

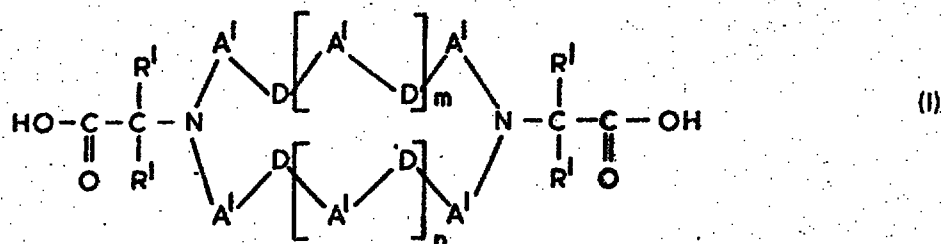
SPECIFICATION

Macrocyclic compounds and their preparation

The invention relates to macrocyclic compounds which can be used, for example, in a process for cleaning a well penetrating an underground formation and/or cleaning formation parts in the vicinity of the said well, and to the preparation of such compounds.

Such a cleaning process wherein the well and/or the formation parts in the vicinity of the well are contacted with an aqueous composition suitable for dissolving barium sulphate scale forms the subject of parent U.K. Patent No. 2024822.

The present invention provides macrocyclic compounds of the general formula:



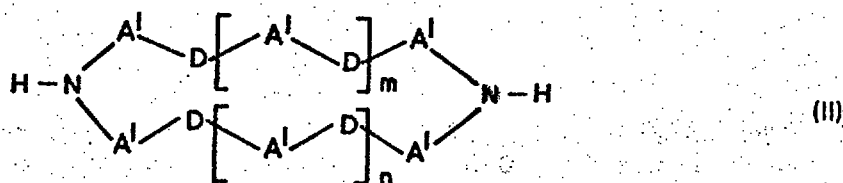
wherein each A¹ which may be the same or different represents a hydrocarbon radical having up to 12 carbon atoms and each D which may be the same or different represents an oxygen or a sulphur atom or a hydrocarbon radical having up to 12 carbon atoms or a group N—R², R² representing a hydrogen atom or a hydrocarbon radical having up to 12 carbon atoms, a hydrocarbonsulphonyl radical having up to 12 carbon atoms, an alkoxycarbonyl or alkoxycarbonyl-methylene radical having up to 4 carbon atoms or a carboxymethylene radical, at least two of the said D members representing an oxygen or a sulphur atom or a group N—R², and each R¹ which may be the same or different represents a hydrogen atom or an alkyl group having up to 6 carbon atom or a carboxy group and m and n are integers from 0 to 5 inclusive, the macrocyclic compound according to the general formula I being compatible with a barium ion, as hereinafter defined, and salts thereof—with the exception of 1,10-di(carboxymethyl)-1,10-diaza-4,7,13,16-tetraoxa-cyclooctadecane and salts thereof.

The expression "the macrocyclic compound of the general formula I being compatible with a barium ion" is used to denote that the macrocyclic compound of the general formula I is capable of accommodating a barium ion in the intra-molecular cavity. The expression "salt of a macrocyclic compound of the general Formula I" is used to denote a carboxylate salt of this macrocyclic compound.

Preferred compounds according to formula I are those wherein A¹ represents a hydrocarbon radical having in the range of from 2 to 8 carbon atoms, or a 1,2-phenylene radical; D represents an oxygen atom or a group N—R² wherein R² represents an alkyl group of up to 8 carbon atoms, a hydrocarbonsulphonyl radical of up to 8 carbon atoms or an alkoxycarbonyl radical of up to 4 carbon atoms; at least 4 of the said D members representing an oxygen atom; and each R¹ represents a hydrogen atom or an alkyl group having up to 4 carbon atoms or a carboxy atom and m and n are in the range of from 1 to 3.

More preferred compounds according to formula I are those wherein A¹ represents an ethylene, diethylene, triethylene or tetra ethylene radical, particularly an ethylene radical; D represents an oxygen atom or a group N—R² wherein R² represents an alkyl group of up to 4 carbon atoms, particularly a methyl group a hydrocarbonsulphonyl radical of up to 4 carbon atoms or a methoxy- or ethoxycarbonyl radical; at least 4 of the said D members representing an oxygen atom, and each R¹ represents a hydrogen atom or a methyl, ethyl or carboxy group and m and n are 1 or 2.

The salts of the macrocyclic compounds according to the general formula I may be prepared in a manner known per se by reacting the corresponding macrocyclic compound of the general formula:



with a salt of an alpha-halocarboxylic acid, such as 2-chloroacetic acid, 2-bromoacetic acid, 2-chloro- or 2-bromobutyric acid, in the presence of a base. Examples of suitable salts of, for instance, 2-chloroacetic acid and 2-bromoacetic acid are alkali metal salts. Suitable bases comprise alkali metal hydroxides, for example lithium hydroxide and potassium hydroxide. It is also possible to react a macrocyclic compound according to the general formula II with an alpha-halocarboxylic acid in the presence of a base, and preferably in the presence of an excess of a suitable base. Acidification of an aqueous solution of the salts of the macrocyclic compounds according to the general formula I yields the macrocyclic compounds according to the general formula I. Further acidification gives quaternary

ammonium salts of the macrocyclic compounds of formula I, which inner salts are also considered to be within the scope of the present invention. In the event that at least one of the groups R¹ represents a carboxy group, it was found convenient to use a halomalononic ester which after subsequent hydrolysis gives the macrocyclic compound according to the general formula I.

5 Example 1

The compound 1,10-di(alpha-ethylcarboxymethyl)-1,10-diaza-4,7,13,16-tetraoxacyclooctadecane was prepared *in situ*, i.e. in the presence of barium sulphate (3 moles per litre) by reacting 1,10-diaza-4,7,13,16-tetraoxacyclooctadecane (0.1M) and 2-chlorobutyric acid (0.2M) and lithium hydroxide (0.8M) at 70°C. The compound was characterised by ¹H and ¹³C nuclear magnetic resonance technique in D₂O.

The following signals were assigned:

¹H NMR (H₂O as ppm):

−1.2 (m, 16H; 1,2); −1.8 (t, 2H, 3); −2.1 (t, 8H, 4); −3.2 (m, 4H, 5); −4.0 (t, 6H, 6) ppm.

¹³C NMR (external reference):

183.4 (7); 73.2 (1, 2, 3); 54.4 (4); 23.4 (5); 14.6 (6) ppm.

The compound was formed in about 14% yield.

Example 11

20 The novel compound bis(dicarboxymethyl)-1,10-diaza-4,7,13,16-tetraoxacyclooctadecane was prepared by reacting dimethylbromomalonate (1.61 g, 7.2 mmol) with 1,10-diaza-4,7,13,16-tetraoxacyclooctadecane (1 g, 3.8 mmol) in dry benzene (26 ml) under reflux for 6 hours. After cooling the reaction mixture was filtered and the filtrate evaporated and purified by column chromatography (Al_2O_3 , CH_2Cl_2 as eluent) yielding the tetramethyl ester of compound C (23%, 0.45 g).

25 The tetramethyl ester (0.35 g, 0.67 mmol) was dissolved in tetrahydrofuran (30 ml) to which lithium hydroxide (67.5 mg, 4 equivalents on ester) and water (2 ml) were added. After 5 days stirring at ambient temperature, the precipitate formed was isolated (0.21 g) as the tetralithium salt of the compound (about 65%).

Upon acidification (excess HCl) and treatment with acetone/ethanol to remove LiCl, the desired compound was obtained as a hygroscopic HCl salt.

Analysis: for $C_{18}H_{52}Cl_4N_2O_{20}$ (compound C $4HCl \cdot 8H_2O$)

30 Calculated: C: 28.6%; H: 6.9%; Cl: 18.8%; N: 3.7%
 Found: C: 24.6%; H: 5.4%; Cl: 20%; N: 3.5%.

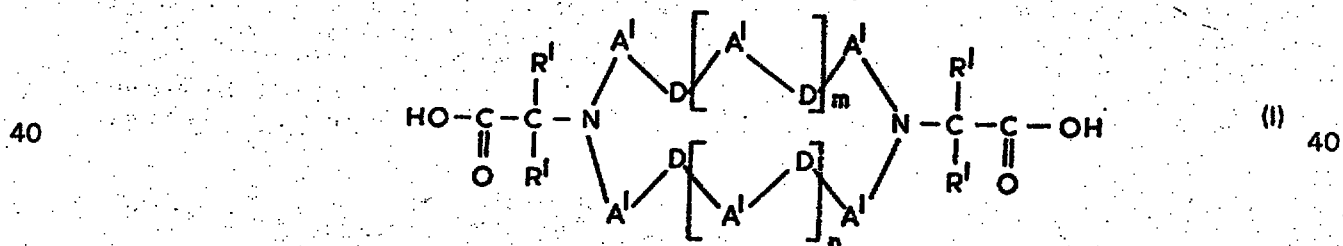
P.M.R.—data were in accordance with the expected structure.

As an alternative to lithium hydroxide, sodium hydroxide can be used, and preferred reaction conditions are an excess of the base and a reaction temperature of up to 80°C.

35 In the following claims the excepted compounds, namely 1,10-di(carboxymethyl)-1,10-diaza-4,7,13,16-tetraoxa-cyclooctadecane and salts thereof, are known per se, and "Accounts of Chemical Research" 11 (1978) 49—57 is referred to in this respect.

Claims

1. A macrocyclic compound of the general formula:



wherein each A¹ which may be the same or different represents a hydrocarbon radical having up to 12 carbon atoms and each D which may be the same or different represents an oxygen or a sulphur atom or a hydrocarbon radical having up to 12 carbon atoms or a group N—R², R² representing a hydrogen atom or a hydrocarbon radical having up to 12 carbon atoms, a hydrocarbon sulphonyl radical having up to 12 carbon atoms, an alkoxy carbonyl or alkoxy carbonylmethylene radical having up to 4 carbon atoms or a carboxymethylene radical, at least two of the said D members representing an oxygen or a sulphur atom or a group N—R², and each R¹ which may be the same or different represents a hydrogen atom or an alkyl group having up to 6 carbon atoms or a carboxy group and m and n are integers from 0 to 5 inclusive, the macrocyclic compound according to the general formula I being compatible with a barium ion, as hereinbefore defined, and salts thereof—with the exception of 1,10-di(carboxymethyl)-1,10-diaza-4,7,13,16-tetraoxacyclooctadecane and salts thereof.

50 barium ion, as hereinbefore defined, and salts thereof—with the exception of 1,10-di(carboxymethyl)- 50
1,10-diaza-4,7,13,16-tetraoxacyclooctadecane and salts thereof.



* C L M S *

ammonium salts of the macrocyclic compounds of formula I, which inner salts are also considered to be within the scope of the present invention. In the event that at least one of the groups R^1 represents a carboxy group, it was found convenient to use a halomalonate ester which after subsequent hydrolysis gives the macrocyclic compound according to the general formula I.

5 Example I

The compound 1,10-di(alpha-ethylcarboxymethyl)-1,10-diaza-4,7,13,16-tetraoxacyclooctadecane was prepared *in situ*, i.e. in the presence of barium sulphate (3 moles per litre) by reacting 1,10-diaza-4,7,13,16-tetraoxacyclooctadecane (0.1M) and 2-chlorobutyric acid (0.2M) and lithium hydroxide (0.8M) at 70°C. The compound was characterised by ^1H and ^{13}C nuclear magnetic resonance technique in D_2O .

The following signals were assigned:

^1H NMR (H_2O as ppm):

—1.2 (m, 16H; 1,2); —1.8 (t, 2H, 3); —2.1 (t, 8H, 4); —3.2 (m, 4H, 5); —4.0 (t, 6H, 6) ppm.

^{13}C NMR (external reference):

183.4 (7); 73.2 (1, 2, 3); 54.4 (4); 23.4 (5); 14.6 (6) ppm.

The compound was formed in about 14% yield.

Example II

The novel compound bis(dicarboxymethyl)-1,10-diaza-4,7,13,16-tetraoxacyclooctadecane was prepared by reacting dimethylbromomalonate (1.61 g, 7.2 mmol) with 1,10-diaza-4,7,13,16-tetraoxacyclooctadecane (1 g, 3.8 mmol) in dry benzene (26 ml) under reflux for 6 hours. After cooling the reaction mixture was filtered and the filtrate evaporated and purified by column chromatography (Al_2O_3 , CH_2Cl_2 as eluent) yielding the tetramethyl ester of compound C (23%, 0.45 g).

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Analysis: for $\text{C}_{18}\text{H}_{52}\text{Cl}_4\text{N}_2\text{O}_{20}$ (compound C 4HCl . $8\text{H}_2\text{O}$)

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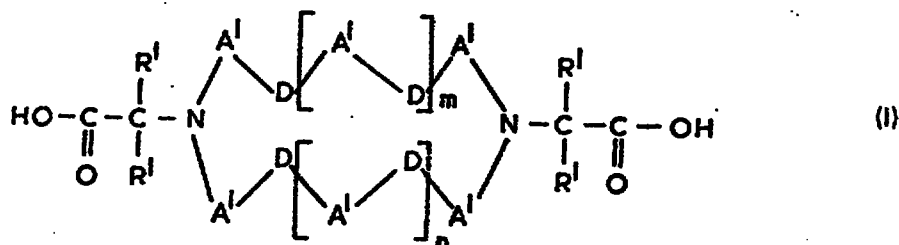
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As an alternative to lithium hydroxide, sodium hydroxide can be used, and preferred reaction conditions are an excess of the base and a reaction temperature of up to 80°C.

In the following claims the excepted compounds, namely 1,10-di(carboxymethyl)-1,10-diaza-4,7,13,16-tetraoxa-cyclooctadecane and salts thereof, are known per se, and "Accounts of Chemical Research" 11 (1978) 49—57 is referred to in this respect.

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2. A compound as claimed in Claim 1, in which A¹ represents an ethylene, diethylene, triethylene or tetraethylene radical; D represents an oxygen atom or a group N—R², wherein R² represents an alkyl group of up to 4 carbon atoms, a hydrocarbon sulphonyl radical of up to 4 carbon atoms or a methoxy- or ethoxy-carbonyl radical; at least 4 of the said D members representing an oxygen atom and each R¹ represents a hydrogen atom or a methyl, ethyl or carboxy group and m and n are 1 or 2.

3. A compound as claimed in Claim 2, in which R² represents a methyl group.

4. 1,10-Di(alpha-ethylcarboxymethyl)-1,10-diaza-4,7,13,16-tetraoxacyclooctadecane.

5. Bis (dicarboxymethyl)-1,10-diaza-4,7,13,16-tetraoxacyclooctadecane.

6. Process for the preparation of macrocyclic compounds according to the general formula I or salts thereof as claimed in any one of Claims 1—5, which comprises reacting a macrocyclic compound according to formula II as defined in the foregoing description with an alpha-halocarboxylic acid or salt thereof in the presence of a base.

7. Process as claimed in Claim 6, in which 1,10-diaza-4,7,13,16-tetraoxacyclooctadecane is reacted with a 2-halocarboxylic acid and sodium hydroxide or lithium hydroxide.

8. Process as claimed in Claim 7, in which there is used an excess of sodium hydroxide or lithium hydroxide at a temperature up to 80°C.

9. Process as claimed in any one of Claims 6—8, in which the reaction is carried out in the presence of solid barium sulphate.

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