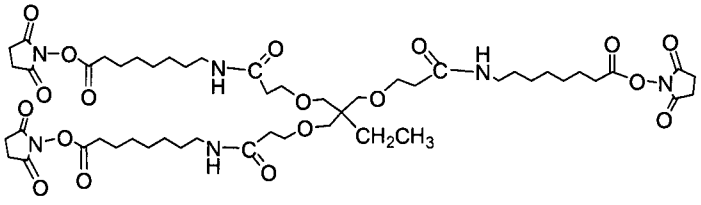

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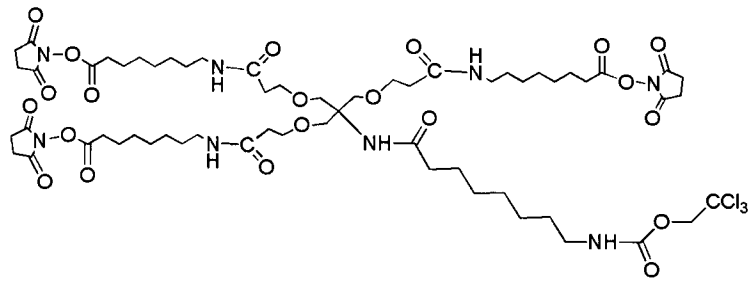

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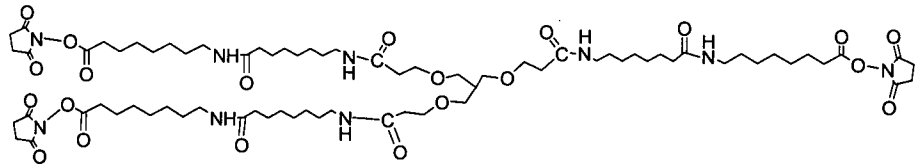

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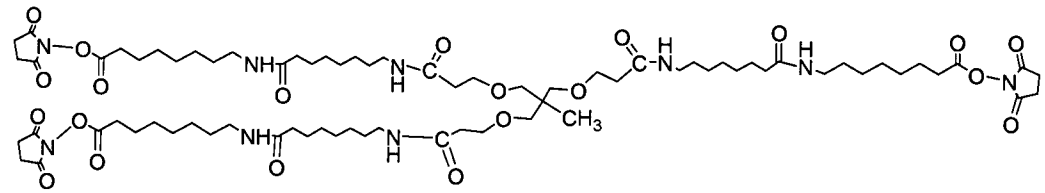

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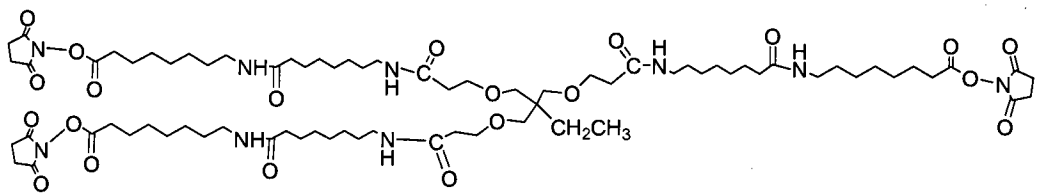

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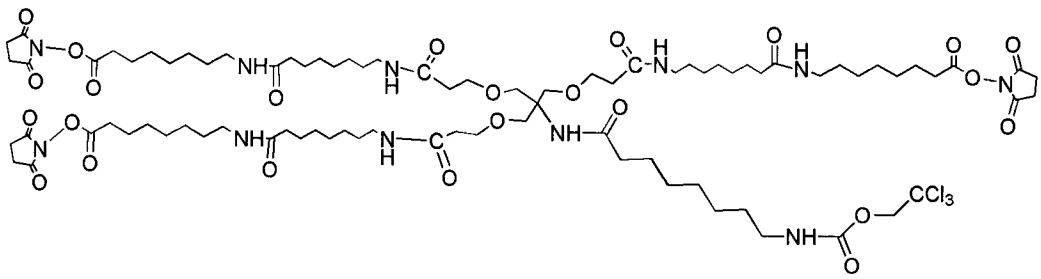

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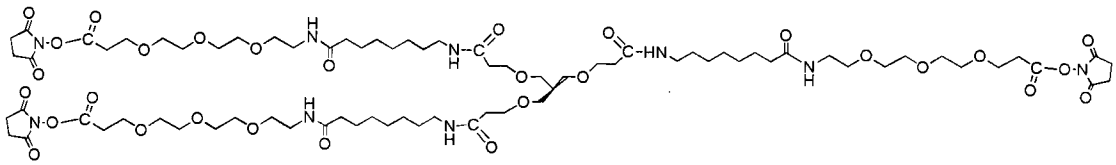

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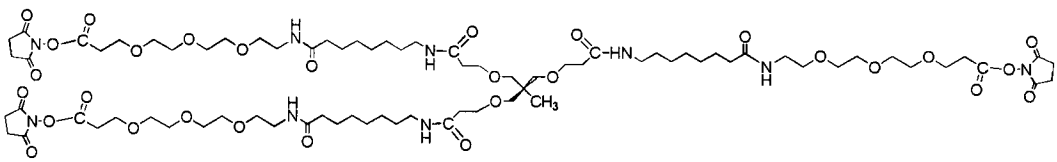

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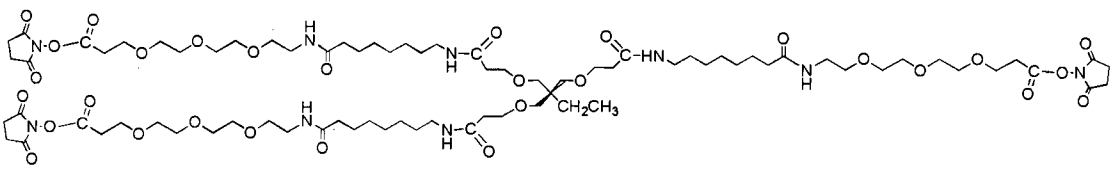

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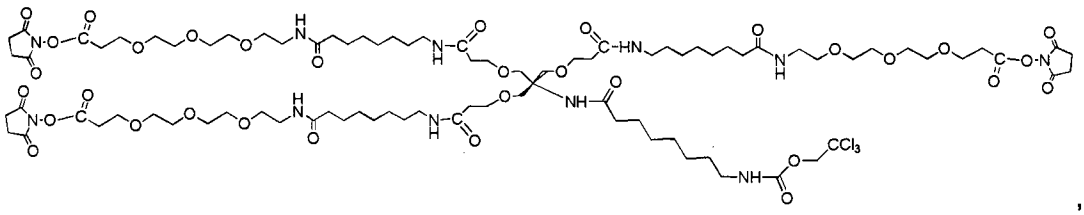

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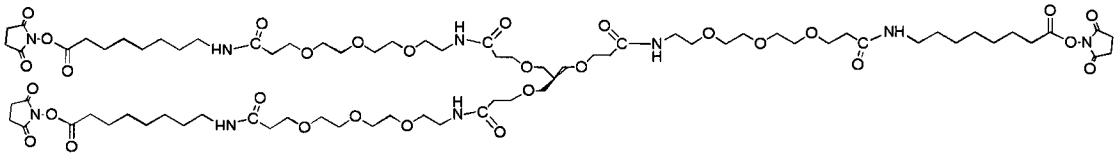

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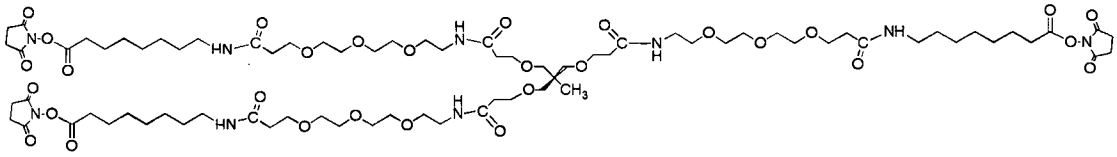

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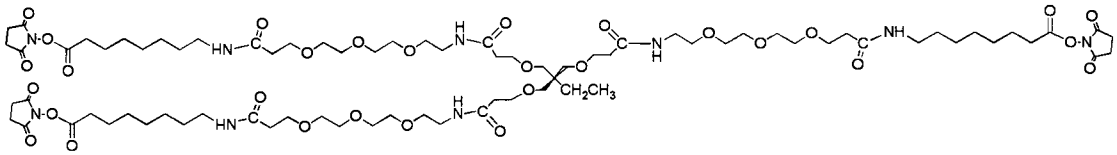

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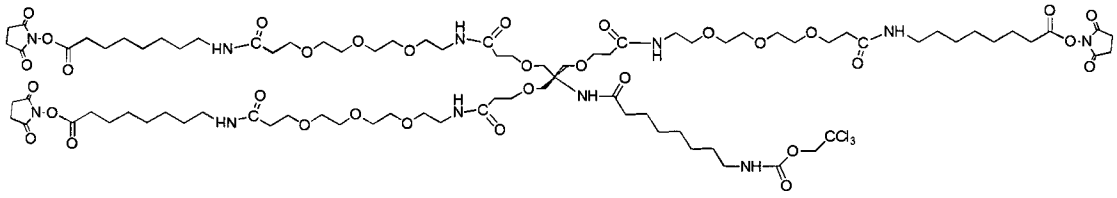

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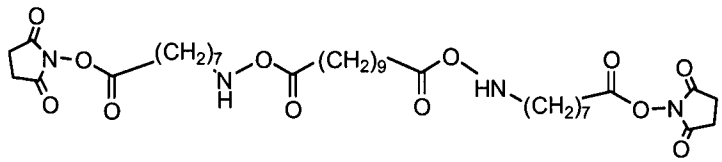

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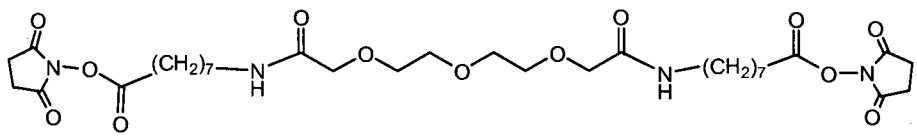

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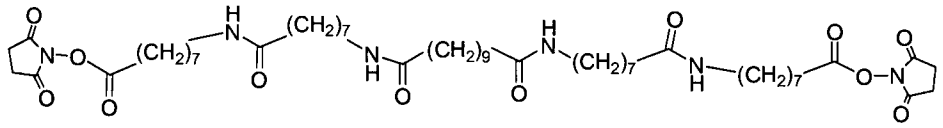

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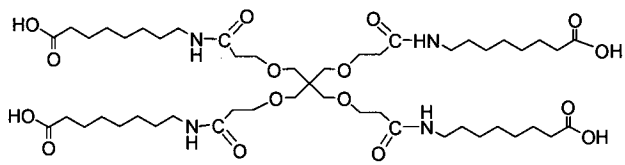

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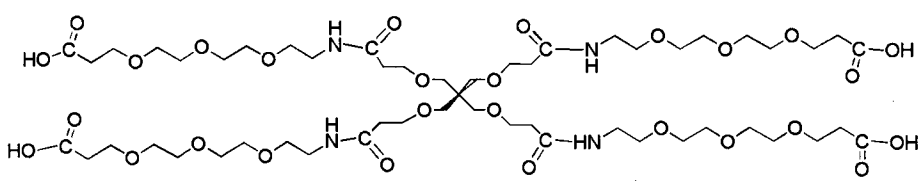

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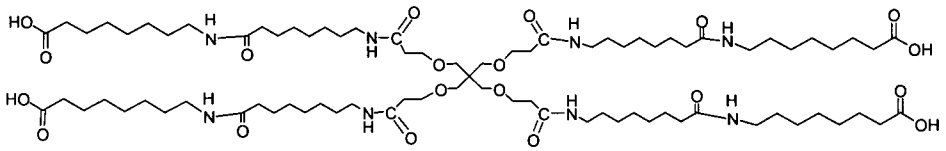

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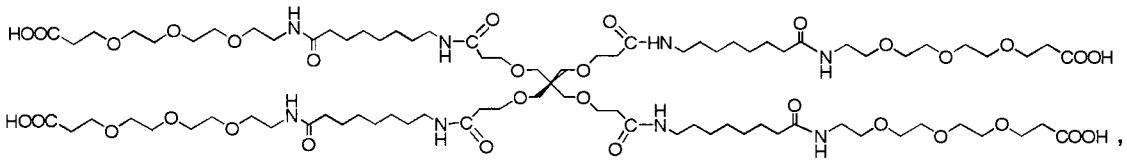

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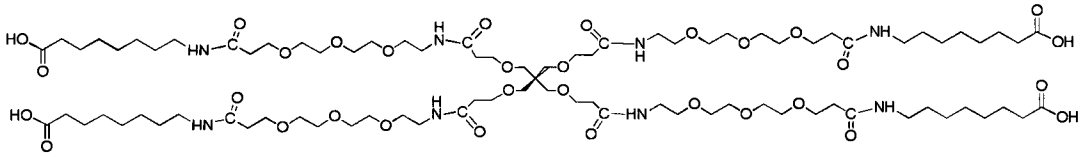

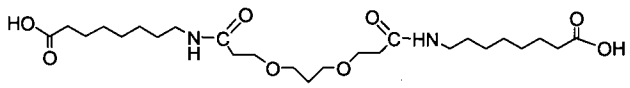

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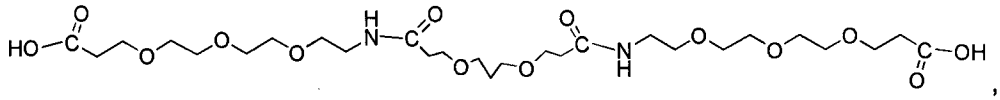

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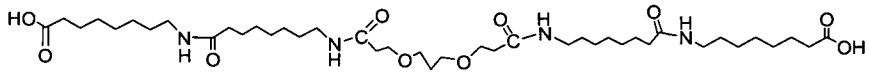

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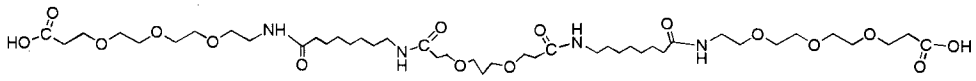

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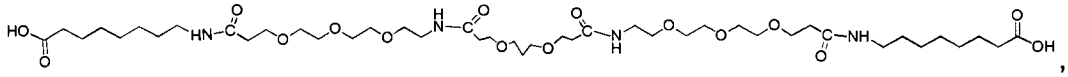

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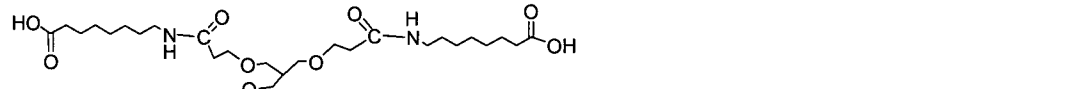

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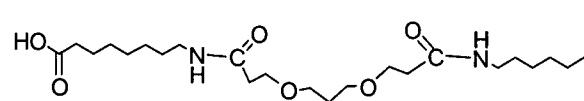

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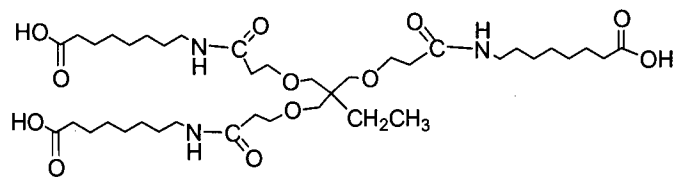

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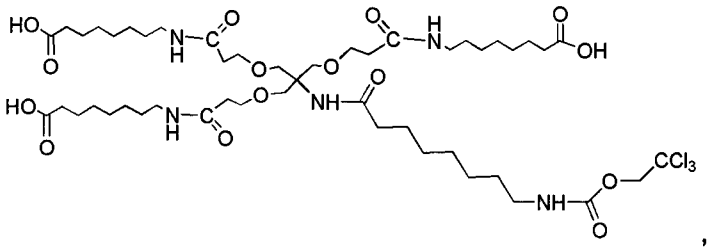

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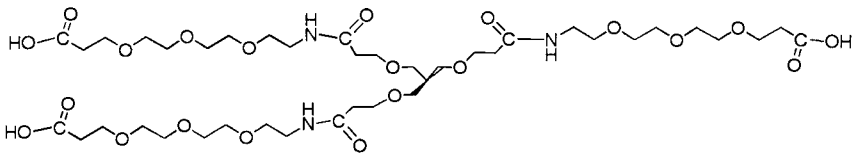

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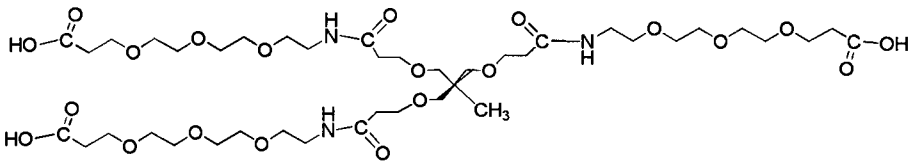

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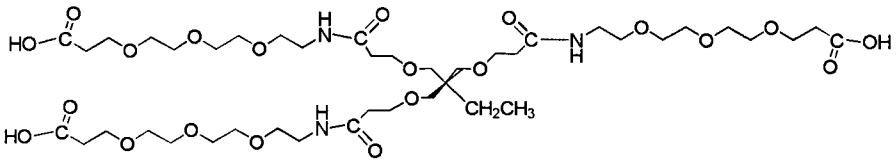

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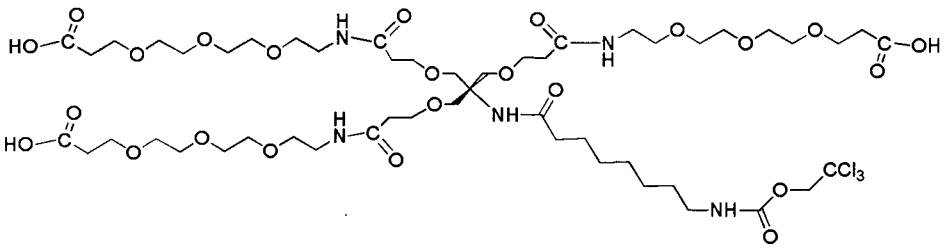

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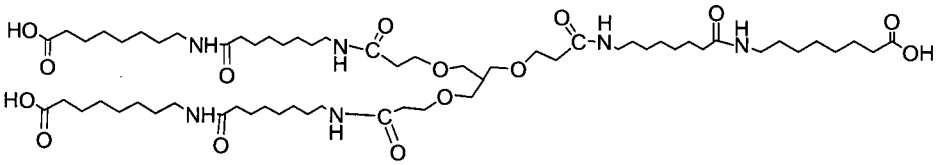

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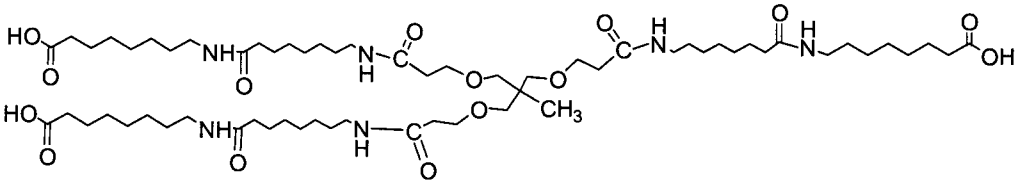

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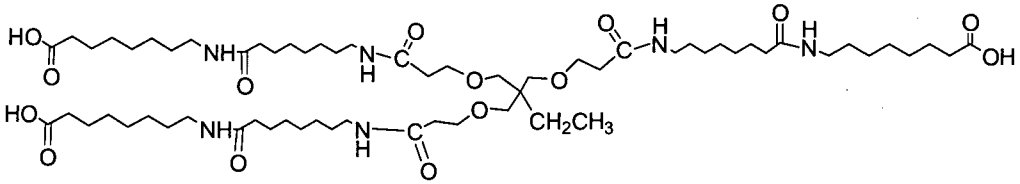

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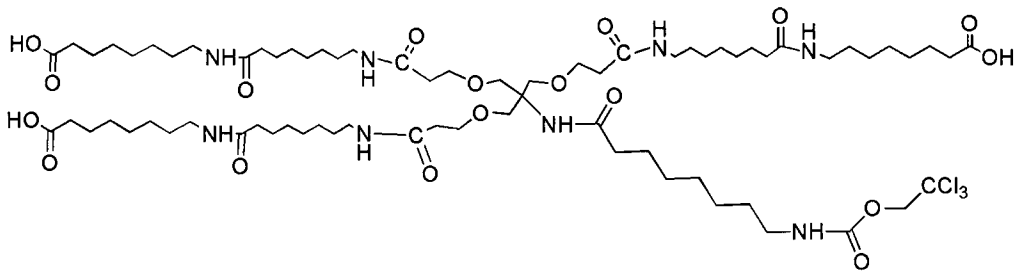

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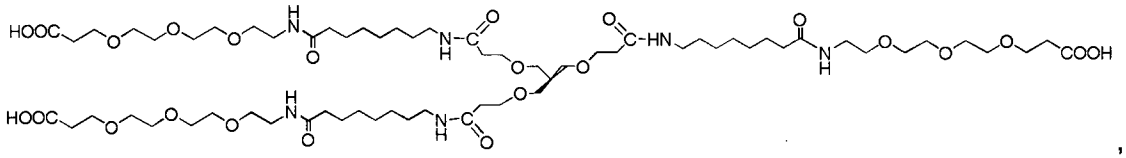

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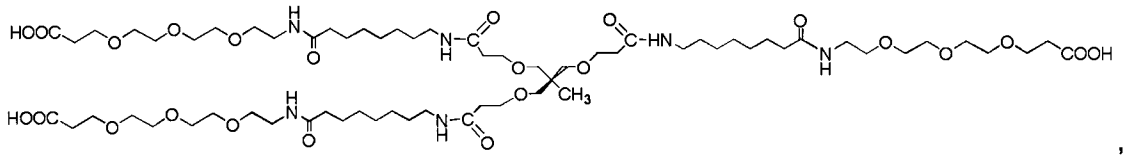

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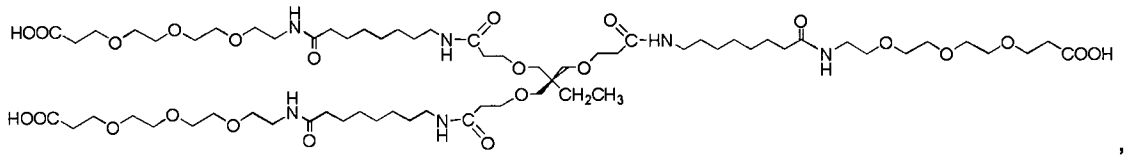

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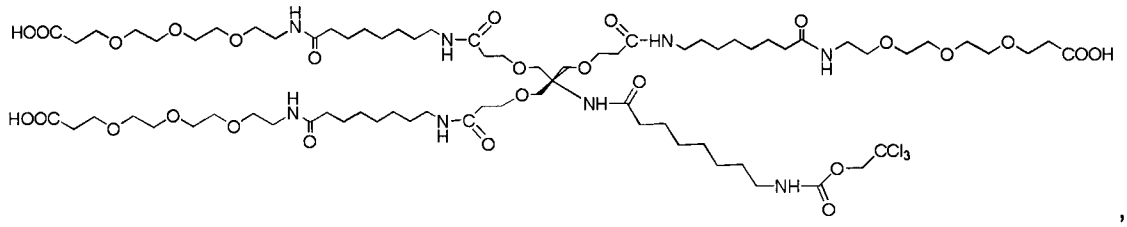

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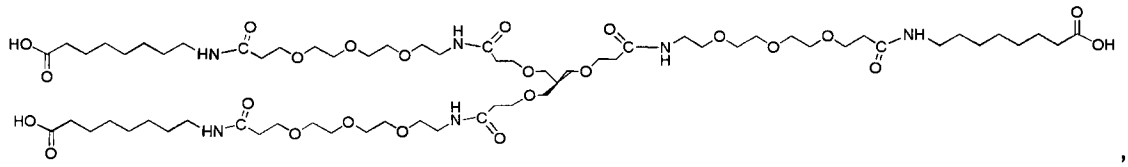

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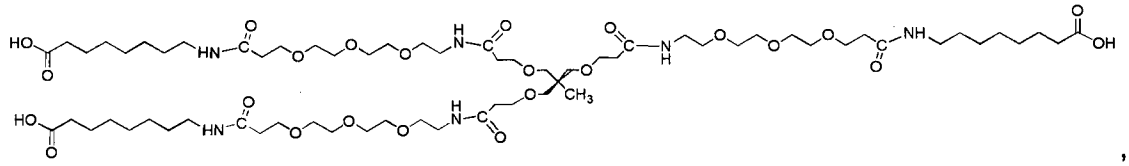

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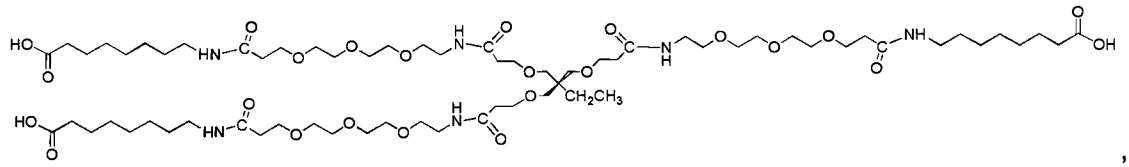

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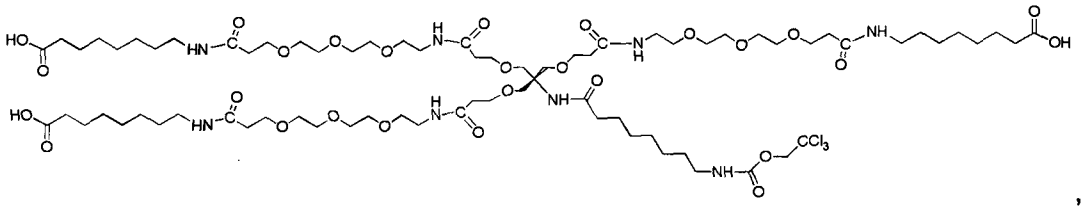

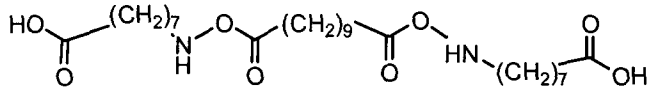

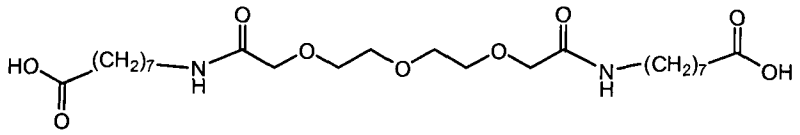

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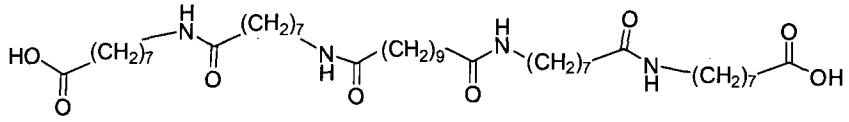

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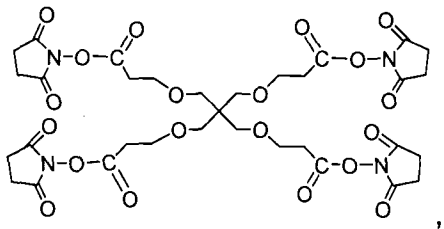
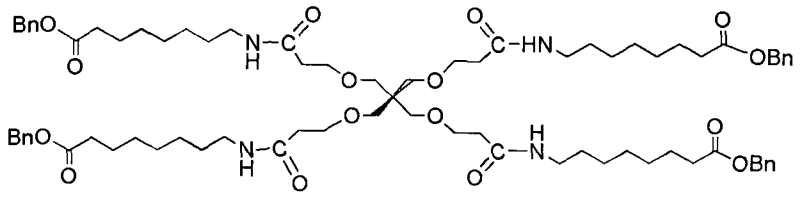
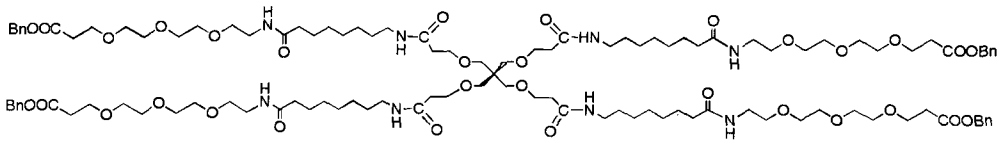
33. A compound selected from the group consisting of:







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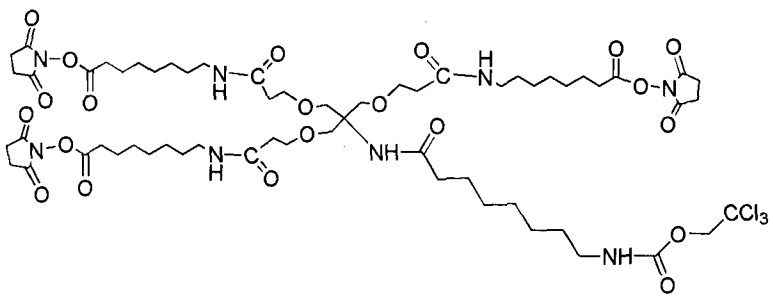

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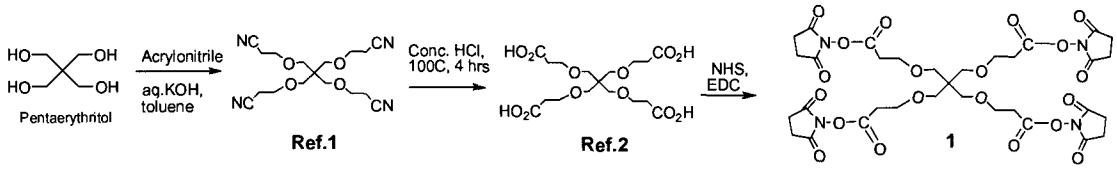
Synthesis of the Compounds of the Invention

The compounds of the invention may be prepared by a variety of different methods. The following are representative non-limiting general methods for synthesising compounds of the invention.

Those skilled in the art will realise that Schemes 2 to 7 below show compounds of the invention where R^5 is succinimidyl group. However, compounds of the invention where R^5 is other than succinimidyl can be prepared analogously. For example, compounds where R^5 is H can be prepared by treatment of the OBn precursors (e.g. Schemes 2-7, below) with palladium on carbon or palladium hydroxide on carbon or platinum on carbon catalysts in solvents such as aqueous THF, methanol, ethanol, ethyl acetate, stirred under a hydrogen atmosphere at ambient temperature and pressure or at 5-50 psi, preferably at 5-25 psi.

"Tetrameric" dendritic core compounds of the invention (where R^1 and R^2 are both a radical of formula (i) or a radical of formula (ii)) are prepared from compound 1, which is synthesised in three steps from pentaerythritol (Scheme 1).

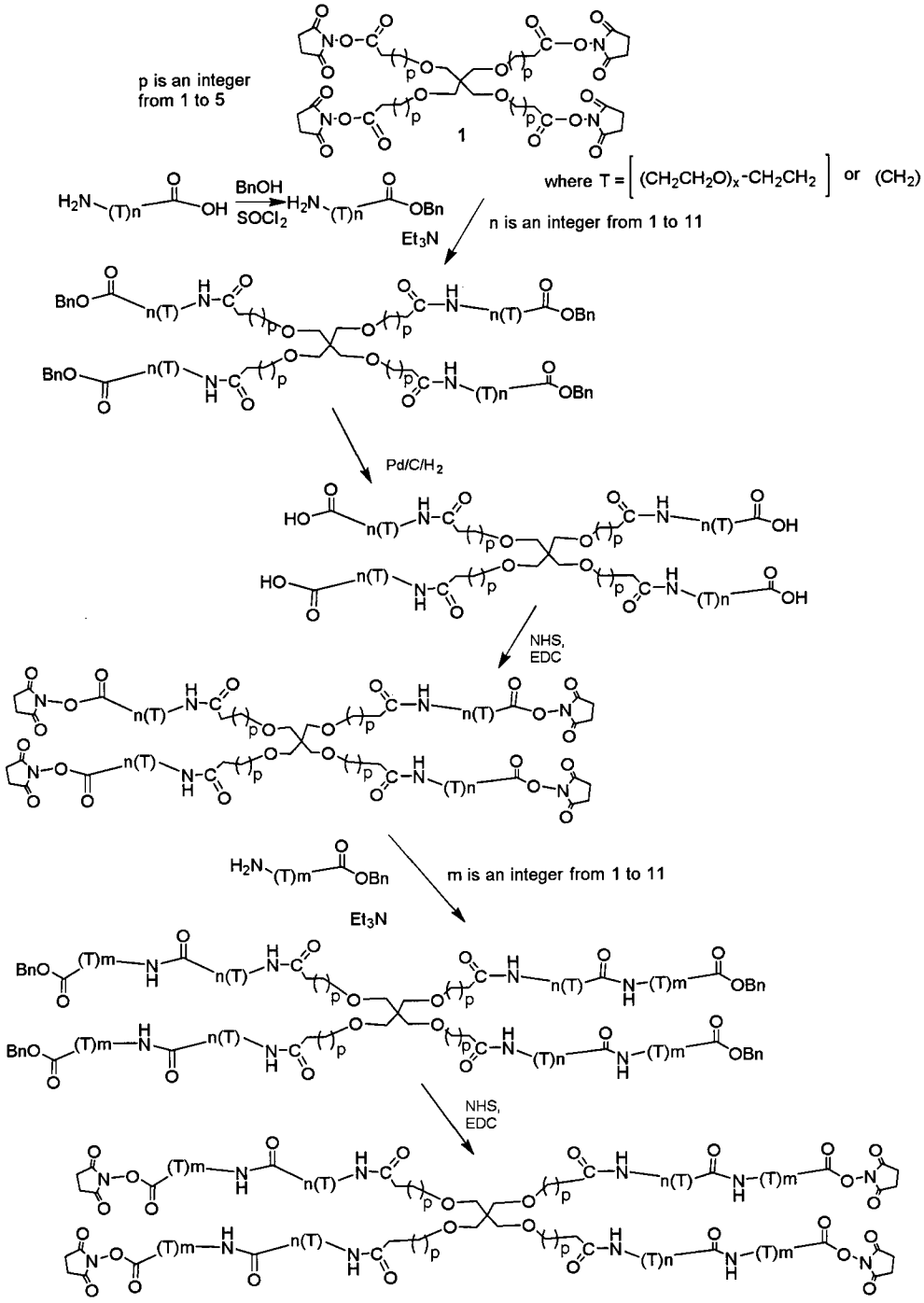
Scheme 1



(**Ref.1**, Hukkämaki, J.; Pakkanen, T.T. *Journal of Molecular Catalysis A: Chemical* **2001**, 174, 205-211; **Ref. 2**, Newcombe, G. R.; Mishra, A; Moorfield, C. N. *J. Org. Chem.* 2002, 67, 3957-3960).

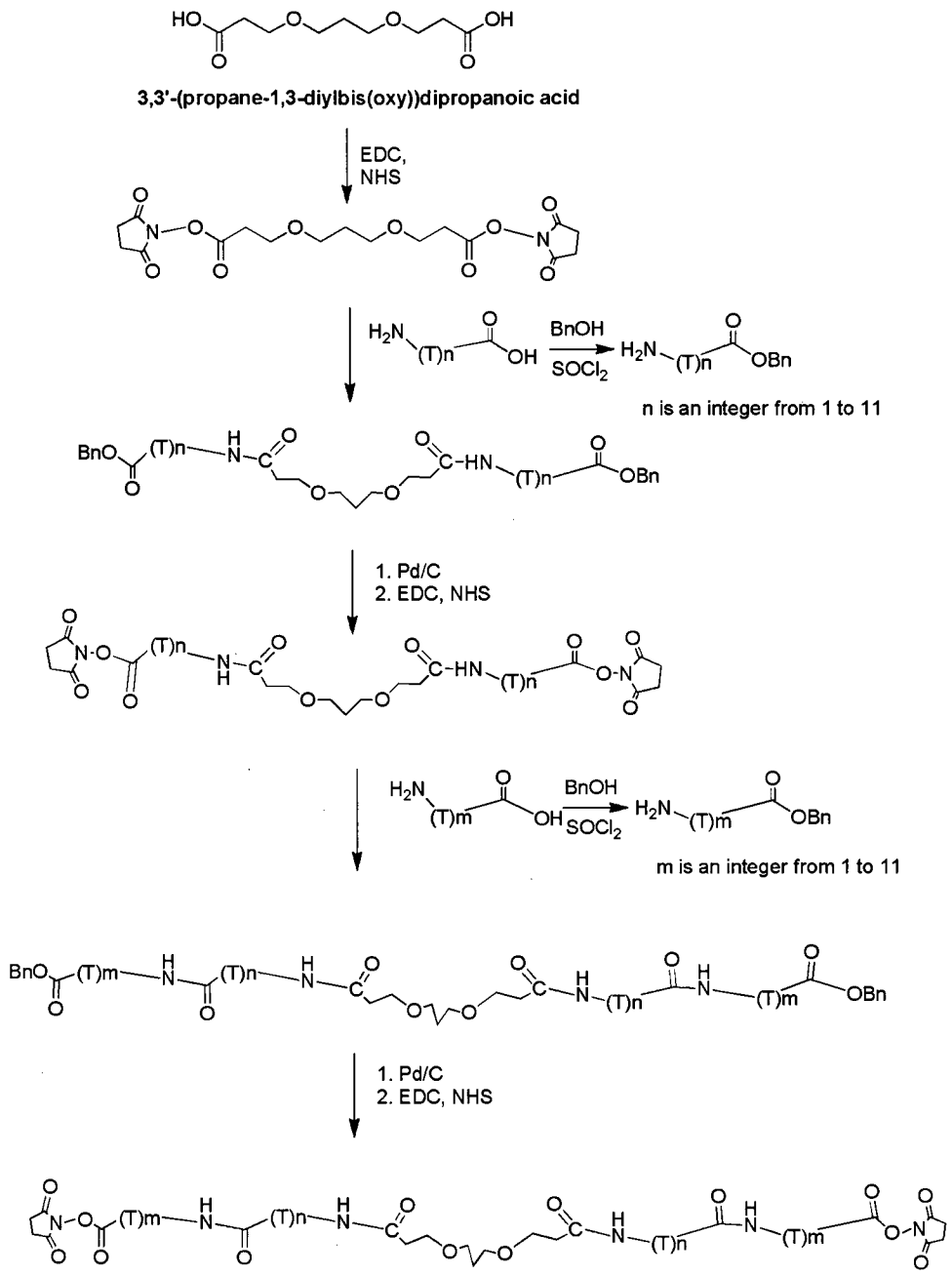
Compound 1 is then converted to compounds of formula (I) via reaction with a suitable amino-substituted carboxylic acid, such as 3-aminopropanoic acid, 4-aminobutanoic acid, 5-aminopentanoic acid, 6-aminohexanoic acid, 7-aminoheptanoic acid, 8-aminooctanoic acid, 9-aminononanoic acid, 10-aminodecanoic acid, 11-aminoundecanoic acid or 12-aminododecanoic acid (Scheme 2).

Scheme 2



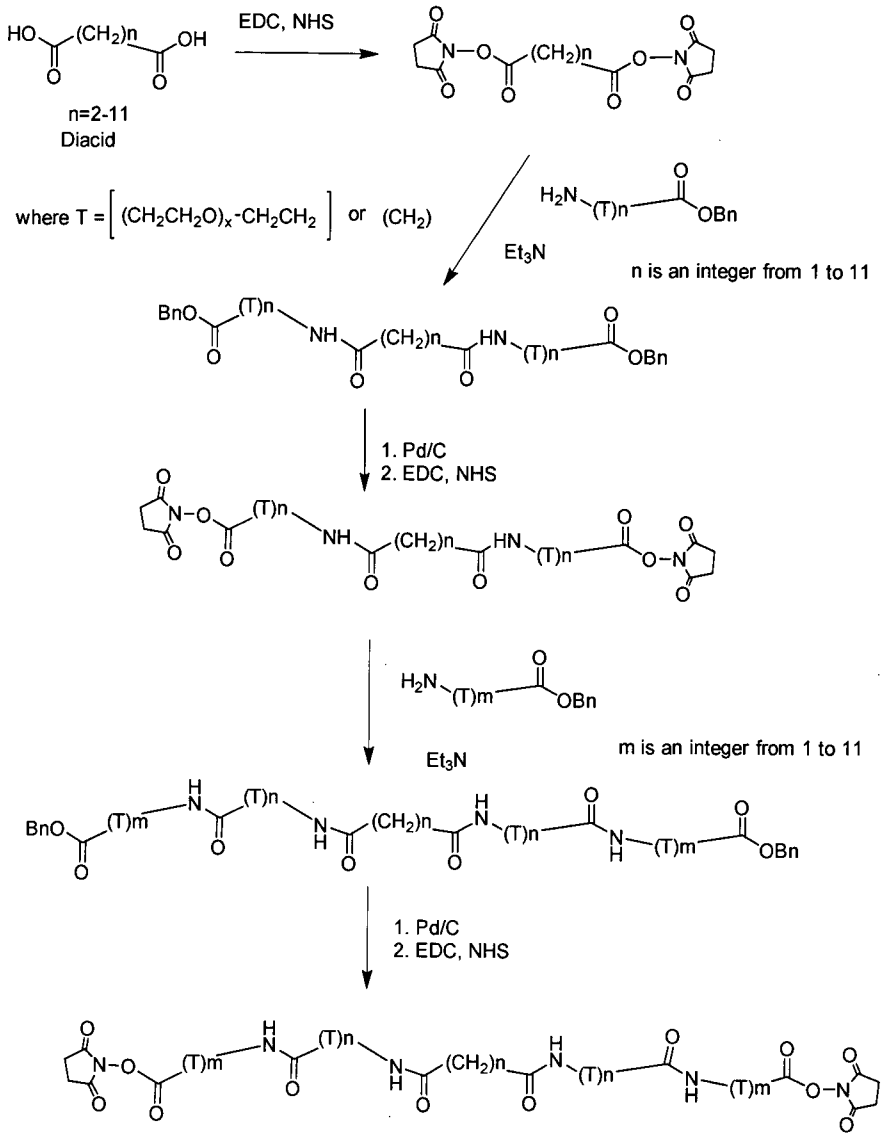
"Dimeric" dendritic core compounds of the invention where Y is C and R^1 and R^2 are both H are prepared from 3,3'-(propane-1,3-diylbis(oxy)dipropanoic acid, using a suitable amino-substituted carboxylic acid, such as 3-aminopropanoic acid, 4-aminobutanoic acid, 5-aminopentanoic acid, 6-aminohexanoic acid, 7-aminoheptanoic acid, 8-aminooctanoic acid, 9-aminononanoic acid, 10-aminodecanoic acid, 11-aminoundecanoic acid or 12-aminododecanoic acid (Scheme 3).

Scheme 3



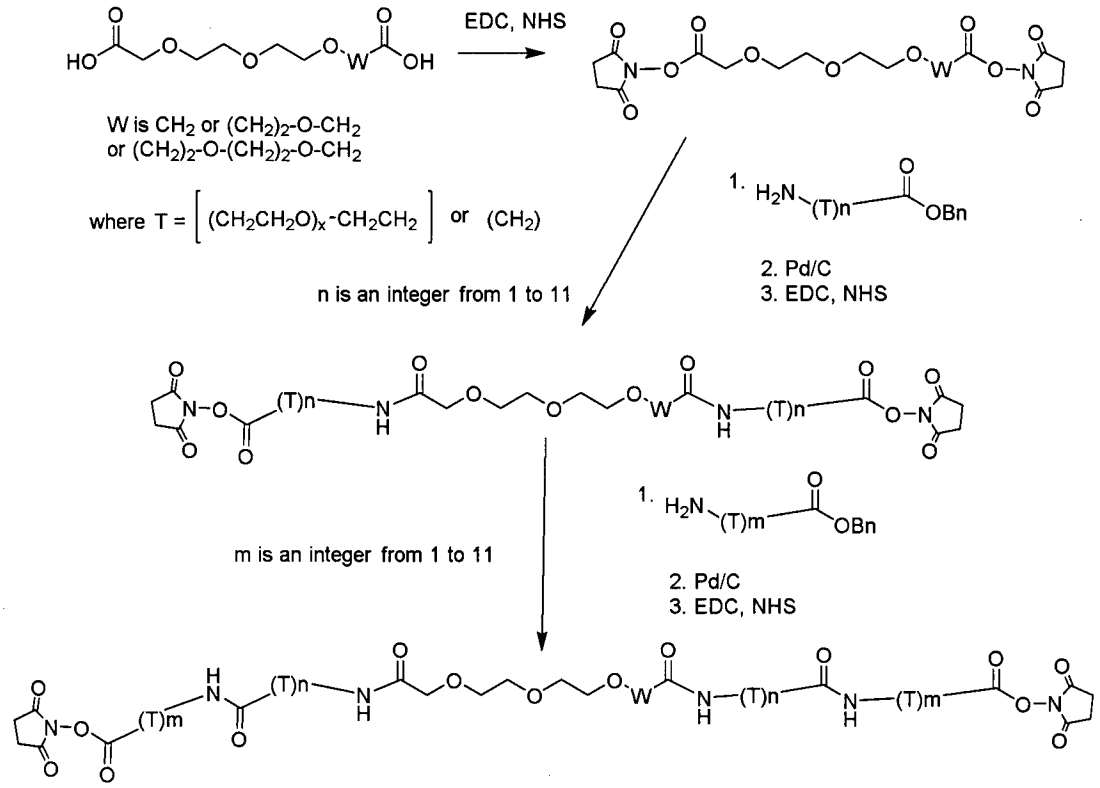
"Dimeric" dendritic core compounds of the invention where Y is C; A is $(CH_2)_u$; and R^1 and R^2 are both H are prepared from a suitable diacid, as shown in Scheme 4.

Scheme 4



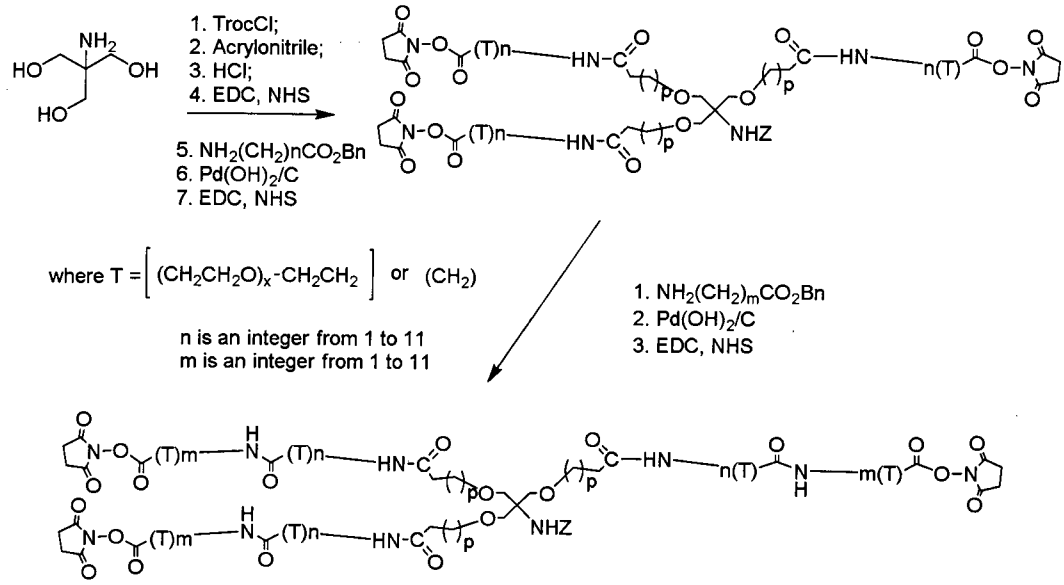
"Dimeric" dendritic core compounds of the invention where Y is O and E is $(CH_2CH_2O)_tCH_2$ are prepared as shown in Scheme 5. Suitable starting materials include, for example, 3,6,9-trioxaundecanedioic acid, 3,6,9,12-tetraoxatetradecanedioic acid or 3,6,9,12,15-pentaoxaheptadecanedioic acid.

Scheme 5



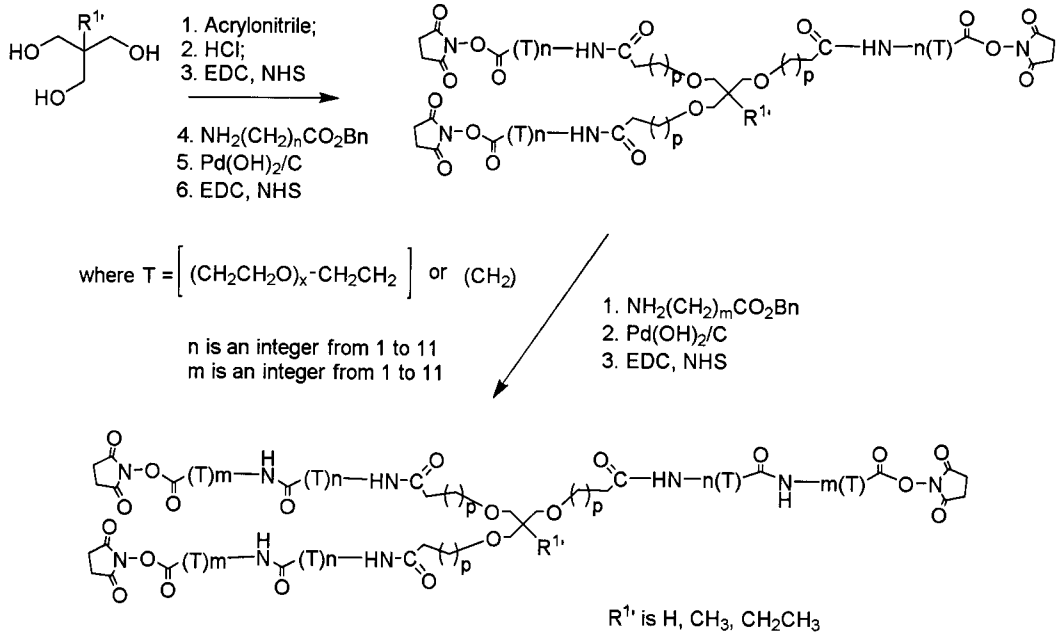
"Trimeric" dendritic core compounds of the invention where Y is C and R^1 is NHZ are prepared from 2-amino-2-hydroxymethyl-propane-1,3-diol, as shown in Scheme 6. Those skilled in the art will appreciate that trimeric dendritic core compounds where R^1 is NH_2 can be used to further elaborate the substitution at the R^1 position. For example, such compounds can be linked to radio- or fluorescent labels or the amino functionality can be converted to other functional groups.

Scheme 6



"Trimeric" dendritic core compounds of the invention where Y is C and R^1 is H, CH_3 or CH_2CH_3 are prepared from 2-hydroxymethyl-propane-1,3-diol, 1,1,1-tris(hydroxymethyl)ethane or 1,1,1-tris(hydroxymethyl)propane, respectively (Scheme 7).

Scheme 7



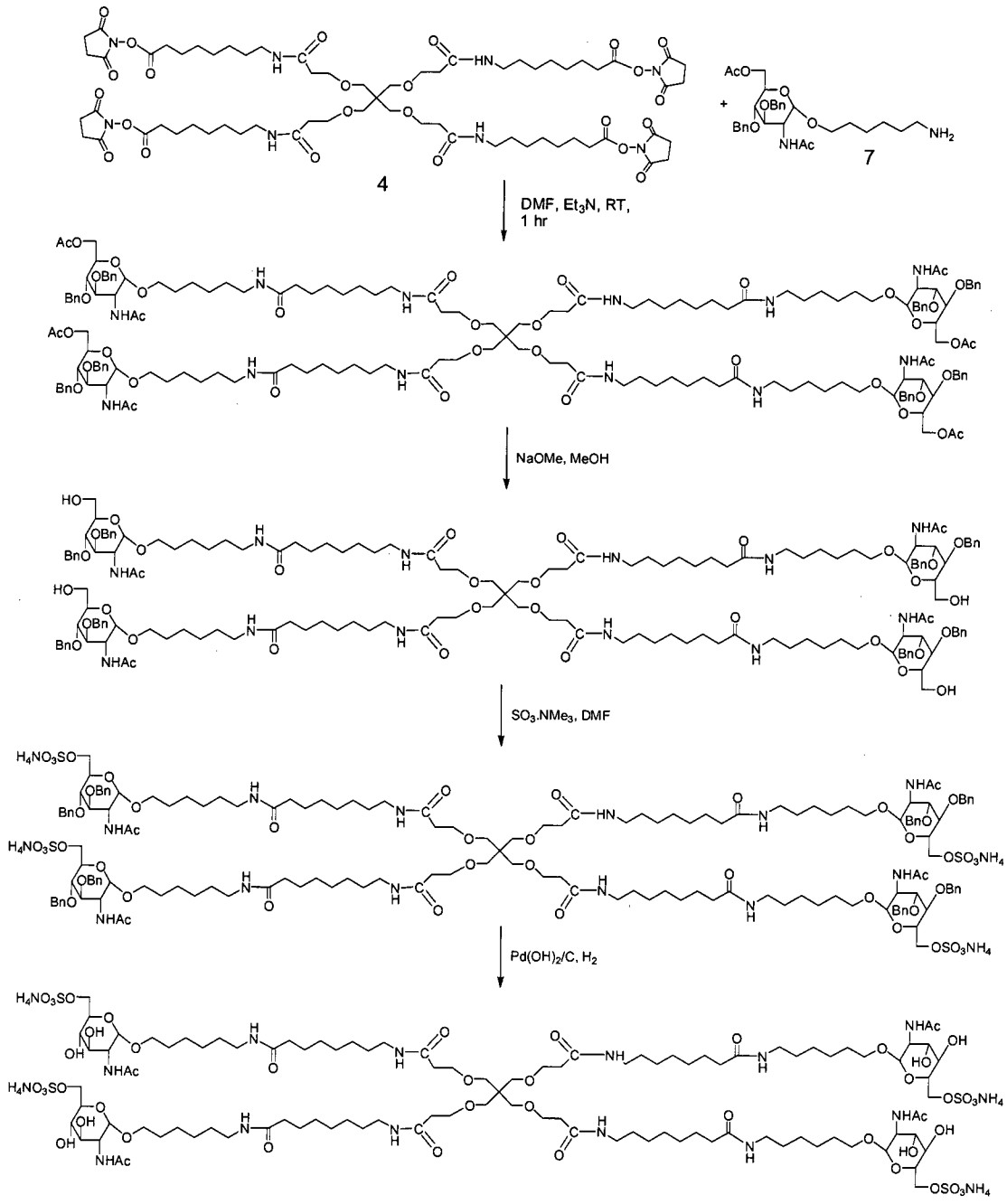
Use of the Compounds of the Invention for Preparing Dendrimers

The compounds of the invention are useful for the preparation of dendritic compounds. Conveniently, the compounds of the invention allow for facile synthesis of dendrimers.

Advantageously, with some compounds of the invention there is no need to use coupling reagents and then to remove an excess of reagents from the dendritic products. The coupling procedure is simple and requires a suitable solvent (DMF, DMSO, water, for example), a small amount of base, e.g. triethylamine, and any glycoside with a free amino group (at least about 2 equivalents of glycoside, e.g. about 2.2 equivalents of glycoside are used for coupling with dimeric compounds of the invention, at least about 3 equivalents of glycoside, e.g. about 3.3 equivalents of glycoside are used for coupling with trimeric compounds of the invention and at least about 4 equivalents of glycoside e.g. about 4.4 equivalents of glycoside are used for coupling with tetrameric compounds of the invention).

Using this method, it is possible to attach a variety of carbohydrate fragments (e.g. heparan sulfates, sulfated monosaccharides, oligosaccharides, amino acids, radioligands, imaging agents, fluorescent probes, antibiotics, cytostatic drugs (chemotherapy), veterinary pharmaceuticals, proton and pH sensors, metal ions and ferrocene) with various linkers to the dendritic cores. By way of example, Scheme 8 shows how a "star burst PET-PEG" dendritic cluster glycomimetic of heparan sulfate can be synthesised from a dendritic core of the present invention. This heparan sulfate mimetic is useful as an inhibitor of Alzheimer's β-secretase.

Scheme 8



Those skilled in the art will appreciated that, using the tetrameric compounds of the invention, it is possible to achieve dendrimers that are a similar size to 16-mer and 32-mer ball-clusters, but which have fewer copies of glycosides attached. Typically, when the use of 16-, 32- and 64-mer dendritic cores is reported, the dendrimer products are described as mixtures with only partial capping of attachment points due to electrostatic repulsion and steric crowding effects. Using the compounds of the invention, with fewer linkers, the glycosides are well separated in space so the capping leads to fully substituted dendrimers. This is advantageous, for example, in the field of pharmaceuticals where it is desirable to produce discrete, well-characterised chemical compounds, rather than mixtures.

ABBREVIATIONS

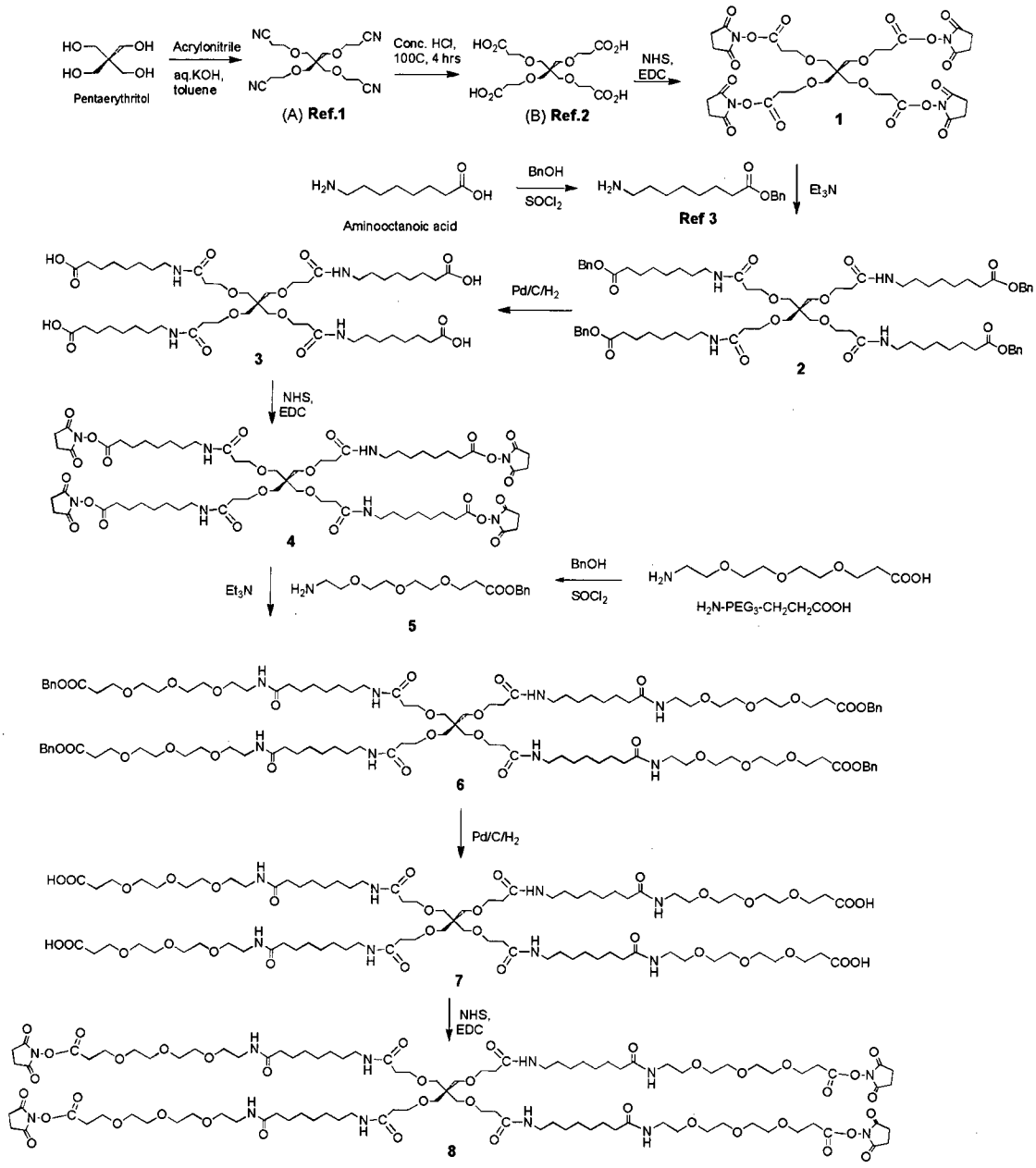
NMR	Nuclear magnetic resonance
HRMS	High resolution mass spectrometry
DCM	Dichloromethane
DMF	N,N-Dimethylformamide
EtOH	Ethanol
MeOH	Methanol
THF	Tetrahydrofuran
EtOAc	Ethyl acetate
RT	Room temperature
TAMRA	4-Carboxytetramethylrhodamine N-succinimidyl ester
BODIPY	4,4-Difluoro-4-bora-3a,4a-diaza-s-indacene
EDC	1-Ethyl-3-[3-dimethylaminopropyl]carbodiimide hydrochloride
NHS	N-Hydroxysuccinimide

EXAMPLES

The following examples further illustrate the invention. It is to be appreciated that the invention is not limited to the examples.

Example 1: Synthesis of Compounds of the Invention

Scheme 9



Preparation of 1

Tetranitrile precursor (**Ref.1**, Hukkamaki, J.; Pakkanen, T.T. *Journal of Molecular Catalysis A: Chemical* **2001**, 174, 205-211) is prepared via Michael-type addition of acrylonitrile to pentaerythritol. Acidic hydrolysis of tetranitrile (**Ref. 2**, Newcombe, G. R.; Mishra, A; Moorfield, C. N. *J. Org. Chem.* 2002, 67, 3957-3960) furnishes the tetraacid. Tetraacid (1.0 g, 2.35 mmol) is dissolved in dry DMF (15 mL). N-Hydroxysuccinimide (1.62 g, 14.14 mmol) and 1-ethyl-3-[3-dimethylaminopropyl]carbodiimide hydrochloride (EDC, 2.71 g, 14.14 mmol) are added to the reaction mixture at room temperature and stirring continued for 24 hrs. The mixture is diluted with DCM and washed with water, then with diluted HCl and water, dried over magnesium sulfate and concentrated. The residue is purified by flash chromatography on silica gel eluting

with EtOAc followed by EtOAc:MeOH, 19:1 → 9:1 → 7:1 → 4:1 to give the tetra-succinimidyl ester (**1**, 1.2 g, 1.48 mmol, 63%). R_f = 0.25 (Ethyl Acetate:MeOH, 9:1). ^{13}C-NMR (125MHz, DMSO-D_6) δ 170.7, 170.1, 68.7, 65.5, 44.9, 31.5, 25.7. HRMS calcd for $C_{33}H_{40}N_4O_{20}Na$ $(M+Na)^+$ *m/z* 835.2134, found 835.2128.

Preparation of 2

Aminooctanoic acid is treated with benzyl alcohol in the presence of thionyl chloride (**Ref. 3**, Patel, R. P; Price, S. *J. Org Chem.* **1965**, 30 (10), 3575-3576) to give a tetra benzyl ester (2 g, 8.12 mmol). This and tetra-succinimidyl ester (**1**, 1.1 g, 1.35 mmol) are dissolved in a mixture of dry THF (55 mL) and dry DMF (3 mL) and treated with triethylamine (1.5 mL, 10.83 mmol). After stirring for 24 hrs the mixture is diluted with ethyl acetate and washed with water twice, dried over magnesium sulfate and concentrated. The residue is dissolved in hot EtOAc, the crystals are filtered off and discharged. The mother liquor is concentrated and the residue is purified by flash chromatography on silica gel eluting with Chloroform : EtOAc : MeOH, 5:2:0.5 to afford the tetra-benzyl ester (**2**, 1.7 g, 1.26 mmol, 93%). R_f = 0.3 (Chloroform : Ethyl Acetate : MeOH, 5:2:1). ^{13}C-NMR (125MHz, $CDCl_3$) δ 173.5, 171.2, 136.1, 128.5, 128.2, 128.1, 69.1, 67.4, 66.1, 45.3, 39.5, 36.9, 34.2, 29.6, 29.4, 28.9, 26.7, 26.6, 24.8. HRMS calcd for $C_{77}H_{112}N_4O_{16}Na$ $(M+Na)^+$ *m/z* 1371.7971, found 1371.7977.

Preparation of 3

Tetra benzyl ester (**2**, 0.595 g, 441 µmol) is dissolved in dry THF (16 mL). Water (4 mL) and glacial acetic acid (5 drops) are added. The reaction mixture is treated with palladium hydroxide on carbon (20% Pd, 1 g) and stirred for 3 hours under hydrogen at ambient temperature and pressure. The catalyst is filtered off and washed with 50% aqueous EtOH. The solution is concentrated to dryness to give a "long-armed" tetraacid (**3**, 0.42 g, 429 µmol, 97%). The product is used in the next step without further purification. R_f = 0.0 (base line, Chloroform : Ethyl Acetate : MeOH, 5:2:1). ^{13}C-NMR (125MHz, DMSO-D_6) δ 174.5, 169.9, 68.8, 67.3, 45.0, 39.0, 38.4, 36.1, 33.8, 29.1, 28.5, 38.4, 26.3, 25.2, 24.5. HRMS calcd for $C_{49}H_{87}N_4O_{16}$ $(M-H)^-$ *m/z* 987.6117, found 987.6110.

Preparation of 4

"Long-armed" tetraacid (**3**, 424 mg, 429 µmol) is dissolved in dry DMF (7 mL). *N*-Hydroxysuccinimide (296 mg, 2.57 mmol) and 1-ethyl-3-[3-dimethylaminopropyl]carbodiimide hydrochloride (EDC, 493 mg, 2.57 mmol) are added to the reaction mixture at room temperature and stirring continued for 24 hrs. The mixture is diluted with DCM and washed with water, then with diluted HCl and water, dried over magnesium sulfate and concentrated. The residue is purified by flash chromatography on silica gel eluting with Chloroform : Ethyl Acetate : MeOH,

5:2:0.5 → 5:4:1 to give the "long-armed" tetra-succinimidyl ester (**4**, 415 mg, 301 µmol, 70.3 %). R_f = 0.25 (DCM:MeOH, 9:1). ^{13}C-NMR (125MHz, $CDCl_3$) δ 171.5, 169.4, 168.6, 68.9, 67.4, 45.3, 39.4, 36.7, 30.8, 29.5, 29.4, 28.6, 28.5, 26.6, 25.5, 25.4, 24.4. HRMS calcd for $C_{65}H_{100}N_8O_{24}Na$ $(M+Na)^+$ *m/z* 1399.6748, found 1399.6737.

Preparation of 5

$H_2N(PEG)_3CH_2CH_2COOH$ (or PEG aminoacid) (1.0 g, 4.52 mmol) is dissolved in benzyl alcohol (30 mL, 287 mmol) and cooled to 0°C. Thionyl chloride (6 mL, 82.2 mmol) is added slowly dropwise. The reaction mixture is stirred at 0°C for 15 min followed by heating at 100°C for 5 hours. Then this is diluted with diethyl ether and the oily residue is collected and purified by flash chromatography on silica gel eluting with Dichloromethane: MeOH, 9:1 → 1:1 to afford the benzyl ester (**5**, 1.2 g, 3.9 mmol, 85%). R_f = 0.15 (Dichloromethane: MeOH, 9:1). ^{13}C-NMR (125MHz, $CDCl_3$) δ 171.6, 135.8, 128.5, 128.2, 128.1, 70.2, 70.14, 70.13, 69.9, 66.7, 66.4, 66.3, 50.0, 39.7, 35.0. HRMS calcd for $C_{16}H_{26}NO_5$ $(M+H)^+$ *m/z* 312.1811, found 312.1806.

Preparation of 6

The benzyl ester **5** (65 mg, 210 µmol) and tetra-succinimidyl ester (**4**, 58 mg, 42.1 µmol) are dissolved in dry DMF (2 mL) and treated with triethylamine (47 µL, 336 µmol). After stirring for 24 hrs the mixture is diluted with ethyl acetate and washed with water twice, dried over magnesium sulfate and concentrated. The residue is dissolved in hot EtOAc, the crystals are filtered off and discharged. The mother liquor is concentrated and the residue is purified by flash chromatography on silica gel eluting with Chloroform : EtOAc : MeOH, 5:2:0.5 to afford the tetra-benzyl ester (**6**, 71 mg, 32.8 µmol, 78%). R_f = 0.3 (Chloroform : Ethyl Acetate : MeOH, 5:2:1). ^{13}C-NMR (125MHz, $CDCl_3$) δ 173.2, 171.3, 135.8, 128.5, 128.2, 128.1, 70.5, 704, 70.2, 69.9, 69.2, 67.5, 66.5, 66.3, 45.3, 39.4, 39.1, 36.9, 36.5, 35.1, 29.6, 29.1, 29.0, 26.7, 25.5.

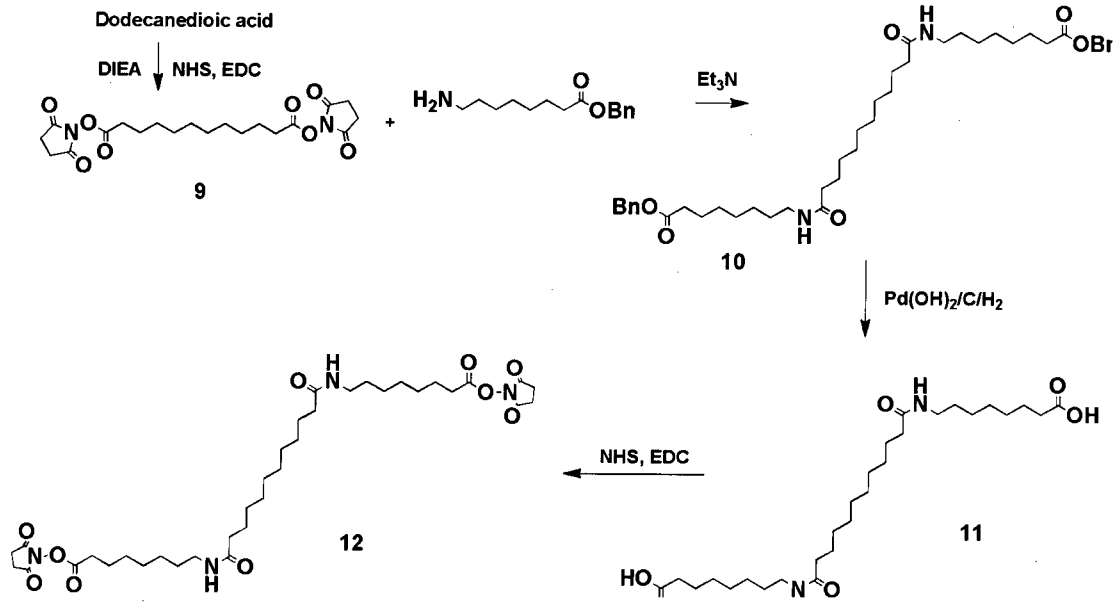
Preparation of 7

Tetra benzyl ester (**6**, 16 mg, 7.21 µmol) is dissolved in dry THF (4 mL). Water (1 mL) and glacial acetic acid (2 drops) are added. The reaction mixture is treated with palladium hydroxide on carbon (20% Pd, 20 mg) and stirred for 3 hours under hydrogen at ambient temperature and pressure. The catalyst is filtered off and washed with 50% aqueous EtOH. The solution is concentrated to dryness to give a "long-armed" PEG tetraacid (**7**, 13 mg, 7.21 µmol, 97%). The product is used in the next step without further purification. R_f = 0.0 (base line, Chloroform : Ethyl Acetate : MeOH, 5:2:1). ^{13}C-NMR (125MHz, MeOD) δ 176.7, 174.2, 71.4, 71.3, 71.2, 70.6, 68.8, 67.8, 62.8, 48.5, 40.6, 40.3, 37.8, 37.1, 35.8, 30.4, 30.2, 30.1, 30.0, 27.9, 26.9.

Preparation of 8

"Long-armed" PEG tetraacid (**7**, 13 mg, 7.21 µmol) is dissolved in dry DMF (1 mL). *N*-Hydroxysuccinimide (5.1 mg, 43.2 µmol), DIPEA (7.6 µL, 43.2 µmol) and 1-ethyl-3-[3-dimethylaminopropyl]carbodiimide hydrochloride (EDC, 8.3 mg, 43.2 µmol) are added to the reaction mixture at room temperature and stirring continued for 24 hrs. The mixture is diluted with DCM and washed with water, then with diluted HCl and water, dried over magnesium sulfate and concentrated. The residue is purified by flash chromatography on silica gel eluting with Chloroform : Ethyl Acetate : MeOH, 5:2:0.5 → 5:4:1 to give the "long-armed" PEG tetra-succinimidyl ester (**8**, 15 mg, 6.85 µmol, 94 %). R_f = 0.25 (DCM:MeOH, 9:1).

Scheme 10



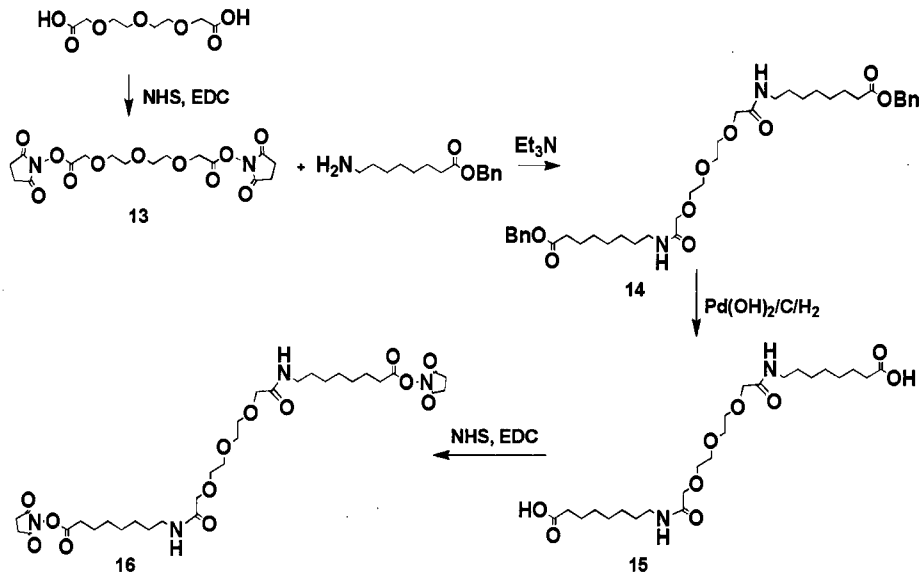
Preparation of 9

Dodecanedioic acid (1.0 g, 4.34 mmol) is dissolved in dry DMF (10 mL). N-Hydroxysuccinimide (1.51 g, 13.0 mmol, 3 eq.) and 1-ethyl-3-[3-dimethylaminopropyl]carbodiimide hydrochloride (EDC, 2.55 g, 13.0 mmol, 3 eq.) and *N,N*-diisopropylethylamine (1.53 mL, 8.68 mmol) are added to the reaction mixture at room temperature and stirring continued for 24 hrs. The mixture is diluted with DCM and washed with water, then with diluted HCl and water, dried over magnesium sulfate and concentrated. The residue is re-crystalized from hot EtOAc to give the di-succinimidyl ester (**9**, 1.84 g, 4.2 mmol, 98%). ^{13}C-NMR (125MHz, DMSO-D_6) δ 170.2, 168.9, 30.2, 28.7, 28.4, 27.9, 25.4, 24.2. HRMS calcd for $C_{20}H_{28}N_2O_8Na$ $(M+Na)^+$ *m/z* 447.1743, found 447.1743.

Preparation of 10

Di-succinimidyl ester (**9**, 500 mg, 1.18 mmol) and an amino benzyl ester (881 mg, 3.53 mmol, 3 eq.) are dissolved in dry DMF (8 mL) and treated with triethylamine (0.66 mL, 4.71 mmol, 4 eq.). After stirring for 24 hrs the mixture is concentrated. The residue is dissolved in hot MeOH, a few drop of chloroform added, the crystals are filtered off and dried to afford the di-benzyl ester (**10**, 0.75 g, 1.1 mmol, 92%). ^{13}C-NMR (125MHz, MeOD) δ 176.2, 175.5, 137.4, 129.8, 129.4, 129.4, 67.5, 40.6, 37.6, 35.5, 30.7, 30.6, 30.5, 30.2, 30.1, 27.9, 27.2, 26.1. HRMS calcd for $C_{42}H_{64}N_2O_6Na$ $(M+Na)^+$ *m/z* 715.4662, found 715.4664.

Scheme 11



Preparation of 14

3,6,9-Trioxaundecanedioic acid (500 mg, 2.25 mmol) is dissolved in dry DMF (10 mL). N-Hydroxysuccinimide (785 mg, 6.75 mmol, 3 eq.), 1-ethyl-3-[3-dimethylaminopropyl]carbodiimide hydrochloride (EDC, 1.32 g, 6.75 mmol, 3 eq.) and *N,N*-diisopropylethylamine (2.38 mL, 13.5 mmol) followed by benzyl 8-aminooctanate (1.68 g, 6.75 mmol, 3 eq.) are added to the reaction mixture at room temperature and stirring continued for 4 hrs. The mixture is diluted with DCM and washed with water, then with diluted HCl and water, dried over magnesium sulfate and concentrated. The residue is dissolved in hot EtOAc, the crystals are filtered off and discharged. The mother liquor is concentrated and the residue is purified by flash chromatography on silica gel eluting with Chloroform : EtOAc : MeOH, 5:2:0.3 to afford the di-benzyl ester (**14**, 1.1 g, 1.61 mmol, 71%). ^{13}C-NMR (125MHz, $CDCl_3$) δ 173.4, 169.9, 136.1, 128.4, 128.3, 128.1, 127.8, 127.7, 65.9, 63.9, 60.3, 39.5, 36.8, 31.9, 30.9, 29.3, 28.8, 26.6, 25.3, 24.7, 24.4, 21.2, 20.9. HRMS calcd for $C_{38}H_{56}N_2O_9Na$ $(M+Na)^+$ *m/z* 707.3884, found 707.3876.

Preparation of 15

Di-benzyl ester (**14**, 204 mg, 297 µmol) is dissolved in dry THF (8 mL). Water (2 mL) and glacial acetic acid (3 drops) are added. The reaction mixture is treated with palladium hydroxide on carbon (20% Pd, 0.5 g) and stirred for 3 hours under hydrogen at ambient temperature and pressure. The catalyst is filtered off and washed with 50% aqueous EtOH. The solution is concentrated to dryness to give a "long-armed" diacid (**15**, 150 mg, 297 µmol, 99.8%). The product is used in the next step without further purification. R_f = 0.0 (base line, Chloroform : Ethyl Acetate : MeOH, 5:2:1). ^{13}C-NMR (125MHz, MeOD) δ 178.1, 175.3, 172.9, 72.3, 71.7, 71.6, 40.4, 35.5, 30.9, 30.6, 30.5, 28.3, 26.5. HRMS calcd for $C_{24}H_{44}N_2O_9Na$ $(M+Na)^+$ *m/z* 527.2945, found 527.2943.

Preparation of 16

"Long-armed" diacid (**15**, 150 mg, 297 µmol) is dissolved in dry DMF (4 mL). *N*-Hydroxysuccinimide (104 mg, 892 µmol), 1-ethyl-3-[3-dimethylaminopropyl]carbodiimide hydrochloride (EDC, 174 mg, 892 µmol) and *N,N*-diisopropylethylamine (0.157 mL, 892 µmol) are added to the reaction mixture at room temperature and stirring continued for 24 hrs. The mixture is diluted with DCM and washed with water, then with diluted HCl and water, dried over magnesium sulfate and concentrated. The residue is purified by flash chromatography on silica gel eluting with Chloroform:Ethyl Acetate : MeOH, 5:2:0.5 → 5:4:1 to give the "long-armed" di-succinimidyl ester (**16**, 188 mg, 269 µmol, 90 %). R_f = 0.25 (DCM:MeOH, 9:1). ^{13}C-NMR (125MHz, $CDCl_3$) δ 170.9, 169.9, 169.5, 168.5, 70.7, 70.6, 70.5, 70.4, 70.0, 38.7, 31.4, 30.7, 29.4, 28.6, 28.5, 28.4, 26.5, 25.5, 24.4. HRMS calcd for $C_{32}H_{50}N_4O_{13}Na$ $(M+Na)^+$ *m/z* 721.3272, found 721.3259.

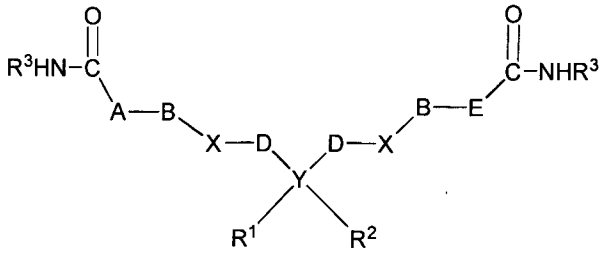
Although the invention has been described by way of example, it should be appreciated that variations and modifications may be made without departing from the scope of the invention. Furthermore, where known equivalents exist to specific features, such equivalents are incorporated as if specifically referred to in the specification.

INDUSTRIAL APPLICABILITY

The invention relates to compounds that are useful for the preparation of dendrimer compounds, the use of these compounds for preparing dendrimers and processes for preparing the compounds.

CLAIMS

1. A compound of formula (I)



wherein:

Y is O;

B is O;

R^1 and R^2 are absent; and

either A, E, D and X are all CH_2; or A, D and X are all CH_2 and E is $(CH_2CH_2O)_t{}^{\#}CH_2$;

wherein # indicates a point of attachment of E to its adjacent carbonyl group;

t is an integer from 1 to 10;

or wherein:

Y is C;

R^1 and R^2 are both H; and

A, E, B and D are CH_2 and X is O;

or wherein:

Y is C;

A is $(CH_2)_u$

R^1 and R^2 are both H;

B, X, D and E are all absent; and

u is an integer from 1 to 10;

or wherein:

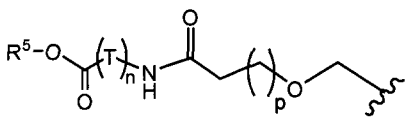
Y is C;

X is O;

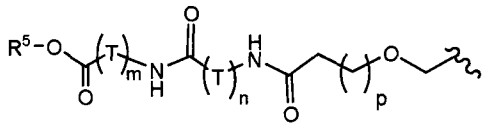
B is $(CH_2)_p$;

A, E and D are all CH_2; and

R^1 is H, NHZ or $C_{1\text{-}6}$alkyl and R^2 is a radical of formula (i) or a radical of formula (ii)



(i)



(ii) ;

Z is H, acyl, $C(O)(CH_2)_wN(H)G$, $*CH_3*C(O)$- where *C denotes ^{13}C or ^{14}C, 4-carboxytetramethylrhodamine, resorcinolphthalein, 7-amino-4-methyl-6-sulfocoumarin-3-acetic acid, 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene or 1-{3-{[4-(2-cyclooctyn-1-ylmethyl)benzoyl]amino}propyl}-4-{2-[4-(dimethylamino)phenyl]ethenyl}pyridinium hexafluorophosphate;

w is an integer from 1 to 11;

G is H, acyl, t-butoxycarbonyl, 2,2,2-trichloroethyloxycarbonyl, 9-fluorenylmethoxycarbonyl, benzyloxycarbonyl,$*CH_3*CO$- where *C denotes ^{13}C or ^{14}C, 4-carboxytetramethylrhodamine, resorcinolphthalein, 7-amino-4-methyl-6-sulfocoumarin-3-acetic acid, 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene or 1-{3-{[4-(2-cyclooctyn-1-ylmethyl)benzoyl]amino}propyl}-4-{2-[4-(dimethylamino)phenyl]ethenyl}pyridinium hexafluorophosphate;

or wherein:

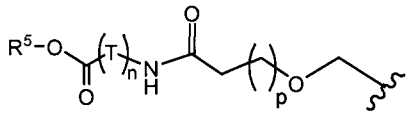
Y is C;

X is O;

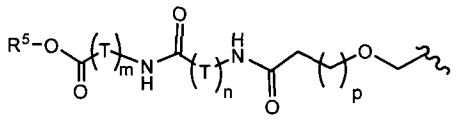
B is $(CH_2)_p$;

A, E and D are all CH_2; and

R^1 and R^2, both the same, are a radical of formula (i) or a radical of formula (ii)

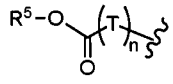


(i)

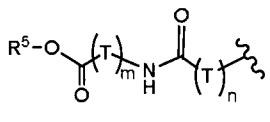


(ii) ;

R^3 is a radical of formula (iii) or a radical of formula (iv)



(iii)



(iv) ;

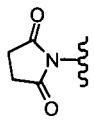
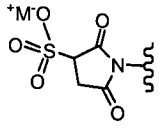
each T is independently selected from the group consisting of $(CH_2CH_2O)_xCH_2CH_2$ and CH_2;

each x is independently an integer from 1 to 12;

m is an integer from 1 to 11, provided that when T is $(CH_2CH_2O)_xCH_2CH_2$ then m is 1;

n is an integer from 1 to 11, provided that when T is $(CH_2CH_2O)_xCH_2CH_2$ then n is 1;

p is an integer from 1 to 5;

R^5 is H,  or  ; and

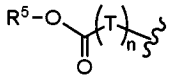
M is sodium or ammonium.

2. A compound as claimed in claim 1 wherein each T is CH_2.

3. A compound as claimed in claim 1 wherein at least one T is $(CH_2CH_2O)_xCH_2CH_2$.

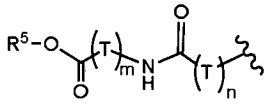
4. A compound as claimed in any one of claims 1 to 3 wherein Y is C.

5. A compound as claimed in any one of claims 1 to 4 wherein R^3 is a radical of formula (iii)



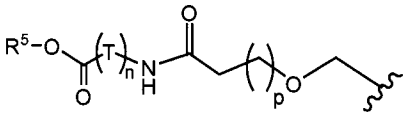
(iii)

6. A compound as claimed in any one of claims 1 to 4 wherein R^3 is a radical of formula (iv)



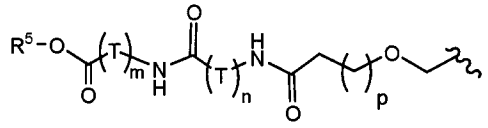
(iv)

7. A compound as claimed in any one of claims 1 to 6 wherein R^1 and R^2 are both a radical of formula (i)

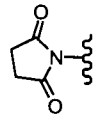


(i)

8. A compound as claimed in any one of claims 1 to 6 wherein R^1 and R^2 are both a radical of formula (ii)



(ii)

9. A compound as claimed in any one of claims 1 to 8 wherein R^5 is  .

10. A compound as claimed in any one of claims 1 to 3, 5 to 6 or claim 9 wherein Y is O; B is O; R^1 and R^2 are absent; and either A, E, D and X are all CH_2 or A, D and X are all CH_2 and E is $(CH_2CH_2O)_tCH_2$; and t is an integer from 1 to 10.

11. A compound as claimed in any one of claims 1 to 6 or claim 9 wherein Y is C; R^1 and R^2 are both H; A, E, B and D are CH_2 and X is O.

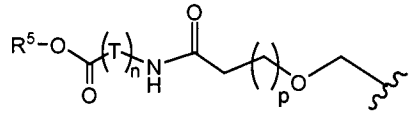
12. A compound as claimed in any one of claims 1 to 6 or claim 9 wherein Y is C; A is $(CH_2)_u$; R^1 and R^2 are both H; B, X, D and E are all absent; and u is an integer from 1 to 10.

13. A compound as claimed in any one of claims 1 to 6 or claim 9 wherein:

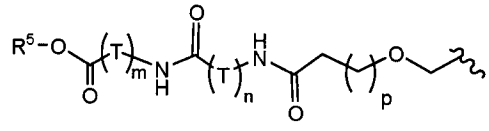
Y is C; X is O; A, E and D are all CH_2; B is $(CH_2)_p$;

R^1 is H, NHZ or $C_{1\text{-}6}$alkyl;

R^2 is a radical of formula (i) or a radical of formula (ii)



(i)



(ii)

; and

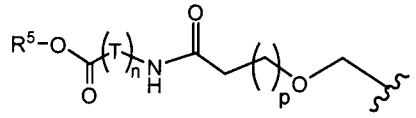
Z is H, acyl, $C(O)(CH_2)_wNHG$, $*CH_3*C(O)$- where *C denotes ^{13}C or ^{14}C, 4-carboxytetramethylrhodamine, resorcinolphthalein, 7-amino-4-methyl-6-sulfocoumarin-3-acetic acid, 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene or 1-{3-{[4-(2-cyclooctyn-1-ylmethyl)benzoyl]amino}propyl}-4-{2-[4-(dimethylamino)phenyl]ethenyl}pyridinium hexafluorophosphate;

w is an integer from 1 to 11;

G is H, acyl, t-butoxycarbonyl, 2,2,2-trichloroethyloxycarbonyl, 9-fluorenylmethoxycarbonyl, benzyloxycarbonyl, $*CH_3*CO$- where *C denotes ^{13}C or ^{14}C, 4-carboxytetramethylrhodamine, resorcinolphthalein, 7-amino-4-methyl-6-sulfocoumarin-3-acetic acid, 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene or 1-{3-

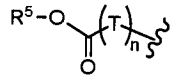
{[4-(2-cyclooctyn-1-ylmethyl)benzoyl]amino}propyl}-4-{2-[4-(dimethylamino)phenyl]ethenyl}pyridinium hexafluorophosphate.

14. A compound as claimed in any one of claims 1 to 7 or claim 9 wherein Y is C; X is O; A, E and D are all CH_2; B is $(CH_2)_p$; R^1 and R^2, both the same, are a radical of formula (i)



(i)

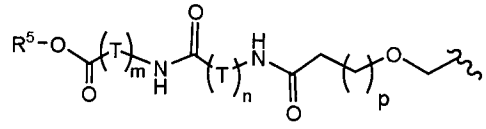
R^3 is a radical of formula (iii)



(iii) ; and

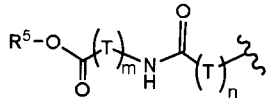
and p is 1.

15. A compound as claimed in any one of claims 1 to 6 or claim 8 or claim 9 wherein Y is C; X is O; A, E and D are all CH_2; B is $(CH_2)_p$; R^1 and R^2, both the same, are a radical of formula (ii)



(ii)

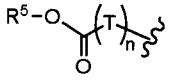
and R^3 is a radical of formula (iv)



(iv) ;

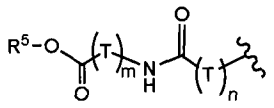
and p is 1.

16. A compound as claimed in any one of claims 1 to 6 or claim 9 or claim 11 wherein Y is C; R^1 and R^2 are both H; A, E, B and D are CH_2; X is O; and R^3 is a radical of formula (iii)



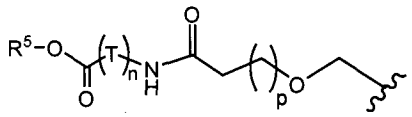
(iii) .

17. A compound as claimed in any one of claims 1 to 6 or claim 9 or claim 11 wherein Y is C; R^1 and R^2 are both H; A, E, B and D are CH_2; X is O; and R^3 is a radical of formula (iv)



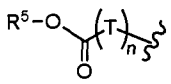
(iv)

18. A compound as claimed in any one of claims 1 to 6 or claim 9 or claim 13 wherein Y is C; X is O; A, E and D are all CH_2; B is $(CH_2)_p$; R^1 is H; R^2 is a radical of formula (i)



(i) ;

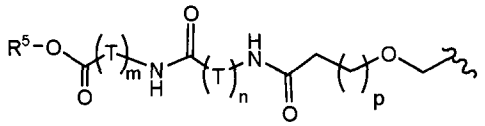
R^3 is a radical of formula (iii)



(iii) ;

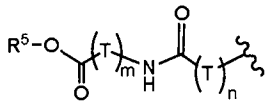
and p is 1.

19. A compound as claimed in any one of claims 1 to 6 or claim 9 or claim 13 wherein Y is C; X is O; A, E and D are all CH_2; B is $(CH_2)_p$; R^1 is H; R^2 is a radical of formula (ii)



(ii) ;

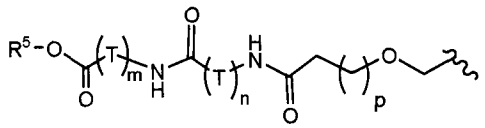
R^3 is a radical of formula (iv)



(iv) ;

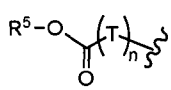
and p is 1.

20. A compound as claimed in any one of claims 1 to 6 or claim 9 or claim 13 wherein Y is C; X is O; A, E and D are all CH_2; B is $(CH_2)_p$; R^1 is H; R^2 is a radical of formula (ii)



(ii) ;

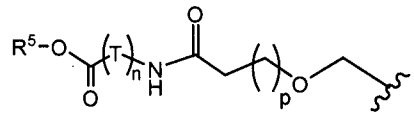
R^3 is a radical of formula (iii)



(iii) ;

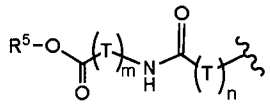
and p is 1.

21. A compound as claimed in any one of claims 1 to 6 or claim 9 or claim 13 wherein Y is C; X is O; A, E and D are all CH_2; B is $(CH_2)_p$; R^1 is H; R^2 is a radical of formula (i)



(i) ;

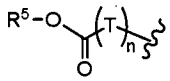
and R^3 is a radical of formula (iv)



(iv) ;

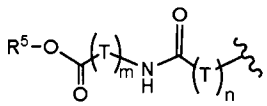
and p is 1.

22. A compound as claimed in any one of claims 1 to 6 or claim 9 or claim 12 wherein Y is C; A is $(CH_2)_u$; R^1 and R^2 are both H; B, X, D and E are all absent; u is an integer from 1 to 10; and R^3 is a radical of formula (iii)



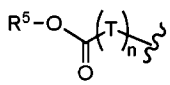
(iii) .

23. A compound as claimed in any one of claims 1 to 6 or claim 9 or claim 12 wherein Y is C; A is $(CH_2)_u$; R^1 and R^2 are both H; B, X, D and E are all absent; u is an integer from 1 to 10; and R^3 is a radical of formula (iv)



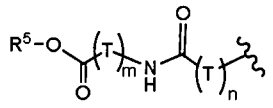
(iv) .

24. A compound as claimed in any one of claims 1 to 6 or claim 9 or claim 10 wherein Y is O; B is O; R^1 and R^2 are absent; and either A, E, D and X are all CH_2 or A, D and X are all CH_2 and E is $(CH_2CH_2O)_tCH_2$; t is an integer from 1 to 10; and R^3 is a radical of formula (iii)



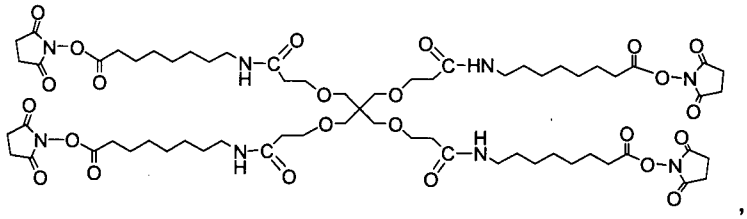
(iii) .

25. A compound as claimed in any one of claims 1 to 6 or claim 9 or claim 10 wherein Y is O; B is O; R^1 and R^2 are absent; and either A, E, D and X are all CH_2 or A, D and X are all CH_2 and E is $(CH_2CH_2O)_tCH_2$; t is an integer from 1 to 10; and R^3 is a radical of formula (iv)



(iv)

26. A compound as claimed in claim 1, selected from the group consisting of:



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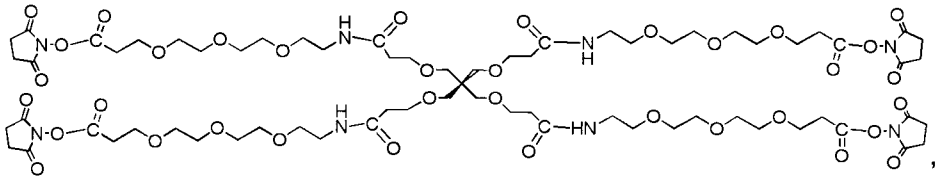

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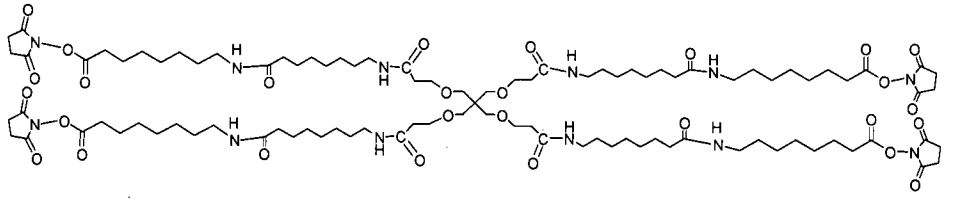

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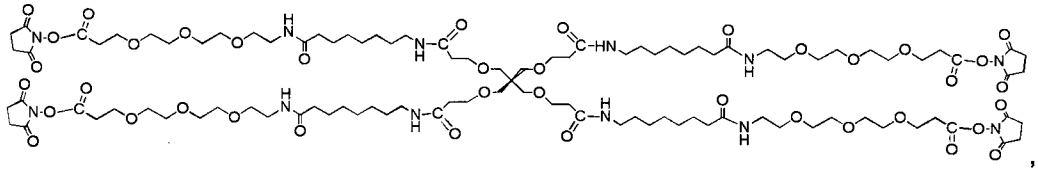

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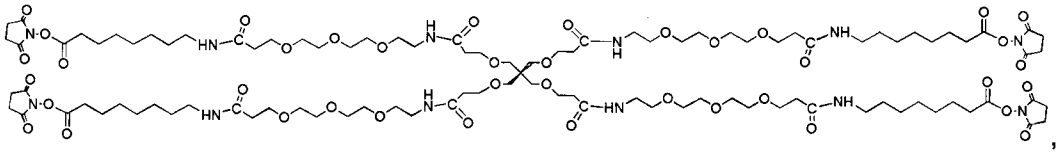

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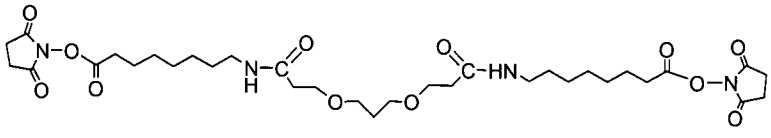

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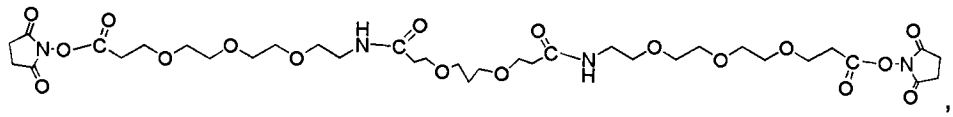

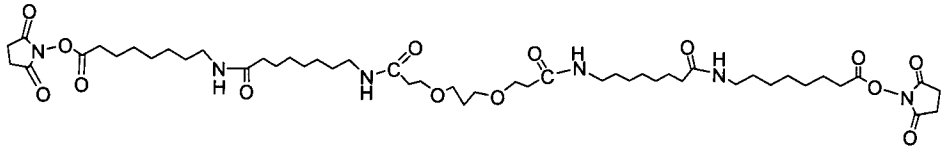

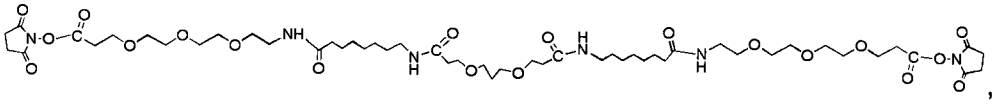

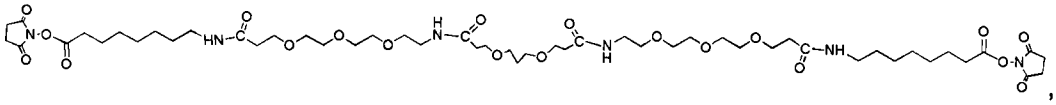

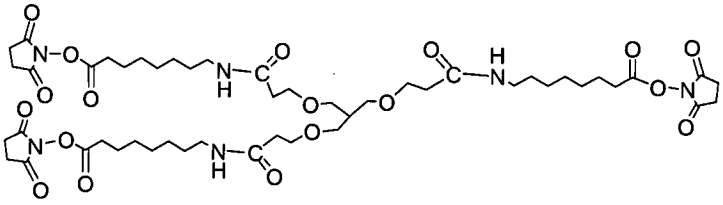

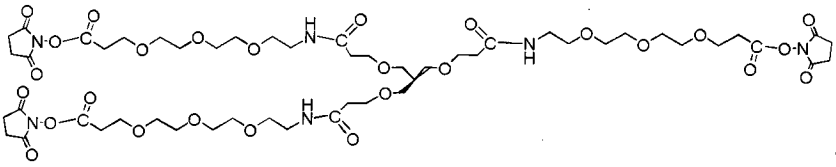

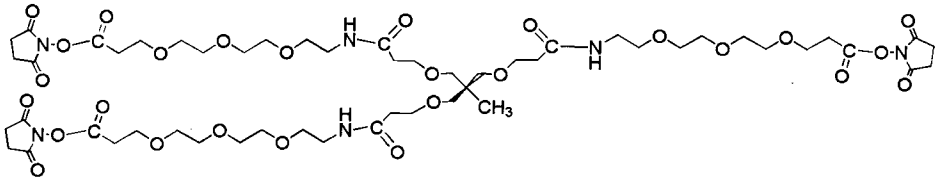

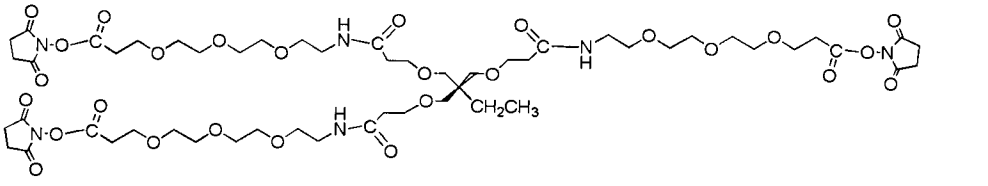

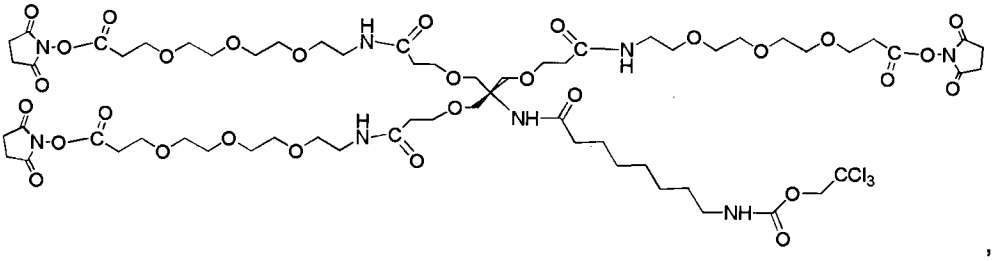

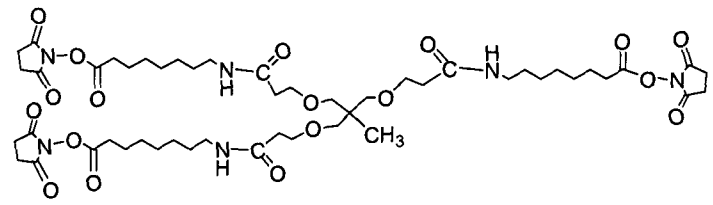

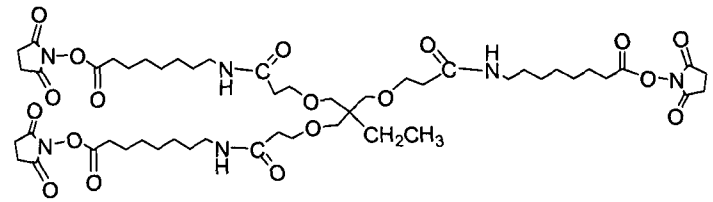

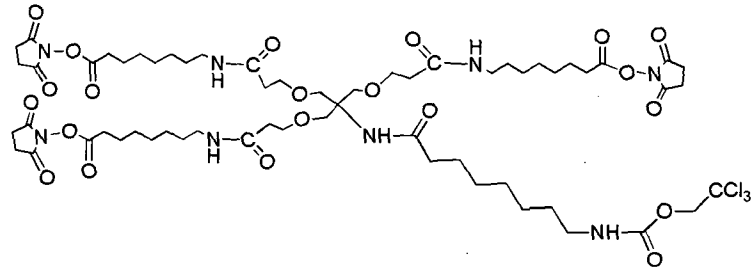

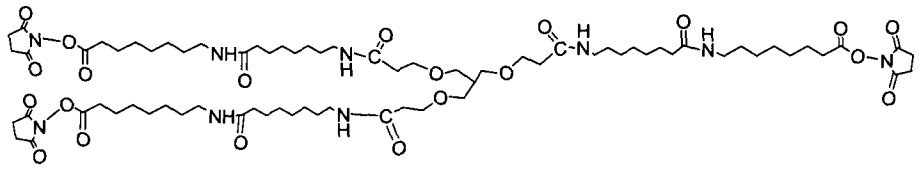

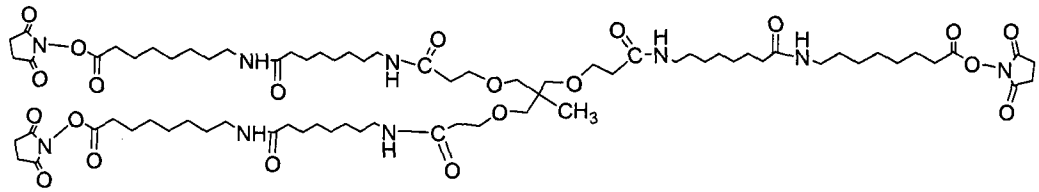

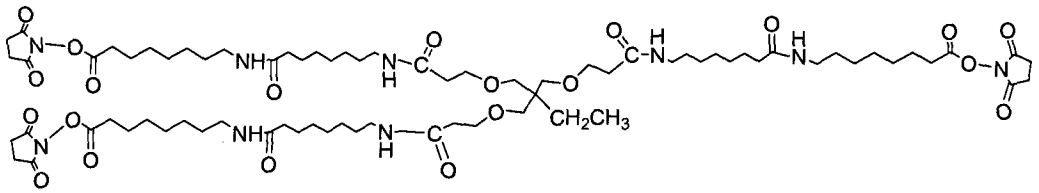

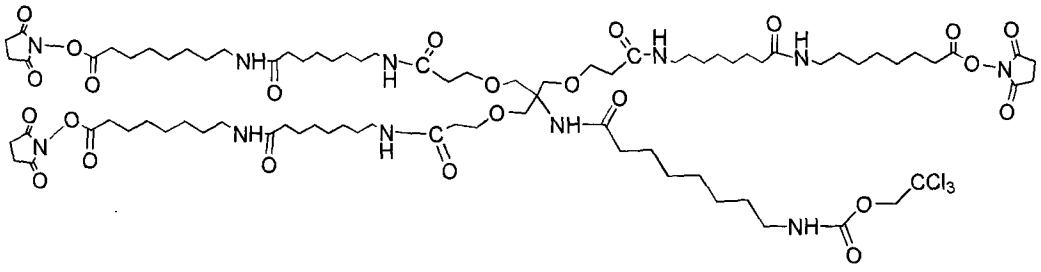

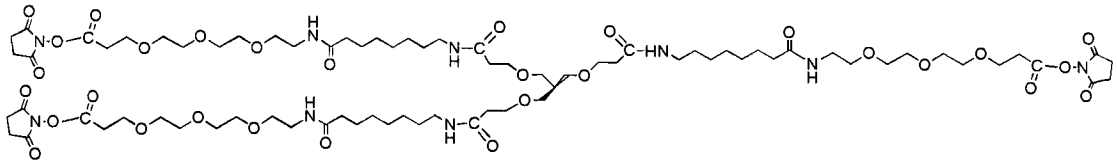

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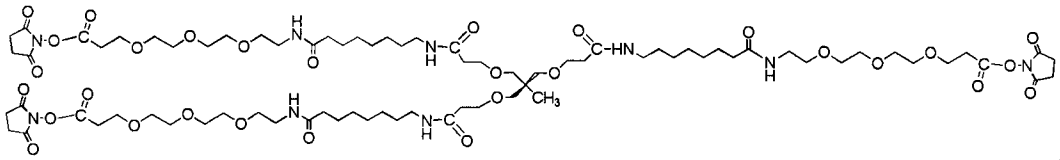

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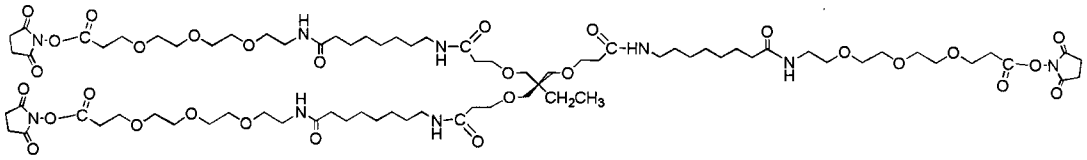

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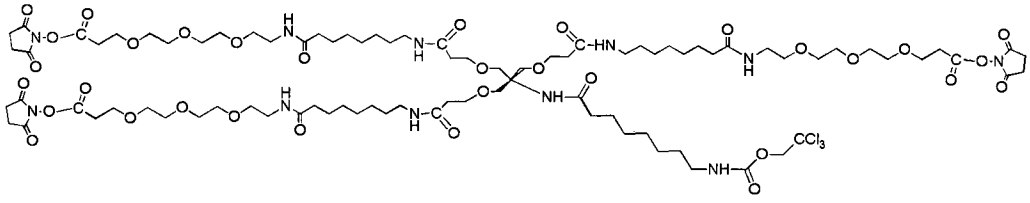

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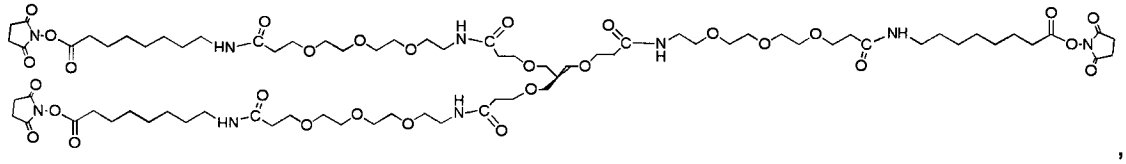

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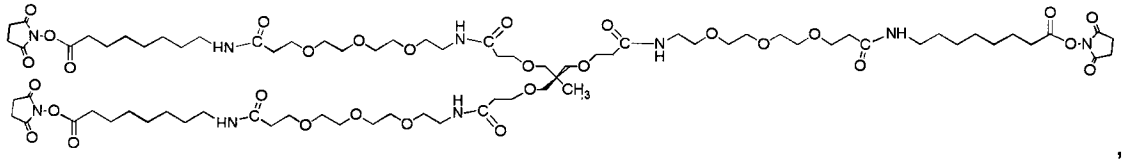

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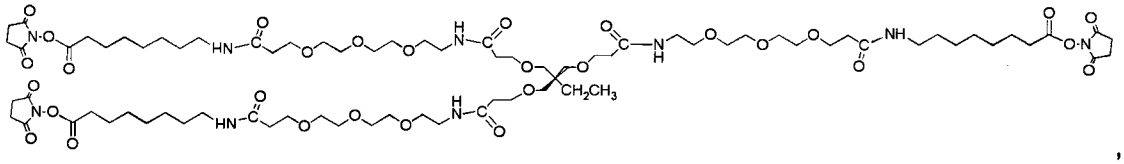

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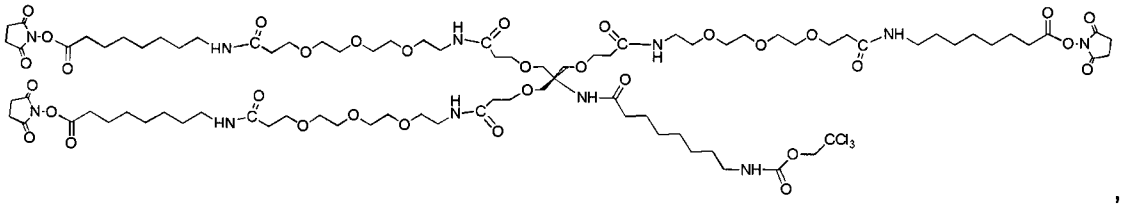

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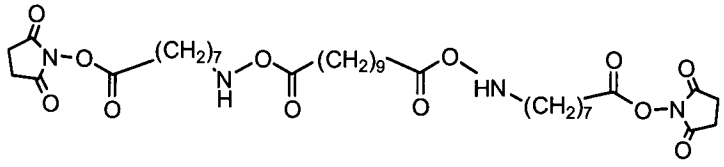

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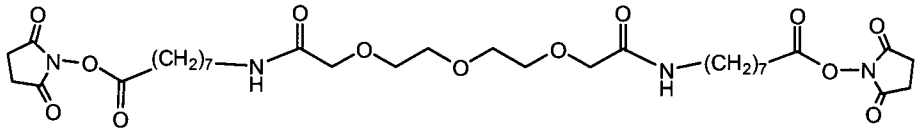

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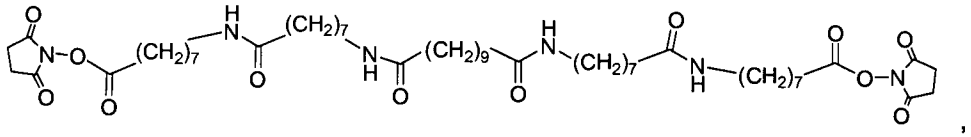

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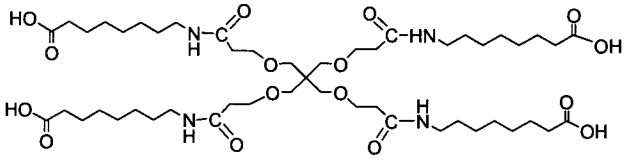

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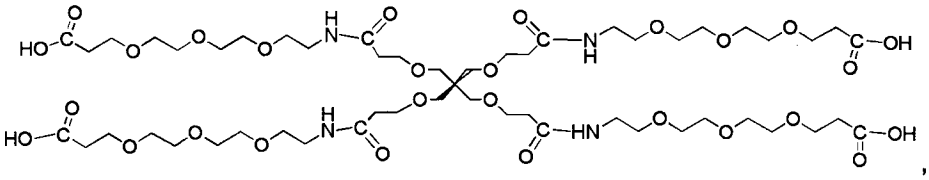

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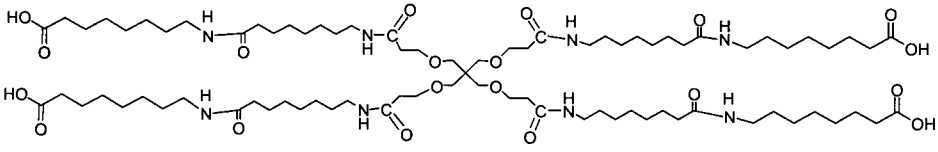

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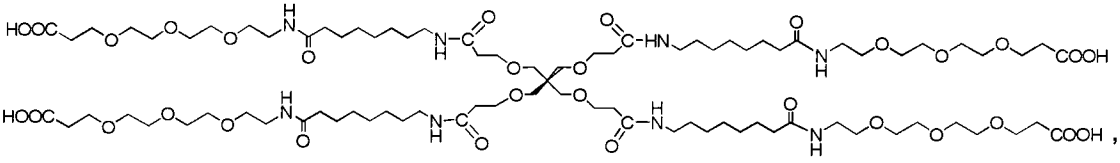

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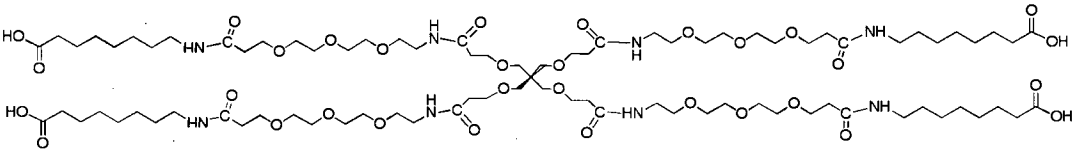

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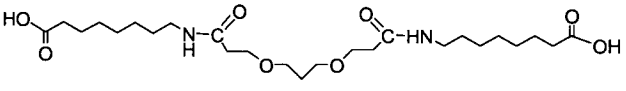

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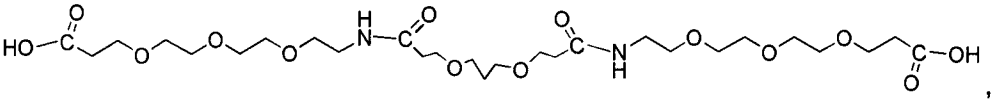

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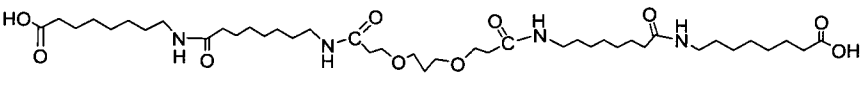

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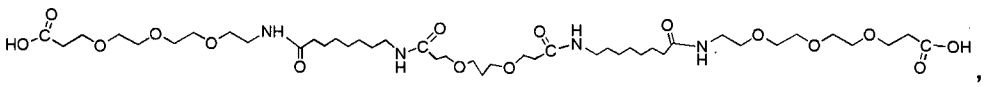

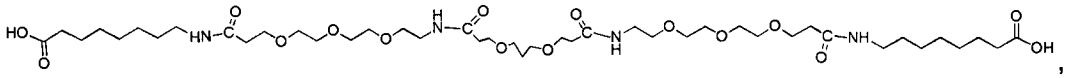

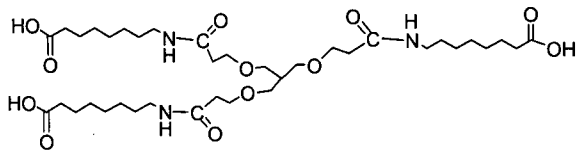

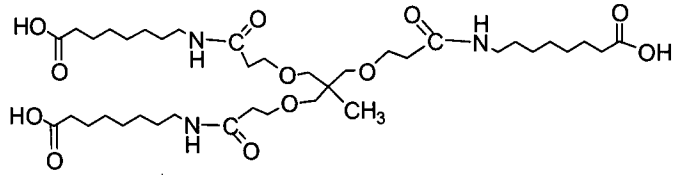

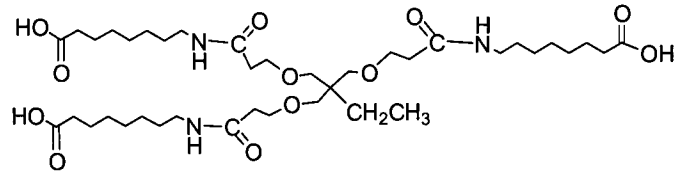

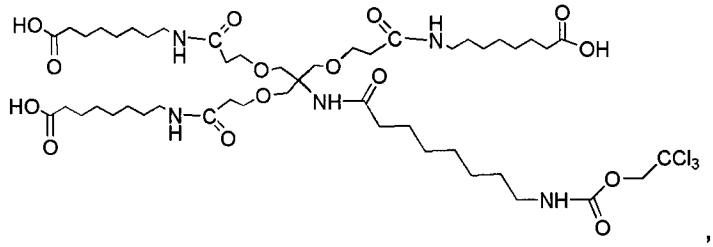

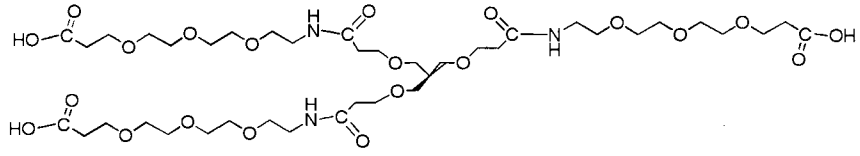

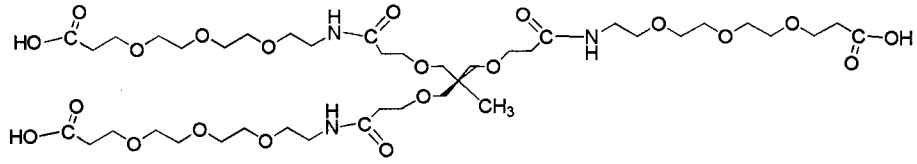

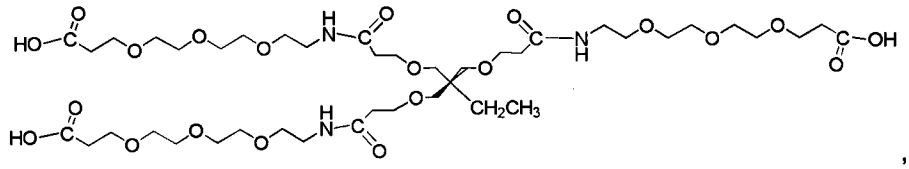

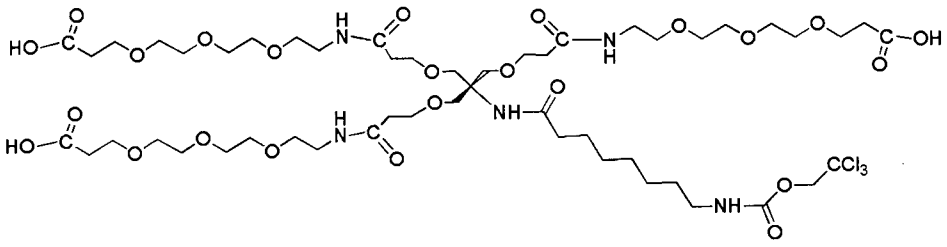

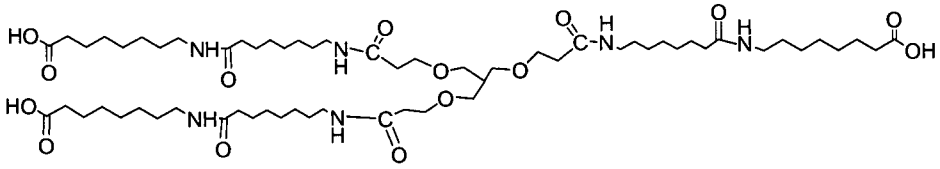

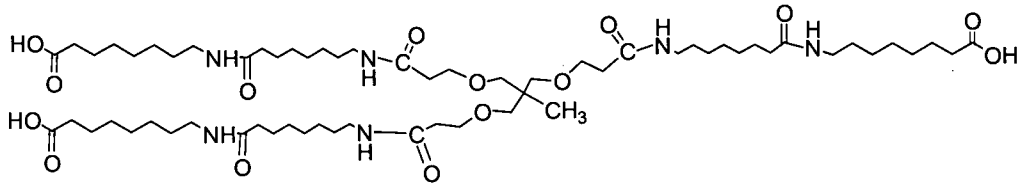

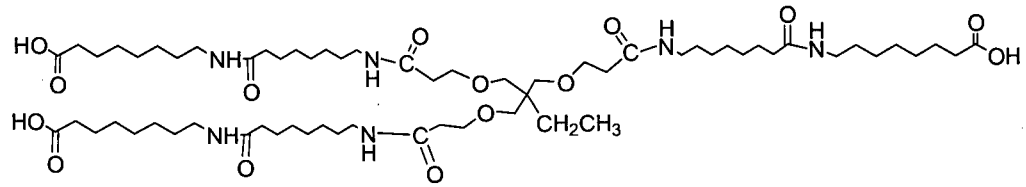

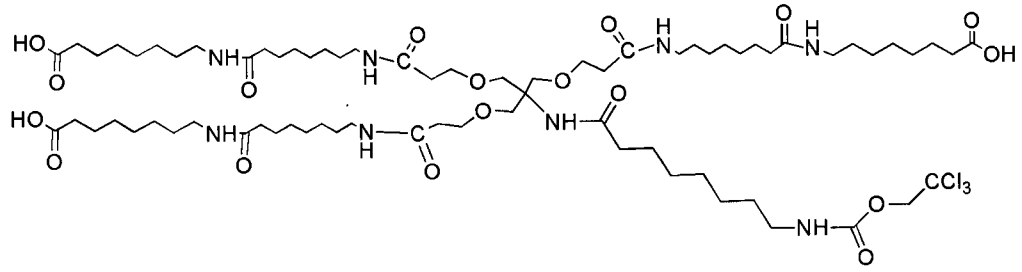

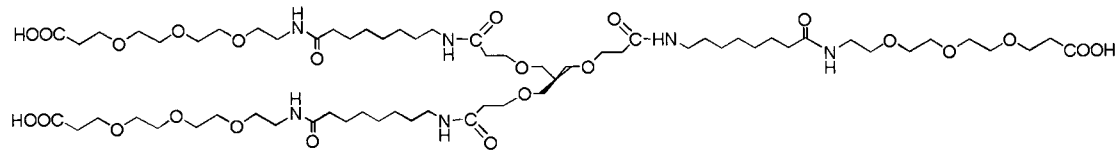

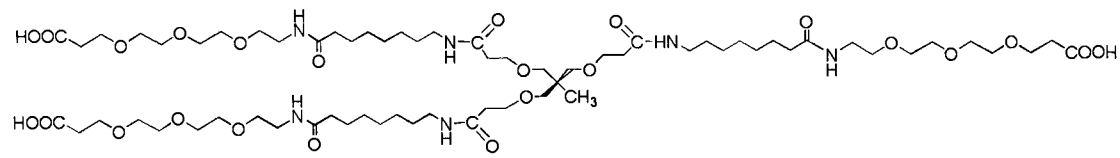

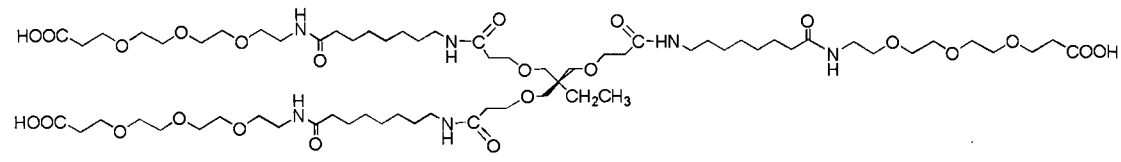

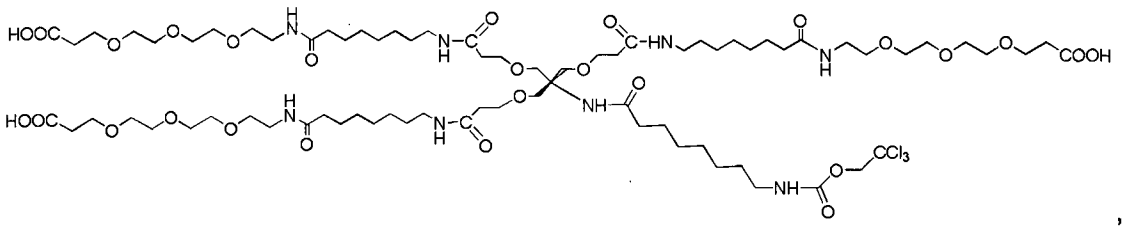

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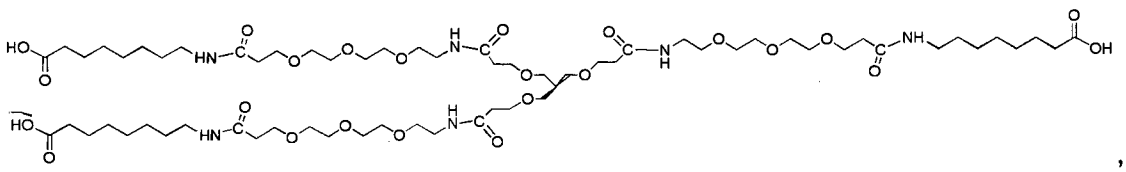

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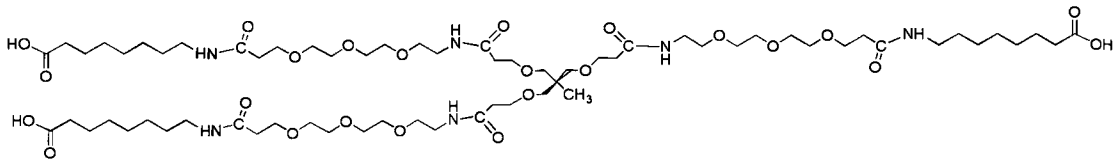

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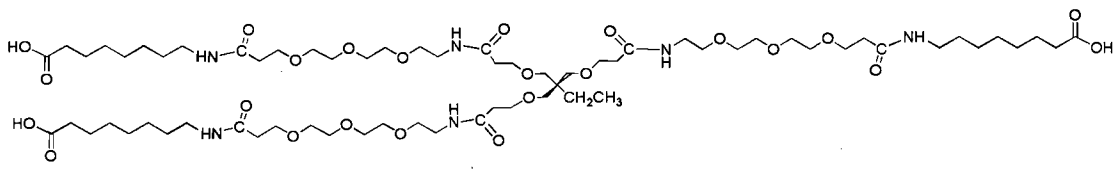

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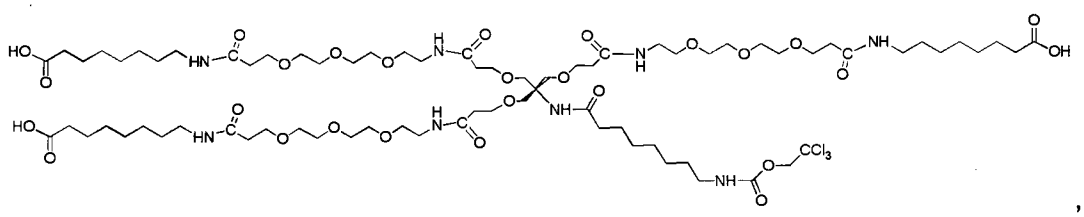

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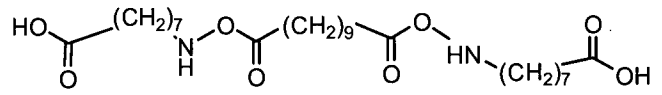

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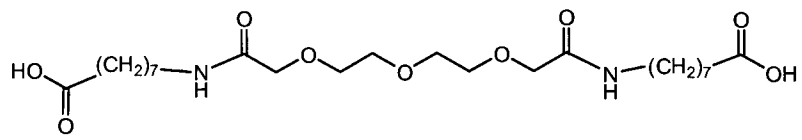

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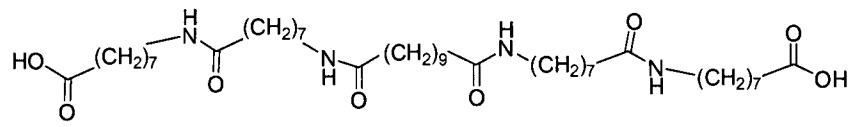

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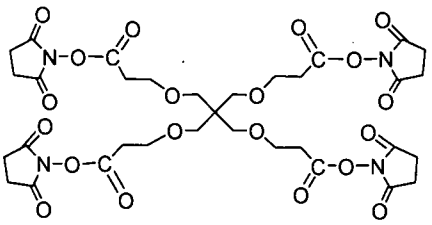
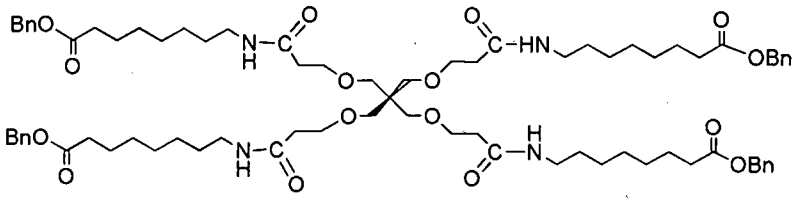
27. A compound selected from the group consisting of:





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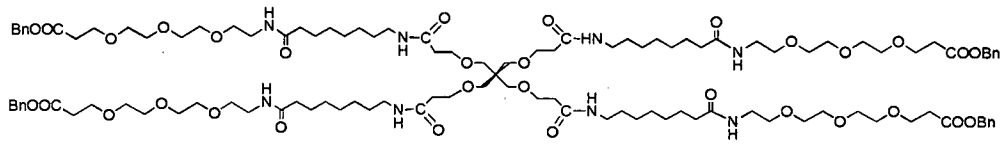

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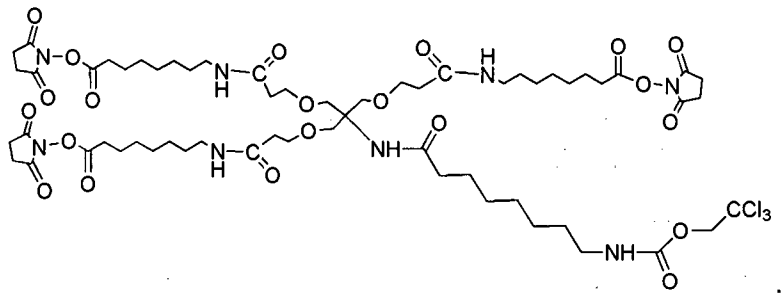

INTERNATIONAL SEARCH REPORT

International application No.
PCT/NZ2013/000215

A. CLASSIFICATION OF SUBJECT MATTER

C07D 207/40 (2006.01) C07C 233/47 (2006.01) C07C 235/12 (2006.01) C07C 235/34 (2006.01)

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

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

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

REGISTRY and CAPLUS: Sub-structure search based on formula (I) of claim 1 and molecular formula search of the first compound at the top of page 62 and the third last compound on page 65.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	Documents are listed in the continuation of Box C	

[X] Further documents are listed in the continuation of Box C [X] See patent family annex

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

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

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
17 February 2014	17 February 2014

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INTERNATIONAL SEARCH REPORT C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		International application No. **PCT/NZ2013/000215**
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5104815 A (GARNER et. al.) 14 April 1992 Col. 11 to 12, compound 6	1-2, 4-5, 9, 12, 22
X	US 6030640 A (SHIMIZU et. al.) 29 February 2000 & CAPLUS ACCESSION NO. 1998:176160 Caplus abstract, compound with registry no. 204259-42-7	1-2, 4, 6, 12, 23
X	US 2010/0272660 A1 (MALLE) 28 October 2010 & CAPLUS ACCESSION NO. 2009:427447 Caplus abstract, compound with registry no. 25580-91-0	1-2, 4-5, 12, 22
X	EP 0891875 B1 (RICOH COMPANY, LTD. et. al.) 01 October 2003 Pages 10-11, Table 1, compounds (1)-(8), (11)-(15), (17)-(21), (24) and (26)-(28)	1-2, 4-5, 12, 22
X	DESARAJU, P. et. al. "Synthesis and iron complexation studies of bis-hydroxamic acids", J. Coordination Chem., 1986, 14, 241-248. Figure 3 and Table 1, compounds 1a-f and 2a-f	1-2, 4-5, 9, 12, 22
X	JP 11152256 A (RICOH CO. LTD. et. al.) 08 June 1999 & CAPLUS ACCESSION NO. 1999:370092 Caplus abstract, compounds with registry nos. 25611-85-2 and 227204-06-0	1-2, 4-5, 12, 22
X	MASAKI KOGISO et. al. "Dicarboxylic oligopeptide bolaamphiphiles: Proton-triggered self-assembly of microtubes with loose solid surfaces", Langmuir, 1998, 14, 4978-4986. Chart 1, compounds 1a to 1f	1-2, 4, 6, 12, 23
X	TOSHIMI SHIMIZU. "Organic supramolecular self-assembled materials stabilized by multiple hydrogen bonds", Transactions of the Materials Research Society of Japan, 1999, 24(3), 431-436. Page 433, right hand column, compound 2, wherein n = 6, 8, 9, 10 and 11 and m =2	1-2, 4, 6, 12, 23

INTERNATIONAL SEARCH REPORT Information on patent family members	International application No. **PCT/NZ2013/000215**

This Annex lists known patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document/s Cited in Search Report		Patent Family Member/s	
Publication Number	**Publication Date**	**Publication Number**	**Publication Date**
US 5104815 A	14 Apr 1992	EP 0460576 A1	11 Dec 1991
		EP 0460576 B1	28 Aug 1996
		JP H04228098 A	18 Aug 1992
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		JP 2796613 B2	10 Sep 1998
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		JP 2010540604 A	24 Dec 2010
		US 2010272660 A1	28 Oct 2010
		WO 2009053584 A2	30 Apr 2009
EP 0891875 B1	01 Oct 2003	EP 0891875 B1	01 Oct 2003
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End of Annex

Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.