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Cross-linked vinyl polymers with bile acid adsorbing effect

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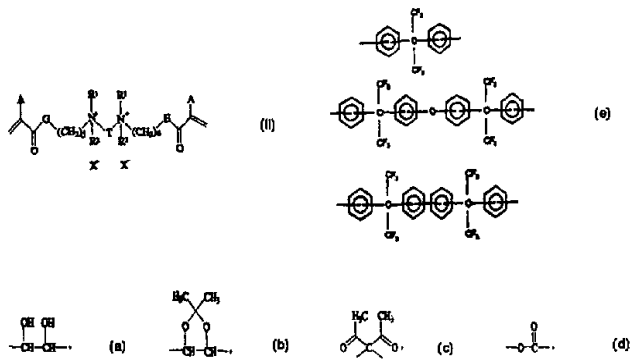
(54) Title: CROSS-LINKED VINYL POLYMERS WITH BILE ACID ADSORBING EFFECT

(54) Bezeichnung: VERNETZTE VINYLPOLYMERE MIT GALLENSÄURE-ADSORBERWIRKUNG



(57) Abstract

Compounds have the general formula (II), in which A stands for hydrogen or C_{1-9}-alkyl; G and E independently represent O or NH; d and a independently represent an integer from 2 to 10; R^1 and R^2 independently represent C_{1-9}-alkyl; T stands for C_{2-200}-alkylene, optionally interrupted by phenylene, one of the groups (a), (b), (c), (d) or (e), 1 to 10 non-adjacent oxygen atoms or groups $-N^+R^3R^4-$, in which R^3 and R^4 independently represent C_{1-9}-alkyl, and X^- stands for an acid anion. Also disclosed are polymers produced from these compounds and their use as lipid lowering agents.

Crosslinked vinyl polymers having bile acid adsorber action

The invention relates to vinyl polymers which are crosslinked by quaternary ammonium salts and have bile acid adsorber action, to monomers thereof, to a process for their preparation and to the use of the polymers as medicaments for lowering the bile acid resorption in the intestine with the aim of lowering the serum cholesterol levels in the blood (therapy of hypercholesterolemia).

Bile acids and their salts are natural detergents and have an important physiological function in fat digestion and fat absorption. As the end products of cholesterol metabolism, they are synthesized in the liver, stored in the gall bladder and released from there as a constituent of the bile into the intestine, where they display their physiological action. The largest part (about 85-90%) of the secreted bile acids (about 16 g/day) is absorbed again from the intestinal wall via the enterohepatic circulation, chiefly in the terminal ileum, and transported back to the liver, i.e. recycled. Only 10-15% of the bile acids are excreted with the feces. In the liver, a reduction in the amount of bile acid can be compensated for up to a certain degree via a control loop system by de novo synthesis of bile acids from cholesterol. A reduction in the liver cholesterol level leads to the increase of the absorption of cholesterol from the blood serum and thus lowers the cholesterol level in the blood serum. Finally, by suppression of bile acid readsorption by means of suitable inhibitors or bile acid adsorbers, the enterohepatic circulation can thus be interrupted in the intestine and as a result the serum cholesterol level in the blood lowered. Too high a serum cholesterol level is recognized in medicine as serious, since it leads to atherosclerosis and thus increases the risk of cardiac infarct. There are therefore many therapeutic approaches for the treatment of hypercholesterolemia. One of these approaches is the interruption of the enterohepatic circulation. Using this approach, it is furthermore possible to treat all diseases in which an inhibition of bile acid reabsorption in the small intestine appears to be desirable.

Nonabsorbable bile acid adsorbers have been used therapeutically for some time for binding of bile acids. In particular, insoluble, usually crosslinked polymers, which contain quaternized nitrogen centers and act as anion exchangers, are employed for this purpose. Such polymers are

described in US 5,607,699. These polymers bind some of the bile acid anions occurring in the intestine by means of mainly ionic interactions and transport them away from the intestine. Commercial products of this type contain, for example, the active compounds cholestyramine and colestipol. They are employed, for example, for the therapy of hypercholesterolemia.

In addition to the polymeric bile acid adsorbers, the active bile acid absorption inhibition approach (receptor blockers) has also been pursued. The bile acid receptor sites in the terminal ileum are blocked here by molecules which, analogously to the bile acids, can interact with the receptors, but unlike the bile acids are not absorbed. As a result of this receptor blockade, the bile acids can no longer be absorbed and are then excreted with the feces. Examples of polymeric bile acid receptor blockers are found in EP-A-0 549 967. Bile acid polymers and oligomers are described therein in which bile acid molecules are linked laterally to a polymer backbone.

The known compounds have the following disadvantages.

The disadvantage of all polymeric bile acid adsorbers on the market to date is the high dosage (10-30 g/day; recommended dose in the case of cholestyramine, for example, 12 g/day). In the case of the polymers known to date, the high daily dose is to be attributed to a low binding rate or to a partial re-release of the adsorbed bile acids in the isotonic intestinal medium.

Low compliance in patients, on account of the fishy odor and unpleasant, sandy taste and the sandy consistency of the powder of the adsorber (for example cholestyramine). The present administration form is problematic, since the adsorber powder does not dissolve in water but can only be suspended. To improve compliance, in some cases more than 50% of taste- and odor-improving additives must be added, so that as a result the daily dose of adsorber medicament is further increased.

Moreover, the adsorbers known to date do not act selectively enough and also bind vitamins (for example vitamin K) and other physiologically important substances, so that deficiency symptoms (for example avitaminoses) can occur.

Furthermore, a damping action on the cholesterol metabolism of the intestinal bacteria is lacking.

An unpleasant side effect which can occur with the bile acid absorption inhibitors known to date, because the increase in the bile acid concentration in the intestine caused by the receptor blockade, is diarrhoea.

Polymers which are suitable for use as ion exchangers or fluoride ion donors and which contain quaternary ammonium ions are known, for example, from US 5,118,717 and WO 96/22761.

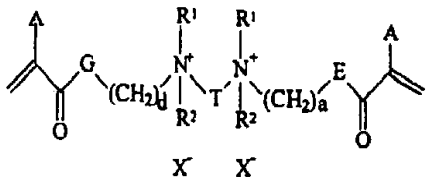
Thus, there is a need in the art to provide a nonsystemically acting polymeric active compound to interrupt the enterohepatic circulation which no longer has the abovementioned disadvantages.

The present invention is based upon incorporating quaternary nitrogen centers into crosslinkable monomer building blocks which carry two polymerizable vinylic groups. These monomers are subsequently homopolymerized or copolymerized with one or more other monomers. The crosslinked polymer obtained in this manner is purified and isolated. The resulting polymer has excellent bile acid absorber properties; after oral administration, it binds in the intestine some of the bile acids required for digesting fat, thus removing it from the body's circulation. As a result, synthesis of new bile acids is required. To this end, the liver makes use of blood cholesterol, which leads to a lowering of the cholesterol and lipid level in the blood. The polymeric bile acid absorbers of the invention have better cholesterol-lowering properties than customary systems.

Polymers of this type thus have a dual action. On the one hand, they act as polymeric bile acid absorption inhibitors due to the covalently firmly bonded receptor blocker units and, on the other hand, as bile acid absorbers.

Thus, the present invention relates to polymers constructed of compounds of the formula II (where the numerical values refer to the

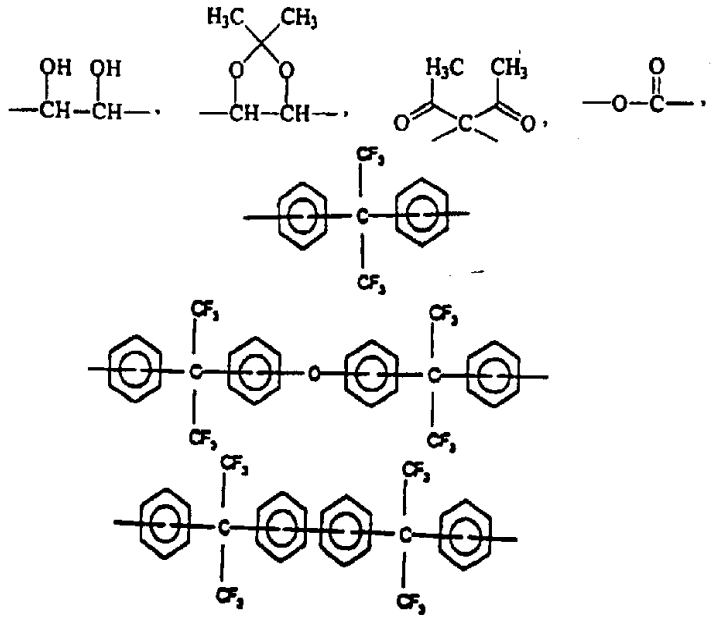
individual monomers and, if monomer mixtures are used, average values for the polymer result which do not have to be integral)



(II)

in which

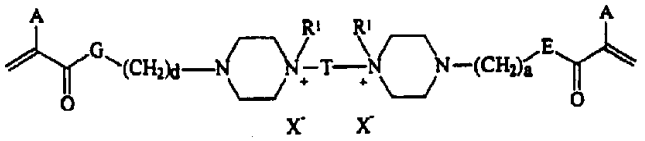
A	is hydrogen or C_{1-9}-alkyl,
G and E	independently of one another are O or NH, preferably both NH,
d and a	independently of one another are an integer from 2 to 10, preferably both the same number,
R^1 and R^2	independently of one another are C_{1-9}-alkyl, preferably of the same kind,
T	is C_{2-200}-alkylene, which may be interrupted by phenylene



or 1 to 10 not directly adjacent oxygen atoms or groups $-N^+R^3R^4-$ where R^3 and R^4 independently of one another are C_{1-9}-alkyl, preferably of the same kind, where T in the individual polymerized monomer structural units of the formula II within the molecule does not have to be constant, but can vary within the given range. Thus, the polymer can be constructed of one or more different monomers of the formula II, and

X^- is an acid anion, or

compounds of the formula III



(III)

in which A, G, d, e, R^1, T are as defined above.

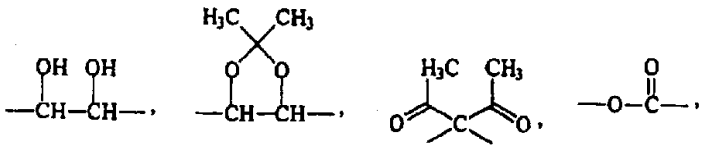
Preference is given to compounds having one or more, preferably all, of the following features:

The polymer can be constructed of one or more different types of monomers, so that in the polymer d and a, for example, are average values and the number of the groups $-N^+R^3R^4-$ in the radical T may be an average value. There may, for example, be from 0 to 10 interruptions in the radical T in the individual monomers, so that an average value results for the polymer. The preferred values below refer to the monomers. The values resulting for the monomer mixtures and polymers are generally not integers.

- A is hydrogen or c_{1-4}-alkyl, preferably hydrogen or C_{1-3}-alkyl, particularly preferably hydrogen or methyl,
- d and e are integers from 2 to 5, preferably 2 or 3
- R^1 and R^2 are C_{1-4}-alkyl, preferably C_{1-3}-alkyl, particularly preferably methyl or ethyl,
  X is halide, preferably chloride or bromide.

T is preferably selected from

- linear or branched C_{4-50}-alkylene, preferably C_{6-30}-alkylene,
- linear or branched C_{2-22}-alkylene which is interrupted by phenylene,



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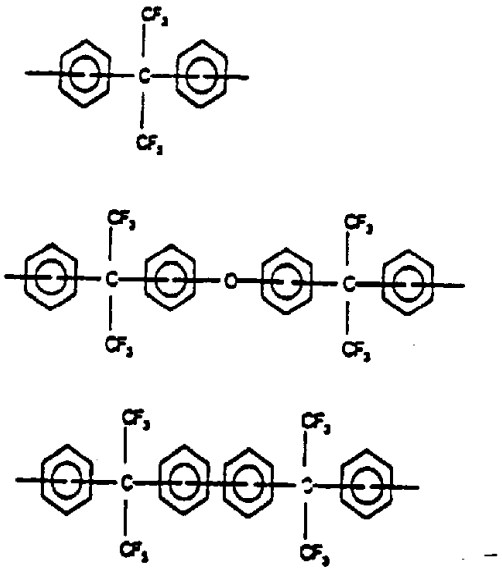


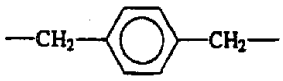
where the phenylene groups are preferably 1,4-phenylene groups. The interruption is preferably approximately in the middle of the alkylene group,

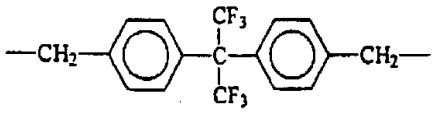
- linear or branched C_{4-16}-alkylene which is interrupted by 1 to 7 not directly adjacent oxygen atoms and preferably has units $-CH_2-CH_2-O-$,

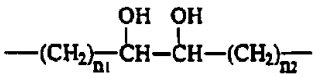
- linear or branched C_{20-140}-alkylene which is interrupted by 2 to 8 not directly adjacent groups $-N^+R^3R^4-$ where R^3 and R^4 are C_{1-4}-alkyl, preferably C_{1-3}-alkyl, in particular methyl or ethyl.

T is selected, in particular, from

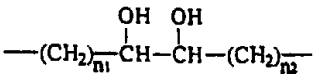
- linear or branched C_{6-30}-alkylene



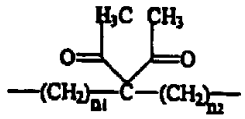




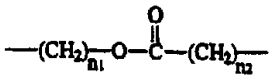
where n1 and n2 independently of one another are integers from 4 to 10, especially from 6 to 8,



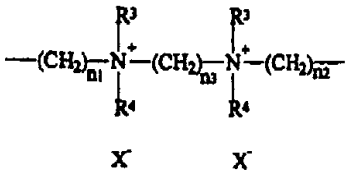
where n1 and n2 independently of one another are integers from 4 to 10, especially from 6 to 8,



where n1 and n2 independently of one another are integers from 4 to 10, especially from 6 to 8,

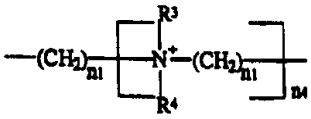


where n1 and n2 independently of one another are integers from 6 to 12, especially from 7 to 9,

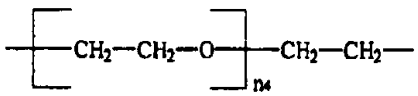


where

R^3 and R^4 are C_{1-3}-alkyl, especially methyl or ethyl, X is halide, especially chloride or bromide, n1 and n2 independently of one another are integers from 6 to 16, especially from 8 to 12, and n3 is an integer from 2 to 6, especially from 3 to 5,

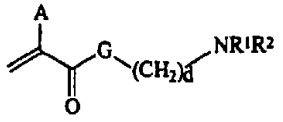


where R^3 and R^4 are C_{1-3}-alkyl, especially methyl or ethyl, X^- is halide, especially chloride or bromide, n1 is a number from 8 to 16, preferably from 12 to 16, especially from 12 to 14 and n4 has an average value of from 1 to 10, preferably from 2 to 7, particularly preferably from 2 to 5, especially from 3 to 4,

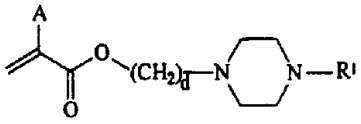


where n4 has an average value of from 1 to 6, preferably 2 to 5, especially 3 to 4.

The compounds of the formula II and/or [lacuna] are preferably prepared by reacting compounds of the formula IV [lacuna]



(IV)



(VI)

with compounds of the formula V

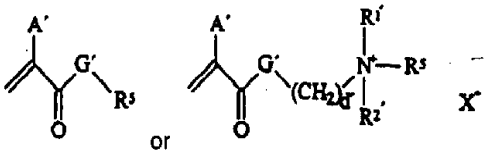
X-T-X V

where A, G, d, R^1, R^2, T are as defined and X is halogen.

The crosslinked polymers according to the invention are constructed of the monomeric basic structural units A1, A2 and A3, the total amount of which is 100% by weight.

a1: from 0.5 to 100% by weight of difunctional basic structural units of the formulae II and/or III, as described above, or mixtures thereof, as component A1,

a2: from 0 to 99.5% by weight of monomers, selected from compounds of the formulae



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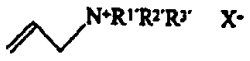

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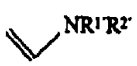

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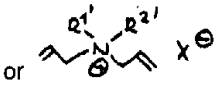
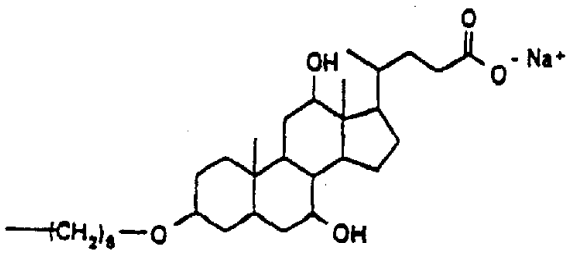
or 

in which A' has one of the meanings given for A, G' has one of the meanings given for G, d' has one of the meanings given for d, $R^{1'}$ has one of the meanings given for R^1, $R^{2'}$ has one of the meanings given for R^2, $R^{3'}$ has one of the meanings given for R^3 and R^5 is selected from the group consisting of

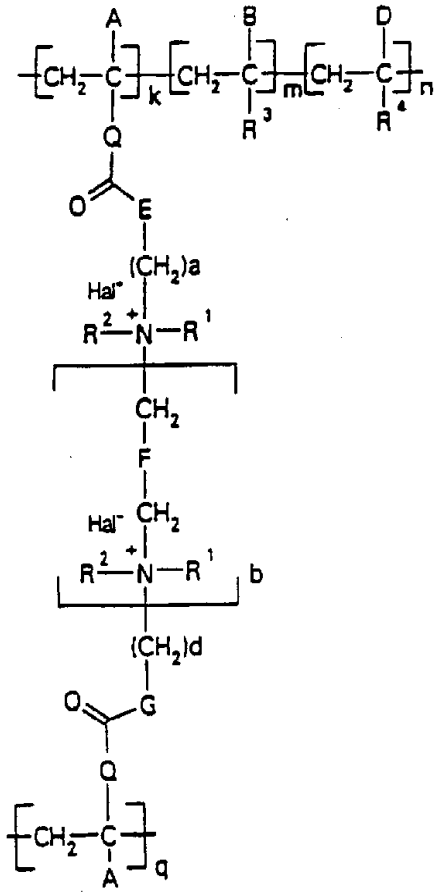
hydrogen, C_{1-9}-alkyl, preferably C_{1-3}-alkyl, in particular methyl and ethyl and



or mixtures thereof, for example (meth)acrylic acid, (meth)acrylamide or polyvinylamine as component A2,

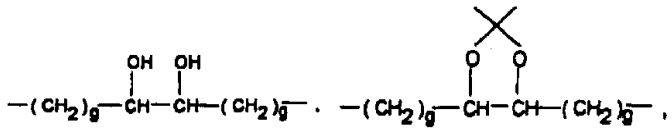
a3: from 0 to 99.5% by weight of other copolymerizable basic structural units, such as vinylic monomers, for example olefins, as component A3.

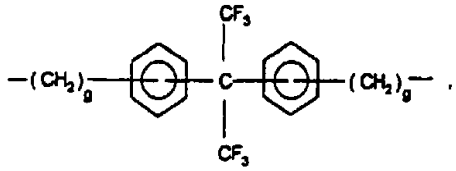
The invention also relates to crosslinked vinyl polymers of the formula I

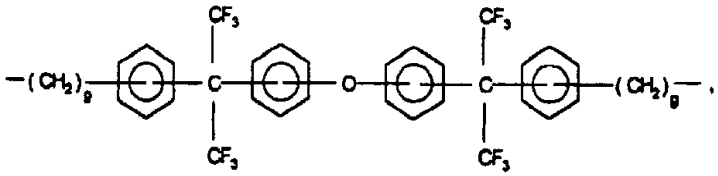


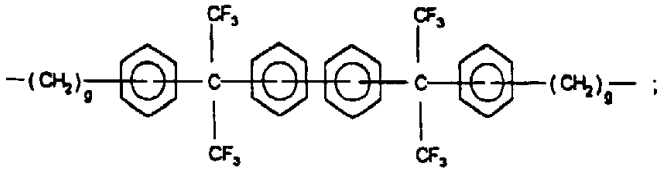
in which

A, B and D	independently of one another are H, $CH_3(CH_2)_f$;
f	is from 0 to 8;
E and G	independently of one another are O or NH;
F	are linear or branched alkylene units having g carbon atoms, such as $(CH_2)_g$, phenylene;





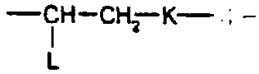




g is from 0 to 36;

r is from 0 to 36;

K is NH, CH_2NH or CH_2CH_2NH;

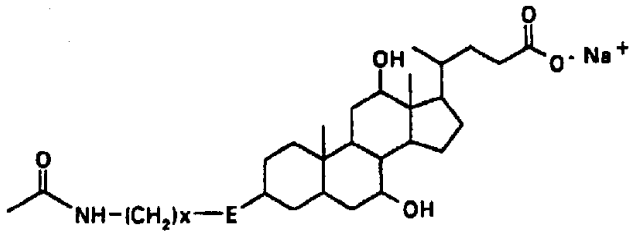
Q is a bond,  ;

L is H, CH_3;

R^1 and R^2 independently of one another are $(C_1\text{-}C_8)$-alkyl;

R^3 and R^4 independently of one another are NH_2, NHR^5, NR^5R^6, $^+NH_3Cl^-$, $^+NH_2R^5Cl^-$, $^+NHR^5R^6Cl^-$, $^+NR^5R^6R^7Cl^-$, $(CH_2)_wNH_2$, $(CH_2)_wNHR^5$, $(CH_2)_wNR^5R^6$, $(CH_2)_w{}^+NH_3Cl^-$,

$(CH_2)_w{}^+NH_2R^5Cl^-$, $(CH_2)_w{}^+NHR^5R^6Cl^-$,
$(CH_2)_w{}^+NR^5R^6R^7Cl^-$, $-COOR^8$, $-CONHR^8$,



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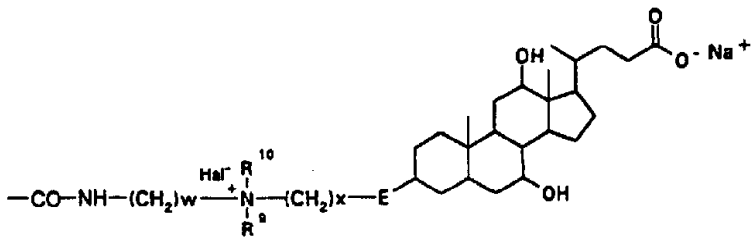


w is from 1 to 18;

10 R^5, R^6, R^7, R^9 and R^{10} independently of one another are $(C_1\text{-}C_{14})$-alkyl;

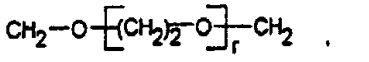
R^8 is NH_2, NHR^5, NR^5R^6, $^+NH_2Cl^-$, $^+NH_2R^5Cl^-$, $^+NHR^5R^6Cl^-$, $^+NR^5R^6R^7Cl^-$, $(CH_2)_wNH_2$, $(CH_2)_wNHR^5$, $(CH_2)_wNR^5R^6$, $(CH_2)_w{}^+NH_3Cl^-$,
15 $(CH_2)_w{}^+NH_2R^5Cl^-$, $(CH_2)_w{}^+NHR^5R^6Cl^-$, $(CH_2)_w{}^+NR^5R^6R^7Cl^-$;

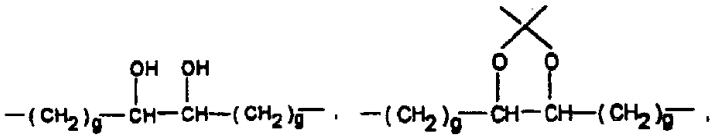
a and d independently of one another are from 2 to 10;
b is from 0 to 3;
20 x is from 2 to 22;
Hal^- is Cl^-, Br^-, I^-,
k and q independently of one another are from 0.005 to 1;
m and n independently of one another are from 0 to 0.995.

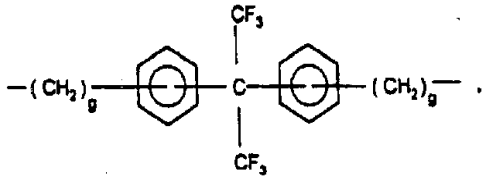
Preference is given to compounds of the formula I in which A, B and D independently of one another are: H, $CH_3(CH_2)_f$, where f is a number from 0 to 8; particularly preferably: H, CH_3.

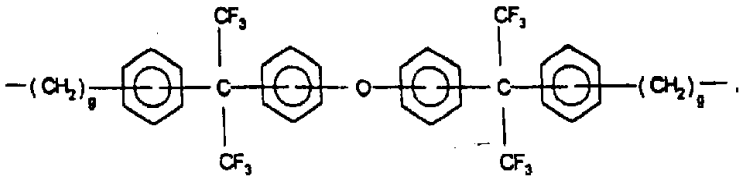
Preference is given to compounds of the formula I in which E and G are NH.

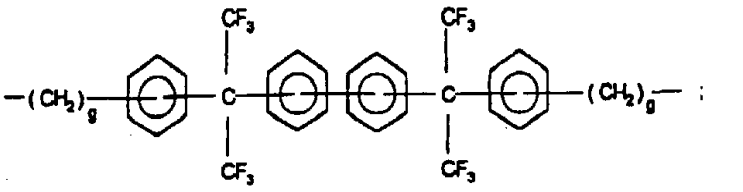
Preference is given to compounds of the formula I in which F is

$(CH_2)_g$, phenylene;  ,

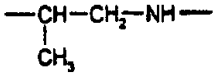
 ,

 ,

 ,

 ;

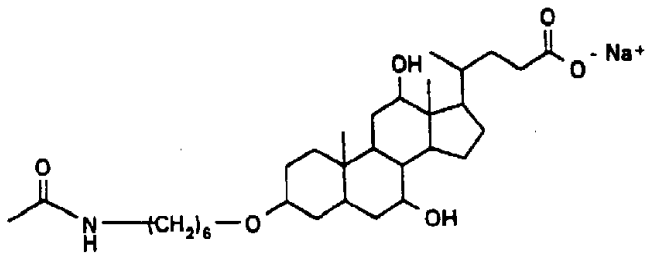
in which g is a number from 8 to 24 and r is a number from 0 to 18; particularly preferably $(CH_2)_g$ in which g is a number from 8 to 22.

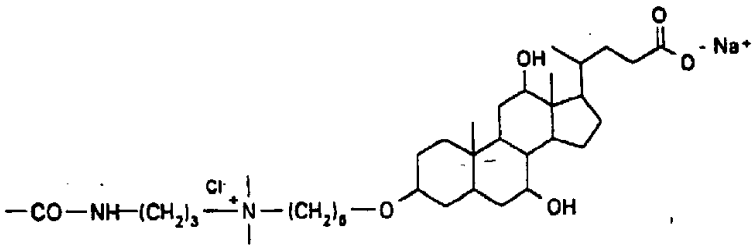
Preference is given to compounds of the formula I in which Q is: a bond or  ; particularly preferably a bond.

Preference is given to compounds of the formula I in which R^1 and R^2 are CH_3 or CH_2-CH_3, particularly preferably CH_3.

Preference is given to compounds of the formula I in which R^3 and R^4 independently of one another are

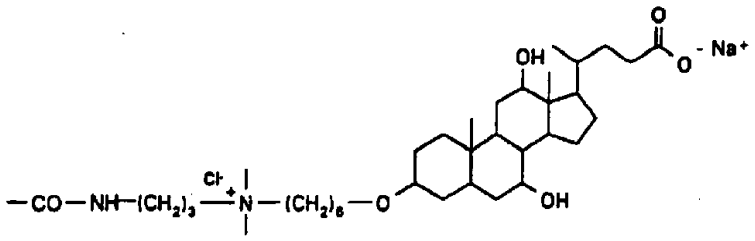
NH_2, $^+NH_3Cl^-$, CH_2-NH_2, CH_2-$^+NH_3Cl^-$, -$CONHR^8$,





in which R^8 is $(CH_2)_w{}^+N(CH_3)_3Cl^-$, where w is a number from 1 to 8;

particularly preferably:



Preference is given to compounds of the formula I in which a and d are each 3.

Preference is given to compounds of the formula I in which b is 1.

Preference is given to compounds of the formula I in which k is from 0.1 to 1.

Preference is given to compounds of the formula I in which q is from 0.1 to 1.

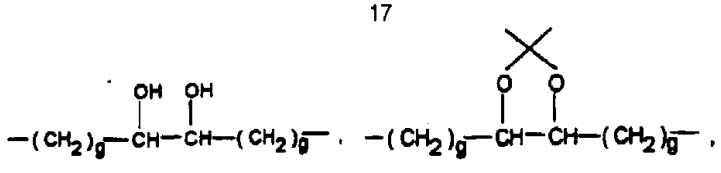
Preference is given to compounds of the formula I in which m is from 0 to 0.8.

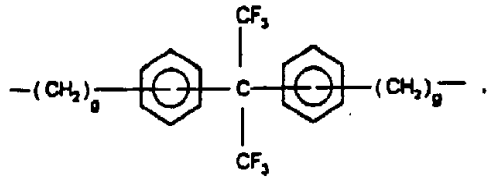
Preference is given to compounds of the formula I in which n is from 0 to 0.8; particularly preferably 0.

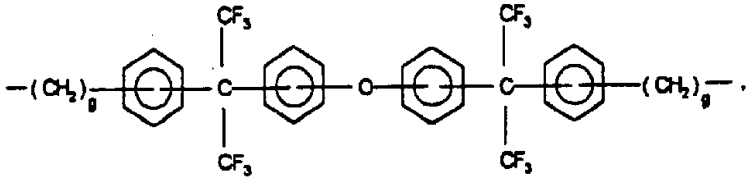
The sum of k + q + m + n has to be 1.

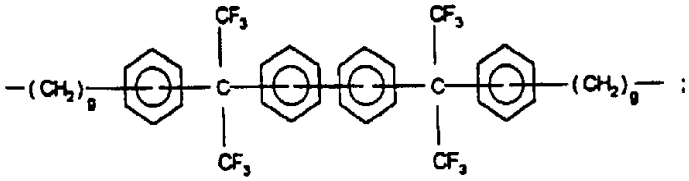
Preference is given to compounds which contain the following combinations:

A, B and D	independently of one another are H, $CH_3(CH_2)_f$;
F	is from 0 to 8;
E and G	are NH;
F	is $(CH_2)_g$, phenylene; $CH_2-O-\left[(CH_2)_2-O\right]_r-CH_2$.



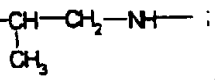






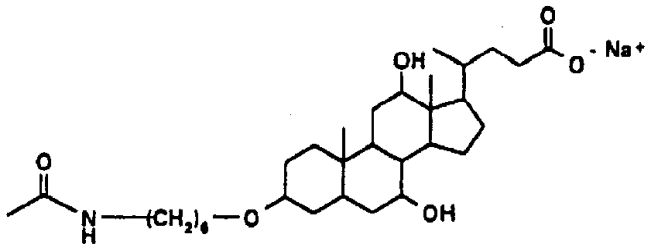
g is from 8 to 34;

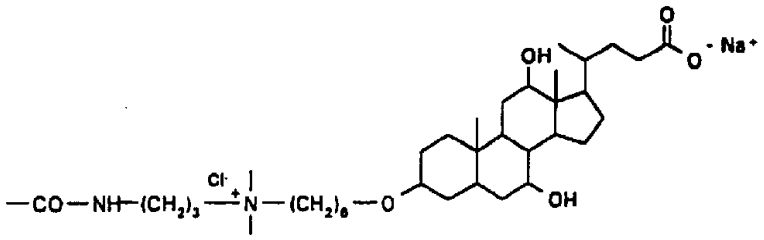
r is from 0 to 18;

Q is a bond,  ;

R^1 and R^2 are CH_3, $-CH_2-CH_3$;

R^3 and R^4 independently of one another are NH_2, $^+NH_3Cl^-$, CH_2-NH_2, $CH_2-^+NH_3Cl^-$, $-CONHR^8$



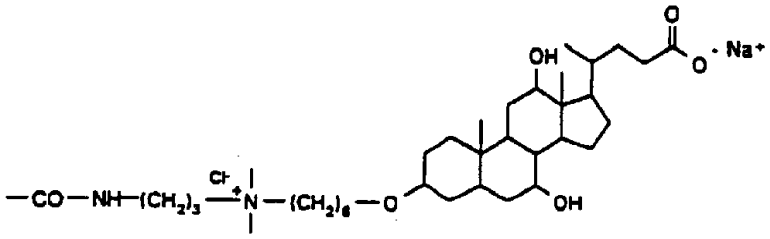


	R^8	is $(CH_2)_w{}^+N(CH_3)_3Cl^-$;
	w	is from 1 to 8;
	a and d	are each 3;
	b	is 1;
	Hal^-	is Cl^-, Br^-, I^-;
	k	is from 0.1 to 1;
	q	is from 0.1 to 1;
	m	is from 0 to 0.8;
	n	is from 0 to 0.8;

where the sum of k + q + m + n is 1.

Particular preference is given to compounds which contain the following combinations:

A, B and D	independently of one another are H, CH_3;
Q	is a bond;
E and G	are NH;
F	is $(CH_2)_g$;
g	is from 8 to 22;
R^1 and R^2	are CH_3;
R^3 and R^4	are



a and d are each 3;
b is 1;
Hal^- is Cl^-, Br^-;
k is from 0.1 to 1;
q is from 0.1 to 1;
m is from 0 to 0.8;
n is 0;
where the sum of k + q + m + n is 1.

The invention furthermore relates to a process for preparing the polymers according to the invention which comprises either homopolymerizing or copolymerizing, with other vinylic monomers, such as allylamine hydrochloride, or the other given monomers, an appropriate bis(meth)acrylate monomer or bis(meth)acrylamide monomer which contains at least one quaternary ammonium center in aqueous medium in the presence of a water-soluble radical initiator, in a free-radical reaction.

The invention also relates to a process for preparing the polymers according to the invention which comprises reacting an appropriate bis(meth)acrylate monomer or bis(meth)acrylamide monomer which contains at least one quaternary ammonium center in a Michael addition with an amino-group-containing vinylic polymer such as polyvinylamine in basic medium in a polymer-analogous manner.

The monomers can furthermore preferably be prepared as follows:

Preparation of the monomers:

1. A monomer having a terminal dialkylamino group, for example a dimethylamino alkyl ester or a dimethylaminoalkylamide of acrylic acid, is reacted with a 1,omega-dihalide, quaternary ammonium centers being formed.

2. A 1,omega-dihalogen compound is reacted with a secondary amine or a salt thereof in the presence of sodium hydride in a suitable solvent, such as DMF. By appropriate choice of the ratio of the components used, the targeted preparation of 1,omega-dihalogen compounds having additional dialkylammonium centers in the chain is possible. What is produced are mixtures of different chain lengths which can be separated, if desired. However, these mixtures can advantageously also be processed further as such to give bisacrylates of the formula II.
3. Monomers having steroid groups can be prepared analogously to Hoe96/F223 or EP-A-0 549 967.
4. By reacting tetramethylpropylenediamine with 1,omega-dihalides it is possible to prepare, analogously to 2., 1,omega-dihalides which carry quaternary ammonium centers linked by a propylene group in the chain.
5. By double alkylation with 1,3-diketones with 1,omega-dihalogen compounds, it is possible to obtain 1,omega-dihalides which carry two additional acyl groups on the same carbon atom in the chain.

Preparation of the polymers:

The polymerization is carried out by customary methods, such as, for example, described in Houben-Weyl. It can be initiated thermally, by free-radical initiators, cationically or anionically or by Michael addition. The polymerization is preferably carried out in a free-radical manner. Suitable solvents here are the solvents which are customarily used for polymerizations. It is also possible to use water as solvent if the starting materials are water-soluble. The polymerization itself is carried out at room temperature or at elevated temperatures. Work-up of the resulting polymers can be carried out by filtration or, in the case of water-swellable

or water-soluble polymers, by ultrafiltration. Drying is carried out by suitable processes, such as freeze-drying.

In general, 1,omega-bis(meth)acrylate and/or -amide monomers which carry one or more quaternary ammonium centers in the chain can be homopolymerized or copolymerized with comonomers in aqueous or alcoholic medium at low temperatures (for example 45°C) using suitable water- or alcohol-soluble free-radical initiators (for example VA-044 from Wako), giving gels which can be worked up by customary methods. By stirring with suitable salt solutions, the anions can be exchanged as desired.

The invention furthermore relates to medicaments, comprising at least one polymer according to the invention and, if appropriate, one or more other lipid-lowering active compounds, customary excipients, auxiliaries and/or additives.

The invention furthermore relates to a process for preparing such a medicament by mixing the components.

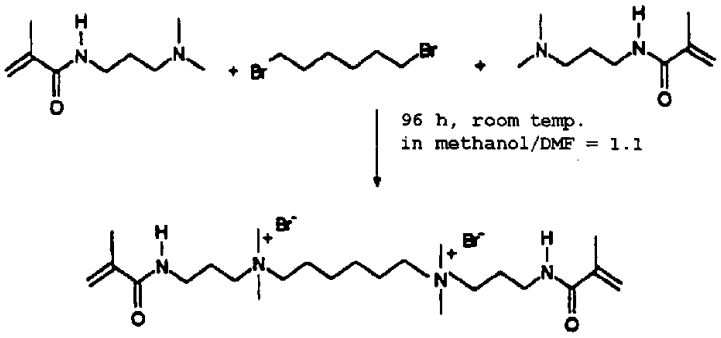
The invention furthermore relates to the use of the polymers according to the invention as medicaments; in particular as antihyperlipidemic.

The invention furthermore relates to the use of the polymers according to the invention for preparing a medicament or pharmaceutical preparation for the treatment of disorders of lipid metabolism, and of hyperlipidemia, for the concentration-dependent reduction of bile acid absorption in the gastrointestinal tract, for the nonsystemic lowering of elevated serum cholesterol and blood fat values for the prevention arteriosclerotic symptoms.

The invention furthermore relates to mixtures of the abovementioned polymers with other polymers and/or biologically active substances.

The examples below serve to illustrate the invention in more detail, without limiting it to the products and embodiments described in the examples.

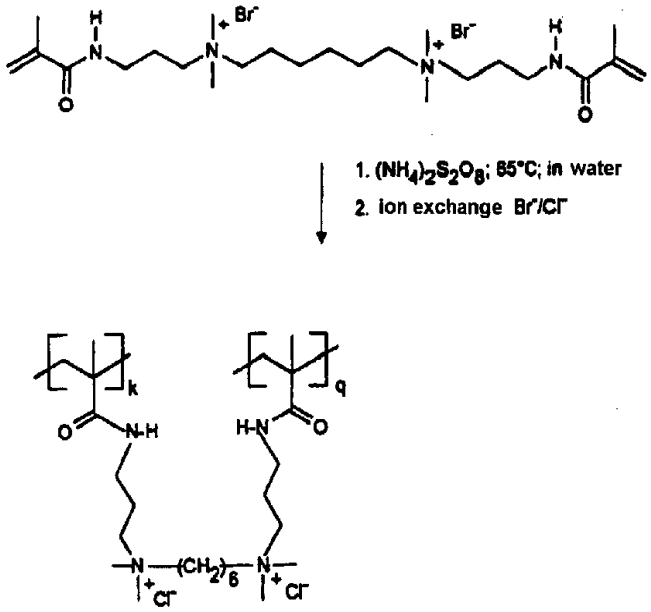
Example 1a:



48.8 g (30.5 ml; 0.20 mol) of 1,6-dibromohexane, 76.0 g (80.8 ml; 0.45 mol) of N-[3-(dimethylamino)propyl]methacrylamide and 1.0 g of hydroquinone were dissolved in a mixture of 50 ml of DMF and 50 ml of methanol. The solution was stirred at room temperature for 96 hours. The mixture was then cooled to <7°C and added dropwise to acetone which had a temperature of 5°C. The resulting crystalline precipitate was filtered off under reduced pressure, stirred with 500 ml of cold acetone in an ice-bath for 1 hour and then filtered off once more. Yield: 110.6 g of Example 1a.

^{1}H NMR (D_2O): δ = 1.42 ppm (m, 4H, CH_2), 1.76 (m, 4H, CH_2), 1.95 (brd. s, 6H, allyl-CH_3), 2.05 (m, 4H, CH_2), 3.09 (s, 12H, CH_3), 3.26-3.42 (m, 12H, alkylene-CH_2), 5.50 (brd. s, 2H, vinyl-H), 5.74 (brd. s, 2H, vinyl-H).

Example 1b:

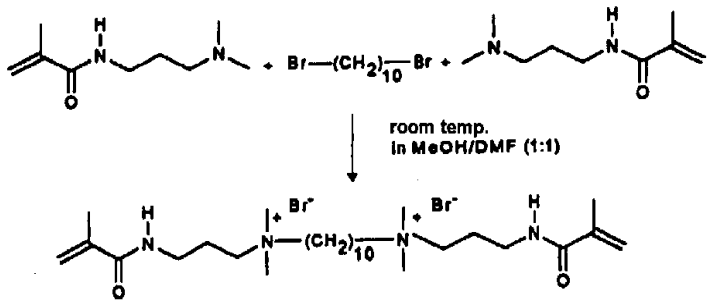


Under an atmosphere of nitrogen, 45 mg of ammonium peroxodisulfate and a minute amount of iron(II) chloride were added to a solution of 3.0 g of Example 1a in 12 ml of water, and the mixture was stirred for 2 hours. Another 45 mg of ammonium peroxodisulfate were then added, and the mixture was heated at 65°C for 2 hours. This gave a colorless gel. This gel was filtered off with suction and pressed through a screen having a mesh size of 200 µm. It was then stirred with 150 ml of water for 30 minutes. The polymer was filtered off under reduced pressure and washed first with saturated aqueous sodium chloride solution and then with with water. The polymer was dried at 40°C in a drying cabinet for 18 hours. Yield: 2.1 g of Example 1b.

Elemental analysis:

Calculated:	C 58.1%	H 9.8%	N 11.3%	Cl 14.3%
Found:	C 58.3%	H 9.7%	N 11.4%	Cl 14.0%

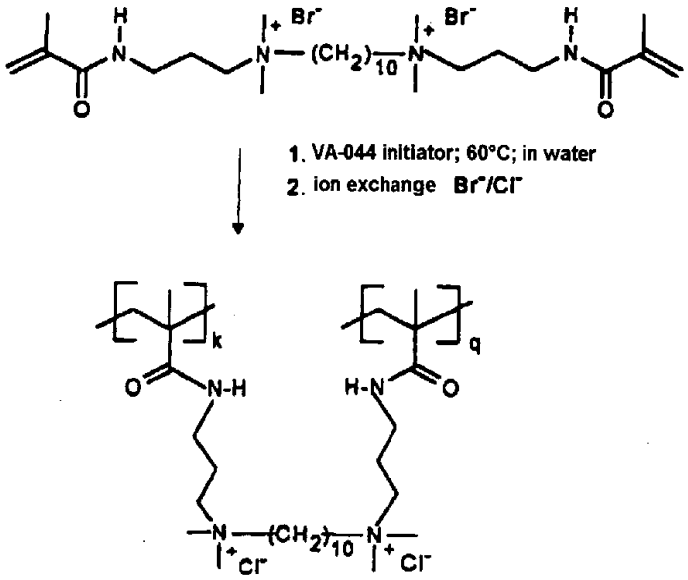
Example 2a:



30.0 g (0.10 mol) of 1,10-dibromodecane (from Acros Chimica), 34.0 g (0.20 mol) of N-[3-(dimethylamino)propyl]methacrylamide and 0.60 g (5.4 mmol) of hydroquinone were dissolved in a mixture of 37.5 ml of DMF and 37.5 ml of methanol. The solution was stirred at room temperature and in the dark for 14 days. The mixture was then cooled to <5°C and added dropwise to ice-cold acetone. The resulting crystalline precipitate was filtered off under reduced pressure and washed with 500 ml of cold acetone. Yield: 58.2 g of Example 2a.

^{1}H NMR (D_2O): δ = 1.34 ppm (m, 4H, CH_2), 1.72 (m, 4H, CH_2), 1.95 (brd. s, 6H, allyl-CH_3), 2.04 (m, 4H, CH_2), 3.08 (s, 12H, CH_3), 3.26-3.41 (m, 20H, alkylene-CH_2), 5.50 (brd. s, 2H, vinyl-H), 5.74 (brd. s, 2H, vinyl-H).

Example 2b:

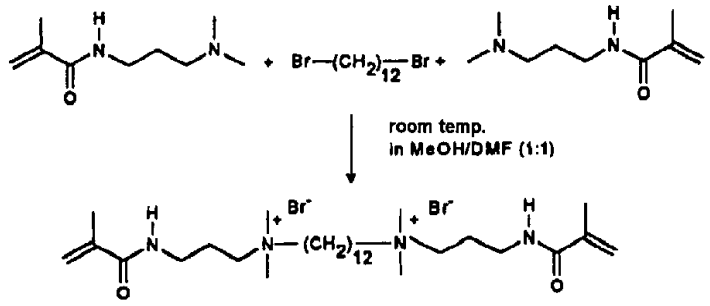


490 mg (1.0% by weight) of the free-radical initiator VA-044 (2,2'-azobis[2-(2'-imidazolin-2-yl)propane] dihydrochloride, from Wako) were added to a solution of 49.4 g (77.27 mmol) of Example 2a in 200 ml of water. The mixture was degassed in an ultrasonic bath for 1 hour and then stirred under an atmosphere of nitrogen at 45°C for 5 hours and then at 60°C for 1 hour. Another 167 mg of VA-044, dissolved in a little degassed water, were then added and the mixture was stirred at 60°C for 9 hours. Since it was still possible to detect monomer by TLC, another 350 mg of VA-044, dissolved in a little degassed water, were added, and the mixture was stirred at 60°C for a total of another 35 hours. This gave a colorless gel. This gel was filtered off under reduced pressure and washed with a little water. To exchange the ions (bromide → chloride), the polymer was stirred 3× with saturated aqueous NaCl solution and filtered off under reduced pressure. The polymer was then washed with water and dried at 50°C in a vacuum drying cabinet until its weight remained constant. Yield: 45.1 g of Example 2b.

Elemental analysis:

Calculated:	C 61.0%	H 10.2%	N 10.2%	Cl 12.9%
Found:	C 61.1%	H 10.0%	N 10.3%	Cl 12.5%

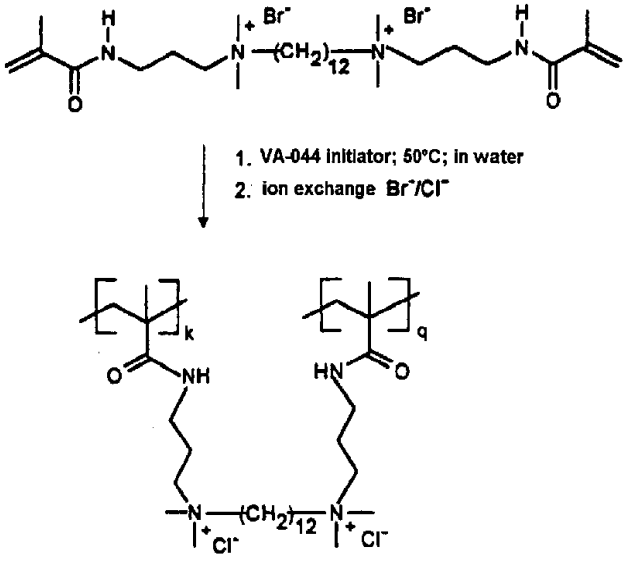
Example 3a:



25.0 g (75 mmol) of 1,12-dibromododecane, 28.1 g (165 mmol) of N-[3-(dimethylamino)propyl]methacrylamide and 500 mg of hydroquinone were dissolved in a mixture of 20 ml of DMF and 20 ml of methanol. The solution was stirred at room temperature and in the dark for 14 days. The mixture was then cooled to <5°C and added dropwise to 1.5 l of ice-cold acetone. The mixture was stirred in an ice-bath for a further 2 hours, and the resulting crystalline precipitate was filtered off under reduced pressure and washed with cold acetone. Yield: 46.6 g of Example 3a.

^{1}H NMR (D_2O): δ = 1.32 ppm (m, 4H, CH_2), 1.72 (m, 4H, CH_2), 1.95 (brd. s, 6H, allyl-CH_3), 2.03 (m, 4H, CH_2), 3.07 (s, 12H, CH_3), 3.25-3.40 (m, 24H, alkylene-CH_2), 5.50 (brd. s, 2H, vinyl-H), 5.74 (brd. s, 2H, vinyl-H).

Example 3b:



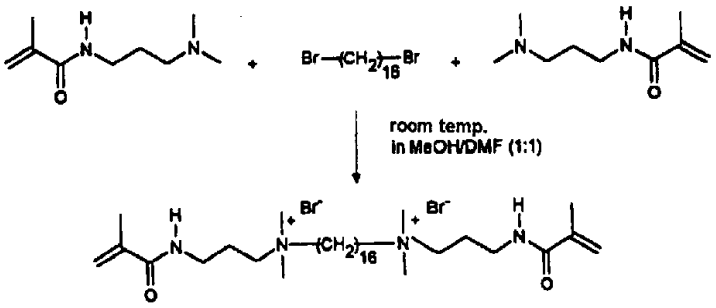
396 mg (1.0% by weight) of free-radical initiator VA-044 (from Wako) were added to a solution of 39.6 g (60.23 mmol) of Example 3a in 160 ml of water. The mixture was degassed in an ultrasonic bath for 1 hour, and nitrogen was then introduced into the solution for 1 hour. The mixture was then stirred at 45°C under an atmosphere of nitrogen for 5 hours. Another 396 mg of VA-044, dissolved in a little degassed water, were then added and the mixture was stirred at 50°C. Even after 30 minutes, the viscosity of the solution increased so much that 200 ml of degassed water had to be added for dilution. The reaction mixture was then stirred at 50°C for another 9 hours. Since it was still possible to detect monomer by TLC, another 100 mg of VA-044, dissolved in a little degassed water, were added, and the mixture was stirred at 50°C for a total of another 28 hours. This gave a colorless gel. This gel was homogenized, filtered off under reduced pressure and washed with a little water. The polymer was dried in a vacuum drying cabinet at 50°C until its weight remained constant. Crude yield: 36.2 g. For ion exchange (bromide → chloride), the polymer was stirred 3× with saturated aqueous NaCl solution and filtered off under reduced pressure. It was then washed with water. The polymer was dried

in a vacuum drying cabinet at 50°C until its weight remained constant. Yield: 33.1 g of Example 3b.

Elemental analysis:

Calculated:	C 62.2%	H 10.4%	N 9.7%	Cl 12.2%
Found:	C 62.3%	H 10.5%	N 9.7%	Cl 12.0%

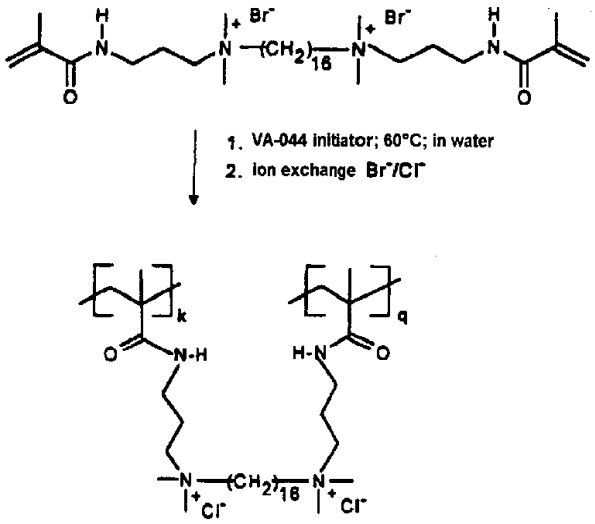
Example 4a:



680 mg of 1,16-dibromohexadecane, 605 mg of N-[3-(dimethylamino)-propyl]methacrylamide and 10 mg of hydroquinone were dissolved in a mixture of 5 ml of DMF and 5 ml of methanol. The solution was stirred at room temperature and in the dark for 7 days. The mixture was then cooled to <5°C and added dropwise to 750 ml of ice-cold acetone. The resulting crystalline precipitate was filtered off under reduced pressure and washed with cold acetone. Yield: 1.06 g of Example 4a.

^{1}H NMR (D_2O): δ = 1.32 ppm (m, 4H, CH_2), 1.72 (m, 4H, CH_2), 1.95 (brd. s, 6H, allyl-CH_3), 2.03 (m, 4H, CH_2), 3.07 (s, 12H, CH_3), 3.25-3.40 (m, 32H, alkylene-CH_2), 5.50 (brd. s, 2H, vinyl-H), 5.74 (brd. s, 2H, vinyl-H).

Example 4b:

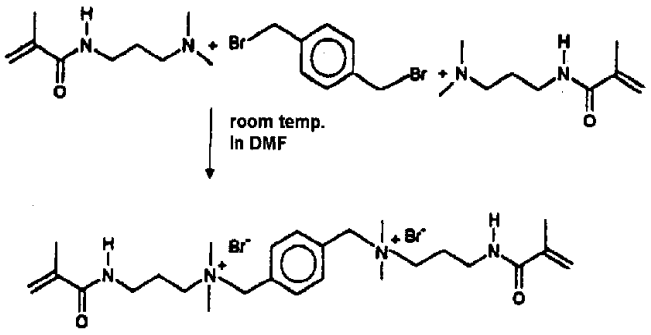


Under an atmosphere of nitrogen, 25 mg of free-radical initiator VA-044 (from Wako) were added at 60°C to a solution of 300 mg of Example 4a in 5.0 ml of water which had been saturated with nitrogen. The mixture was stirred at 60°C for 2.5 hours. The resulting white gel was homogenized using an Ultraturrax (IKA) and then transferred to an ultrafiltration cell (membrane 5kDalton). For ion exchange (bromide → chloride), the polymer was ultrafiltered 2× in saturated aqueous NaCl solution and then in water. The polymer was freeze-dried until its weight remained constant. Yield: 282 mg of Example 4b.

Elemental analysis:

Calculated:	C 64.2%	H 10.8%	N 8.8%	Cl 11.2%
Found:	C 64.%	H 11.0%	N 8.6%	Cl 11.0%

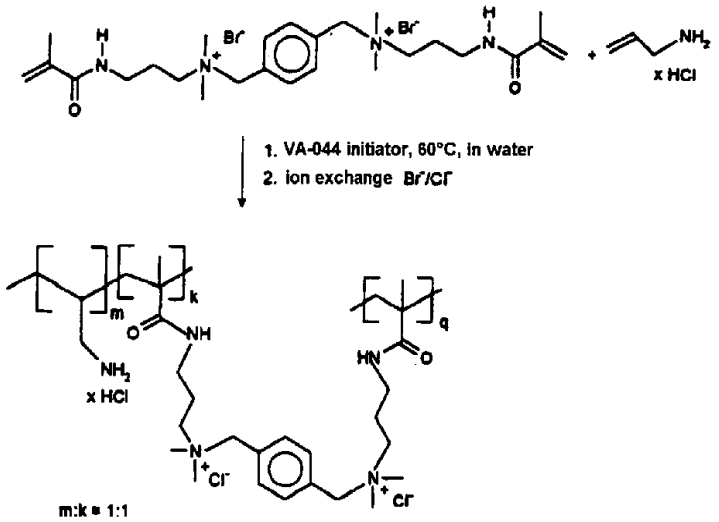
Example 5a:



10.9 g (41.4 mmol) of α,α'-dibromo-p-xylene (Aldrich), 14.1 g (82.7 mmol) of N-[3-(dimethylamino)propyl]methacrylamide and 280 mg of hydroquinone were dissolved in 250 ml of DMF. The solution was stirred at room temperature and in the dark for 14 days. Since it was still possible to detect starting material in the subsequent TLC, the mixture was stirred for another 4 weeks. The mixture was then cooled to <5°C and added dropwise to 1.5 l of ice-cold acetone. The mixture was stirred in an ice-bath for another 1 hour, and the resulting crystalline precipitate was filtered off under reduced pressure and washed with cold acetone. Yield: 22.0 g of Example 5a.

^{1}H NMR (D_2O): δ = 1.95 ppm (brd. s, 6H, allyl-CH_3), 2.19 (m, 4H, CH_2), 3.12 (s, 12H, CH_3), 3.30-3.45 (m, 8H, alkylene-CH_2), 4.60 (s, 4H, aryl-CH_2), 5.50 (brd. s, 2H, vinyl-H), 5.72 (brd. s, 2H, vinyl-H), 7.69 (s, 4H, aryl-H).

Example 5b:

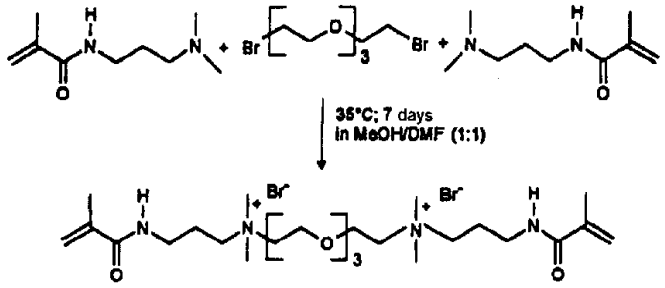


0.86 g (15 mmol) of allylamine (from Riedel-de Haen) was added to a mixture of 1.42 ml of concentrated hydrochloric acid and 20 ml of water. 9.13 g (15 mmol) of Example 5a and 160 mg of free-radical iniator VA-044 (from Wako) were then added. The mixture was degassed and then stirred under an atmosphere of nitrogen at 60°C for 7 hours. This gave a gel. This gel was homogenized, filtered off under reduced pressure and washed first with saturated aqueous sodium chloride solution and then with water. The polymer was dried in a vacuum drying cabinet at 50°C until its weight remained constant. Yield: 6.7 g. Example 5b.

Elemental analysis:

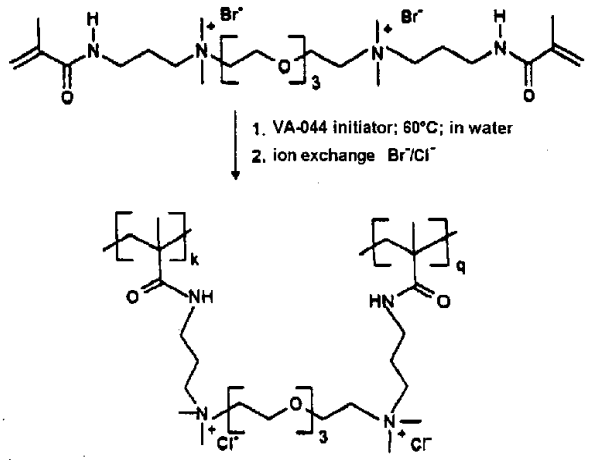
Calculated:	C 60.6%	H 8.6%	N 10.9%	Cl 13.8%
Found:	C 60.5%	H 8.8%	N 10.7%	Cl 13.4%

Example 6a:



1.72 g of α,α'-dibromo-tetraethylene glycol (prepared by bromination of tetraethylene glycol with tetrabromomethane in the presence of triphenylphosphine), 1.71 g of N-[3-(dimethylamino)propyl]methacrylamide and 290 mg of hydroquinone were dissolved in a mixture of 7.5 ml of DMF and 7.5 ml of methanol. The mixture was stirred at 35°C and in the dark for 7 days. The mixture was then cooled to <5°C and added dropwise to an ice-cold mixture of acetone/ether (1:1). The resulting crystalline precipitate was filtered off under reduced pressure, washed with cold acetone and dried. Yield: 2.60 g of Example 6a.

Example 6b:

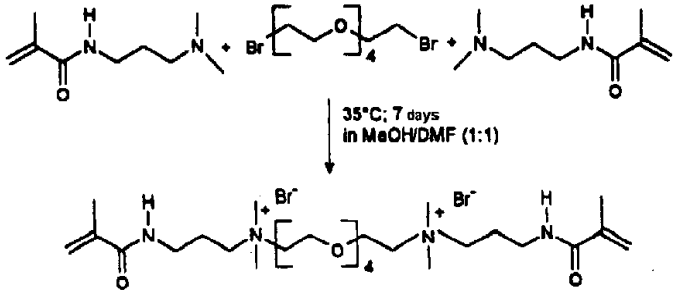


Under an atmosphere of nitrogen, 20 mg of free-radical initiator VA-044 (from Wako) were added at 60°C to a solution of 250 mg of Example 6a in 5.0 ml of water which had been saturated with nitrogen. The mixture was stirred at 60°C for 3 hours. The resulting gel was transferred to an ultrafiltration cell (membrane 5000 Å). For ion exchange (bromide → chloride), the polymer was washed 2× with saturated aqueous NaCl solution and once with water. The retentate was freeze-dried. Yield: 226 mg of Example 6b.

Elemental analysis:

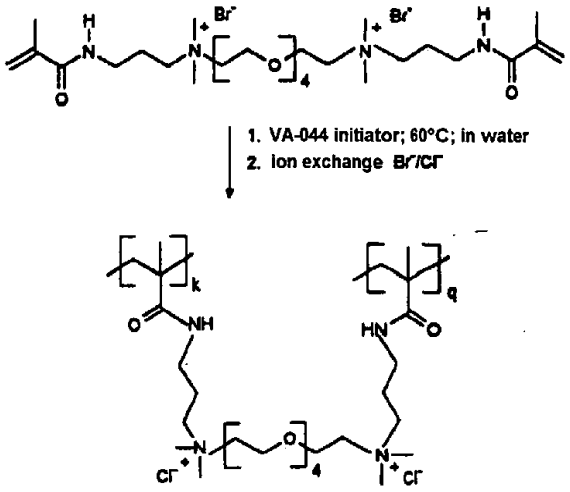
Calculated:	C 56.5%	H 8.8%	N 9.4%	Cl 11.9%
Found:	C 56.2%	H 9.1%	N 9.1%	Cl 11.6%

Example 7a:



1.56 g of α,ω-dibromo-pentaethylene glycol (prepared by bromination of tetraethylene glycol with tetrabromomethane in the presence of triphenylphosphine), 1.37 g of N-[3-(dimethylamino)propyl]methacrylamide and 100 mg of hydroquinone were dissolved in a mixture of 7.5 ml of DMF and 7.5 ml of methanol. The solution was stirred at 35°C and in the dark for 7 days. The mixture was then cooled to <5°C and added dropwise to an ice-cold mixture of acetone/ether (1:1). The resulting crystalline precipitate was filtered off under reduced pressure, washed with cold acetone and dried. Yield: 1.82 g of Example 7a.

Example 7b:



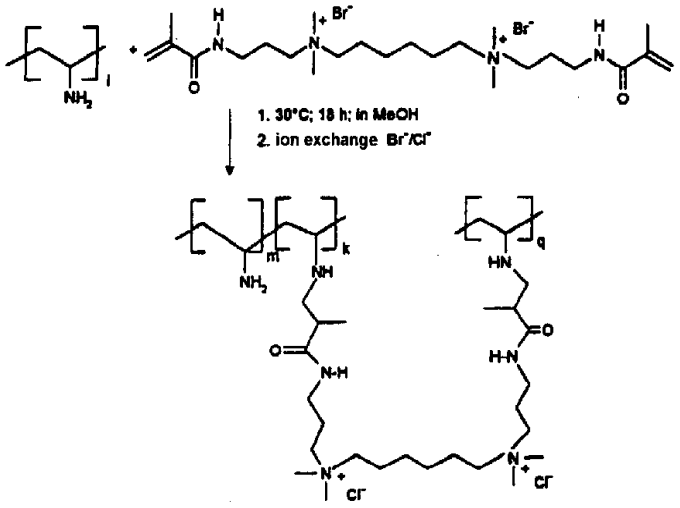
Under an atmosphere of nitrogen, 25 mg of free-radical initiator VA-044 (from Wako) were added at 60°C to a solution of 300 mg of Example 7a in

5.0 ml of water which had been saturated with nitrogen. The mixture was stirred at 60°C for 2.5 hours. The resulting gel was transferred to an ultrafiltration cell (membrane 5000 Å). For ion exchange (bromide → chloride), the polymer was washed 2× with saturated aqueous NaCl solution and once with water. The retentate was freeze-dried. Yield: 282 mg of Example 7b.

Elemental analysis:

Calculated:	C 56.3%	H 8.8%	N 8.8%	Cl 11.1%
Found:	C 56.2%	H 8.9%	N 8.6%	Cl 10.8%

Example 8:



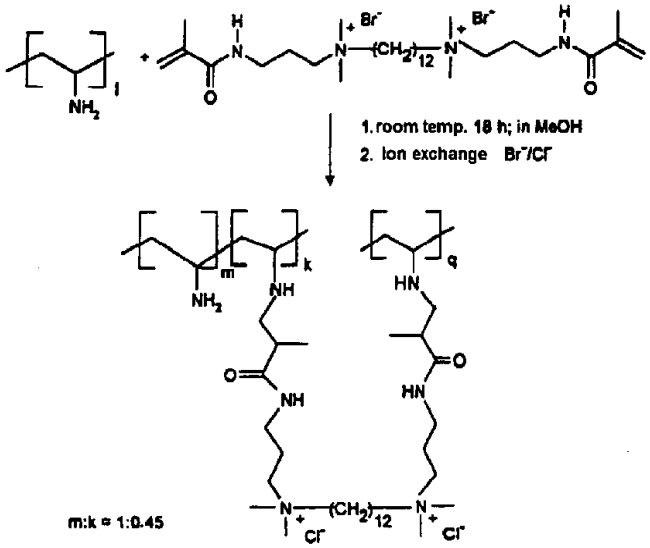
A solution of 6.2 g (11 mmol) of Example 1a in 50 ml of methanol was added to a solution of 1.0 g (23 mmol) of polyvinylamine in 15 ml of methanol. The mixture was stirred at 30°C for 18 hours. The mixture was diluted with 50 ml of water and then stirred for 30 minutes. The resulting polymer was filtered off under reduced pressure, washed with water and then freeze-dried. Yield: 4.3 g of Example 8.

Elemental analysis:

Calculated:	C 56.5%	H 11.0%	N 25.4%
Found:	C 56.5%	H 11.1%	N 25.9%

The elemental analysis corresponds to a degree of crosslinking of 45%.

Example 9:



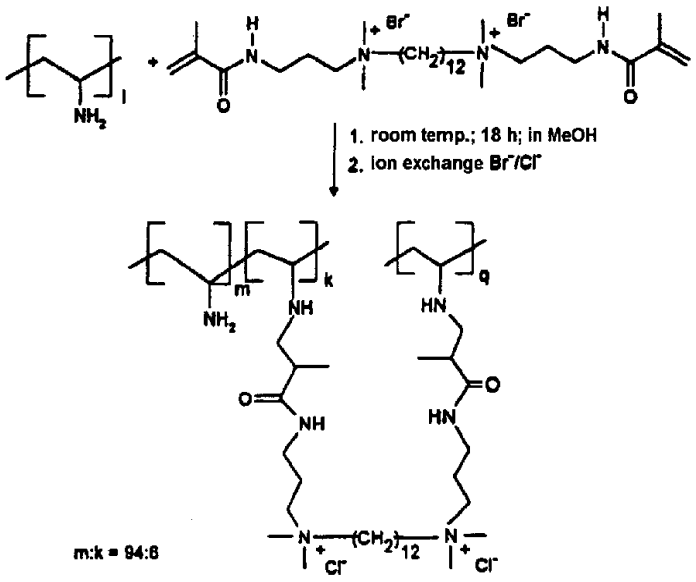
A solution of 3.84 g (5.8 mmol) of Example 3a in 20 ml of methanol was added to a solution of 0.50 g (11.5 mmol) of polyvinylamine in 7.5 ml of methanol. The mixture was stirred for 18 hours. The methanol was distilled off using a rotary evaporator. 200 ml of water were then added. The polymer was purified by two ultrafiltrations (membrane 5000 Å) in saturated aqueous sodium chloride solution and in water and then freeze-dried. Yield: 2.76 g of Example 8.

Elemental analysis:

Calculated:	C 57.8%	H 11.2%	N 24.9%
Found:	C 57.6%	H 11.3%	N 16.0%

The elemental analysis shows that the degree of crosslinking is 40%.

Example 10:

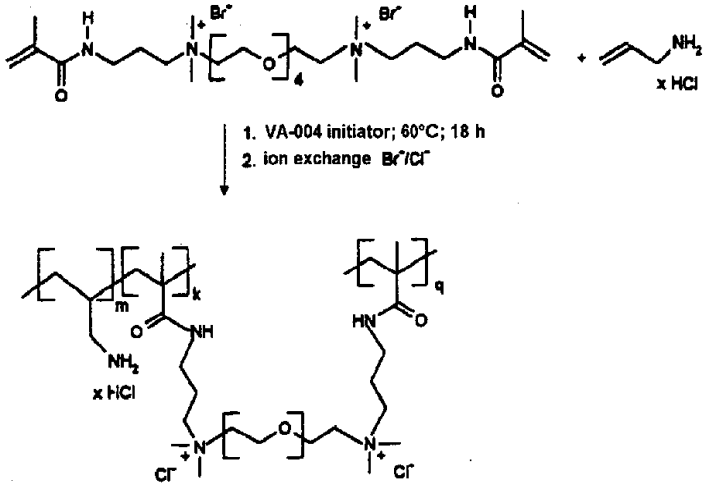


A solution of 1.54 g (2.3 mmol) of Example 3a in 10 ml of methanol was added to a solution of 1.00 g (23.0 mmol) of polyvinylamine in 15 ml of methanol. The mixture was stirred at room temperature for 18 hours. The methanol was distilled off using a rotary evaporator. The residue was stirred with 200 ml of water and transferred to an ultrafiltration cell. The polymer was purified by two ultrafiltrations (membrane 5000 Å) and saturated aqueous sodium chloride solution and in water and then freeze-dried. Yield: 2.21 g of Example 10.

Elemental analysis: (calculated for a ratio of vinylamine: Example 3a: = 94:6)

Calculated:	C 56.4%	H 11.6%	N 30.2%	Cl 1.2%
Found:	C 56.2%	H 11.6%	N 31.2%	Cl 0.8%

Example 11:

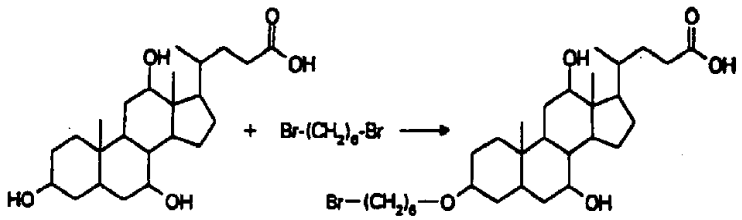


342 mg (469 µmol) of Example 7a and 107 mg (1870 µmol) of allylamine were dissolved in 7.5 ml of 1N aqueous hydrochloric acid. The solution was saturated with nitrogen. Under an atmosphere of nitrogen, the mixture was heated to 60°C. 22 mg of free-radical initiator VA-044 were then added. The mixture was stirred at 60°C for 18 hours. The resulting mixture was homogenized. The polymer was purified by two ultrafiltrations (membrane 5000 Å) in saturated aqueous sodium chloride solution and in water and then freeze-dried. Yield: 319 g of Example 11.

Elemental analysis: (calculated for a ratio of Example 7a: allylamine = 1:4)

Calculated:	C 61.7%	H 9.9%	N 21.3%
Found:	C 61.6%	H 9.8%	N 21.2%

Example 12a:

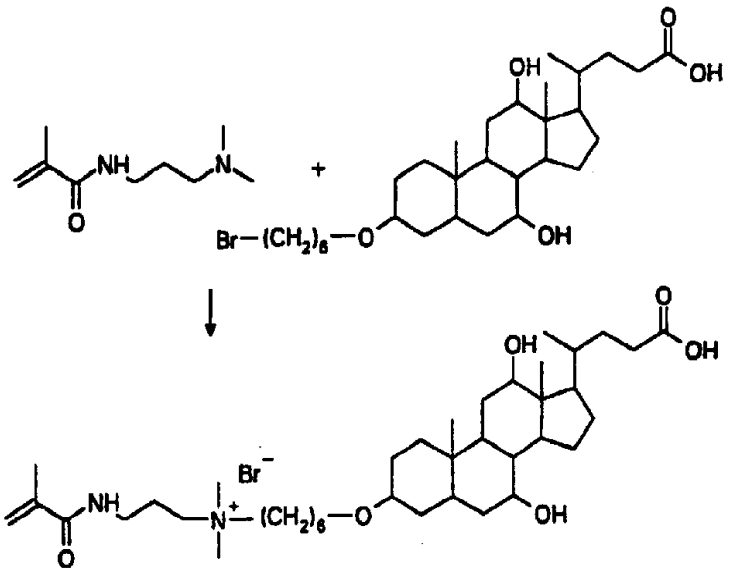


12.3 g (30 mmol) of cholic acid (Aldrich) were dissolved in 200 ml of THF. 73.2 g (300 mmol) of 1,6-dibromohexane were then added, and the mixture was heated under reflux. Over a period of 6 hours, 10.2 g (180 mmol) of potassium hydroxide powder were added a little at a time. The mixture was then stirred for another hour. After cooling, the resulting precipitate was filtered off with suction and washed with THF. The filtrate was concentrated. Excess dibromohexane was distilled off under reduced pressure. The viscous residue was purified by column chromatography (ethyl acetate → ethyl acetate:methanol = 9:1). Yield: 6 g of Example 12a.

^{1}H NMR: ($CDCl_3$) d = 0.68 ppm (s, 3H, cholate-CH_3); 0.89 (brd. m, 6H, cholate-CH_3); 0.99 (d, J= 6.0 Hz, 3H, C<u>H</u>$_3$CH); 1.0-2.4 (m, aliphat. cholate-CH); 1.3-1.8 (brd. m, 2H, CHNH-C<u>H</u>$_2$); 2.6-2.9 (brd. m, 3H); 3.42 (d, J= 6.0 Hz, 2H); 3.84 (brd. s, 1H, C<u>H</u>OH); 3.96 (br. S, 1H, C<u>H</u>OH 4.06 (d, J= 6.0 Hz, 2H).

MS: CI (ammonia): m/z [%]= 590 (M+NH_4 of ^{81}Br isotope, 95); 588 (M+NH_4 of ^{79}Br isotope, 100).

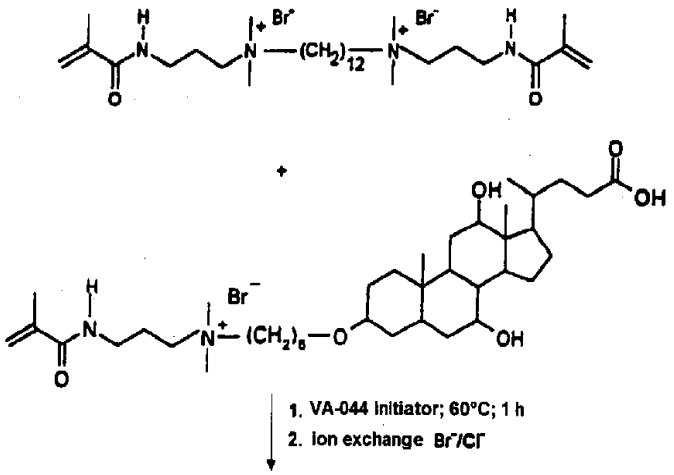
Example 12b:

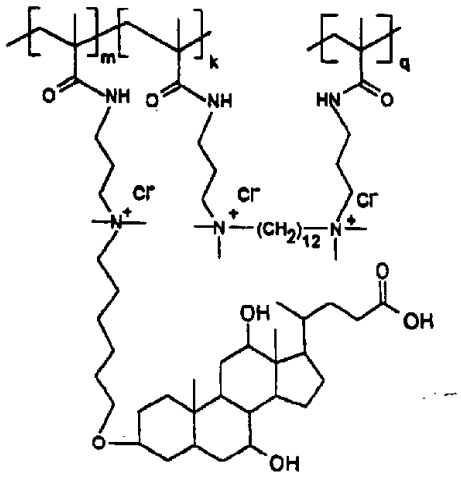


251 g (0.44 mmol) of 3-(6-bromohexyloxy)cholate (Example 12a) were dissolved in 2 ml of methanol, and 75 mg (0.44 mmol) of 3-(N,N-dimethylaminopropyl)methacrylamide were then added. The mixture was heated under reflux for 6 hours and then allowed to stand overnight. The solvent was stripped off and the residue was chromatographed over silica gel (methanol → methanol/water/acetic acid = 99:0.5:0.5). This gave 160 mg of crude product which was purified further over a weakly acidic ion exchanger. Yield: 80 mg of Example 12b.

^{1}H NMR: ($CDCl_3$) d = 0.67 ppm (s, 3H, cholate-CH_3); 0.87 (s, 3H, cholate-CH_3); 0.99 (d, J= 7 Hz, 3H, cholate-CH_3CH), 1.0-2.4 (m, aliphat. CH), 3.1-4.1 (several m, CHOH, CH_2O, inter alia), 3.15 (s, 6H, N-CH_3), 3.86 (s), 5.35 (brd. s, 1H, vinyl-H), 5.85 (brd. s, 1H, vinyl-H).

Example 12c:





m:k = 1:1

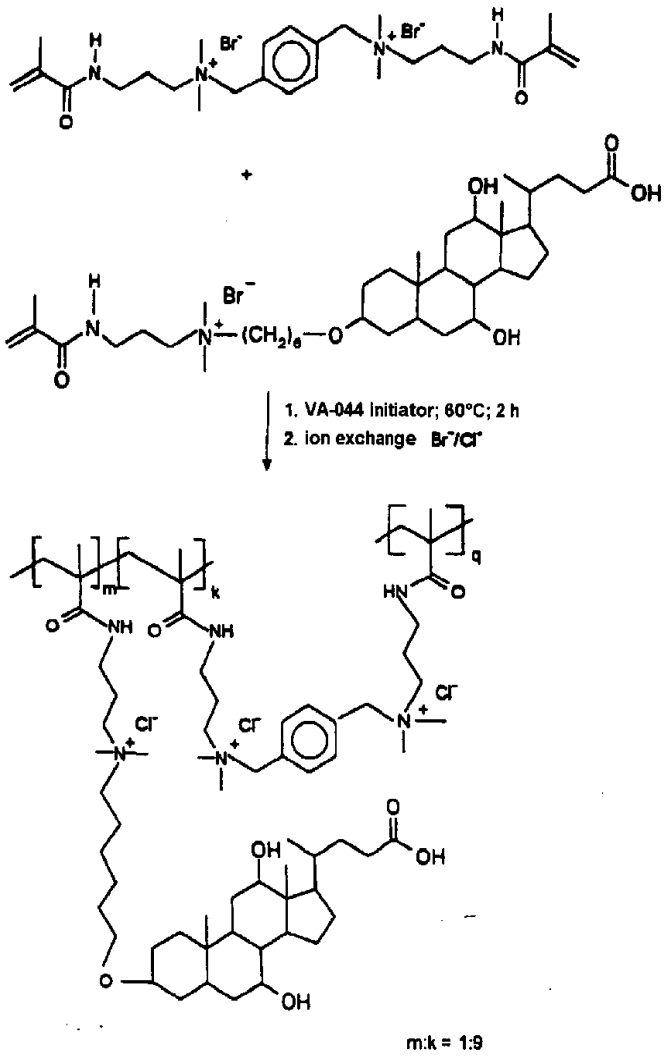
100 mg (150 mmol) of Example 12b and 903 mg (1350 mmol) of Example 3a were dissolved in a mixture of 7.5 ml of water and 7.5 ml of methanol. The solution was saturated with nitrogen and then heated to 60°C. Under an atmosphere of nitrogen, 40 mg of free-radical initiator VA-044 were then

added, and the mixture was stirred at this temperature for 1 hour. The resulting gel was transferred into an ultrafiltration cell (membrane 5000 Å). For ion exchange (bromide → chloride), the polymer was washed 2× with saturated aqueous NaCl solution and once with water. The retentate was freeze-dried. Yield: 912 mg of Example 12c.

Elemental analysis:

Calculated:	C 62.6%	H 10.4%	N 10.1%	Cl 11.5%
Found:	C 62.4%	H 10.6%	N 10.0%	Cl 11.1%

Example 13:



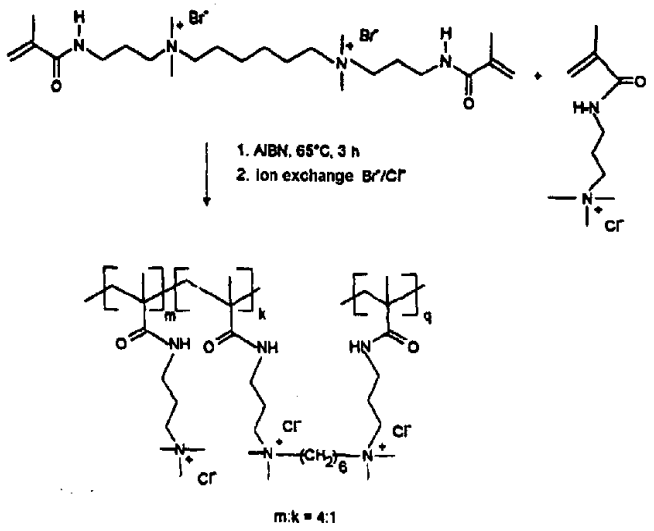
100 mg (150 mmol) of Example 12b and 816 mg (1350 mmol) of Example 5a were dissolved in 15 ml of a mixture of methanol and water (ratio 1:1). 40 mg of free-radical initiator VA-044 (from Wako) were then added. The mixture was degassed and then stirred at 60°C, under an atmosphere of

nitrogen, for 2 hours. The resulting gel was transferred to an ultrafiltration cell (membrane 5000 Å). For ion exchange (bromide → chloride), the polymer was washed 2× with saturated aqueous NaCl solution and once with water. The retentate was freeze-dried. Yield: 849 mg of Example 13.

Elemental analysis:

Calculated:	C 61.5%	H 8.8%	N 11.2%	Cl 12.9%
Found:	C 61.0%	H 8.7%	N 11.1%	Cl 13.1%

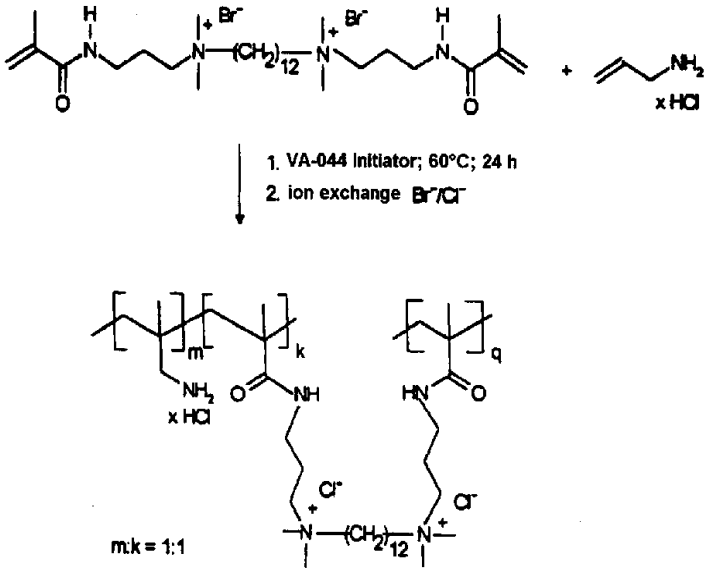
Example 14:



At 60°C, 4.9 g (8 mmol) of Example 1a were dissolved in 70 ml of isopropanol. A mixture of 7.0 g (32 mmol; 16.7 ml) of a 50% strength aqueous solution of [3-(methacryloylamino)propyl]trimethylammonium chloride (from Aldrich) in 70 ml of ethyl acetate was added to this solution. The solution was degassed. Under an atmosphere of nitrogen, 35 mg of azobisisobutyronitrile (AIBN) were then added. The solution was stirred at 65°C for 3 hours. The resulting gel was admixed with 500 ml of water, and the mixture was allowed to stand at room temperature for 2 hours for swelling. 1500 ml of isopropanol were then added, and the mixture was stirred for 4 hours, resulting in precipitation of the polymer. The mixture

was allowed to stand overnight, and the supernatant was then decanted off. The precipitated polymer was stirred first with saturated aqueous sodium chloride solution and then with 100 ml of water and 800 ml of isopropanol for 2 hours. The supernatant was then decanted off. 1500 ml of isopropanol were added to the polymer, and the mixture was stirred for another 2 hours. The polymer was then filtered off under reduced pressure [lacuna] dried. Yield: 11.2 g of Example 14.

Example 15:

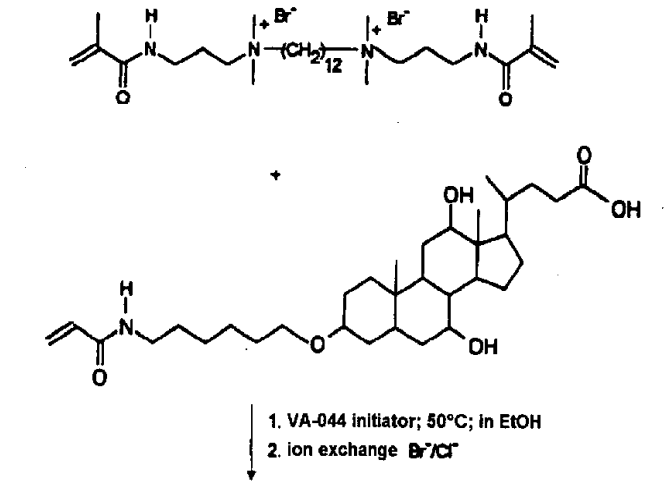


57 mg (1 mmol) of allylamine (from Riedel-de Haen) were added to 3 ml of 1n hydrochloric acid. 668 mg (1 mmol) of Example 3a and 2.4 mg of free-radical initiator VA-044 (from Wako) were then added. The mixture was degassed and then stirred at 60°C under an atmosphere of nitrogen for 24 hours. This gave a gel. The resulting gel was transferred to an ultrafiltration cell (membrane 5000 Å). For ion exchange (bromide → chloride), the polymer was washed 2× with saturated aqueous NaCl solution and once with water. The retentate was freeze-dried. Yield: 636 mg of Example 15.

Elemental analysis:

Calculated:	C 62.2%	H 10.5%	N 11.0%
Found:	C 62.1%	H 11.1%	N 14.9%

Example 16:



m:k = 1:4

5

490 mg (732 mmol) of Example 3a and 100 mg (183 mmol) of the cholate-containing comonomer I (synthesis as described in EP 548793) were dissolved in 2 ml of ethanol. 4.4 mg of free-radical initiator VA-044 (from Wako) were then added. The mixture was degassed and then stirred at 50°C under an atmosphere of nitrogen for 36 hours. This gave a gel which was homogenized using an Ultraturrax. Another 1.1 mg of VA-044 were added, and the mixture was once more degassed and stirred at 50°C under an atmosphere of nitrogen for a further 10 hours. The gel was then transferred to an ultrafiltration cell (membrane 5000 Å). For ion exchange (bromide → chloride), the polymer was washed 2× with saturated aqueous NaCl solution and once with water. The retentate was freeze-dried. Yield: 530 mg of Example 16.

Elemental analysis:

Calculated:	C 63.8%	H 10.4%	N 8.2%
Found:	C 62.4%	H 10.4%	N 8.2%

Example 17:
1,18-Dibromooctadecane

At from 0°C to 5°C, 2.4 g (100 mmol) of magnesium in 100 ml of abs. diethyl ether are stirred under nitrogen with 107 g (440 mmol) of dibromohexane. After 2-3 hours, the magnesium has dissolved, and 4 ml (0.04 mmol) of a 0.1 n solution of dilithium tetrachlorocuprate in THF are added to the mixture, and 300 ml of abs. THF are subsequently added dropwise to the mixture such that the temperature during the exothermic reaction is kept between 10 and 15°C by cooling. The mixture is then stirred at 5-10°C for 1 hour, and then at room temperature for 23 hours. The precipitate is then filtered off with suction and the filtrate is concentrated. The residue is stirred in hot heptane and filtered off with suction. The concentrated filtrate is distilled.
B.p.: 200°C at 15 [lacuna] uncorr. M.p.: 62°C
Yield: 7.0 g = 34.0% (based on the magnesium)

^{1}H NMR: ($COCl_3$) δ = 1.2-1.5 (several m, 28 H, aliphat. CH_2), 1.8-1.9 (m, 4H, aliphat. CH_2), 3.4 (t, 4 H, Br-CH_2) ppm.

Example 18:

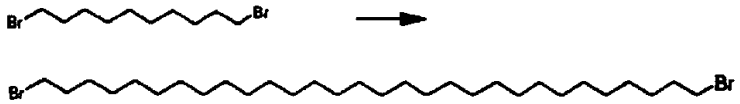
1,24-Dibromotetraeicosane

As in Example 17 using 1,18-dibromooctane. For work-up, the reaction mixture is filtered and the 1,8-dibromooctane is then initially distilled off, and the mixture is then boiled with 250 ml of heptane and filtered hot. The product crystallizes from the heptane. Repeated crystallization from heptane gives 11.5 g = 46.4% of product (based on magnesium)
M.p.: 72-75°C of a waxy substance

^{1}H NMR: ($COCl_3$) δ = 1.2-1.5 (several m, 40 H, aliphat. CH_2), 1.8-1.9 (m, 4H, aliphat. CH_2), 3.4 (t, 4 H, Br-CH_2) ppm.

Example 19:

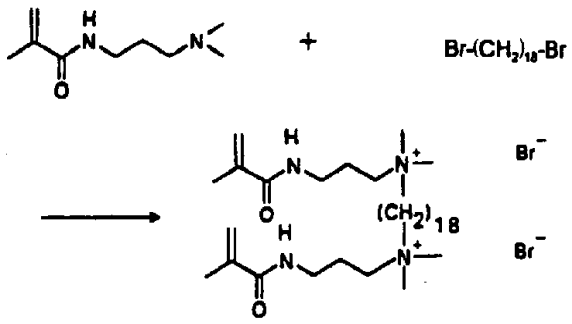
1,30-Dibromotriacontane



As Example 18 m.p.: 78°C
Yield: 12.5 g = 56.8% (based on magnesium)

^{1}H NMR: ($COCl_3$) δ = 1.2-1.5 (several m, 52 H, aliphat. CH_2), 1.8-1.9 (m, 4H, aliphat. CH_2), 3.4 (t, 4 H, Br-CH_2) ppm.

Example 20:
1,18-Di[N,N-dimethyl,N-(3-methacrylamidopropyl)ammonium]octadecane dibromide

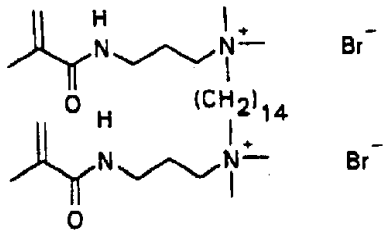


7.0 g (17 mmol) of 1,18-dibromooctadecane and 5.8 g (34 mmol) of dimethylaminopropylmethacrylamide in 120 ml of DMF are stirred at 80°-90° for 2.5 hours. The DMF is then distilled off and the residue is dissolved in 50 ml of methylene chloride. The solution is stirred into 1 ltr. of hexane and the clear supernatant is discarded after 1 hour. The residue is once more precipitated as described above.
Yield: 11.7 g = 91%

^{1}H NMR: (D_2O) δ = 1.2-1.5 (m, 28 H, aliphat. CH_2), 1.6-1.8 (m, 4H, aliphat. CH_2), 2.0-2.1 (m, 4 H, aliphat. CH_2), 1.95 (s, 6 H, methacrylate-CH_3), 3.08 (s, 12 H, N-CH_3), 3.2-3.4 (several m, 12 H, aliphat. CH_2, N-CH_2), 5.50 (m, 1 H, vinyl-H), 5.75 (m, 1 H, vinyl-H) ppm.

Example 21:
1,14-Di[N,N-dimethyl, N-(3-metharylamidopropyl)ammonium]tetradecane dibromide

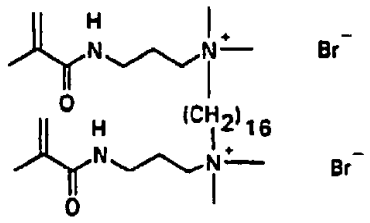
50



22.6 g (63.5 mmol) of 1,14-dibromotetradecane and 25.4 g (140 mmol) of dimethylaminopropylmethacrylamide together with 0.5 g of hydroquinone in 50 ml of DMF and 30 ml of methanol are allowed to stand in the dark for 2 weeks. The product is then precipitated by addition of diethyl ether and isohexane. The supernatant is decanted off and the residue is stirred with acetone, resulting in crystallization. The crystals are filtered off with suction and washed with acetone, giving 39.8 g = 90.1% (based on 1,14-dibromotetradecane).

^{1}H NMR: (D_2O) δ = 1.2-1.4 (several m, 20 H, aliphat. CH_2), 1.6-1.8 (m, 4H, aliphat. CH_2), 2.0-2.1 (m, 4 H, aliphat. CH_2), 1.95 (s, 6 H, methacrylate-CH_3), 3.08 (s, 12 H, N-CH_3), 3.2-3.4 (several m, 12 H, aliphat. CH_2, N-CH_2), 5.50 (m, 1 H, vinyl-H), 5.75 (m, 1 H, vinyl-H) ppm.

Example 22:
1,16-Di[N,N-dimethyl, N-(3-methacrylamidopropyl)ammonium]hexadecane dibromide



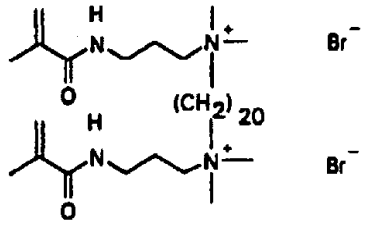
2.9 g (7.5 mmol) of dibromohexadecane and 2.6 g (15 mmol) of dimethylaminopropylmethacrylamide in 80 ml of DMF are stirred at 40-50°C for 27 hours. Work-up as in Example 21.

Yield: 4.8 g = 87.3%

^{1}H NMR: (D_2O) δ = 1.2-1.4 (several m, 24 H, aliphat. CH_2), 1.6-1.8 (m, 4H, aliphat. CH_2), 2.0-2.1 (m, 4 H, aliphat. CH_2), 1.95 (s, 6 H, methacrylate-CH_3), 3.08 (s, 12 H, N-CH_3), 3.2-3.4 (several m, 12 H, aliphat. CH_2, N-CH_2), 5.50 (m, 1 H, vinyl-H), 5.75 (m, 1 H, vinyl-H) ppm.

Example 23:

1,20-Di[N,N-dimethyl, N-(3-methacrylamidopropyl)ammonium]eicosane dibromide



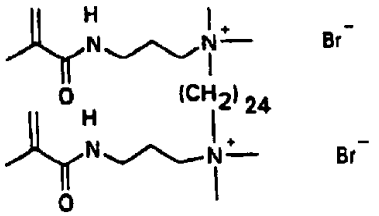
As in Example 21 using 1,20-dibromoeicosane. Reaction time: 30 hours 70-80°C.

Yield: 2.0 g = 95.2%

^{1}H NMR: (D_2O) δ = 1.2-1.4 (several m, 32 H, aliphat. CH_2), 1.6-1.8 (m, 4H, aliphat. CH_2), 2.0-2.1 (m, 4 H, aliphat. CH_2), 1.95 (s, 6 H, methacrylate-CH_3), 3.08 (s, 12 H, N-CH_3), 3.2-3.4 (several m, 12 H, aliphat. CH_2, N-CH_2), 5.50 (m, 1 H, vinyl-H), 5.75 (m, 1 H, vinyl-H) ppm.

Example 24:

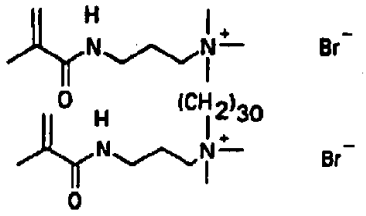
1,24-Di[N,N-dimethyl, N-(3-methacrylamidopropyl)ammonium]tetra-eicosane dibromide



As in Example 21 using 1,24-dibromotetraeicosane
Reaction time: 18 hours at 50-60°C.
Yield: 12.1 g = 91.7%.

^{1}H NMR: (D_2O) δ = 1.2-1.4 (several m, 32 H, aliphat. CH_2), 1.6-1.8 (m, 4H, aliphat. CH_2), 2.0-2.1 (m, 4 H, aliphat. CH_2), 1.95 (s, 6 H, methacrylate-CH_3), 3.08 (s, 12 H, N-CH_3), 3.2-3.4 (several m, 12 H, aliphat. CH_2, N-CH_2), 5.50 (m, 1 H, vinyl-H), 5.75 (m, 1 H, vinyl-H) ppm.

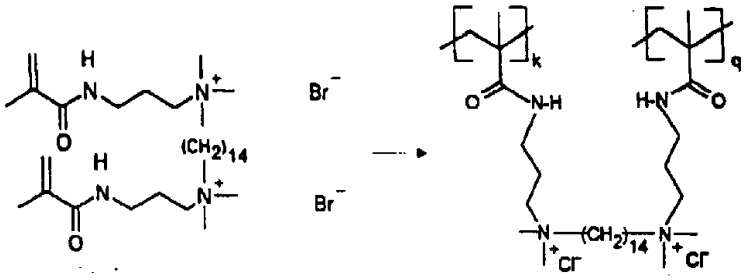
Example 25:
1,30-Di[N,N-dimethyl, N-(3-methacrylamidopropyl)ammonium]triacontane dibromide



As in Example 21 using 1,30-dibromotriacontane
Reaction time: 30 hours at 80°C.
The solution is then cooled to 0°C, and the product crystallizes out.
It is filtered off with suction and washed with a little DMF. Drying. 15.2 g = 77%.

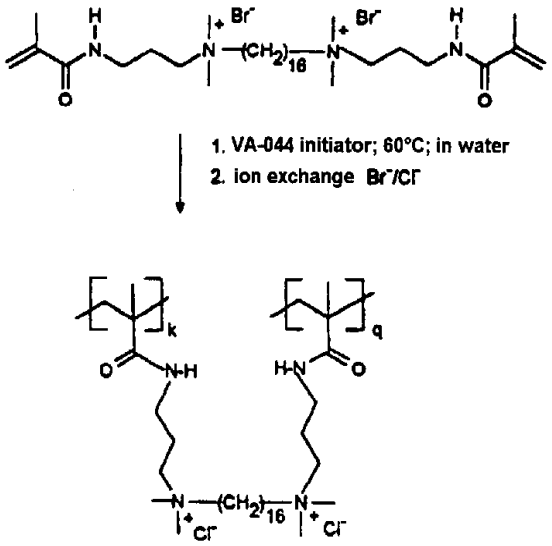
^{1}H NMR: (D_2O) δ = 1.2-1.4 (m, 32 H, aliphat. CH_2), 1.6-1.8 (m, 4H, aliphat. CH_2), 2.0-2.1 (m, 4 H, aliphat. CH_2), 1.95 (s, 6 H, methacrylate-CH_3), 3.08 (s, 12 H, N-CH_3), 3.2-3.4 (several m, 12 H, aliphat. CH_2, N-CH_2), 5.50 (m, 1 H, vinyl-H), 5.75 (m, 1 H, vinyl-H) ppm.

Example 26:



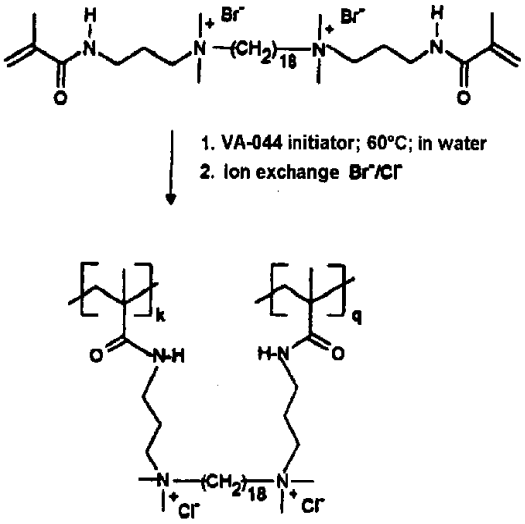
Under nitrogen, 10 g (14.4 mmol) of 1,14-di[N,N-dimethyl, N-(3-methacrylamidopropyl)ammonium]tetradecane dibromide are dissolved in 40 ml of water. 0.15 g of 2,2'-azobis[2(2-imidazolin-2-yl)propane] dihydrochloride are added, and the mixture is then heated with stirring to 50-60°C. After 1-2 hours, another 0.05 g of initiator are added to the reaction mixture, and stirring is continued until all the starting material has polymerized. 100 ml of saturated sodium chloride solution are then added to the reaction mixture, and the product is filtered off with suction. The product is washed free of chloride by ultrafiltration (membrane 5000 Å). Freeze drying gives 8 g of pure polymer. The product is insoluble in water.

Example 27:



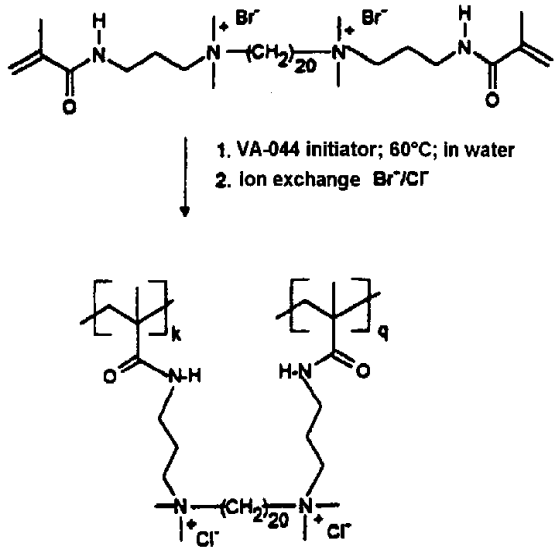
As in Example 26 using 1,16-di[N,N-dimethyl, N-(3-methacrylamidopropyl)-ammonium]hexadecane dibromide.
Yield: 8.4 g = 95.2%
The product is insoluble in water.

Example 28:



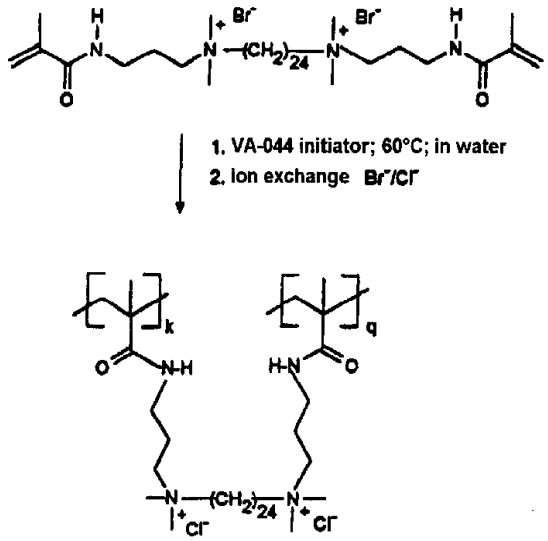
As Example 26 using 1,18-di[N,N-dimethyl, N-(3-methacrylamidopropyl)-ammonium]octadecane dibromide.
Yield: 5.0 g = 96.1%
The product is insoluble in water.

Example 29:



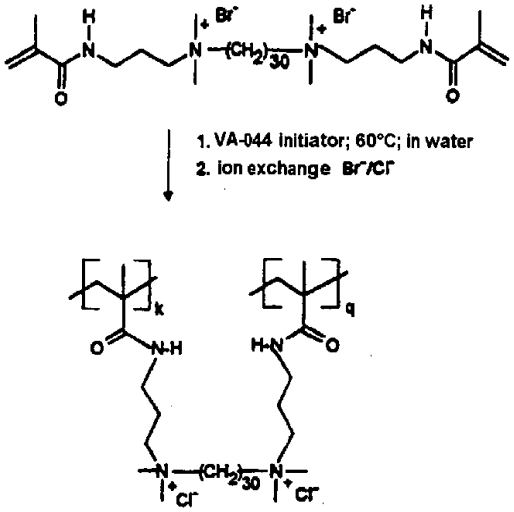
As Example 26 using 1,20-di[N,N-dimethyl, N-(3-methacrylamidopropyl)-ammonium]eicosane dibromide.
Yield: 1.8 g = 95.3%
The product is insoluble in water.

Example 30:



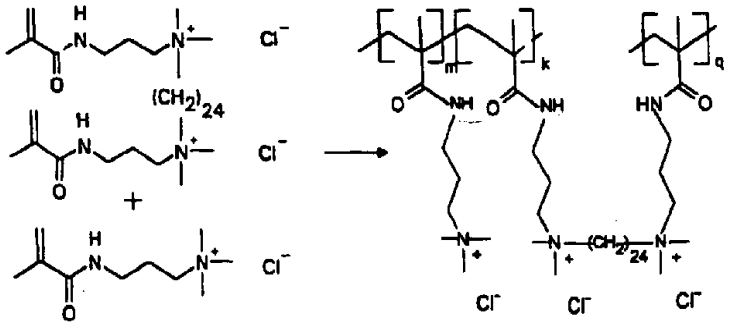
As Example 26 using 1,24-di[N,N-dimethyl, N-(3-methacrylamidopropyl)-ammonium]tetraeicosane dibromide.
Yield: 5.9 g = 81%
The product is insoluble in water.

Example 31:



As Example 26 using 1,30-di[N,N-dimethyl, N-(3-methacrylamidopropyl)-ammonium]triacontane dibromide.
Yield: 12.5 g = 83.4%
The product is insoluble in water.

Example 32:



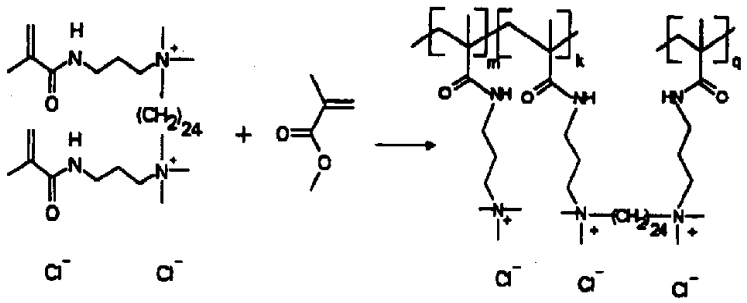
Under nitrogen, 3.4 g (10 mmol) of a 50% strength solution of N-(3-trimethylammoniumpropyl)methacrylamide chloride and 0.25 g of 2,2'-azo-bis[2(2-imidazolin-2-yl)propane] dihydrochloride are added to 8.4 g

(10 mmol) of 1,24-di[N,N-dimethyl, N-(3-methacrylamidopropyl)-ammonium]tetraeicosane dibromide in 50 ml of water. With stirring, the mixture is polymerized at 60°C until both starting materials have reacted completely. After 2 hours, 200 ml of a saturated sodium chloride solution are added to the mixture, and the product is filtered off with suction. The polymer is then washed free of chloride by ultrafiltration (membrane: 5000 Å).

Yield: 10.2 g = 100%

The product is insoluble in water.

Example 33:



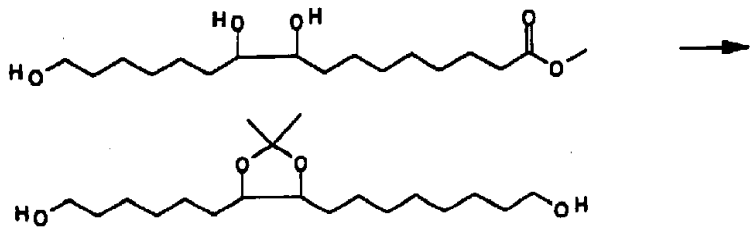
Under nitrogen, 3.6 g (4.4 mmol) of 1,24-di[N,N-dimethyl, N-[3-methacrylamidopropyl)ammonium]tetraeicosane dibromide in 25 ml of water and 10 ml of methanol are admixed with 3.6 g (36.4 mmol) of methyl methacrylate. At 60°C, 0.15 g of 2,2'-azobis[2(2-imidazolin-2-yl)propane] dihydrochloride is added with stirring, and the mixture is stirred at 60°C until the starting materials have reacted. Work-up as in Example 32.

Yield: 5.9 g = 80.5%

The product is insoluble in water.

Example 34:

1,7,8,16-Tetrahydroxyhexadecane 7,8-ethylene ketal



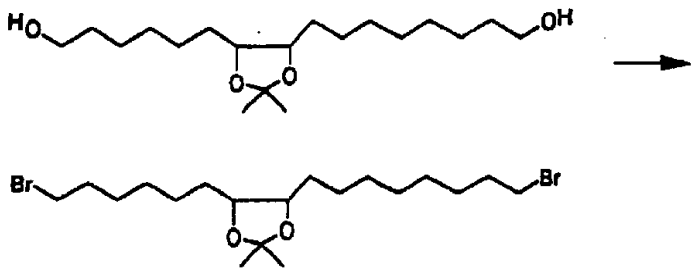
35 g (105.3 mmol) of ethyl 9,10,16-trihydroxyhexadecanoate in 200 ml of 2,2'-dimethoxypropane with ½ drop of conc. H_2SO_4 are stirred until the starting material has reacted completely (TLC: ethyl acetate/isohexane 3/7). The mixture is then poured into a solution of sodium bicarbonate, and the organic phase is, after separation, dried over sodium sulfate. Concentration gives 44.5 g of acetal which are, under nitrogen, dissolved in 250 ml of abs. THF. 41 g (132 mmol) of a solution of sodium bismethoxyethylaluminum hydride in toluene (Aldride, "Red-Al") are added with slight cooling at 25°C, and the mixture is stirred for 2 hours. The mixture is then poured onto ice and the THF is distilled off under reduced pressure. The mixture is then acidified using glacial acetic acid and extracted repeatedly with ethyl acetate. The concentrated organic phase is dissolved in 50 ml of methylene chloride and with 5 ml of glacial acetic acid and 5 ml of water admixed with methanol until a clear solution results. The mixture is subsequently stirred until thin layer chromatography (ethyl acetate/isohexane 3/7) shows a uniform product. The mixture is then poured into 0.5 n aqueous sodium hydroxide solution and extracted with ethyl acetate. The extract is dried over sodium sulfate and then concentrated.

Yield: 34 g = 98.0% light-yellow oil

^{1}H NMR: ($CDCl_2$) δ = 1.2-1.6 (several m, 30 H, aliphat. CH_2 and acetal-CH_3), 3.54-3.64 (m, 2 H, CH-O), 3.63 (2 t, 4 H, CH_2-O) ppm.

Example 35:

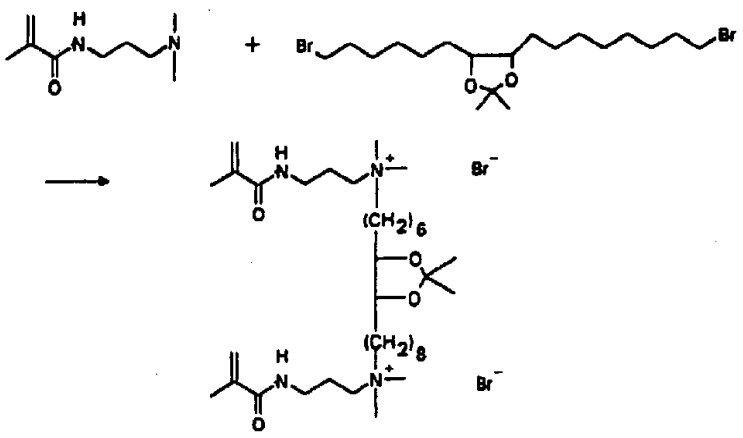
1,16-Dibromo-7,8-dihydroxyhexadecane-7,8-ethylene ketal



33 g (100 mmol) of 1,7,8,16-tetrahydroxyhexadecane 7,8-ethylene ketal (Example 34) are, together with 83 g (250 mmol) of tetrabromomethane, dissolved in 350 ml of acetonitrile. At 0-5°C, 79 g (300 mmol) of triphenylphosphine are subsequently added a little at a time over a period of 2-3 hours, and stirring is continued at 0°C for another hour. The progress of the reaction is monitored by thin-layer chromatography (silica gel; isohexane/ethyl acetate 9/1). Once the product has disappeared, the mixture is filtered and the residue is washed with ethyl acetate. The filtrate is concentrated under reduced pressure, dissolved in ethyl acetate and washed with sodium bicarbonate solution until the solution no longer reacts acidic. The combined organic phases are dried over sodium sulfate and then concentrated. The syrup that remains is purified over silica gel (isohexane/ethyl acetate 9/1). Yield: 43.3 g = 94.9%

^{1}H NMR: ($CDCl_2$) δ = 1.2-1.6 (several m, 26 H, aliphat. CH_2 and acetal-CH_3), 1.85 (m, 4 H, Br-CH_2CH_2-), 3.4 (2 t, 4 H, Br-CH_2), 3.54-3.62 (m, 2 H, CH-O) ppm.

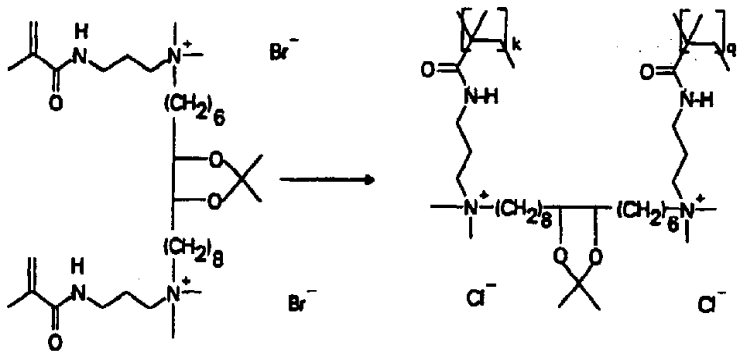
Example 36:



43 g (94.2 mmol) of 1,16-dibromo-7,8-dihydrohexadecane 7,8-ethylene ketal (Example 35) in 100 ml of DMF are stirred in the dark with 34 g (200 mmol) of dimethylaminopropylmethacrylamide and 1 g of hydroquinone. The reaction is monitored by thin-layer chromatography (silica gel; isohexane/ethyl acetate 9/1 and n-butanol/glacial acetic acid/water 10/4/1). When all of the starting material has reacted and the end product is substantially uniform, the mixture is poured with stirring into 2 ltr. of ethyl acetate. The mixture is subsequently decanted. The syrup-like residue is stirred with ethanol and decanted three times.
Yield: 75 g

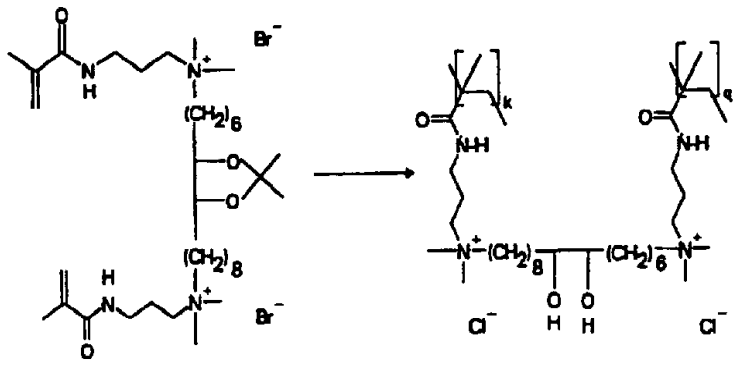
^{1}H NMR: (D_2O) δ = 1.3-1.8 (several m, 28 H, aliphat. CH_2 and acetal-CH_3), 1.95 (s, 6 H, methacrylate-CH_3), 1.95-2.1 (m, 4 H, aliphat. CH_2), 3.2-3.4 (several m, 12 H, aliphat. CH_2, N-CH_2), 3.08 (s, 12 H, N-CH_3), 3.8 (several m, 2 H, CH-O, 5.5 (m, 1 H, vinyl-H), 5.75 (m, 1 H, vinyl-H) ppm.

Example 37:



25 g (31 mmol) of monomer (Example 36) are dissolved in 180 ml of methanol and, under nitrogen, heated at 50°C. After 30 minutes, 0.75 g of 2,2'-azobis[2(2-imidazolin-2-yl)propane] dihydrochloride is added. Once the mixture has solidified, it is admixed with 50 ml of water and homogenized using an Ultraturrax. The mixture is then heated at 60°C for 2 hours. The mixture is then stirred with 100 ml of saturated sodium chloride solution and filtered. The residue is washed twice with saturated sodium chloride solution. It is subsequently washed free of chloride with water and dried.
Yield: 22.0 g = 88%
The product is insoluble in water.

Example 38:

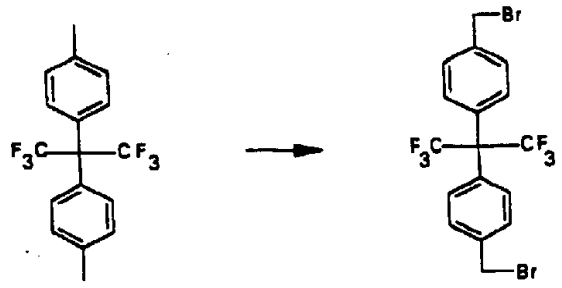


25 g (31 mmol) of monomer (Example 36) are dissolved in 500 ml of 2 n HCl. After 24 hours, the solution is concentrated under reduced pressure. (To check the reaction, an NMR in D_2O is recorded. Acetalic protons should no longer be visible). The residue that remains is dissolved in 100 ml of water and adjusted to pH 7 using 2 n NaOH. The mixture is then heated at 60°C under nitrogen. After 30 minutes, the mixture is polymerized and purified as described in Example 21.

Yield: 16.4 g = 78.3%

The product is insoluble in water.

Example 39:
2,2-Di(4-bromomethylphenyl)hexafluoropropane

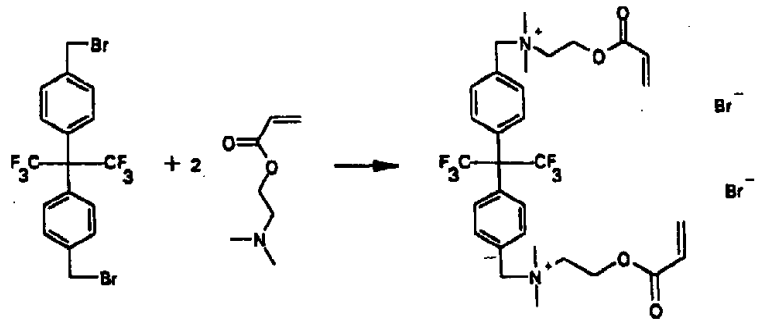


26.5 g (80 mmol) of 2,2-di(4-bromomethylphenyl)hexafluoropropane are dissolved in 300 ml of CCl_4 and heated to the boil and irradiated using a UV lamp. Over a period of 1.5 hours, 27.2 g (170 mmol) of bromine in 100 ml of CCl_4 are added dropwise. The mixture is then heated at reflux for 30 minutes. After cooling, the organic phase is de-acidified using sodium bicarbonate solution, dried over Na_2SO_4 and concentrated. The residue is dissolved in 400 ml of hot heptane. After cooling, pure 2(4-bromomethylphenyl)-2(dibromomethylphenyl)hexafluoropropane is filtered off with suction, and the filtrate is concentrated to half its volume. After cooling, more 2(4-bromomethylphenyl)-2(4-dibromomethylphenyl)hexafluoropropane is filtered off with suction. The concentrated filtrate gives impure 2,2'-di(4-bromomethylphenyl)hexafluoropropane, which is sufficiently pure to be processed further. Yield: 16.4 g

^{1}H NMR: ($CDCl_3$) δ = 4.8 (s, 4 H, Br-CH_2-), 7.32-7.44 (m, 8 H, aromatic) ppm.

Example 40

2,2-Di[4(N,N-dimethyl, N-(2-acryloxyethyl)ammonium)methyl]phenylhexafluoropropane dibromide



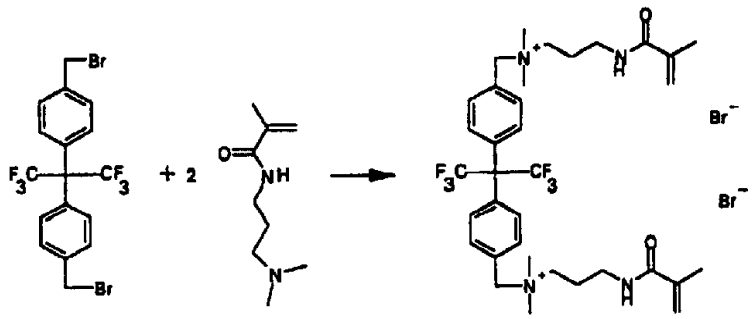
12.3 g (25 mmol) of 2,2-di(4-bromomethylphenyl)hexafluoropropane (crude product, Example 39) together with 7.2 g (50 mmol) of dimethylaminoethyl acrylate are stirred in 100 ml of DMF for 30 hours. The DMF is then distilled off under reduced pressure and the residue is dissolved in a little methylene chloride. The solution is stirred into 1.5 ltr. of methylene chloride, and an oil precipitates out which gradually solidifies. The solid

residue is comminuted, stirred with methylene chloride, filtered off with suction and dried. Yield: 11.4 g = 92%.

^{1}H NMR: (D_2O) δ = 3.2 (s, 12 H, N-CH_3), 3.8-3.9 (m, 4 H, aliphat. CH_2), 4.7 (s, 4H, CH_2-N), 4.7-4.8 (m, 4 H, aliphat. CH_2), 6.04-6.56 (m, 6H, vinyl-H), 7.64-7.74 (m, 8 H, aromatic) ppm.

Example 41:

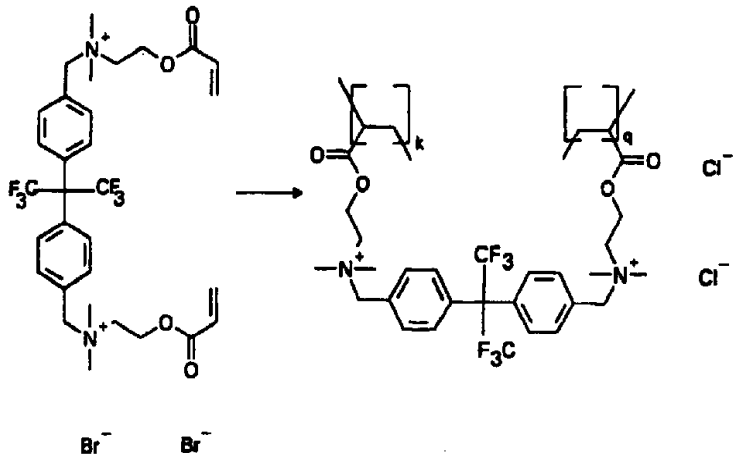
2,2-Di[4(N,N-dimethyl, N-(3-methacrylamidopropyl)ammonium)methyl]-phenylhexafluoropropane dibromide



9.8 g (20 mmol) of 2,2-di(4-bromomethylphenyl)hexafluoropropane (crude product, Example 39) together with 6.8 g (40 mmol) of 3-dimethylamino-propylmethacrylamide are allowed to stand in 100 ml of DMF at room temperature for 70 hours. The DMF is then distilled off under reduced pressure, and the residue is dissolved in a little methanol and stirred into 1 ltr. of methylene chloride. The emulsion is concentrated to about 300 ml under reduced pressure. It is then allowed to settle, and the supernatant is decanted off from the syrup-like residue. By repeating the purification process several times, 9.6 g = 91% of pure product are obtained.

^{1}H NMR: (D_2O) δ = 1.9 (s, 6 H, methacrylate-CH_3), 2.14-2.28 (m, 4 H, aliphat. CH_2), 3.1-3.2 (s, 12 H, N-CH_3), 3.26-3.38 (m, 4 H, aliphat. CH_2), 3.40-3.48 (m, 4 H, aliphat. CH_2), 4.6 (s, 4 H, CH_2-N), 5.6 and 5.72 (m, 2 H, vinyl-H), 7.55-7.65 (m, 8 H, aromatic) ppm.

Example 42:

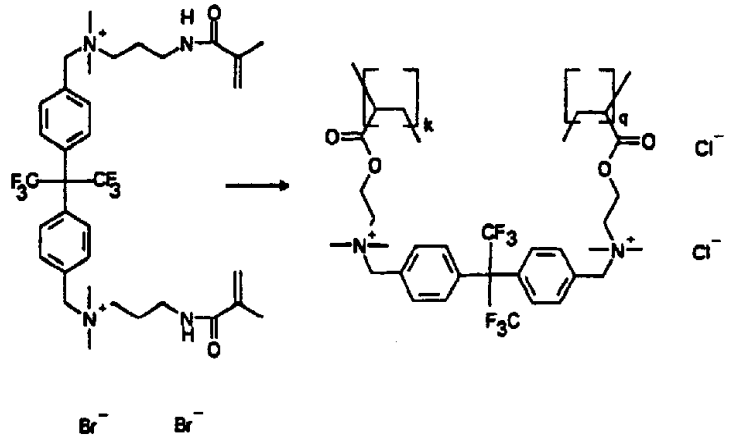


7 g (9 mmol) of 2,2-di[4-(N,N-dimethyl, N-(2-acryloxyethyl)ammonium)-methyl]phenylhexafluoropropane dibromide (Example 40) in 50 ml of water are heated under nitrogen to 60°C. Polymerization is initiated by addition of 0.14 g of 2,2'-azobis[2(2-imidazolin-2-yl)propane] dihydrochloride. Within a short period of time, the mixture can no longer be stirred, and another 20 ml of water and 0.07 g of polymerization initiator are then added and the entire mixture is homogenized using an Ultraturrax. After a further 2 hours at 60°C, the mixture is stirred with 200 ml of saturated sodium chloride solution and filtered off with suction, and the residue is washed once more with saturated sodium chloride solution and subsequently washed free of chloride with water.

Yield: 6.7 g = 95.7%

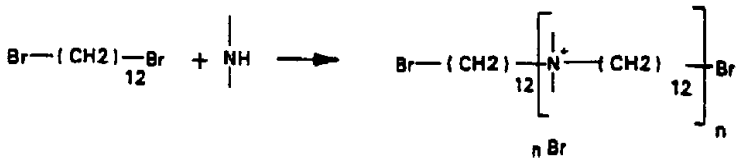
The product is insoluble in water.

Example 43:



As in Example 42 using 2,2-di[4(N,N-dimethyl, N(3-methacrylamidopropyl)-ammonium)methyl]phenylhexafluoropropane dibromide.
Yield: 95.7%
The product is insoluble in water.

Example 44a



50 g (152.3 mmol) of 1,12-dibromododecane and 2.9 g (35 mmol) of dimethylamine hydrochloride are initially charged in 15 ml of abs. DMF and 15 ml of abs. THF. 2.1 g (70 mmol) of sodium hydride (80%, in oil) are added a little at a time. After 24 hours, a further 0.9 g (11 mmol) of dimethylamine hydrochloride and, a little at a time, 0.7 g (23 mmol) of sodium hydride (80%, in oil) are added. The mixture is stirred at room temperature for 20 hours and then, for 5 hours, at 50-60°C. The reaction mixture is poured onto ice/conc. HBr and extracted repeatedly with hexane. After concentration, the hexane phase contained 23 g = 46% of 1,2-dibromododecane. The aqueous phase is extracted 4× with dichloromethane. Drying and concentration gives 30 g of crude product. This is concentrated using an oil pump. To remove residual amounts of DMF, the product is shaken 3× with ether and subsequently cooled to -50°C. The ether phases are discarded. After drying at 50°C using an oil pump, 24 g of product are obtained. For further purification, the product is subjected to column chromatography over silica gel.

Mobile phase: ethyl acetate; later: acetone/dichloromethane/methanol/ethyl acetate/water/glacial acetic acid 9:6:2:2:2:1.

Fraction 1: n = 1; 4.5 g

^{1}H NMR: (DMSO) δ = 3.5 (t, 4H, CH_2-Br), 3.2-3.3 (m, 4H, N-CH_2), 3.0 (s, 6H, N-CH_3), 1.8 (m, 4H, aliph. CH_2), 1.6-1.7 (m, 4H, aliphat. CH_2), 1.2-1.4 (m, 32 H, aliph. CH_2) ppm.

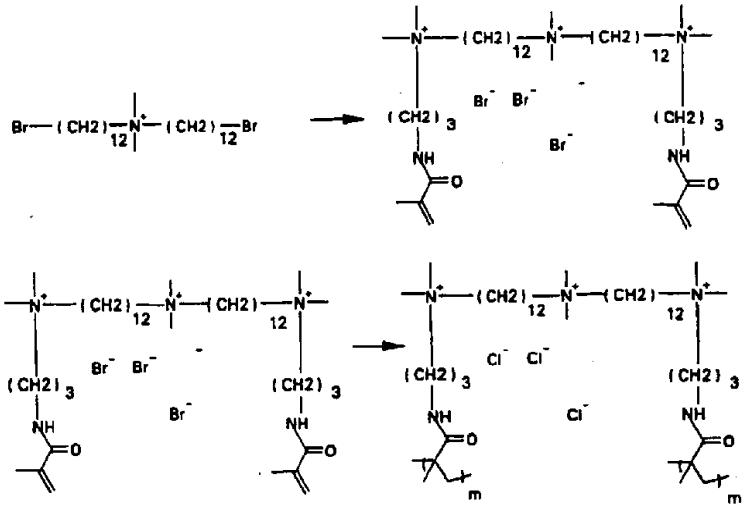
Fraction 2: n = 2; 2.7 g

^{1}H NMR: (DMSO) δ = 3.5 (t, 4H, CH_2-Br), 3.2-3.3 (m, 8H, N-CH_2), 3.0 (s, 12H, N-CH_3), 1.8 (m, 4H, aliph. CH_2), 1.6-1.7 (m, 8H, aliphat. CH_2), 1.2-1.4 (m, 48 H, aliph. CH_2) ppm.

Fraction 3: n = 3; 1.8 g

^{1}H NMR: (DMSO) δ = 3.5 (t, 4H, CH_2-Br), 3.2-3.3 (m, 12H, N-CH_2), 3.0 (s, 18H, N-CH_3), 1.8 (m, 4H, aliph. CH_2), 1.6-1.7 (m, 12H, aliphat. CH_2), 1.2-1.4 (m, 64 H, aliph. CH_2) ppm.

Example 44b



10.5 g (about 17 mmol) of fraction 1 from Example 44a, 8.5 g (50 mmol) of N-(3-N,N-dimethylaminopropyl)methacrylamide and 0.5 g of hydroquinone are initially charged in 40 ml of DMF. The mixture is then stirred at room temperature for 4 days and at 50°C for 35 hours. The DMF is distilled off under reduced pressure. The residue is subsequently stirred 5× with 250 ml of acetone each time. The viscous brown residue is then dried under reduced pressure.

Weight 12 g

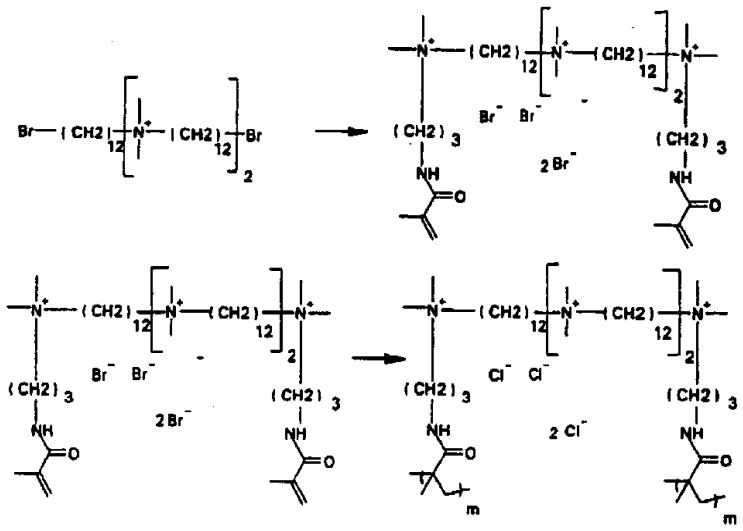
Under nitrogen, the product in water is heated to 50°C, whereupon it dissolves. Polymerization is initiated by addition of 2,2'-azobis[2(2-imidazolin-2-yl)propane] dihydrochloride and carried out by the customary method. The product is then stirred into saturated NaCl solution. The precipitate is filtered off with suction, washed free of NaCl and subjected to ultrafiltration. The residue is subsequently freeze-dried.

Yield: 10.6 g

Analysis values for $C_{44}H_{90}N_5O_2Cl_3+2H_2O$

Calculated:	C 61.2%	H 11.0%	N 8.1%
Found	C 61.1%	H 10.4%	N 8.0%

Example 44c



6.3 g (6.9 mmol) of fraction 2 from Example 44a, 3.4 g (20 mmol) of n-(3-N,N-dimethylaminopropyl)methacrylamide and 0.3 g of hydroquinone are initially charged in 25 ml of DMF. The mixture is then stirred at room temperature for 4 days and at 50° for 35 hours. The DMF is subsequently distilled off under reduced pressure. The residue is repeatedly triturated with acetone, dissolved in methanol and precipitated with acetone and isohexane. The precipitate is dried under reduced pressure.

Weight 4.1 g.

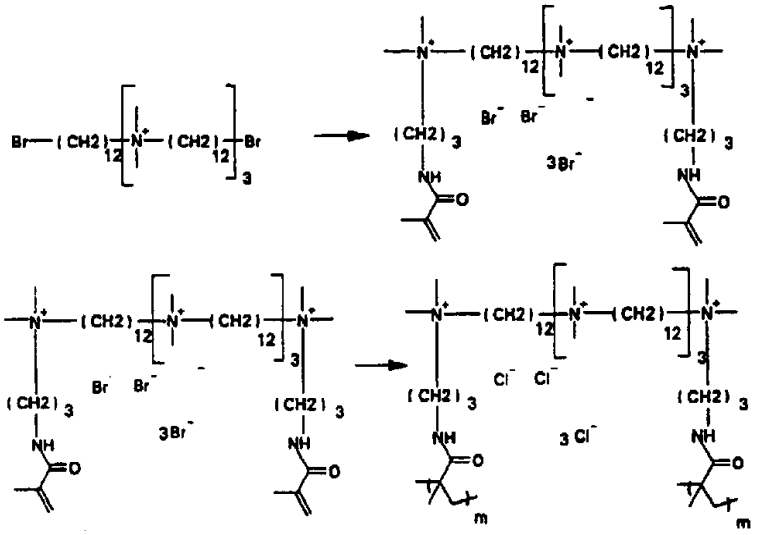
Under nitrogen, the product is dissolved in water at 50°C. Polymerization is initiated by addition of 2,2'-azobis[2(2-imidazolin-2-yl)propane] dihydrochloride and carried out by the customary method. A gel-like material is finally formed. This material is then stirred into saturated NaCl solution. The gel-like material is washed free of NaCl by ultrafiltration. The residue is freeze-dried.

Yield: 3.0 g

Analysis values for $C_{58}H_{120}N_6O_2Cl_4 + 3H_2O$

Calculated.	C 61.9%	H 11.3%	N 7.4%
Found	C 62.1%	H 11.1%	N 7.7%

Example 44d



4.9 g (4 mmol) of fraction 3 from Example 44a, 2 g (12 mmol) of N-(3-N,N-dimethylaminopropyl)methacrylamide and 0.3 g of hydroquinone are initially charged in 20 ml of DMF. The mixture is then stirred at room temperature for 4 days and at 50°C for 40 hours. The DMF is distilled off under reduced pressure. The residue is repeatedly triturated with acetone and dried under reduced pressure.

Yield: 4.3 g

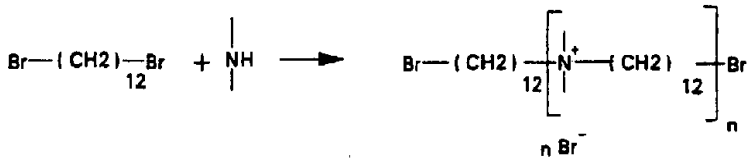
Under nitrogen, the product in water is heated to 50°C, whereupon it dissolves. Polymerization is initiated by addition of 2,2'-azobis[2(2-imidazolin-2-yl)propane] dihydrochloride and carried out by the customary method. A granular product is formed. This granular product is then stirred into saturated NaCl solution. The product is washed free of NaCl by ultrafiltration. The residue is freeze-dried.

Yield: 2.84 g

Analysis values for $C_{72}H_{150}N_7O_2C_{15} + 2H_2O$

Calculated.	C 63.6%	H 11.4%	N 7.2%
Found	C 63.5%	H 11.1%	N 6.8%

Example 45a

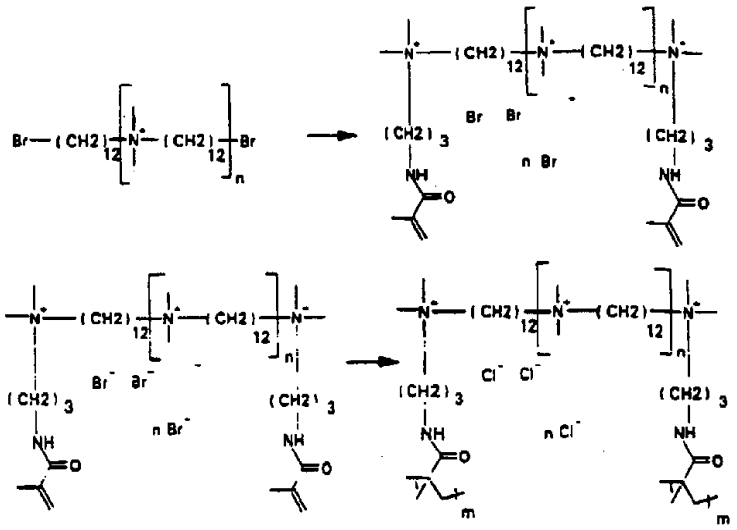


29 g (88 mmol) of dibromododecane and 3.6 g (44 mmol) of dimethylamine hydrochloride are initially charged in 60 ml of abs. DMF at room temperature. 1.4 g of NaH (80%, in oil) are added a little at a time at 35°C. The mixture is then stirred at 30°C for 3 days. The DMF is distilled off under reduced pressure. The residue is extracted with hexane. By concentrating the hexane, unreacted 1,12-dibromododecane is recovered. The residue is subsequently extracted with dichloromethane. The dichloromethane is concentrated, giving 23.5 g of a residue.

13.5 g of the dichloromethane residue are chromatographed over silica gel. Mobile phase: acetone/dichloromethane/methanol/ethyl acetate/water-/glacial acetic acid 9:6:2:2:2:1.

Evaluation of the ratio of the CH_2-Br protons to the N-CH_3 protons gives an average value of 2 for n.

Example 45b



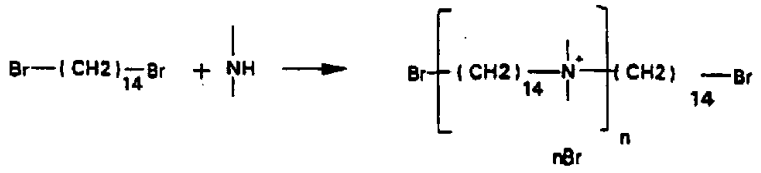
10 g of the mixture from Example 45a, 4.3 g (25 mmol) of N-(3-N,N-dimethylaminopropyl)methacrylamide and 0.5 g of hydroquinone are initially charged in 40 ml of DMF. The mixture is then stirred for 4 days at 25°C and for 4 days at 45°C. The DMF is distilled off under reduced pressure. The residue is repeatedly triturated with acetone. Under nitrogen, the viscous brown residue (8 g) is heated in water to 50°C, whereupon it dissolves. Polymerization is initiated by addition of 2,2'-azobis[2(2-imidazolin-2-yl)propane] dihydrochloride and carried out by the customary method. Saturated NaCl solution is then added. The precipitate that is formed after stirring is filtered off with suction and washed free of NaCl, and the gel-like material is subjected to ultrafiltration. The residue is freeze-dried.

Yield: 4.9 g

Analysis values for $C_{58}H_{120}N_6O_2Cl_4 + 5H_2O$

Calculated	C 61.9%	H 11.3%	N 7.4%
Found	C 59.9%	H 10.8%	N 7.2%

Example 46a

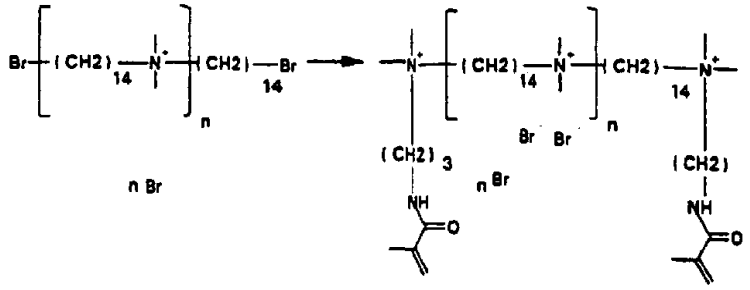


25.65 g (72 mmol) of 1,14-dibromotetradecane and 1.96 g (24 mmol) of dimethylamine hydrochloride are initially charged in 60 ml of abs. DMF at 40°C. 1.5 g (50 mmol) of sodium hydride (80%, in oil) are added a little at a time at 30°C. The mixture is then stirred at 45°C for 6 hours. The DMF is distilled off under reduced pressure. The residue is poured into 200 ml of 2n HBr and repeatedly extracted with hexane. Unreacted dibromotetradecane can be recovered by concentrating the hexane. The residue is subsequently extracted repeatedly with dichloromethane. The dichloromethane is concentrated. Drying of the residue gives 14.9 g of product.

^{1}H NMR: (DMSO) δ = 3.5 (t, 4H, CH_2-Br), 3.2-3.3 (m, 8H, N-CH_2), 3.0 (s, 12H, N-CH_3), 1.8 (m, 4H, aliph. CH_2), 1.6-1.7 (m, 8H, aliphat. CH_2), 1.2-1.4 (m, 60 H, aliph. CH_2) ppm.

The ratio of the protons to one another gives an average value 2 for n.

Example 46b

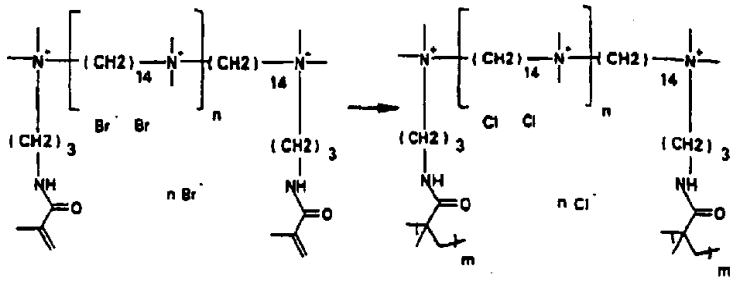


14.9 g (17.8 mmol) of the product from Example 46a, 8.5 g (50 mmol) of N-(3-N,N-dimethylaminopropyl)methacrylamide and 0.6 g of hydroquinone are initially charged in 80 ml of DMF. The mixture is then stirred at 55°C for 7 hours. The DMF is distilled off under reduced pressure. The viscous brown residue is triturated repeatedly with acetone. The acetone is discarded. The residue is dried using an oil pump:
Yield: 14.5 g

^{1}H NMR: (DMSO) δ = 8.2 (t, 2H, NH), 5.7, (5.7, s, 2H, olefin-H), 5.4 (s, 2H, olefin-H), 3.1-3.4 (m, 20H, N-CH_2), 3.0 (2 s, 24 H, N-CH_3), 1.9 (s, 6H, C-CH_3), 1.6 (m; 16H, aliphat-H), 1.2-1.4 (m, 64 H, aliph. CH_2) ppm.

The ratio of the protons gives an average value of 2 for n.

Example 46c

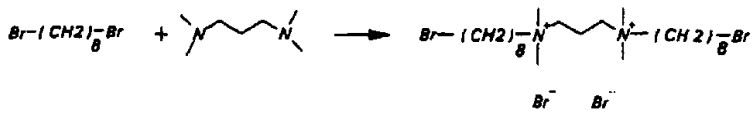


Under nitrogen, 14.5 g of the product from Example 46b in 60 ml of water are heated to 50°C. Polymerization is initiated by addition of 200 mg of 2,2'-azobis[2(2-imidazolin-2-yl)propane] dihydrochloride. After 20 minutes, another 200 mg of polymerization initiator are added. 20 minutes later, the reaction mixture thickens. A further 200 mg of polymerization initiator are added, and the reaction mixture is then diluted with water and homogenized using an Ultraturrax. After a further 2 hours of stirring at 60°C, the mixture is admixed with 100 ml of saturated NaCl solution. The residue is filtered off with suction, washed free of NaCl and dried.
Yield: 10.7 g

Analysis values for n = 2; $C_{64}H_{132}N_6O_2Cl_4 + 4H_2O$

Calculated	C 62.4%	H 11.5%	N 6.8%
Found	C 62.1%	H 11.2%	N 6.9%

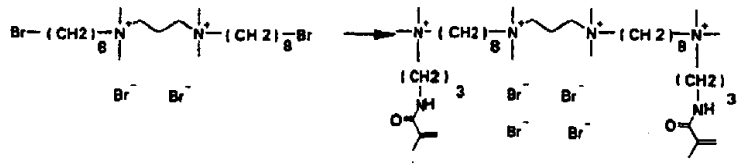
Example 47a



54 g (200 mmol) of dibromooctane are dissolved in 50 ml of DMF. At 50°C, 5.2 g (40 mmol) of N,N,N',N'-tetramethyl-1,3-propanediamine are added over a period of 30 minutes, and a white precipitate is formed. According to TLC, the reaction has ended after 4 hours of stirring at 50°C. The precipitate is filtered off with suction and discarded. The DMF is distilled off using an oil pump. The distillation residue is dissolved in water and extracted 2× with hexane. 33 g of dibromooctane can be recovered by concentrating the hexane phase. The aqueous phase is freeze-dried. The viscous residue is stirred with dichloromethane. The dichloromethane solution is separated from the insoluble residue, giving, after concentration, 20 g of crude product. This is dissolved in a little dichloromethane and stirred into 100 ml of ethyl acetate. The precipitate is dried using an oil pump. Yield: 15 g = 56%.

^{1}H NMR (D_2O) δ = 3.5 (t, 4H, CH_2-Br), 3.4 (m, 8H, N-CH_2), 3.1 (s, 12H, N-CH_3), 2.3 (m, 2H, aliphat. CH_2), 1.7-1.9 (2 m, 8H, aliphat. CH_2), 1.4 (m, 16, aliphat. (H_2) ppm.

Example 47b

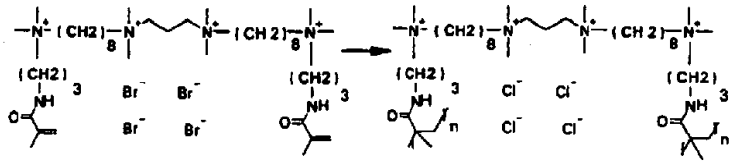


15 g (22 mmol) of the product from Example 47a are dissolved in 100 ml of DMF. After addition of 7.5 g (44 mmol) of N-(3-N,N-dimethylaminopropyl)-methacrylamide, the mixture is heated to 50°C. According to TLC, the reaction has ended after 10 hours of stirring at 50°C. The DMF is distilled off using an oil pump. The distillation residue is stirred 4 times with 500 ml of dichloromethane. After in each case stirring for 15 minutes, the clear supernatant is decanted off and the residue is dried using an oil pump.

Yield: 21 g

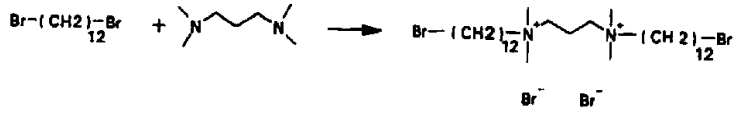
^{1}H NMR (D_2O) δ = 5.7 (s, 2H, olefin-H), 5.5 (s, 2 H, olefin-H), 3.2-3.5 (2 m, 20H, N-CH_2), 3.1 and 3.2 (2s, 24H, N-CH_3), 2.3 (m, 4H, aliphat.H), 2.0 (m, 4H, aliphat.H), 1.9 (s, 6H, C-CH_3), 1.8 and 1.4 (2 m, 24 H, aliphat.H) ppm.

Example 47c



Under nitrogen, 21 g (21 mmol) of acrylamide from Example 47b in 150 ml of water are heated to 70°C. The polymerization is initiated by addition of 160 mg of 2,2'-azobis[2(2-imidazolin-2-yl)propane] dihydrochloride. 5 minutes later, the polymer begins to precipitate out, and the mixture becomes gel-like and difficult to stir. After half an hour, another 150 ml of water and 160 mg of polymerization initiator are added, and the reaction mixture is homogenized using an Ultraturrax. The mixture is stirred at 70°C for another 4 hours, and 100 ml of saturated NaCl solution are then added. After 30 minutes, 500 ml of acetone are stirred into the gel-like solution. The turbid supernatant is decanted off from the viscous precipitate. The precipitate is gelated in 100 ml of water and once more precipitated using acetone. After four reprecipitations, the gel-like residue is freeze-dried. Yield: 5.8 g

Example 48a

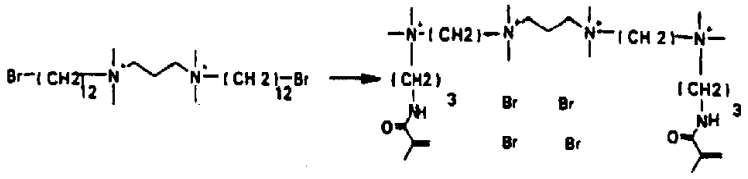


65.6 g (200 mmol) of 1,12-dibromododecane are dissolved in 80 ml of DMF. 5.2 g (40 mmol) of N,N,N',N'-tetramethyl-1,3-propanediamine are added, and the mixture is then heated to 60-70°C. The mixture is stirred at 50°C for 5 hours and then allowed to stand overnight, after which the reaction has ended according to TLC. The DMF in the filtrate is distilled off using an oil pump. The distillation residue is stirred with water and hexane. The aqueous phase is extracted 3× with dichloromethane (3-phases). The middle phase is dried using an oil pump.

Yield: 27.3 g

^{1}H NMR (D_2O) δ = 3.3-3.6 (m, 12H, CH_2-Br and N-CH_2), 3.2 (2s, N-CH_3), 2.2-2.3 (m, 2H, aliphat. CH_2), 1.6-1.9 (m, 8H, aliphat. H), 1.2-1.5 (m, 32H, aliphat. H) ppm.

Example 48b

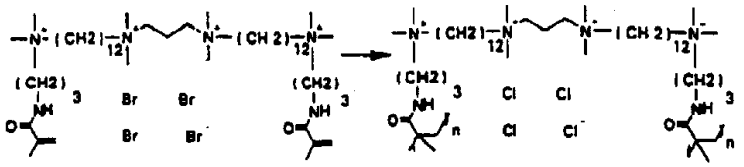


13.7 g (17.5 mmol) of the product from Example 48a are dissolved in 50 ml of DMF. 11.9 g (70 mmol) of N-(3-N,N-dimethylaminopropyl)methacrylamide are added, and the mixture is heated to 60°C. After 4 days of stirring at 70°C, the reaction has ended according to TLC. The DMF is distilled off using an oil pump. The distillation residue is dissolved in 50 ml of dichloromethane and slowly stirred into approximately 300 ml of acetone. The mixture is stirred for 15 minutes, 200 ml of hexane are added and stirring is continued for another 10 minutes. The clear supernatant is decanted off (discarded), and the residue is dried using an oil pump.

Yield: 14.0 g

1-H NMR (D_2O) δ = 5.8 (s, 2H, olefin-H), 5.5 (s, 2H, olefin-H), 3.2-3.5 (m, 20H, N-CH_2), 3.1 and 3.2 (2s, 24H, N-CH_3), 2.3 (m, 2H, aliph.H), 2.0 (m, 4H, aliph.H), 2.0 (s, 6H, C-CH_3), 1.7-1.9 and 1.3-1.5 (2m, 40H, aliphat.H) ppm.

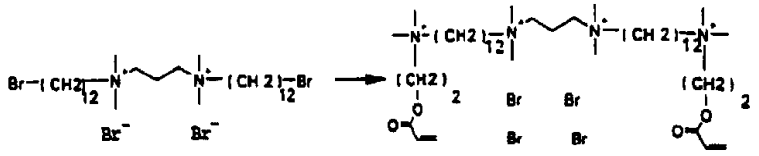
Example 48c



12.2 g (10.8 mmol) of the product from Example 48b are dissolved in 180 ml of water and, under nitrogen, heated to 70°C. The polymerization is initiated to addition of 150 mg of 2,2'-azobis[2(2-imidazolin-2-yl)propane] dihydrochloride. After 6 minutes, the mixture has gelled. 200 ml of water and 150 mg of polymerization initiator are added, and the reaction mixture is homogenized using an Ultraturrax. After a further 4 hours of stirring at 70°C, 100 ml of saturated NaCl solution are added. The mixture is allowed to stand overnight and then subjected to ultrafiltration until the permeate is free of NaCl. The retentate is freeze-dried.

Yield: 6.3 g

Example 49a

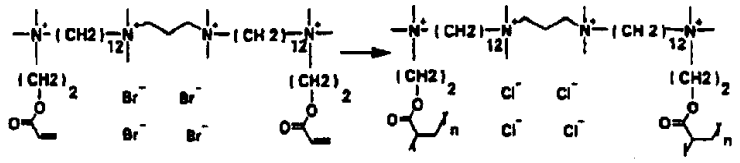


13.7 g (17.5 mmol) of the product from Example 48a are dissolved in 50 ml of DMF. 10.0 g (70 mmol) of N'N-dimethylaminoethyl acrylate are added, and the mixture is then heated to 60°C. The mixture is stirred at 60°C for 4 days, after which the reaction has ended according to TLC. The DMF is distilled off using an oil pump. The distillation residue is dissolved in 30 ml of propanol and 30 ml of dichloromethane and slowly stirred into approximately 400 ml of acetone. The mixture is stirred for 15 minutes, 300 ml of hexane are added and stirring is continued for another 10 minutes. The clear supernatant is decanted off and the residue is dried using an oil pump.

Yield: 14.0 g

1-H NMR (D_2O) δ = 6.0-6.5 (m, 6H, olefin-H), 4.7 (m, 4H, O-CH_2), 3.8 (m, 4H, N-CH_2), 3.4 (m, 12H, N-CH_2), 3.1 and 3.2 (2s, 24H, N-CH_3), 2.3 (m, 2H, aliph.H), 1.7-1.9 and 1.3-1.5 (2m, 32H, aliphat.H) ppm.

Example 49b



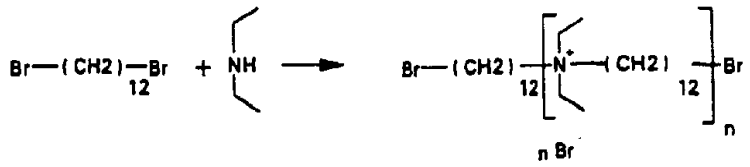
Under nitrogen, 13.7 g of the compound from Example 49a in 300 ml of water are heated to 70°C. Polymerization is initiated by addition of 180 mg of 2,2'-azobis[2(2-imidazolin-2-yl)propane] dihydrochloride. After 30 minutes, another 180 mg of polymerization initiator are added. After 60 minutes, another 180 mg of polymerization initiator are added. After 90 minutes, another 250 mg of polymerization initiator are added. After 4 hours, 100 ml of saturated NaCl solution are added, whereupon the solution becomes turbid. After addition of more water, the reaction mixture is subjected to ultrafiltration until it is free of NaCl. The permeate is freeze-dried.

Yield: 8.5 g

Analysis values: for $C_{41}H_{92}N_4O_4Cl_4 + 3H_2O$

Calculated	C 54.7%	H 11.0%	N 6.2%
Found	C 55.1%	H 11.0%	N 6.1%

Example 50a

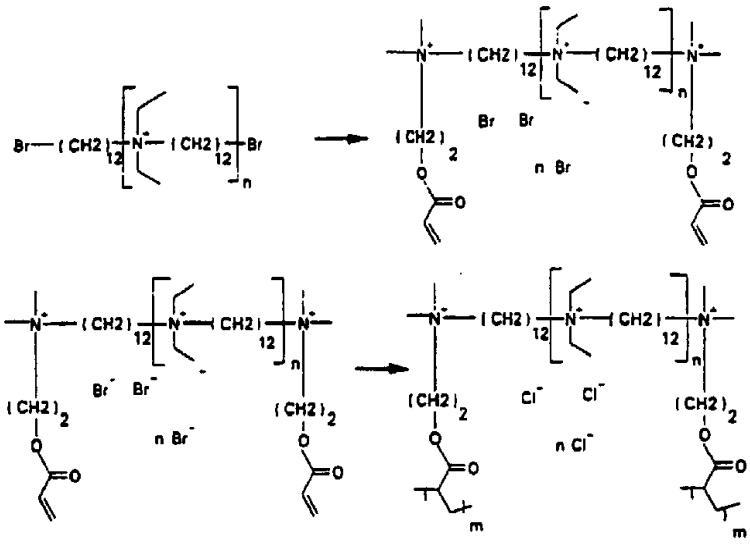


In a stream of nitrogen substance, 32.8 g (100 mmol) of 1,12-dibromododecane are dissolved with heating to 30°C in 50 ml of absolute DMF. With stirring, 2.4 g (33 mmol) of diethylamine are added, and the mixture is stirred at room temperature for 1 hour. 1.0 g (33 mmol) of sodium hydride (80% in oil) is added a little at a time over a period of 1 hour. The mixture is allowed to stand overnight, after which the DMF is stripped off using an oil pump. The residue is dissolved in water and made strongly acidic using hydrobromic acid. The turbid solution is extracted 3× with hexane (3 phases: hexane-oil-water). The hexane phase is discarded. The middle and the lower phases are extracted 3 times with dichloromethane. The combined methylene chloride phases are dried and concentrated. n has an average value of 1.

Yield: 19.3 g

^{1}H NMR: (DMSO) δ = 3.5 (t, 4H, CH_2-Br), 2.9-3.3 (3m, 16H, N-CH_2), 1.8 (m, 4H, aliphat. CH_2), 1.1-1.7 (4m, 72 H, aliphat. C-CH_3) ppm.

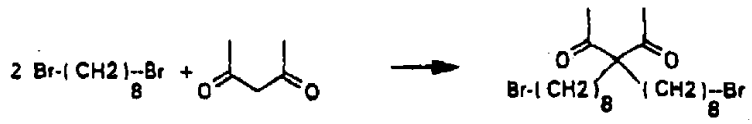
Example 50b



9.5 g (9.8 mol) of the product from Example 50a are dissolved in 50 ml of DMF. 2.8 g (19.6 mmol) of N'N-dimethylaminoethyl acrylate are added, and the mixture is heated to 60°C. After 3 days of stirring at 60°C, the reaction has ended according to TLC. The DMF is distilled off using an oil pump. The distillation residue is dissolved in 50 ml of dichloromethane and slowly stirred into approximately 300 ml of acetone. After 15 minutes of stirring, 200 ml of hexane are added and stirring is continued for 10 minutes. The clear supernatant is decanted off (discarded), and the residue is dried using an oil pump.
Yield: 8.1 g

The residue is dissolved in 50 ml of water and, under nitrogen, heated to 70°C. Polymerization is initiated by addition of 100 mg of 2,2'-azobis[2(2-imidazolin-2-yl)propane] dihydrochloride. After 10 minutes, the reaction mixture has gelled. 150 ml of water and 100 mg of polymerization initiator are added. The reaction mixture is subsequently homogenized using an Ultraturrax. After a further 4 hours of stirring at 70°C, 100 ml of saturated NaCl solution are added. The mixture is allowed to stand overnight and then subjected to ultrafiltration until the permeate is free of NaCl. The retentate is freeze-dried.
Yield: 5.7 g

Example 51a

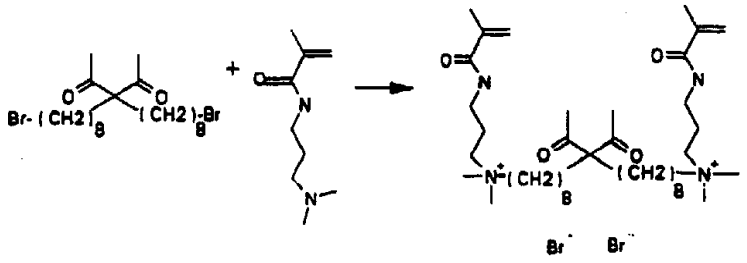


81.6 g (300 mmol) of 1,8-dibromooctane are initially charged in 150 ml of toluene. 2.4 g of tetrabutylammonium chloride (vacuum-dried) are added, and the mixture is heated to 70°C. At 30 minute intervals, 7.5 g (75 mmol) of acetylacetone and 60 g of potassium carbonate (dried) are added in 3 portions. After 5 hours of stirring at 70°C, the reaction has ended according to TLC. The cooled reaction mixture is admixed with water and extracted twice with toluene. The dried organic phase is concentrated using a rotary evaporator, and the excess dibromooctane is distilled off using an oil pump. The distillation residue of 29 g is chromatographed over a silica gel column. Mobile phase: hexane, later hexane/dichloromethane 1:1.

Yield: 9.2 g = 25%

^{1}H NMR: ($CDCl_3$) δ = 3.4 (t, 4H, CH_2-Br), 2.1 (s, 6H, CH_3CO), 1-1.8 (4 m, 28H, aliphat. CH_2) ppm.

Example 51b

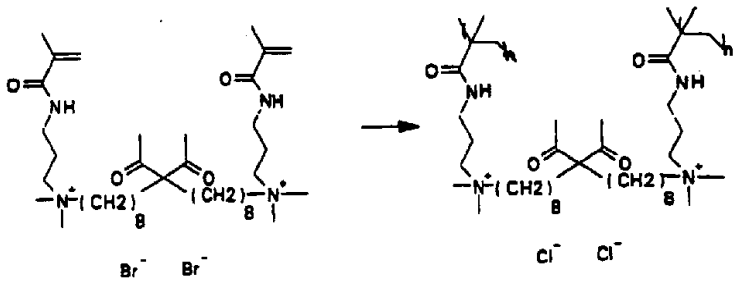


7.5 g (15.5 mmol) of the product from Example 51a are dissolved in 50 ml of DMF. After addition of 5.3 g (31 mmol) of N-(3-N,N-dimethylaminopropyl)methacrylamide, the mixture is heated to 70°C. After 8 hours of stirring at 70°C and 60 hours at room temperature, the reaction has ended according to TLC. The DMF is distilled off using an oil pump. The distillation residue is dissolved in 50 ml of dichloromethane and slowly stirred into approximately 1 l of hexane. The mixture is stirred for 1.5 hours, after which the clear supernatant is decanted off, and the residue is dissolved in water and freeze-dried.

Yield: 12.8 g

^{1}H NMR: (D_2O) δ = 5.4 and 5.8 (2 s, 4 H, olefin. H), 3.2-3.4 (m, 12H, N-CH_2), 3.1 (s, 12 H, N-CH_3), 2.1 (s, 6 H, CH_3-CO), 1.9 (s, 6H, CH_3), 1.0-2.0 (5 m, 32 H, aliphat. H) ppm.

Example 51c



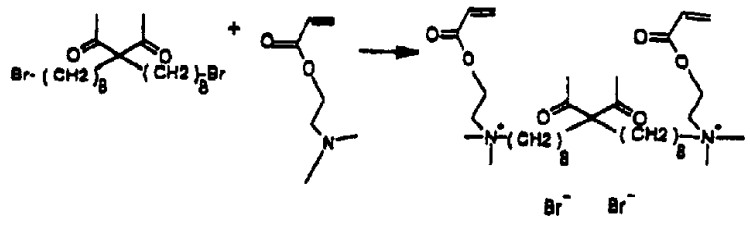
12.8 g (15.6 mmol) of the product from Example 51b are dissolved in 100 ml of water and, under nitrogen, heated to 70°C. Polymerization is initiated by addition of 120 mg of 2,2'-azobis[2(2-imidazolin-2-yl)propane] dihydrochloride. 3 minutes later, the polymer begins to precipitate out. After half an hour, another 120 mg of polymerization initiator are added, and the reaction mixture is homogenized using an Ultraturrax. After a further 4 hours of stirring at 70°C, 100 ml of saturated NaCl solution are added. The mixture is allowed to stand overnight and then subjected to ultrafiltration until the permeate is free of NaCl. The retentate is freeze-dried.

Yield: 10.3 g

Analysis values for: $C_{37}H_{74}N_4O_4Cl_2 + 4H_2O$

Calculated	C 56.8%	H 10.6%	N 7.9%
Found	C 57.6%	H 9.6%	N 6.8%

Example 52a

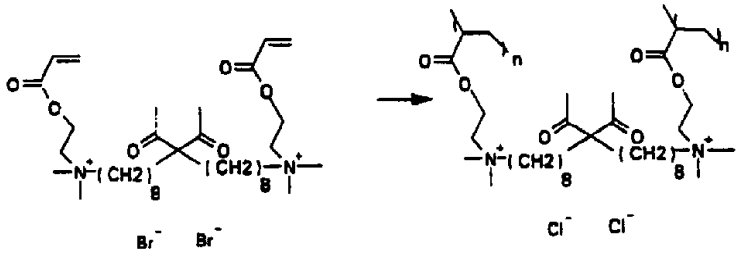


7.5 g (15.5 mmol) of the product from Example 51a are dissolved in 50 ml of DMF. After addition of 5.3 g (31 mmol) of N-(3-N,N-dimethylaminopropyl)methacrylamide, the mixture is heated to 70°C. After 8 hours of stirring at 70°C and 60 hours at room temperature, the reaction has ended according to TLC. The DMF is distilled off using an oil pump. The distillation residue is dissolved in 50 ml of dichloromethane and slowly stirred into approximately 1 l of hexane. The mixture is stirred for 1.5 hours, after which the clear supernatant is decanted off, and the residue is dissolved in water and freeze-dried.

Yield: 11.8 g

^{1}H NMR: (DMSO) δ = 6.4-6.0 (m, 6 H, olefin H), 4.5 (m, 4H, O-CH_2, 3.7 (m, 4 H, N-CH_2), 3.1 (s, 12 H, N-CH_3), 2.0 (s, 6 H, CH_3CO), 0.9-1.8 (4 m, 28 H, aliphat. H) ppm.

Example 52b



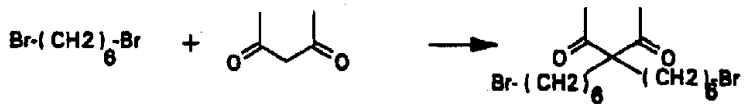
11.8 g (15.4 mmol) of the product from Example 52a are dissolved in 100 ml of water and 20 ml of methanol and, under nitrogen, heated to 70°C. Polymerization is initiated by addition of 110 mg of 2,2'-azobis[2(2-imidazolin-2-yl)propane] dihydrochloride. 3 minutes later, the polymer begins to precipitate out. After half an hour, another 110 mg of polymerization initiator are added, and the reaction mixture is homogenized using an Ultraturrax. The mixture is stirred at 70°C for another 4 hours, and 100 ml of saturated NaCl solution are then added. The mixture is allowed to stand overnight and then subjected to ultrafiltration until the permeate is free of NaCl. The retentate was freeze-dried.

Yield: 8.4 g

Analysis values for $C_{33}H_{64}N_{42}O_6Cl_2 + 2H_2O$

Calculated	C 57.3%	H 9.9%	N 4.1%
Found	C 57.6%	H 9.9%	N 3.8%

Example 53a

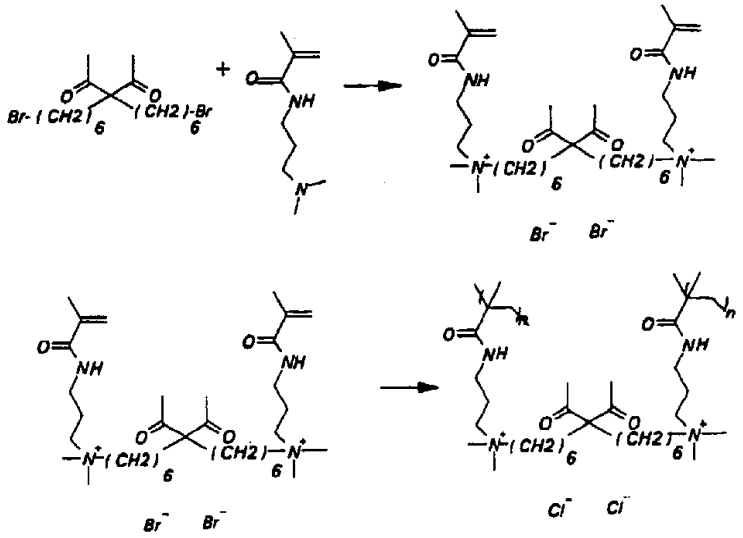


73.2 g (300 mmol) of 1,6-dibromohexane are initially charged in 150 ml of toluene. 2.4 g of tetrabutylammonium chloride (vacuum-dried) are added, and the mixture is then heated to 70°C. Over a period of 1 hour, 7.5 g (75 mmol) of acetylacetone are added dropwise, and 60 g of potassium carbonate (dried) are added a little at a time. After 4 hours of stirring at 70-80°C, the reaction has ended according to TLC. The cooled reaction mixture is admixed with water and extracted twice with toluene. The dried organic phase is concentrated using a rotary evaporator, and the excess dibromohexane is distilled off using an oil pump. The distillation residue of 25 g is chromatographed over a silica gel column. Mobile phase: hexane, later hexane/dichloromethane 1:1.

Yield: 8.7 g = 27%

^{1}H NMR: ($CDCl_3$) δ = 3.4 (t, 4H, CH_2-Br), 2.1 (s, 6 H, CH_3CO), 1-1.8 (4 m, 20 H, aliphat. CH_2) ppm.

Example 53b

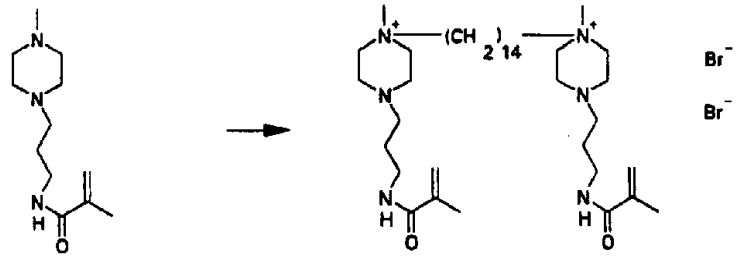


8.7 g (20.4 mmol) of the product from Example 53a are dissolved in 80 ml of DMF. 6.9 g (40.8 mmol) of N-(3-N,N-dimethylaminopropyl)methacrylamide are added, and the mixture is then heated to 70°C. After 2 days of stirring at 70°C, the reaction has ended according to TLC. The DMF is distilled off using an oil pump. The distillation residue is dissolved in 100 ml of dichloromethane and slowly stirred into approximately 1 l of hexane. After 1 hour of stirring, the clear supernatant is decanted off, and the residue is dissolved in water and freeze-dried. Yield: 1 g.

^{1}H NMR: (D_2O) δ = 5.4 and 5.8 (2 s, 4 H, olefin. H), 3.2-3.4 (m, 12H, N-CH_2), 3.1 (s, 12 H, N-CH_3), 2.1 (s, 6 H, CH_3-CO), 1.9 (s, 6H, CH_3), 1.0-2.0 (5 m, 24 H, aliphat. H) ppm

The polymerization is carried out as in Example 52b, giving 13 g of polymer.

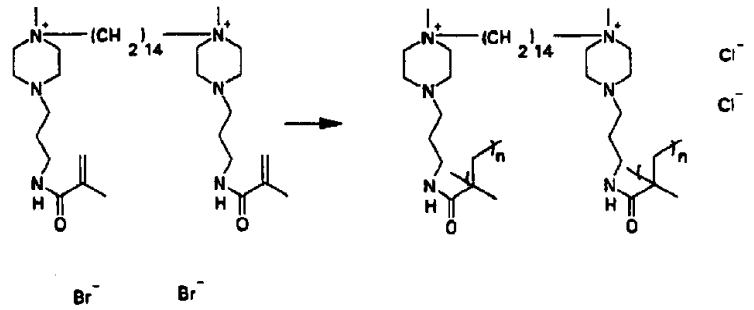
Example 54a



6.6 g (18.5 mmol) of dibromotetradecane, 10.1 g (45 mmol) of N-[3-(4-methylpiperazino)propyl]methacrylamide and 0.5 g of hydroquinone are dissolved in 20 ml of DMF and, under nitrogen, stirred at 40°C. After 3 more days of stirring at 55°C, the solution is concentrated under reduced pressure. The residue is stirred with approximately 30 ml of acetone and at the same time cooled to -70°C. The acetone supernatant is decanted off. This procedure is repeated 5 times, and the residue is then dried. Weight 7 g.

^{1}H NMR: (DMSO) δ = 5.3 and 5.6 (2 s, 4 H, olefin. H), 3.0 (s, 6H, N-CH_3), 1.6, 1.2, 2.4, 2.6, 2.7, 3.1 and 3.3 (7 m, aliphat. CH_2), 1.8 (s, 6H, CH_3) ppm.

Example 54b



5 7 g of the product from Example 54a are dissolved in 40 ml of water and polymerized with addition of 150 mg of initiator as in Example 53b. After the polymerization has ended, the product is washed free of chloride using a Nutsche filter and dried in a desiccator. Grinding gives 3.9 g of a brown powder.

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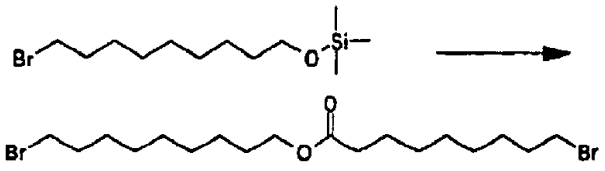
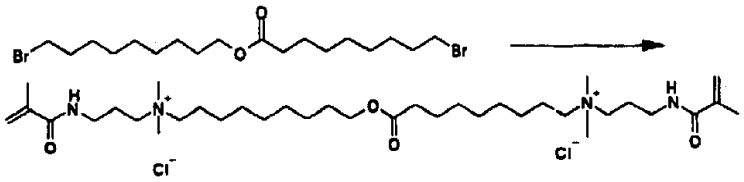
Example 55a



27.5 g (93 mmol) of 9-bromononanol trimethylsilyl ether are dissolved in 250 ml of carbon tetrachloride and heated at reflux temperature. 19.9 g (106 mmol) of N-bromosuccinimide and 1.5 g (9.3 g) of azoisobutyronitrile are added in small portions in intervals of 5 minutes over 1 hour. As long as the starting material can be seen in the TLC, more N-bromosuccinimide and azoisobutyronitrile are added at 10 minute intervals. The mixture is then stirred under reflux for one hour. After cooling, the precipitate is filtered off and the filtrate is concentrated. Approximately 500 ml of hexane are added with stirring to the residue. The precipitate that forms is filtered off with suction, and the filtrate is concentrated. This gives 29 g of an oily liquid. Column chromatography (mobile phase: hexane/dichloromethane 8:2, later 1:1, adsorbent material: silica gel) gives 7.2 g of product..

^{1}H NMR ($CDCl_3$) δ = 4.0 (t, 2H,., OCH_2), 3.4 (t, 4H, $BrCH_2$), 2.3 (t, 2H, CH_2CO), 1.2-1.9 (4m, 26H, aliphat. CH_2) ppm.

Example 55b

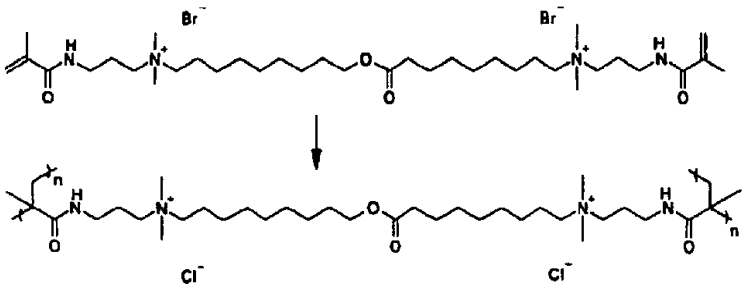


7.6 g (17.2 mmol) of the product from Example 55a are dissolved in 100 ml of DMF. 5.8 g (34.4 mmol) of N-(3-N,N-dimethylaminopropyl)methacrylamide are added, and the mixture is heated to 50°C. After 3 days of stirring at 50°C, the reaction has ended. The DMF is distilled off using an oil pump. The distillation residue is dissolved in dichloromethane and slowly stirred into hexane. After the mixture has been stirred for some, the clear supernatant is decanted off (discarded). The residue is once more reprecipitated as described, and then dissolved in water and freeze-dried.

Yield: 12.2 g

H NMR ($CDCl_3$) δ = 5.5 and 5.8 (2s, 4H, olefin. H), 4.1 (t, 2H,., OCH_2) 3.0-3.4 (2m, 12H, NCH_2), 3.1 (s, 12 H, N-CH_3), 2.4 (t, 2H, CH_2CO), 1.4-2.0 (3m, 30H, aliphat. CH_2), 2.0 (s, 6H, CH_3), ppm.

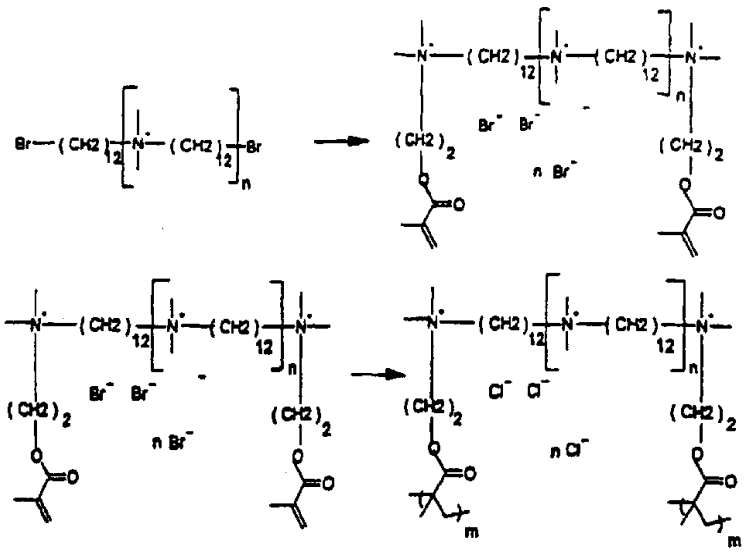
Example 55c



12.2 g of the product from Example 55b are dissolved in 80 ml of water and, under nitrogen, heated to 70°C. Polymerization is initiated by addition of 120 mg of 2,2'-azobis[2(2-imidazolin-2-yl)propane] dihydrochloride. The polymerization starts after 20 minutes. After 30 minutes, 20 ml of water and 120 mg of polymerization initiator are added, and the reaction mixture is homogenized using an Ultraturrax. After a further 4 hours of stirring at 70°C, 100 ml of saturated NaCl solution are added. The mixture is allowed to stand overnight and then filtered off with suction through a G4 frit and stirred with another 100 ml of saturated NaCl solution. The mixture is then filtered off with suction.. Following this, it is subjected to ultrafiltration until the permeate is free of NaCl. The retentate is freeze-dried.

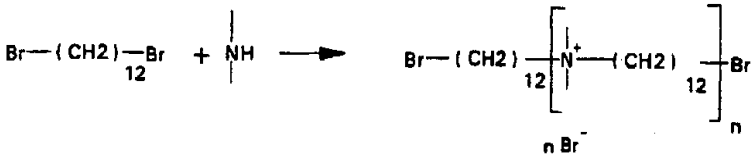
Yield: 9.6 g

Example 56



The procedure of Example 45b is employed, but using 2-dimethylamino-ethyl acrylate. n = 2.

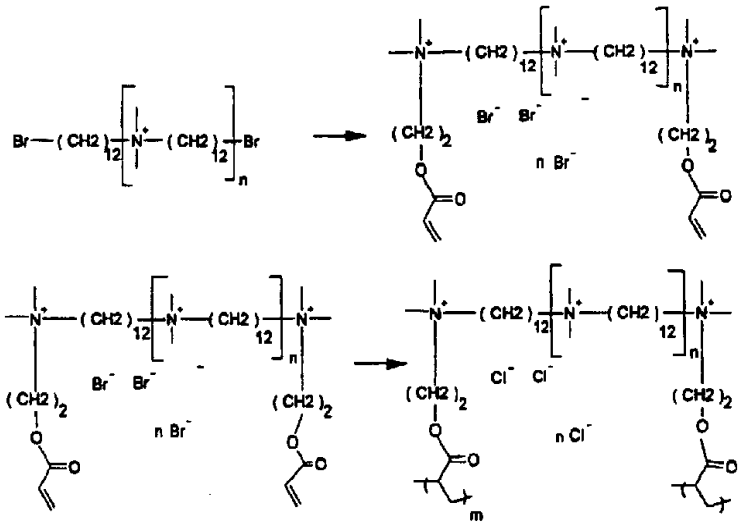
Example 57a



35 g of dibromododecane and 3.3 g of dimethylamine hydrochloride are initially charged in 70 ml of abs. DMF at room temperature. 3.3 g of NaH (80%, in oil) are added a little at a time, at 25-35°C. The mixture is then stirred at room temperature for 5 hours and at 60°C for 6 hours. After cooling, the mixture is stirred into aqueous HBr and extracted with isohexane. The mixture is subsequently extracted with dichloromethane. The dichloromethane is concentrated. The residue is repeatedly triturated with diethyl ether and dried under reduced pressure, giving a residue of 41.7 g.

Evaluation of the ratio of the CH_2Br protons to the N-CH_3 protons gives an average value of 3-4 for n.

Example 57b



31 g of the mixture from Example 57a, 18.6 g of N,N-dimethylaminoethyl acrylate and 0.5 g of hydroquinone are initially charged in 50 ml of DMF. The mixture is then stirred at 75°C for 20 hours. The DMF is distilled off under reduced pressure. The residue is repeatedly triturated with acetone. Under nitrogen, the viscous brown residue (37 g) is heated in water to 50°C, whereupon it dissolves. Polymerization is initiated by addition of 2,2'-azobis[2(2-imidazolin-2-yl)propane] dihydrochloride and carried out by the customary method. Saturated NaCl solution is then added. The precipitate that is formed after stirring is filtered off with suction and washed free of NaCl, and the gel-like material is subjected to ultrafiltration. The residue is freeze-dried.
Yield: 21 g

Demonstration of the superiority of the polymers according to the invention compared to cholestyramine in the in vivo test:

The superiority of the polymers according to the invention compared to cholestyramine could be shown using the in vivo model "golden Syrian hamster". To this end, the polymers according to the invention from Examples 2b and Example 3b were tested in an exemplary manner by

comparison with cholestyramine. For this purpose, the experiments described below were carried out.

Nine groups of Syrian golden hamsters were fed for 21 days with different feed. Cholesterol, the compound from Example 2b, the compound from Example 3b and cholestyramine were mixed into the feed and offered ad libitum to the animals. None of the treatment groups showed any irregularities in feed consumption. The development of the body weight was comparable for all groups.

Groups	Feed	Number of animals
Grp. 1:	Control Teklad 8604	n=6
Grp. 2:	T 8604 + 0.1% cholesterol	n=5
Grp. 3:	T 8604 + 0.1% cholesterol + 0.50% cholestyramine	n=5
Grp. 4:	T 8604 + 0.1% cholesterol + 1.00% cholestyramine	n=6
Grp. 5:	T 8604 + 0.1% cholesterol + 0.25% Example 3b	n=5
Grp. 6:	T 8604 + 0.1% cholesterol + 0.50% Example 3b	n=5
Grp. 7:	T 8604 + 0.1% cholesterol + 1.00% Example 3b	n=6
Grp. 8:	T 8604 + 0.1% cholesterol + 0.25% Example 2b	n=5
Grp. 9:	T 8604 + 0.1% cholesterol + 0.50% Example 2b	n=5

After the 21 days had passed, the plasma cholesterol level and the 7-α-hydroxylase activity were determined:

A) Determination of the plasma cholesterol level

The plasma cholesterol level was determined using the plasma cholesterol essay from Sigma (order No. 352-100, catalog from 1996) and the cholesterol calibrator (order No. C7921, catalog from 1996).
Table 1 shows the results of the determination.

Table 1.

Group	Plasma cholesterol [mg/dl]
1	103
2	173
3	155
4	137
5	143
6	102
7	75
8	130
9	126

Whereas 0.5% cholestyramine (group 3) effected a plasma cholesterol reduction of only 10%, it was possible to effect a 41% reduction and a 27% reduction with the same dose of the compound from Example 3b (group 6) and with the same dose of the compound from Example 2b (group 9), respectively.

B) Determination of the 7-α-hydroxylase activity

Preparation of 7-α-hydroxylase microsomes

New preparation: (from Journal of Biol. Chem. Vol. 205, 1990, pp. 4541-4546: Purification of 7-alpha hydroxylase from Human and Rat Liver...)

Buffer A:
100 mM dipotassium hydrogen phosphate pH 7.4 (17.4 g/l)
1.5% potassium chloride (15 g/l)
50 mM sodium fluoride (2.1 g/l)

Buffer B:
100 mM dipotassium hydrogen phosphate pH 5.4 (4.35 g/250 ml)
5 mM DTT (dithiothreitol) (0.1925 g/250 ml)
1 mM EDTA (ethylenediamine tetracetate, Na salt 0.0925 g/250 ml)
50 mM sodium fluoride (0.525 g/250 ml)

Preparation procedure at 4°C

The liver is removed and washed in cold 0.9% strength aqueous sodium chloride solution.

The required small piece of liver is transferred into an ice-cooled UC tube. (Kontron polycarbonate 38.5 ml)

The liver is comminuted with 5 ml of buffer A per g of liver using an Ultraturrax. Small Turrax rod, setting: red = 13,500 min^{-1}

The homogenate is centrifuged at 10,000 × g, 4°C, for 20 min.

UC: TFT 55.38 = 10,000 rpm
Sorvall: SA34 = 10,000 rpm

The supernatant is transferred into a clean UZ tube and the pellet is discarded. The tube is filled with buffer A, and its weight is adjusted (± 0.05 g)
Centrifugation at 100,000 × g, 1.5 hours, 4°C
TFT 55.38 = 32,000 rpm

The supernatant is discarded.
The pellet is then taken up in 1 ml of buffer B per g of liver
Small Turrax rod, setting: yellow = 8000 min^{-1}
(If it is not possible to homogenize the pellet without foaming using the Ultraturrax, a 22 G cannula should be used and the suspension should be drawn up and ejected 2-3 times.)

Aliquots of 500 µl are shock-frozen in liquid nitrogen and stored at -80°C. Additionally one 100 µl aliquot for protein determination.

Determination of the 7-α-hydroxylase activity in liver microsomes using HPLC

Microsome samples are carefully drawn up and ejected twice using a 1 ml syringe with cannula No. 18 (26 G), 200 µl of microsome solution are used

in the case of hamsters and 75 µl of microsome solution in the case of rats. The remaining microsome solution is kept for protein determination (according to BCA, diluted 1:20).

Batch in thermomixer 37°C, with constant shaking (position 12).

200 µl of microsome solution are transferred into an Eppendorf tube and the tube is filled with buffer 1 to 1 ml (determination in duplicate). Addition of 20 µl of cholesterol - cyclodextrin solution (CD):
incubation for 10 minutes (in the case of rats without CD)
Addition of 200 µl of freshly prepared regeneration solution: incubation for 20 minutes
Addition of 60 µl of stock solution, brief shaking
100 µl of 0.1% cholesterol oxidase solution are added using a pipette,
incubation for 15 minutes
The solution is then transferred into a ground-glass tube which had been initially charged with 2 ml of ethanol.
The tube is vortexed.
Now 3 extractions with 6 ml of petroleum ether.
In each extraction, the tube is shaken/vortexed for 1 minute and then centrifuged for approximately 5 minutes at 4°C, 1000 rpm, the supernatants are combined in another tube and in each case evaporated in a heating block at 40°C, with excess of air.
The dried extract is taken up in 1 ml of petroleum ether and transferred into an Eppendorf tube.
The mixture is once more evaporated.
The extract is taken up in 120 µl of 60% acetonitrile/30% methanol/10% chloroform, shaken at 40°C in a thermomixer for 10 minutes, vortexed and then briefly centrifuged.
The extracts are transferred into plastic vials for HPLC which are closed using aluminum lids.
As standard: 30 µl 7 hydroxycholesterol solution + 30 µl of 7-α-hydroxy-cholesterol solution (oxidized), mixed with 60 µl of solvent.
Mobile phase for HPLC: 70% acetonitrile/30% methanol (possibly 80% acetonitrile/20% methanol)
Run time: 40 minutes, 240 nm, 0.01 AUFS.

Calculation of the peaks:

Internal standard 7-α-hydroxycholesterol = 1 µg of the material employed
Area standard for example = 496543 = 1 µg
Area sample for example = 68807 = X
X = 0.139 µg of 7-α-hydroxycholesterol

Calculation of the amount of protein used:
For example 10 mg/ml (according to protein determination) × 200 µl (protein solution employed): 1000 = 2 mg of protein
Converted into nmol of enzyme activity per mg of protein per hour (7 alpha MW 403 g/mol)

0.139 µg X 3 (because only incubated for 20 min): amount of protein used, for example, 2 mg = 0.208 µg X 1000 = 208 ng/mg/h

403 ng = 1 nmol
208 ng = 0.516 nmol

0.516 nmol/mg/h

Buffer 1 (to be stored at 4°C)
100 mM dipotassium hydrogenphosphate pH 7.2 (8.7 g/500 ml)
50 mM NaF (1.05 g/500 ml)
5 mM DTT (0.385 g/500 ml)
1 mM EDTA (0.186 g/500 ml)
20% glycerol (100 g/500 ml)
0.015% CHAPS (3-[(cholamide)dimethylammonio]-1-propanesulfonate (0.076 g/500 ml)

Buffer 2 (to be stored at 4°C)
10 mM dipotassium hydrogenphosphate pH 7.4 (0.174 g/100 ml
1 mM DTT (0.015 g/100 ml)
20% glycerol (20 g/100 ml)

Cholesterol - cyclodextrin solution (to be stored at 4°C)
1 mg/ml of cholesterol in 45% hydroxypropyl cyclodextrin
(4.5 g of cyclodextrin are stirred with approximately 3 ml of doubly distilled water in a 10 ml measuring flask until it is dissolved + 10 mg of cholesterol are stirred overnight in a cooled-storage room (very poor solubility), and the flask is then filled to 10 ml).

Regeneration buffer (always fresh!)
10 mM Na isocitrate (25.8 mg/2 ml)
10 mM magnesium chloride (20.3 mg/2 ml)
1 mM NADPH (8.3 mg/2 ml) (β-nicotinamide adenine dinucleotide phosphate, reduced Na_4 salt)
0.15 U isocitrate deydrogenase (50 µl/2 ml)

Isocitrate dehydrogenase (-20°C)
One bottle (50 U) is to be taken up in 1 ml of buffer 1 + 600 µl of glycerol.

Stop solution (to be stored at -20°C)
20% cholic acid Na salt which contains 1 µg of 7-OH-CH (internal standard) per 60 µl.
A 1 mg 7-OH-CH (7-hydroxycholesterol)/ml solution in ethanol is prepared. 1000 mg of cholic acid are dissolved in 3 ml of distilled H_2O, 83.33 µl of 1 mg/ml 7-OH-CH solution is added and the solution is made up with ethanol to 5 ml.
(83.33 µl = 83.33 µg in 5 ml of stop solution = 1 µg in 60 µl of stop solution).

0.1% cholesterol oxidase (to be stored at -20°C)
1 mg/ml solution in buffer 2.

Table 2 shows the results of the determination of 7-α-hydroxylase activity.

Table 2.

Group	Plasma cholesterol [mg/dl]
1	83
2	100
3	119
4	198
5	203
6	307
7	536
8	203

9	380

Whereas 0.5% cholestyramine (group 3) caused an increase of 7-α-hydroxylase activity of only 19%, an activity increase of 207% and 280% could be effected using the same dose of the compound from Example 3b (group 6) and the compound from Example 2b (group 9), respectively.

The determination of the adsorption activity of the polymers according to the invention with respect to bile acid can be carried out in an in vitro model. For this purpose, the substance is stirred or shaken for a certain time with glyco- and taurocholic acid in an aqueous salt solution which mimics the conditions in the small intestine, and the amounts of bile acids which remain in the solution are determined after filtration or centrifugation using HPLC. The strength of the adsorption is determined by stirring the residue with aqueous salt solution and determining the liberated bile acids in the salt solution using HPLC.

Bile acid desorption
Test conditions

1: Solutions for use

a: Standard solution: as in the determination of adsorption

b: Salt solution: standard solution without bile acids

NaCl	8.00 g/l	137.00 mmol/l
KCl	0.20 g/l	2.70 mmol/l
Na_2HPO_4, $2H_2O$	1.40 g/l	8.00 mmol/l
KH_2PO_4	0.20 g/l	1.45 mmol/l

2: Practice

The polymer sample is weighed and the standard solution is added to give a concentration of 5 mg of sample/ml of standard solution. (50 mg/10 ml). This solution is stirred at room temperature for 2 hours.

It is then filtered using membrane filtration (0.45 µm).

A: Filtrate: determination of adsorption

B: Filter cake

The filter with the filter cake is transferred into a glass vessel.

A volume of salt solution identical to that of the standard solution is added.

The mixture is stirred at room temperature for 2 hours.

It is then filtered using membrane filtration.

a: Filtrate: determination of desorption

b: Filter cake: procedure B is repeated.

Some polymer samples are difficult to filter or adhere to the wall. In this case, the solution is, instead of being filtered, centrifuged at 4500 rpm.

3: HPLC

Column: RP 18 Licrospher 5 µm (250 × 4 mm)

Mobile phase: 900 ml of acetonitrile

1100 ml H_2O

6.8 g of tetrabutylammonium hydrogen sulfate

Flow rate: 1 ml/min

Detection: 210 nm

Injection volume: 5 µl

Retention time: GCA 4 min

TCA 5 min

Standard and samples are each injected 3 times.

4: Calculation

$$Ads\% = \frac{\text{area standard - area sample}}{\text{area standard}} * 100$$

Bile acid desorption

Test conditions

1: Preparation of the salt solution

a) Stock solution:

NaCl	160 g
KCl	4 g
$Na_2HPO_4, 2H_2O$	28 g
KH_2PO_4	4 g
per 1 l of H_2O	

b) Solution for use - standard

The stock solution is diluted 1:20 with water and the bile acid salts are added.

Bile acid salts: 8 mmol/l

Na glycocholate/Na taurocholate	= 2/l	
Na glycocholate (bCA)	2.60 g/l	5.33 mmol/l
Na taurocholate (TCA)	1.43 g/l	2.67 mmol/l
NaCl	8.00 g/l	137 mmol/l
KCl	0.20 g/l	2.7 mmol/l
$Na_2HPO_4, 2H_2O$	1.40 g/l	8.0 mmol/l
KH_2PO_4	0.20 g/l	1.45 mmol/l

2: Adsorption

The polymer sample is weighed and the standard solution is added to give a concentration of 5 mg of polymer/ml of standard.

(10 mg/2 ml)

The solutions are stirred at room temperature for 2 hours.

The solutions are then filtered (0.2 µm)

Comparison: colestyramine

The pH of the filtrate is checked.

3: Determination of bile acids

GCA and TCA determination by HPLC (see determination of adsorption)

4: Adsorption

$$Ads\% = \frac{\text{area standard - area filtrate A}}{\text{area standard}} * 100$$

5: Desorption

$$Des\% = \frac{\text{area a} * 100}{\text{area standard - area filtrate A}}$$

these measurements gave the following values:

GCA: glycocholic acid
TCA: taurocholic acid

Com-pounds	Mean value for n	Adsorption	Adsorption	Desorption	Desorption
from	[-Cl2-N-]n	GCA %	TCA %	GCA %	TCA %
Cholestyra-mine		54.3	75.0	42.9	22.0
Example 57b	3-4	82.0	91.6	16.7	7.1

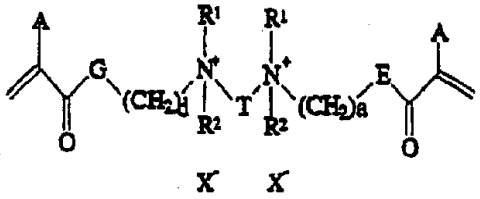
The best results were achieved for average values for n in the range from 3 to 4.

Throughout this specification and the claims which follow, unless the context requires otherwise, the word "comprise", or variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated integer or group of integers or steps but not the exclusion of any other integer or group of integers or steps.

The reference to any prior art in this specification is not, and should not be taken as, an acknowledgement or any form of suggestion that the prior art forms part of the common general knowledge in Australia.

The claims defining the invention are as follows:

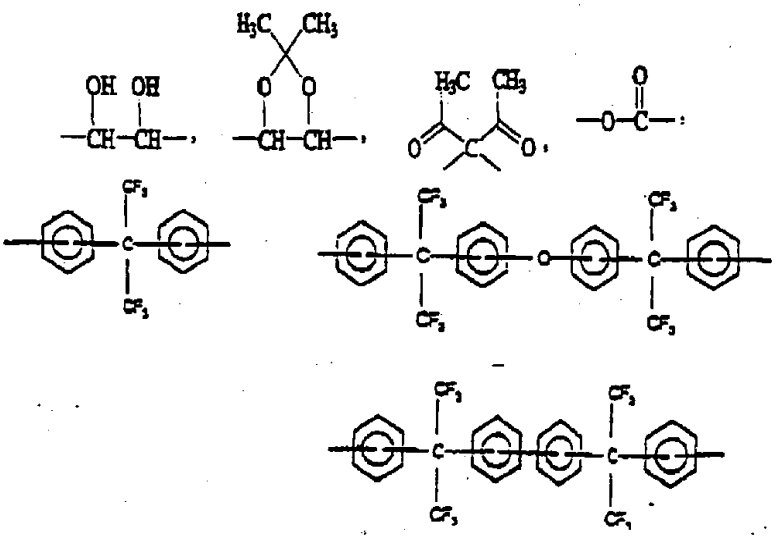
1. A compound of the formula II



(II)

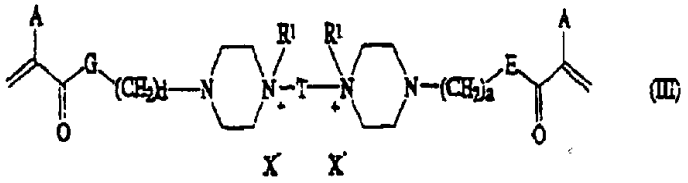
in which

A	is hydrogen or C_{1-9}-alkyl
G and E	independently of one another are O or NH
d and a	independently of one another are an integer from 2 to 10
R^1 and R^2	independently of one another are C_{1-3}-alkyl
T	is C_{2-200}-alkylene, which may be interrupted by phenylene,



or 1 to 10 not directly adjacent oxygen atoms or groups $-N^+R^1R^2-$ where R^1 and R^2 independently of one another are C_{1-9}-alkyl, and X^- is an acid anion.

2. A compound of the formula III



(III)

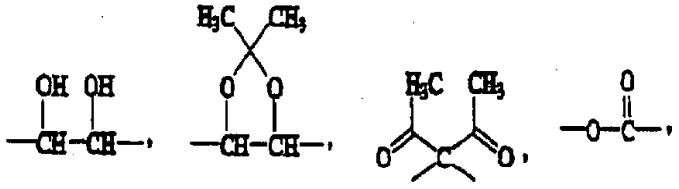
in which A, G, d, a, R^1, T, E and X are as defined in claim 1.

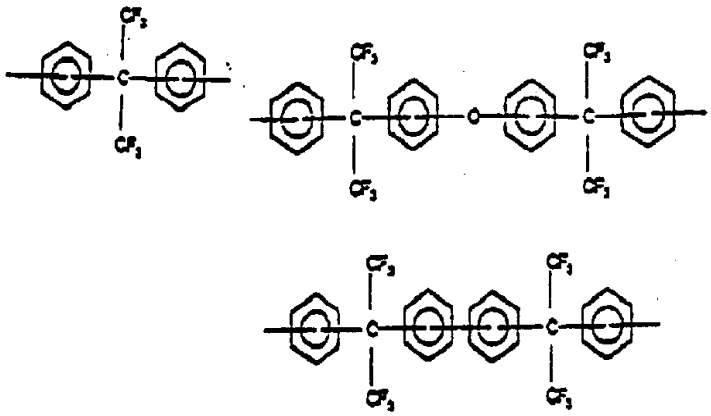
3. The compounds as claimed in either claim 1 or claim 2, having one or more of the following features:

- A is hydrogen or C_{1-4}-alkyl
- d and a are integers from 2 to 5
- R^1 and R^2 are C_{1-4}-alkyl
- X^- is halide.

4. The compounds as claimed in anyone of claims 1-3, wherein T is selected from

- linear or branched C_{4-50}-alkylene
- linear or branched C_{2-22}-alkylene which is interrupted by

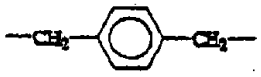


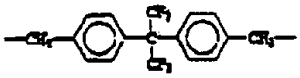


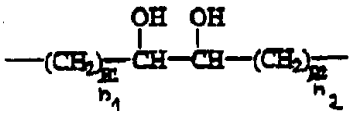
- linear or branched C_{4-16}-alkylene which is interrupted by 1 to 7 not directly adjacent oxygen atoms,
- linear or branched C_{20-140}-alkylene which is interrupted by 2 to 8 not directly adjacent groups $-N^+R^1R^2-$ where R^1 and R^4 are C_{1-4}-alkyl.

5. Compounds according to anyone of claims 1-4, wherein T is selected from

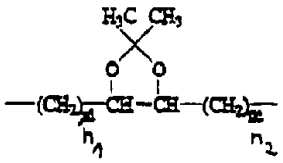
- linear or branched C_{6-30}-alkylene



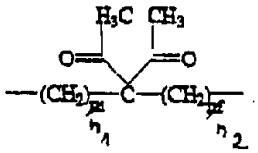




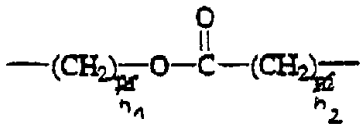
where n_1 and n_2 independently of one another are integers from 4 to 10,



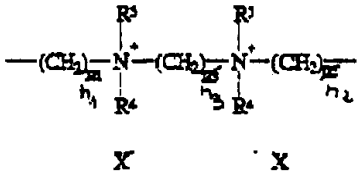
where n_1 and n_2 independently of one another are integers from 4 to 10,



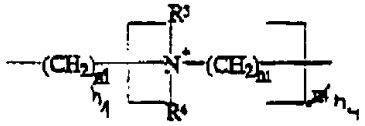
where n_1 and n_2 independently of one another are integers from 4 to 10,



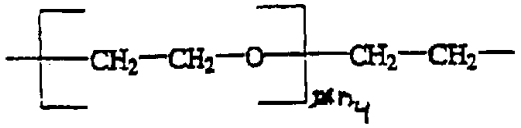
where n_1 and n_2 independently of one another are integers from 6 to 12,



where
R^1 and R^2 are C_{1-3}-alkyl, X^- is halide,
n_1 and n_2 independently of one another are integers from 6 to 16 and n_3 is an integer from 2 to 6,

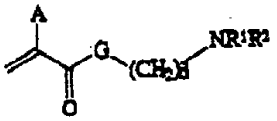


where R^1 and R^2 are C_{1-3}-alkyl, X^- is halide, n_1 is a number from 8 to 16 and n_4 has an average value of from 1 to 10,

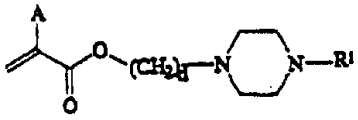


where n_4 has an average value of from 1 to 6.

6. A process for preparing compounds of the formula II and/or III as claimed in anyone of claims 1 to 5 which comprises reacting compounds of the formulae IV or VI



(IV)



(VI)

with compounds of the formula V

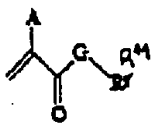
X - T - X (V)

where A, G, d, R^1, R^2, T are as defined and X is halogen.

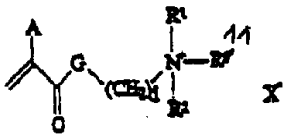
7. A crosslinked polymer from the monomeric basic structural units A1, A2 and A3, the total amount of which is 100% by weight,

a1: from 0.5 to 100% by weight of difunctional basic structural units of the formulae II and/or III as claimed in any of claims 1 to 5, or mixtures thereof, as component A1,

a2: from 0 to 99.5% by weight of monomers selected from compounds of the formulae



or

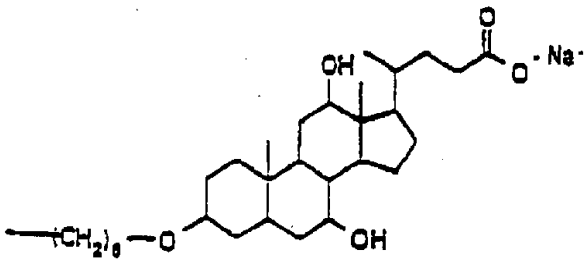


or  or 

or  or 

or 

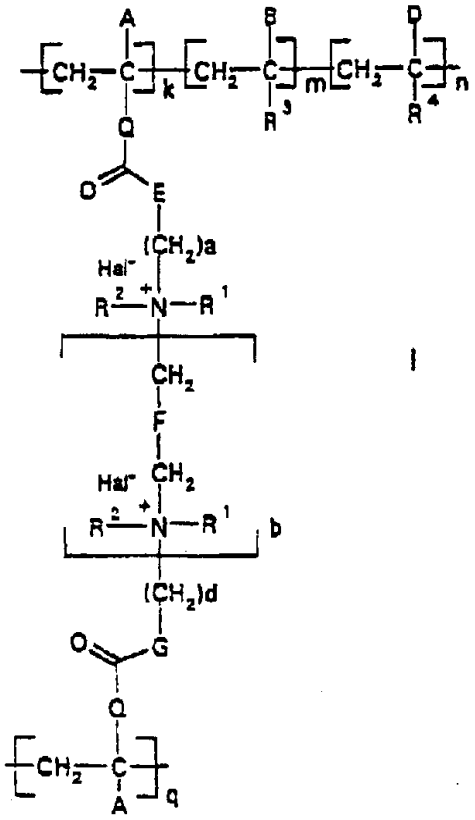
in which the radicals A, G, R^1, R^2 and the index d are as defined in claim 1 and R^{11} is selected from the group consisting of hydrogen, C_{1-9}-alkyl and



or mixtures thereof
or polyvinylamine
as component A2,

a3: from 0 to 99.5% by weight of other copolymerizable basic structural units as component A3.

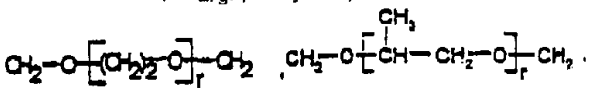
8. A crosslinked vinyl polymer of the formula I

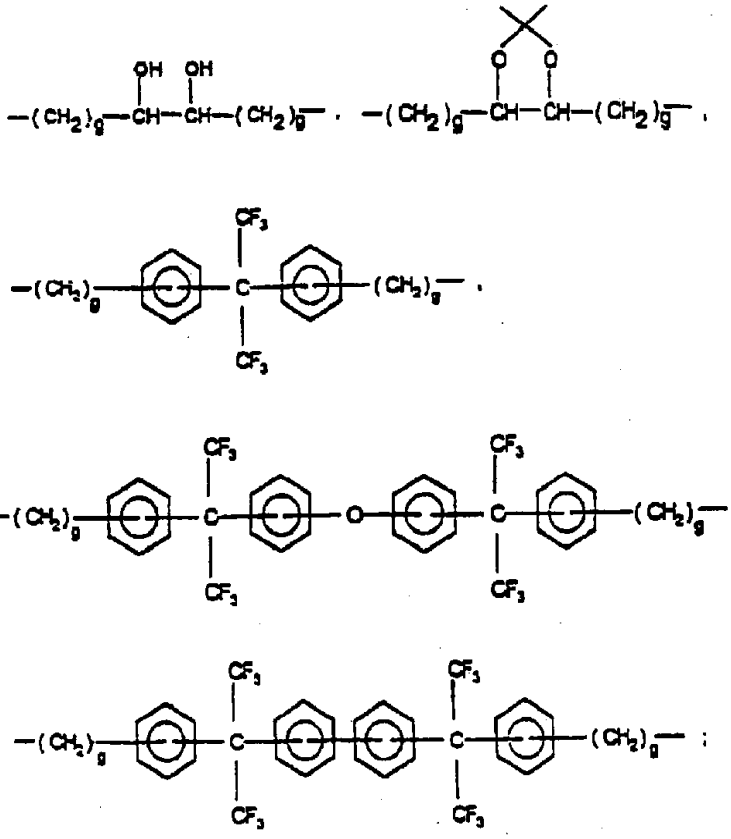


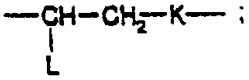
I

in which:

A, B and D	independently of one another are H, $CH_3(CH_2)_f$;
f	is from 0 to 8;
E and G	independently of one another are O or NH;
F	is $(CH_2)_g$, phenylene;





	g	is from 0 to 36;
5	r	is from 0 to 36;
	K	is NH, CH_2NH or CH_2CH_2NH;
	Q	is a bond,  ;
	L	is H, CH_3;
10	R^1 and R^2	independently of one another are (C_1-C_8)-alkyl;

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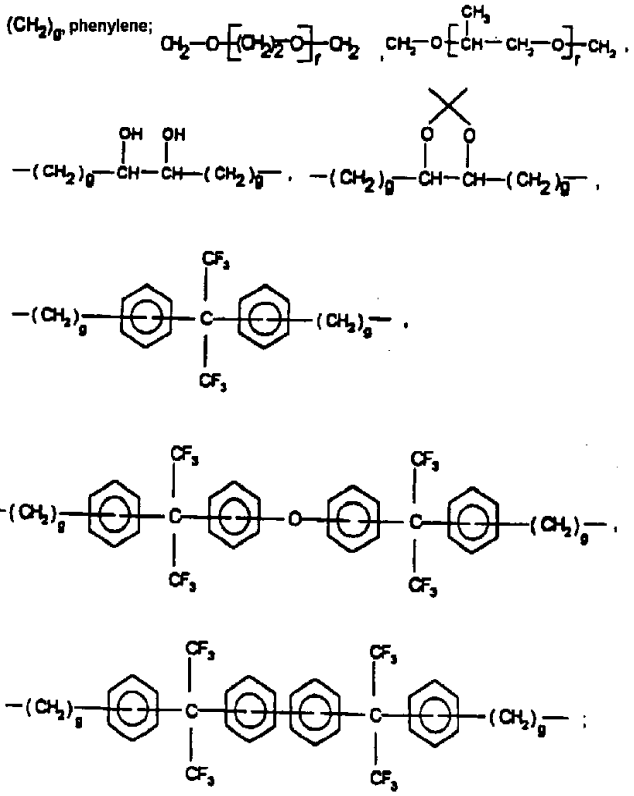
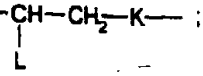
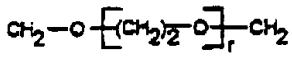
F $(CH_2)_g$, phenylene; 

	g	is from 0 to 36;
	r	is from 0 to 36;
5	K	is NH, CH_2NH or CH_2CH_2NH;
	Q	is a bond,  ;
	L	is H, CH_3;
	R^1 and R^2	independently of one another are (C_1-C_8)-alkyl;
10	R^3 and R^4	independently of one another are NH_2, NHR^5, NR^5R^6, $^+NH_2Cl^-$, $^+NH_2R^5Cl^-$, $^+NHR^5R^6Cl^-$, $^+NR^5R^6R^7Cl^-$, $(CH_2)_wNH_2$, $(CH_2)_wNHR^5$, $(CH_2)_wNR^5R^6$, $(CH_2)_w{}^+NH_3Cl^-$, $(CH_2)_w{}^+NH_2R^5Cl^-$,

where the sum of k + q + m + n equals 1 and k and q independently of one another are at least 0.005.

9. The cross-linked vinyl polymer as claimed in claim 8, wherein one or more of the radicals has or have the following meaning:

A, B and D	independently of one another are H, $CH_3(CH_2)_f$;
F	is from 0 to 8;
E and G	are NH;
F	is $(CH_2)_g$, phenylene;



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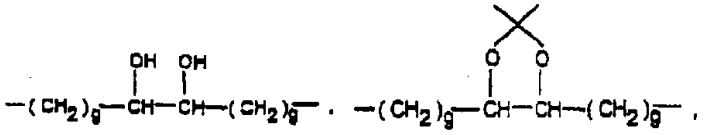

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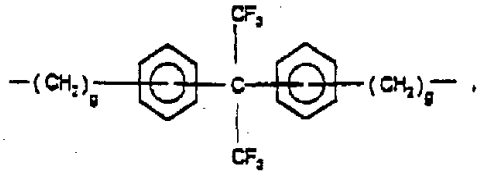

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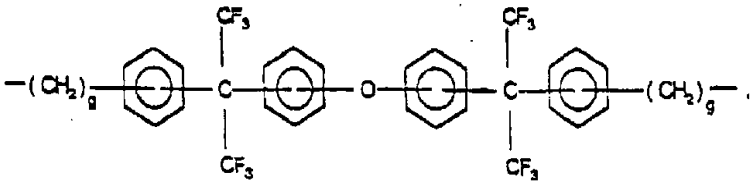

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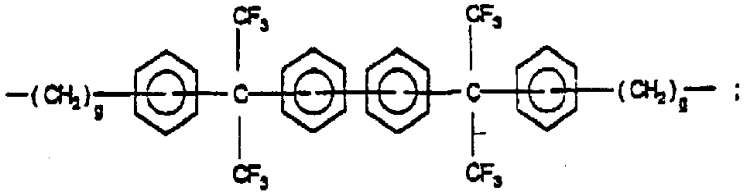
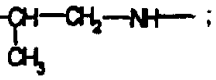


;

g	is from 8 to 34;
r	is from 0 to 18;
Q	is a bond,  ;

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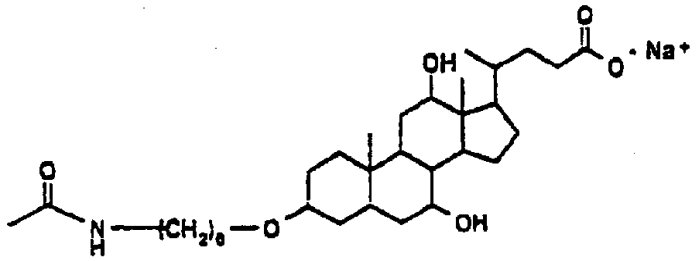
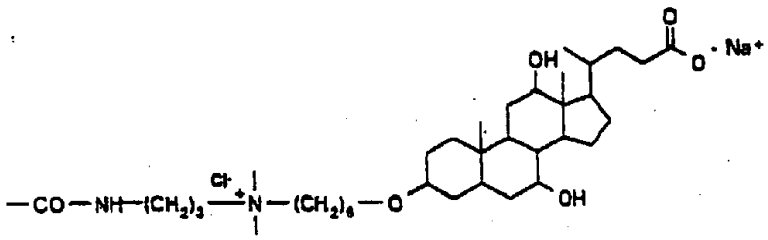
R^1 and R^2	are CH_3, $-CH_2-CH_3$;
R^3 and R^4	independently of one another are NH_2, $^+NH_3Cl^-$, CH_2-NH_2, $CH_2-^+NH_3Cl^-$, $-CONHR^8$





R^8	is $(CH_2)_w{}^+N(CH_3)_3Cl^-$;
w	is from 1 to 8;
a and d	are each 3;
b	is 1;
Hal^-	is Cl^-, Br^-, I^-;
k	is at least 0.1
q	is at least 0.1

where the sum of k + q + m + n equals 1.

10. The cross-linked vinyl polymer as claimed in either claim 8 or claim 9, wherein one or more of the radicals has or have the following meaning:

A, B and D	independently of one another are H, CH_3;
Q	is a bond;
E and G	are NH;
F	is $(CH_2)_g$;

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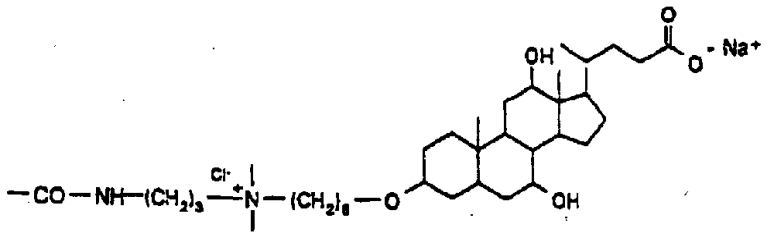
g	is from 8 to 22;
R^1 and R^2	are CH_3;
R^3 and R^4	are



a and d	are each 3;
b	is 1;
Hal^-	is Cl^-, Br^-;
k	is at least 0.1
q	is at least 0.1
m	is from 0 to 0.8;
n	is 0;

where the sum of k + q + m + n equals 1.

11. A process for preparing polymers as claimed in anyone of claims 7 to 10, which comprises either homopolymerizing or copolymerizing, with other vinylic monomers, such as allylamine hydrochloride, an appropriate bis(meth)acrylate monomer or bis(meth)acrylamide monomer, which contains at least one quaternary ammonium center in aqueous medium in the presence of a water-soluble radical initiator, in a free-radical reaction.

12. A process for preparing polymers as claimed in anyone of claims 7 to 10, which comprises reacting an appropriate bis(meth)acrylate monomer or bis(meth)acrylamide monomer which contains at least one quaternary ammonium center in a Michael addition with an amino-group-containing vinylic polymer such as polyvinylamine in basic medium in a polymer-analogous manner.

13. A medicament, comprising at least one polymer as claimed in anyone of claims 7 to 10 and one or more other lipid-lowering active compounds, customary excipients, auxiliaries and/or additives.

14. A process for preparing a medicament as claimed in claim 13 by mixing the components.

15. The use of polymers as claimed in anyone of claims 7 to 10 for preparing pharmaceutical preparations for use as an antihyperlipidemic, for the treatment of disorders of lipid metabolism, for the treatment of hyperlipidemia, for the concentration-dependent reduction of bile acid sorption in the gastrointestinal tract and/or for the nonsystemic lowering of elevated serum cholesterol and blood fat values for the prevention of arteriosclerotic manifestations.

16. A mixture of the polymers as claimed in anyone of claims 7 to 10 with other polymers and/or biologically active substances.

17. A method for the treatment of disorders of lipid metabolism, for the treatment of hyperlipidemia, for the concentration-dependent reduction of bile acid sorption in the gastrointestinal tract and/or for the nonsystemic lowering of elevated serum cholesterol and blood fat values for the prevention of arteriosclerotic manifestations which comprises administering to a subject in need of such treatment or prevention at least one polymer as claimed in any one of claims 7 to 10 or a medicament according to claim 13.

18. Use of polymers as claimed in anyone of claims 7 to 10 or a medicament according to claim 13 as an antihyperlipedmic.

19. Compounds of the formula I or III, or processes for their preparation, substantially as hereinbefore described with reference to the Examples.

20. Crosslinked polymers from the monomeric basic structural units A1, A2 and A3 or cross-linked vinyl polymers of the formula I, processes for their preparation or medicaments or uses thereof involving/containing them, substantially as hereinbefore described with reference to the Examples.

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AVENTIS RESEARCH AND TECHNOLOGIES GMBH & CO KG
by its Patent Attorneys
DAVIES COLLISON CAVE