

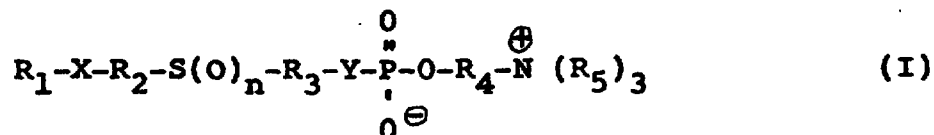
Description

The present invention concerns new sulphur-containing phospholipids, their pharmacologically acceptable salts, processes for their preparation, as well as medicaments which contain these substances.

In DE-AS No. 2009341 is claimed 3-octadecyloxypropanol-(1) phosphoric acid monocholine ester as immunological adjuvant, in DE-AS No. 2009342 its 2-hydroxy derivative as agent for increasing the natural resistance of the organism and in DE-OS No. 2619686 its 2-methoxy derivative as anti-tumour agent. Finally, in DE-OS No. 2619715, there is described the dodecyloxypropylphosphorylcholine as tumour antigen.

It has now been found that alkanol phosphoric acid monoammonium alkyl esters, which are substituted by an alkylated mercapto, sulphinyl or sulphonyl group, also act cancerostatically but, in contradistinction to the above-mentioned phospholipids, do not initiate thrombocyte aggregation.

Consequently, the subject of the present invention are compounds of the general formula I



in which X signifies a valency bond, oxygen, sulphur, the sulphinyl or sulphonyl group, the -NHCO-, -CONH- or -NHCONH- group, a C₃ to C₈-cycloalkylene or phenylene

radical, Y oxygen or sulphur, R_1 hydrogen, a straight-
chained or branched, saturated or unsaturated alkyl
radical with 1 to 18 carbon atoms, which is optionally
substituted one or more times by aryl, halogen, a lower
5 alkoxy, alkylmercapto, alkoxycarbonyl, alkanesulphinyl
or alkanesulphonyl group, R_2 a straight-chained or
branched, saturated or unsaturated alkylene chain with
1 to 18 carbon atoms which is optionally substituted
one or more times by halogen, aryl, a lower alkoxy,
10 alkoxycarbonyl, alkylmercapto, alkanesulphinyl or
alkanesulphonyl group, R_3 a straight-chained or branched,
saturated or unsaturated alkylene chain with 2 to 8
carbon atoms which can also be part of a cyclopentane,
cyclohexane or cycloheptane ring optionally substituted
15 by a lower alkyl group and which is optionally substituted
one or more times by hydroxyl, halogen, nitrile, a
cycloalkyl, phenyl, alkoxycarbonyl, optionally alkylated
carbamoyl, alkylmercapto, alkanesulphinyl, alkane-
sulphonyl, optionally acylated amino group or by alkoxy,
20 which, in turn, can be substituted by aryl, alkylmercapto,
alkanesulphinyl, alkanesulphonyl, optionally acylated NH_2 ,
alkoxycarbonyl, nitrile, hydroxyl, alkoxy or optionally
alkylated carbamoyl, R_4 a straight-chained or branched
alkylene chain with 2 to 4 carbon atoms, R_5 hydrogen or
25 a lower alkyl group and n the numbers 0, 1 or 2, with
the proviso that the group R_1-X-R_2 , for the case in
which it represents an alkyl group (X = valency), has

up to 20 C-atoms, as well as their pharmacologically acceptable salts.

In the substituents R_5 , alkyl means a hydrocarbon radical with 1 to 6 carbon atoms, especially the methyl
5 or ethyl radical.

Alkoxy, alkoxycarbonyl, alkylmercapto, alkane-sulphanyl and alkanesulphonyl mean, as a rule, radicals with 1 to 6 carbon atoms but can also be radicals with up to 20 carbon atoms, e.g. octadecylmercapto, tetra-
10 decyloxy, octylmercapto.

By cycloalkylene radical of the group X are to be understood radicals with 3 to 8 carbon atoms, especially the cyclopropylene, cyclopentylene and cyclohexylene radical.

15 Cycloalkane rings, which can also be part of the alkylene chain of the group R_3 , are the cyclopentane, cyclohexane and the cycloheptan ring, whereby the rings can also be substituted by a lower alkyl group.

Halogen means fluorine, chlorine, bromine and
20 iodine, but preferably fluorine.

For the case in which X represents a valency bond, the group R_1-X-R_2 represents an alkyl group with up to 20 carbon atoms which can be straight-chained or branched, saturated or unsaturated. As straight-chained group,
25 there preferably comes into question the eicosyl, octadecyl, heptadecyl, hexadecyl, tetradecyl, dodecyl and the octyl radical. The unsaturated group can contain

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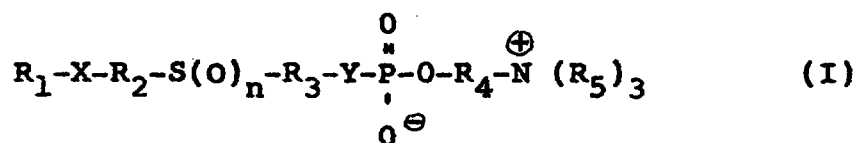
up to 4 double bonds but preferably 1 or 2 double bonds.

The group R_3 preferably consists of a $-\text{CH}_2-\text{CH}_2-\text{CH}_2-$ group, the middle CH_2 group of which can be substituted once or twice by alkyl, alkoxy, alkylmercapto, alkane-
5 sulphinyl, alkanesulphonyl, alkoxyalkylene, benzyloxy, hydroxyl or halogen and which can optionally be substituted on C_1 and C_3 by alkyl groups, whereby these can also form a ring.

The group R_4 preferably means the $-\text{CH}_2-\text{CH}_2-$ group.

10 Preferred compounds of the formula I are especially derivatives of propanol-(1)- or propanethiol-(1)-phosphoric acid monocholine ester which is substituted in the 3-position of the propanol by an alkylmercapto, alkanesulphinyl or alkanesulphonyl radical and option-
15 ally also in the 2-position.

Furthermore, the subject of the invention are processes for the preparation of compounds of the general formula I

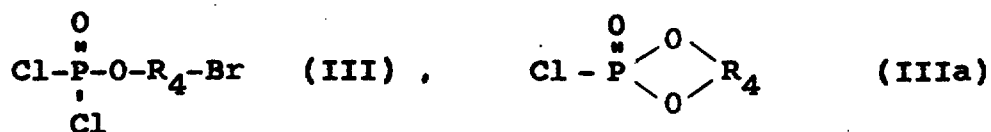


20 in which R_1 to R_5 , X, Y and n have the above-given meaning, whereby one reacts a compound of the general formula II



in which R_1 , R_2 , R_3 , X, Y and n have the above-given
25 meaning, either

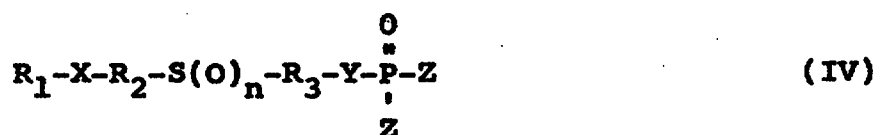
a) with a compound of the general formula III or IIIa



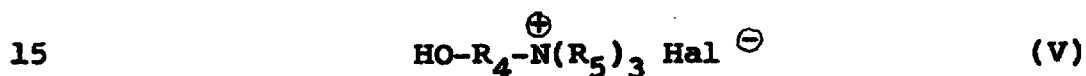
in which R_4 has the above-mentioned meaning, in the presence of an acid binding agent, the reaction product,

5 in the case of use of a compound of the formula III, selectively hydrolysed and the remaining bromine atom exchanged for an optionally alkylated ammonium group, in the case of a compound of formula IIIa treats directly with optionally alkylated ammonia or

10 b) converts into a compound of the general formula IV

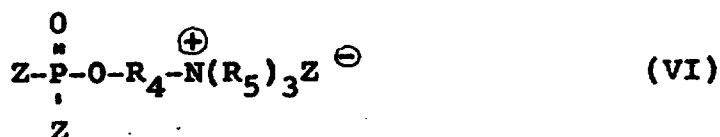


in which R_1 , R_2 , R_3 , Y , X and n have the above-given meanings and Z signifies hydroxyl, chlorine or bromine, and reacts this with a compound of the general formula V



in which R_4 and R_5 have the above-given meanings and $\text{Hal}^\ominus$ is to be chloride, bromide or iodide, in the presence of an acid-binding agent or of an activating reagent, or

20 c) reacts with a compound of the general formula VI



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in which R_4 , R_5 and Z have the above-given meanings and $Z^{\ominus}$ is to be chloride or bromide, in the presence of an acid-binding agent, converts into the inner salt and optionally oxidises.

5 All described processes take place in per se known manner.

As a rule, the process a is so carried out that an alkanol or alkanethiol of the general formula II is reacted with a bromoalkanol phosphoric acid monoester
10 dichloride of the general formula III in the presence of an acid-binding agent, such as e.g. triethylamine, in an absolute, inert organic solvent, such as e.g. chlorinated hydrocarbon or toluene, at temperatures from the freezing point up to room temperature. The selective
15 hydrolysis of the phosphoric acid diester monochloride obtained is achieved directly in two-phase mixture by addition of an aqueous potassium chloride solution at 0 to 50°C. For the substitution of the remaining
bromine atom by an optionally alkylated ammonium group,
20 one dissolves the ammonia or the alkylamine in a medium which sufficiently well dissolves not only the phosphoric acid diester but also ammonia or the amine, for which purpose mixtures of acetonitrile or lower alcohols with chlorinated hydrocarbons are especially suitable, and
25 completes the reaction at a temperature of 20 to 70°C.

In the case of the use of a compound of the formula IIIa, the reaction product is treated directly

with optionally alkylated ammonia.

One can also proceed stepwise, thus first introduce an alkylammonium group and subsequently react with alkyl halide to the di- or trialkylammonium alkyl ester.

5 The removal of the residual halogenide ions preferably takes place in lower alcohols by means of silver acetate or silver oxide. All intermediate stages, as well as end products, can be easily purified column chromatographically with conventional elution agents, 10 such as e.g. ether, ligroin, chlorinated hydrocarbons, lower alcohols or mixtures thereof, on silica gel, whereby, in the case of the betaine-like end product, some water is expediently added thereto.

In the case of process b, if Z means chlorine or 15 bromine, the reaction of a compound of the formula II to the phosphoric ester dihalide of the formula IV is carried out with phosphorus oxyhalide in inert, water-free solvents, such as e.g. halogenated hydrocarbons, in the presence of acid acceptors, preferably pyridine 20 or quinoline. The reaction temperatures lie between 0 and 40°C. The product can be isolated or, without isolation, reacted with alkylammonium-alkanol halides or ammonium-alkanol halides, with the addition of further pyridine or quinoline, at temperatures of 0 to 40°C. to 25 the desired end product. As solvent herefor, one preferably uses halogenated hydrocarbons, as well as acetonitrile or trichloroacetonitrile. For the case that Z

signifies hydroxyl, the compound of general formula IV can be prepared by hydrolysis of the corresponding phosphoric ester dihalide or by hydrogenolysis of the corresponding phosphoric ester diphenyl ester. The
5 further reaction with substances of the general formula V takes place in the presence of sulphonic acid halides, such as p-toluenesulphochloride or triisopropylbenzene-sulphochloride. As solvent, one uses dimethylformamide with an addition of pyridine or pyridine alone. As a
10 rule, the reaction temperature lies at 0 to 40°C.

The substances of the general formula VI in the case of process c can, for the case in which Z signifies hydroxyl, be reacted with generally usual halogenation agents, such as e.g. phosphorus pentachloride, in the
15 presence of an acid acceptor, such as e.g. pyridine, to substances of the general formula VI with Z = chlorine or bromine, which can then be isolated or, without isolation, brought to reaction with compounds of the general formula II. As acid acceptors, as a rule, there
20 are here also employed nitrogen-containing bases, such as pyridine, quinoline or triethylamine. The preferred solvents are water-free halogenated hydrocarbons or also toluene.

The alkylated mercaptoalkanols of the general
25 formula II used as starting materials are also new and can easily be obtained by reaction of halogenalkanes with mercaptocarboxylic acids or esters, or of mercapto-

alkanes with halogenocarboxylic acids or esters in the presence of an acid-binding agent, such as e.g. sodium alcoholate, in a lower alcohol, or by addition of mercaptoalkanes to α,β -unsaturated carboxylic acids or esters in a lower alcohol with base catalysis and subsequent treatment with reducing agents, such as e.g. sodium borohydride in lower alcohols, or lithium aluminium hydride in abs. ether. A further mode of preparation of the compounds of the general formula II consists in the reaction of mercaptoalkanes with alkanols which carry a reactive group, such as e.g. halogen or the sulphonic acid residue, or of halogenoalkanes with mercaptoalcohols in the presence of an acid-binding agent, such as e.g. potassium hydroxide or sodium alcoholate, in a lower alcohol or by addition of a mercaptoalkane to an unsaturated alcohol with base or peroxide catalysis.

The thiols of the general formula II can be synthesised from the alcohols of the general formula II according to per se known methods in that e.g. one prepares from the alcohol of the general formula II a halide or sulphonate, allows this to react with thiourea and splits the resultant isothiuronium salt with alkali. By acidification, one then obtains the desired thiol of the general formula II.

Furthermore, the subject of the invention are all stereoisomeric compounds of the formula I which occur

e.g. on the basis of asymmetric carbon atoms, of the sulphoxide group or on the basis of cis-trans isomerism. A separation of the products obtained in a mixture takes place according to per se known processes.

- 5 One obtains the pharmacologically acceptable salts in the usual way, e.g. by neutralisation of the compounds of the formula I with non-toxic inorganic or organic acids, such as e.g. hydrochloric, sulphuric, phosphoric, hydrobromic, acetic, lactic, citric, malic, salicylic, malonic, maleic or succinic acid.
- 10

The new substances of the formula I according to the invention and their salts can be administered enterally or parenterally in liquid or solid form. All conventional forms of administration hereby come into question, for example tablets, capsules, dragees, syrups, solutions, suspensions. As injection medium, water is preferably used which contains the additives usual in the case of injection solutions, such as stabilising agents, solubilising agents and buffers. Such additives are e.g. tartrate and citrate buffers, ethanol, complex formers (such as ethylenediamine-tetraacetic acid and its non-toxic salts), high molecular polymers (such as liquid polyethylene oxide) for viscosity regulation. Liquid carrier materials for injection solutions must be sterile and are preferably filled into ampoules. Solid carrier materials are e.g. starch, lactose, mannitol, methyl cellulose, talc, highly dispersed

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silicic acids, high molecular fatty acids (such as stearic acid), gelatine, agar-agar, calcium phosphate, magnesium stearate, animal and vegetable fats, solid high molecular polymers (such as polyethylene glycols);
5 compositions suitable for oral administration can, if desired, contain flavouring and sweetening materials.

The dosaging can depend upon various factors, such as mode of administration, species, age and/or individual state. The dosage to be administered daily lies at about
10 0.05 - 1.00 mg./kg. body weight.

Preferred in the sense of the present invention are, apart from the compounds mentioned in the Examples, the following esters:

1. 2,3-Bisoctadecylmercaptopropanol-(1)-phosphoric acid
15 monocholine ester
2. 2-[3-(Hexadecylmercapto)-propoxyphosphoryloxyhydroxy]-
2-methylethylammonium hydroxide
3. 3-Tetradecylmercapto-2-ethoxypropanol-(1)-phosphoric
acid monocholine ester
- 20 4. 3-Hexadecylmercapto-2-ethoxypropanol-(1)-phosphoric
acid monocholine ester; m.p. 69°C. sinters,
238 - 243°C. decomp.
5. 3-(14-Methylmercaptotetradecylmercapto)-propanol-(1)-
phosphoric acid monocholine ester
- 25 6. 3-(17-Methyloctadecylmercapto)-propanol-(1)-phosphoric
acid monocholine ester

7. 3-(8-Fluorooctadecylmercapto)-propanol-(1)-phosphoric acid monocholine ester
8. 2-Hydroxy-3-octadecylmercaptopropanol-(1)-phosphoric acid monocholine ester
- 5 9. 2-Hydroxy-3-octadecansulphinypropanol-(1)-phosphoric acid monocholine ester
- 10 10. 2-Hydroxy-3-octadecansulphonypropanol-(1)-phosphoric acid monocholine ester
11. 2-Methoxy-3-[8-(4-octylcyclohexyl)-octylmercapto]-propanol-(1)-phosphoric acid monocholine ester
12. 3-Hexadecylmercapto-2-methylmercaptopropanol-(1)-phosphoric acid monocholine ester
13. 3-Hexadecylmercapto-2-methanesulphinypropanol-(1)-phosphoric acid monocholine ester
- 15 14. 3-Hexadecylmercapto-2-methanesulphonypropanol-(1)-phosphoric acid monocholine ester
15. 2-Methoxy-3-(2-methoxyoctadecylmercapto)-propanol-(1)-phosphoric acid monocholine ester
16. 2-Methoxy-3-(2-tetradecyloxyoctadecylmercapto)-propanol-(1)-phosphoric acid monocholine ester
- 20 17. 2-Methoxy-3-(14-tetradecyloxyoctadecylmercapto)-propanol-(1)-phosphoric acid monocholine ester
18. 2-Methoxy-3-(14-methylmercaptotetradecylmercapto)-propanol-(1)-phosphoric acid monocholine ester
- 25 19. 2-Methoxy-3-(17-methyloctadecylmercapto)-propanol-(1)-phosphoric acid monocholine ester

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20. 3-(8-Fluorooctadecylmercapto)-2-methoxypropanol-(1)-
phosphoric acid monocholine ester
21. 2-Fluoro-3-octadecylmercaptopropanol-(1)-phosphoric
acid monocholine ester
- 5 22. 2-Fluoro-3-octadecansulphinypropanol-(1)-phosphoric
acid monocholine ester
23. 2-Fluoro-3-octadecansulphonypropanol-(1)-phosphoric
acid monocholine ester
24. 2-Ethylmercapto-3-octadecylmercaptopropanol-(1)-
10 phosphoric acid monocholine ester
25. 3-Hexadecansulphiny-2-methylpropanol-(1)-phosphoric
acid monocholine ester
26. 3-Heptadecylmercapto-2-methylpropanol-(1)-phosphoric
acid monocholine ester; m.p. 74°C., sinters;
15 250 - 254°C., decomp.
27. Cis-3-hexadecylmercaptocyclohexanol-(1)-phosphoric
acid monocholine ester; m.p. 65°C., sinters;
240 - 252°C. decomp.
28. 2,3-Bisooctylmercaptopropanol-(1)-phosphoric acid
20 monocholine ester
29. 2-Methoxy-3-[8-(4-octylphenyl)-octylmercapto]-
propanol-(1)-phosphoric acid monocholine ester
30. 2,2-Dimethyl-3-hexadecansulphinypropanol-(1)-
phosphoric acid monocholine ester
- 25 31. 2,2-Dimethyl-3-hexadecansulphonypropanol-(1)-
phosphoric acid monocholine ester

32. 2-Methoxymethylene-3-octadecylmercaptopropanol-(1)-
phosphoric acid monocholine ester
33. 2,2-Diethoxy-3-hexadecylmercaptopropanol-(1)-
phosphoric acid monocholine ester
- 5 34. 4-Octadecylmercapto-n-butanol-(2)-phosphoric acid
monocholine ester
35. 4-Octadecansulphinyl-n-butanol-(1)-phosphoric acid
monocholine ester
36. 4-Octadecansulphonyl-n-butanol-(1)-phosphoric acid
10 monocholine ester
37. 3-Hexadecansulphinylcyclopentanol-(1)-phosphoric
acid monocholine ester
38. 3-Hexadecansulphonylcyclopentanol-(1)-phosphoric
acid monocholine ester
- 15 39. 4-Octadecylmercapto-n-butanol-(1)-phosphoric acid
monocholine ester
40. 3-Octadecansulphinylcyclohexanol-(1)-phosphoric acid
monocholine ester
41. 3-Octadecansulphonylcyclohexanol-(1)-phosphoric acid
20 monocholine ester
42. 2-Ethyl-3-octadecylmercaptocyclohexanol-(1)-
phosphoric acid monocholine ester
43. 2,2-(6-Methylcyclohex-3-enylidene)-3-hexadecyl-
mercaptopropanol-(1)-phosphoric acid monocholine
25 ester
44. 2-Octadecylmercaptoethanolphosphoric acid monocholine
ester



45. 2-(2-Propynyl)-3-hexadecylmercaptopropanol-(1)-
phosphoric acid monocholine ester; m.p. 54°C.,
sinters; 237 - 239°C. decomp.
- 5 46. 2-Propadienyl-3-hexadecylmercaptopropanol-(1)-
phosphoric acid monocholine ester
47. 2-(1-Propenyl)-3-hexadecylmercaptopropanol-(1)-
phosphoric acid monocholine ester
- 10 48. Trans-3-hexadecylmercaptocyclohexanol-(1)-phosphoric
acid monocholine ester; m.p. 59°C., sinters; 245 -
250°C. decomp.
49. 2-Isopropyl-3-hexadecylmercaptopropanol-(1)-phosphoric
acid monocholine ester; m.p. 68°C., sinters; 242°C.
decomp.
- 15 50. 2-Methyl-3-heptadecylmercaptopropanol-(1)-phosphoric
acid monocholine ester
51. 2-Methyl-3-hexadecansulphonylpropanol-(1)-phosphoric
acid monocholine ester; m.p. 64°C., sinters; 232°C.
foaming up.
- 20 52. 2-Methyl-2-methoxy-3-hexadecylmercaptopropanol-(1)-
phosphoric acid monocholine ester
53. 2,2-Bismethoxymethylhexadecylmercaptopropanol-(1)-
phosphoric acid monocholine ester
- 25 54. 2-Methylmercaptomethyl-3-hexadecylmercaptopropanol-
(1)-phosphoric acid monocholine ester wax 240°C.
decomp.
55. 2-Methanesulphinylmethyl-3-hexadecylmercaptopropanol-
(1)-phosphoric acid monocholine ester

56. 2-Methanesulphonylmethyl-3-hexadecylmercapto-
propanol-(1)-phosphoric acid monocholine ester
57. 2-Methoxyethoxymethyl-3-hexadecylmercaptopropanol-
(1)-phosphoric acid monocholine ester
- 5 58. 2-Cyanomethyl-3-hexadecylmercaptopropanol-(1)-
phosphoric acid monocholine ester
59. 2-Carbamoylmethyl-3-hexadecylmercaptopropanol-(1)-
phosphoric acid monocholine ester
60. 2-N,N-Dimethylcarbamoylmethyl-3-hexadecylmercapto-
10 propanol-(1)-phosphoric acid monocholine ester
61. 2-Ethoxycarbonylmethyl-3-hexadecylmercaptopropanol-
(1)-phosphoric acid monocholine ester
62. 2-Methyl-3-(1-methoxycarbonylheptadecylmercapto)-
propanol-(1)-phosphoric acid monocholine ester;
15 m.p. 84°C. sinters; 239 - 241°C. foaming up
63. Thiophosphoric acid-0-choline ester-S-3-heptadecyl-
mercaptopropyl ester; m.p. 80°C. sinters, 264°C.
decomp.
64. Thiophosphoric acid-0-choline ester-S-2-methyl-3-
20 hexadecanesulphinypropyl ester
65. Thiophosphoric acid-0-choline ester-S-2-methyl-3-
hexadecanesulphonylpropyl ester; m.p. 60°C. sinters,
205 - 208°C. slight foam formation
66. Thiophosphoric acid-0-choline ester-S-2-benzyl-3-
25 octadecylmercaptopropanol ester; m.p. 240°C. decomp.
67. Thiophosphoric acid-0-choline ester-S-2,2-dimethyl-
3-hexadecylmercaptopropyl ester

68. 2-Aminoethyl-3-hexadecylmercaptopropanol-(1)-
phosphoric acid monocholine ester
69. 2-Acetylaminethyl-3-hexadecylmercaptopropanol-(1)-
phosphoric acid monocholine ester
- 5 70. 2-Mesylaminethyl-3-hexadecylmercaptopropanol-(1)-
phosphoric acid monocholine ester
71. 2-Hydroxymethyl-3-heptadecylmercaptopropanol-(1)-
phosphoric acid monocholine ester
72. 2-Cyclopentyl-3-heptadecylmercaptopropanol-(1)-
10 phosphoric acid monocholine ester
73. 2-Cyclohexylmethyl-3-hexadecylmercaptopropanol-(1)-
phosphoric acid monocholine ester
74. 2-p-Methylbenzyl-3-octadecylmercaptopropanol-(1)-
phosphoric acid monocholine ester
- 15 75. 2-Cyano-3-heptadecylmercaptopropanol-(1)-phosphoric
acid monocholine ester
76. 2-Carbamoyl-3-heptadecylmercaptopropanol-(1)-
phosphoric acid monocholine ester
77. 2-Hydroxy-3-hexadecylmercaptopropanol-(1)-
20 phosphoric acid monocholine ester
78. 2-Isopropoxy-3-heptadecylmercaptopropanol-(1)-
phosphoric acid monocholine ester
79. 2-(3-Phenethyloxy)-3-heptadecylmercaptopropanol-(1)-
phosphoric acid monocholine ester
- 25 80. 2-(2-Hydroxyethoxy)-3-octadecylmercaptopropanol-(1)-
phosphoric acid monocholine ester

81. 2-(2-Methylmercaptoethoxy)-3-octadecylmercapto-
propanol-(1)-phosphoric acid monocholine ester
82. 2-(2-Methanesulphinyloethoxy)-3-octadecylmercapto-
propanol-(1)-phosphoric acid monocholine ester
- 5 83. 2-(2-Methanesulphonyloethoxy)-3-octadecylmercapto-
propanol-(1)-phosphoric acid monocholine ester
84. 2-(2-Aminoethoxy)-3-heptadecylmercaptopropanol-(1)-
phosphoric acid monocholine ester
85. 2-(2-Acetylaminoethoxy)-3-heptadecylmercaptopropanol-
10 (1)-phosphoric acid monocholine ester
86. 2-(2-Mesylaminoethoxy)-3-heptadecylmercaptopropanol-
(1)-phosphoric acid monocholine ester
87. 2-Ethoxycarbonylmethoxy-3-hexadecylmercaptopropanol-
(1)-phosphoric acid monocholine ester
- 15 88. 2-Cyanomethoxy-3-hexadecylmercaptopropanol-(1)-
phosphoric acid monocholine ester
89. 2-Carbamoylmethoxy-3-hexadecylmercaptopropanol-(1)-
phosphoric acid monocholine ester
90. 2-Amino-3-hexadecylmercaptopropanol-(1)-phosphoric
20 acid monocholine ester
91. 2-Acetylamino-3-hexadecylmercaptopropanol-(1)-
phosphoric acid monocholine ester
92. 2-Methyl-3-(11-butylureyleneundecylmercapto)-
propanol-(1)-phosphoric acid monocholine ester
- 25 93. 2-Methyl-3-(11-valeroylamino undecylmercapto)-
propanol phosphoric acid monocholine ester

94. 2-N-Dodecylcarboxamidomethoxy-3-hexadecylmercapto-
propanol-(1)-phosphoric acid monocholine ester

95. 2-Ethylidene-3-hexadecylmercaptopropanol-(1)-
phosphoric acid monocholine ester.

5 The following Examples show some of the process
variants which can be used for the synthesis of the
compounds according to the invention.

Example 1.

3-Octadecylmercaptopropanol-(1)-phosphoric acid mono-
10 choline ester.

6.7 g. 3-Octadecylmercaptopropanol, m.p. 53 -
55°C., are dissolved in 70 ml. abs. methylene chloride
and added dropwise at -5°C. to a second solution which
contains 70 ml. bas. methylene chloride, 6.7 g. phosphoric
15 acid mono-2-bromoethyl ester dichloride and 9.7 ml.
triethylamine. After 1 h., one allows it to come to
room temperature and leaves it to stand overnight. One
then adds thereto 80 ml. 0.1N potassium chloride sol-
ution and stirs for 2 h. at 40°C. One now cools, adds
20 130 ml. methanol thereto and adjusts to pH 3 with conc.
hydrochloric acid. One separates off the organic phase,
washes with water, dries and evaporates. The evaporation
residue (8.7 g.), which represents 3-octadecylmercapto-
propanol-(12)-phosphoric acid mono-(2-bromoethyl) ester,
25 is further reacted in the crude state. One dissolves
it in a mixture of 45 ml. each of methanol and chloroform
and passes in trimethylamine. One then stirs under reflux

for 1 h., leaves to stand overnight at room temperature, dissolves in chloroform, filters and mixes the clear filtrate with acetone, whereby 6.1 g. of thin layer chromatographically uniform bromide are obtained. For
5 the removal of the bromide ions, one treats in methanolic solution with silver acetate and finally purifies on a silica gel column with a mixture of chloroform/methanol/water (65:25:4). One thus obtains 2.3 g. = 26%, of the m.p. 238 -240°C. decomp.

10 According to the result of the elementary analysis, the product contains 1.5 mole water.

Here and in all other Examples, the structure is verified by NMR spectrum and elementary analysis, that of the precursors also by mass spectroscopic investigation.
15

The 3-octadecylmercaptopropanol used as starting material is prepared as follows:

0.35 g. sodium are dissolved in 10 ml. methanol, 1.8 g. 3-mercaptopropionic acid methyl ester added
20 dropwise thereto and then a solution of 5.2 g. octadecyl bromide in 20 ml. methanol added thereto. After 3 h. refluxing, it is cooled and the suspension obtained filtered off with suction. For purification, it is chromatographed on a silica gel column. Elution agent:
25 chloroform/ligroin 1:1. There are obtained 4.1 g. 3-octadecylmercaptopropionic acid methyl ester of the m.p. 39 - 41°C. One dissolves in ether and reduces

with lithium aluminium hydride until the ester is no longer to be seen in the thin layer chromatogram. After usual working up, one obtains 2.8 g. 3-octadecylmercaptopropanol, m.p. 53 - 55°C.

- 5 Instead of octadecyl bromide, there can also be used octadecylmercaptan which is then reacted with 3-bromopropionic acid methyl ester or added to acrylic acid methyl ester with sodium methylate catalysis. In both cases, 3-octadecylmercaptopropionic acid methyl
10 ester is obtained.

Finally, 3-octadecylmercaptopropanol can also be obtained by addition of octadecylmercaptan to allyl alcohol.

Example 2.

- 15 3-Octadecanesulphinypropanol-(1)-phosphoric acid monocholine ester.

- 0.25 g. of the precursor described in Example 1, 3-octadecylmercaptopropanol, are mixed in 5 ml. glacial acetic acid with 0.07 ml. perhydrol, after stirring for
20 1 hour at room temperature, rendered weakly alkaline with dilute aqueous sodium hydroxide solution and, after 2 h., the suspension filtered off with suction, washed with water and dried. One thus obtains 0.34 g. of m.p. 74 - 78°C. and further purifies on a silica
25 gel column with chloroform/methanol 99:1, which brings about a melting point increase to 81 - 83°C. With this 3-(octadecanesulphiny)-propanol there is carried out

the synthesis as described in Example 1. One thus obtains 19% of thin layer chromatographically uniform crystals of the m.p. 244°C . decomp. They contain 1 mole of water.

- 5 One also obtains an identical product by selective oxidation of the compound obtained according to Example 1 with perhydrol in glacial acetic acid.

Example 3.

- 3-Octadecanesulphonylpropanol-(1)-phosphoric acid
10 monocholine ester.

- 0.25 g. of the compound described in Example 1 are stirred in 5 ml. glacial acetic acid and 0.1 ml. perhydrol for 8 h. at room temperature. After the addition of water, one then evaporates and stirs up the residue
15 with acetone. One thus obtains 0.23 g. = 87% of crystals of the m.p. $240 - 242^{\circ}\text{C}$. decomp. They contain 2 mole of water.

One also obtains an identical product in the following way:

- 20 0.5 g. of the precursor described in Example 1, 3-octadecylmercaptopropanol, are dissolved in 10 ml. glacial acetic acid and mixed with 0.13 ml. perhydrol. After stirring for 1 hour at room temperature, the hydrogen peroxide addition is repeated and left to stand
25 for 24 h. The resulting suspension is then filtered off with suction and the 0.3 g. of crystals obtained purified on a column. M.p. $92 - 94^{\circ}\text{C}$.

With this compound, there is carried out the synthesis analogously to the procedure given in Example 1. In the thin layer chromatogram, the sulphone can be differentiated not only from the sulfoxide but also from the mercapto compound by the R_F value. In the case of the monitoring of the course of the reaction, it is shown that, as intermediate stage, the sulfoxide described in Example 2 occurs in both methods.

Example 4.

10 3-(Octadec-9t-enylmercapto)-propanol-(1)-phosphoric acid monocholine ester.

3-(Octadec-9t-enylmercapto)-propionic acid methyl ester are obtained as oil with 69% yield according to the method of working described in Example 1 with elaidine bromide. The lithium aluminium hydride reduction leads, with 83% yield, to the 3-(octadec-9t-enylmercapto)-propanol with an m.p. of 38 - 40°C., which is phosphorylated analogously to the procedure given in Example 1 and reacted with trimethylamine. Yield 9%,
20 m.p. 238 - 243°C. The product contains 2 mole of water.

Example 5.

3-(Octadec-9t-enesulphonyl)-propanol-(1)-phosphoric acid monocholine ester.

1.4 g. of the compound obtained according to Example 4 are dissolved in 35 ml. glacial acetic acid, 0.5 ml. perhydrol added thereto in 2 portions within 2 h. and left to stand for 24 h. at room temperature.

It is then mixed with water, evaporated, taken up in chloroform and precipitated out with ether. No melting point can be obtained for the amorphous, hygroscopic product. According to the analysis, it contains 3 mole
5 of water.

Example 6.

3-Hexadecylmercaptopropanol-(1)-phosphoric acid
monocholine ester.

The β -hexadecylmercaptopropionic acid methyl ester
10 is obtained analogously to the procedure given in
Example 1 in 88% yield with 1-hexadecyl bromide (hygro-
scopic crystals) and from this with lithium aluminium
hydride, in 95% yield, 3-hexadecylmercaptopropanol of
the m.p. 50 - 51°C. Finally, the phosphorylation and
15 reaction with trimethylamine yields the desired product
with 11% yield. The thin layer chromatographically
uniform crystals have an m.p. of 240°C. decomp. They
contain 2.5 mole of water.

Example 7.

20 3-Hexadecanesulphonylpropanol-(1)-phosphoric acid
monocholine ester.

The oxidation of the compound described in the
preceding Example in glacial acetic acid with 30%
hydrogen peroxide gives, with 70% yield, the desired
25 compound. A melting point determination cannot be
carried out because the product becomes sticky in the
air. It contains 1.5 mole of water.

Example 8.

3-(3,7,11,15-Tetramethylhexadecylmercapto)-propanol-
(1)-phosphoric acid monocholine ester.

1-Bromo-3,7,11,15-tetramethylhexadecane (prepared
5 according to "Helv. Chim. Acta", 12, 915/1929) is
reacted, analogously to the procedure given in Example 1,
with β -mercaptopropionic ester; 82% yield, yellowish
oil, then reduced with lithium aluminium hydride: 90%
yield, yellowish oil, and finally phosphorylated and
10 reacted with trimethylamine. After the usual purifica-
tion, there is obtained an amorphous product in 15%
yield which contains 3 mole of water.

Example 9.

3-(3,7,11,15)-Tetramethylhexadecanesulphonyl)-
15 propanol-(1)-phosphoric acid monocholine ester.

The oxidation of the compound obtained according
to Example 8 is carried out in the way described in
Example 3 and provides the desired product in 86% yield,
also in an amorphous state. It contains 2 mole of water.

20 Example 10.

3-Heptadecylmercaptopropanol-(1)-phosphoric acid
monocholine ester.

In a way analogous to that described in Example 1,
the following reactions are carried out:

25 1-Bromoheptadecane with β -mercaptopropionic acid
methyl ester, 88% yield, oil.

The lithium aluminium hydride reduction of this

ester gives, with 88% yield, 3-heptadecylmercapto-
propanol, m.p. 48 - 51°C. and with 21% yield there is
obtained the desired compound, m.p. 246°C., decomp.,
after phosphorylation and reaction with trimethylamine.

5 It contains 1 mole of water.

Example 11.

3-Heptadecanesulphonylpropanol-(1)-phosphoric acid
monocholine ester.

The product obtained according to Example 10 is
10 oxidised in the usual way with hydrogen peroxide in
glacial acetic acid. Yield 76%. A melting point
determination is not possible because the product is
sticky. It contains 2 mole of water.

Example 12.

15 3-Eicosylmercapto-
propanol-(1)-phosphoric acid
monocholine ester.

Eicosyl bromide is reacted with β -mercapto-
propionic acid methyl ester, as well as the following
reaction steps, analogously to the procedure given in
20 Example 1. Yield 74%, m.p. 48 - 50°C.

The lithium aluminium hydride reduction gives,
with 76%, 3-eicosylmercapto-
propanol, m.p. 58 - 60°C.
The phosphorylation and choline formation finally give
the desired product with 16% yield. M.p. 235 - 238°C.
25 decomp. It contains 2 mole of water.

Example 13.

3-Eicosanesulphonylpropanol-(1)-phosphoric acid
monocholine ester.

10

The product obtained according to Example 12 is oxidised with perhydrol in glacial acetic acid at room temperature. The yield amounts to 76%, m.p. 210 - 229°C. decomp. The crystals contain 2 mole of water.

5 Example 14.

3-Dodecylmercaptopropanol-(1)-phosphoric acid
monocholine ester.

This synthesis also takes place analogously to the procedure given in Example 1:

10 β -Dodecylmercaptopropionic acid methyl ester, oil, yield quantitative, 3-dodecylmercaptopropanol, oil, which solidifies upon cooling, yield 94%.

The phosphorylation and choline formation take place with 16% yield, m.p. 229 - 231°C., decomp. The
15 product contains 1 mole of water.

Example 15.

3-Dodecanesulphonylpropanol-(1)-phosphoric acid
monocholine ester.

The product obtained according to Example 14 is
20 oxidised in the usual way with hydrogen peroxide in glacial acetic acid. Yield 74%, m.p. 95 - 99°C., decomp. The product contains 2 mole of water.

Example 16.

3-(2-Pentadecyloxyethylmercapto)-propanol-(1)-
25 phosphoric acid monocholine ester.

2.8 g. Sodium are dissolved in 34 ml. ethylene glycol, 53.5 ml. 1-bromopentadecane added thereto and

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stirred for 15 h. at 150°C. After cooling, it is extracted with ethyl acetate/ligroin 1:2, evaporated and chromatographed on a silica gel column with ligroin. Yield 29%, oil, which becomes solid upon standing.

- 5 10 g. thereof are stirred with 1.4 ml. phosphorus tribromide and 0.6 ml. pyridine for 5 h. at room temperature, poured on to ice, extracted with ether and purified on a column. Yield of oily 1-(2-bromoethoxy)-pentadecane 60%. The following reactions are again
- 10 carried out analogously to the procedure given in Example 1. Thus, β -(2-pentadecyloxyethylmercapto)-propionic acid methyl ester is obtained with 69% and 3-(2-pentadecyloxyethylmercapto)-propanol, m.p. 44 - 47°C., with 95% yield.

- 15 After reaction with bromoethylphosphoric acid dichloride and action of trimethylamine, there is obtained the desired product with 31% yield, m.p. 231 - 233°C., decomp. It contains 1 mole of water.

Example 17.

- 20 3-(2-Pentadecyloxy)-ethanesulphonylpropanol-(1)-phosphoric acid monocholine ester.

- The compound described in Example 16 is oxidised in the usual way with perhydrol in glacial acetic acid. After evaporation of the solution mixed with water, it
- 25 is stirred up with ether and crystallisation thereby brought about. There are obtained hygroscopic crystals with the decomposition point of 95°C. with 75% yield.

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They contain 2 mole of water.

Example 18.

3-[3-(Octadecanesulphonyl)-propoxyphosphoryloxy-hydroxy]-propyl trimethylammonium hydroxide.

- 5 3-Bromo-1-propanol is reacted with phosphorus oxychloride analogously to the procedure disclosed in "Helv. Acta Chim.", 33, 349/1958 for 2-bromoethanol and the ester dichloride obtained of b.p. 130 - 134°C./17 mm.Hg ($\approx$ 2.3 kPa) reacted in the way given in
- 10 Example 1 with the 3-(octadecanesulphonyl)-propanol described in Example 3. After reaction has taken place with trimethylamine, there are obtained 25% of the said product of m.p. 226 - 229°C., decomp.

Example 19.

- 15 2-[3-(Octadecanesulphonyl)-propoxyphosphoryloxy-hydroxy]-2-methylethyltrimethylammonium hydroxide.

- 1-Bromo-2-propanol is reacted with phosphorus oxychloride analogously to the procedure disclosed in "Helv. Acta Chim.", 33, 349/1958 for 2-bromoethanol and
- 20 the ester dichloride obtained of b.p. 110°C./18 mm.Hg ($\approx$ 2.4 kPa) reacted in the way given in Example 1 with the 3-(octadecanesulphonyl)-propanol described in Example 3. After reaction has taken place with trimethylamine, there are obtained 3.1% of the desired compound of
- 25 m.p. 203°C., decomp. It crystallises with 2 mole of water.

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Example 20.

2-Methoxy-3-octadecylmercaptopropanol-(1)-phosphoric acid monocholine ester.

- A. To 6.37 g. 2-0-methylglycerol in 70 ml. absolute
5 pyridine one adds dropwise at 0°C., with stirring,
7.7 ml. benzene sulphochloride. The batch is left to
stand overnight in the refrigerator and is then poured
in to 150 g. of ice. One extracts the aqueous phase with
methylene chloride, shakes the organic phase with 2N
10 hydrochloric acid, sodium bicarbonate solution and water,
dries and evaporates. The residue is applied to a silica
gel column (500 g.; elution agent: toluene/acetone 3:1
v/v). One obtains 7.2 g. $\approx$ 48.6% of the 2-0-methyl-
glycerol monobenzene-sulphonate (oil).
- 15 B. One dissolves 1.74 g. of solid potassium hydroxide
in 60 ml. absolute ethanol. At room temperature, one
adds dropwise, with stirring, a solution of 8.88 g.
octadecylmercaptan in 60 ml. absolute ethanol. After
1 h., one adds dropwise the solution of 6.93 g. 2-0-
20 methylglycerol monobenzene-sulphonate in 30 ml. absolute
ethanol thereto and leaves it to stir for 1.5 h. at room
temperature. Subsequently, it is poured on to 1 l. of
ice water. One acidifies with 2N hydrochloric acid,
extracts with ether, dries the organic phase and evapor-
25 ates. One purifies the residue over a silica gel column
(500 g.; elution agent: ether-ligroin 1:1 v/v). One
obtains 6.1 g. $\approx$ 58% of the 2-methoxy-3-octadecylmercapto-

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propanol (m.p. 44 - 47°C.).

C. To 6.0 g. 2-methoxy-3-octadecylmercaptopropanol in 80 ml. absolute toluene one adds 5.67 g. triethylamine and adds dropwise at 0°C., with stirring, the solution of
5 4.91 g. 2-bromoethylphosphoric acid dichloride in 50 ml. absolute toluene. After 4 h. at 0°C., one allows to stir overnight at room temperature, cools to 0°C., adds thereto 67 ml. 0.1 N aqueous potassium chloride solution and allows to stir vigorously for 1 h. at 0°C. and 2 h.
10 at room temperature. The toluene phase is then separated off, dried and evaporated. One takes up the residue in 45 ml. absolute methanol/30 ml. absolute chloroform, filters and saturates the solution with dry triethylamine. It is then boiled under reflux for 16 h. and subsequently
15 evaporated. One takes up the residue in 180 ml. absolute methanol, mixes with 2.88 g. silver acetate, leaves to stir for 1.5 h. at room temperature, filters off with suction, after-washes with absolute methanol and evaporates the filtrate. The residue is then purified over a
20 silica gel column (100 g.; elution agent: chloroform/methanol/water 65:25:4 v/v/v). One thus obtains 1.8 g. $\approx$ 19.6% of the desired 2-methoxy-3-octadecylmercaptopropanol-(1)-phosphoric acid monocholine ester. The amorphous product obtained is brought to crystallis-
25 ation by dissolving in absolute chloroform and precipitating out with acetone (m.p. 251 - 252°C.). The substance contains 2 mole of water.

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Example 21.

2-Methoxy-3-octadecanesulphonylpropanol-(1)-
phosphoric acid monocholine ester.

As described in Example 2, 2-methoxy-3-octadecyl-
5 mercaptopropanol-(1)-phosphoric acid monocholine ester
is treated with 30% hydrogen peroxide in glacial acetic
acid. The crude product is triturated several times
with acetone and thus brought to crystallisation. M.p.
81°C. (sinters), 120 - 122°C. (melts), yield 75.7%.
10 The substance contains 2 mole of water.

Example 22.

2-Methoxy-3-octadecanesulphonylpropanol-(1)-
phosphoric acid monocholine ester.

As described in Example 3, 2-methoxy-3-octadecyl-
15 mercaptopropanol-(1)-phosphoric acid monocholine ester
is treated with 30% hydrogen peroxide in glacial acetic
acid. The crude product is triturated several times
with acetone and thus brought to crystallisation. Yield
53.5%, melting point not determinable. The substance
20 contains 2 mole of water.

Example 23.

3-(2-Pentadecylmercaptoethylmercapto)-propanol-(1)-
phosphoric acid monocholine ester.

Starting from 3-(2-pentadecylmercaptoethylmercapto)-
25 propanol, m.p. 53 - 55°C., according to the procedure
given in Example 1, one obtains the desired compound as
hygroscopic crystals with the decomposition point of



237°C. which contain 2 mole of water.

The starting material is obtained as follows:

A solution of 2.3 g. sodium in 80 ml. methanol, which contains 12 g. 3-mercaptopropionic acid methyl ester and 12.5 g. 2-bromoethanol, is stirred under reflux for 4 h. After evaporation, it is taken up in chloroform, filtered and evaporated. One obtains 16 g. 3-(2-hydroxyethylmercapto)-propionic acid methyl ester as oil.

8.2 g. thereof are dissolved in 27 ml. abs. ether, 0.8 ml. pyridine added thereto and, with ice cooling, 1.9 ml. phosphorus tribromide added dropwise. Subsequently, one stirs at room temperature for 5 h. One then adds ice water thereto, extracts with ether, which is washed with water, dried and evaporated and one thus obtains 10.1 g. of an oil which is chromatographed with 480 g. silica gel. Elution agent: ligroin/ether (2:1). Yield 7.1 g. 3-(2-bromoethylmercapto)-propionic acid methyl ester as oil.

5.9 g. thereof are further reacted as follows.

A solution of 0.6 g. sodium in 30 ml. methanol, which contains 6.3 g. 1-mercaptopentadecane and 5.9 g. of ester, is heated under reflux for 3 h. One then cools and obtains, after dissolving in ether, filtering and evaporating, 9.4 g. crystalline 3-(2-pentadecylmercaptoethylmercapto)-propionic acid methyl ester. This amount is dissolved in 80 ml. absolute ether and added dropwise to a solution of 0.66 g. lithium aluminium hydride in

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50 ml. absolute ether. After 30 min. refluxing, one works up as usual and obtains 7.8 g. 3-(2-pentadecylmercaptoethylmercapto)-propanol as thin layer chromatographically uniform product of m.p. 53 - 55°C.

5 Example 24.

3-[3-Octadecylmercaptopropoxy)-phosphoryloxyhydroxy]-propyltrimethylammonium hydroxide.

A mixture of 1 g. phosphoric acid 3-bromopropyl ester dichloride, 1 g. 3-octadecylmercaptopropanol and 10 1.4 ml. triethylamine in 20 ml. absolute methylene chloride is stirred at 5°C. for 30 min. and in the ice-bath for 1 h. One then leaves to stand overnight at room temperature, hydrolyses, after the addition of 20 ml. 0.1N potassium chloride solution, by stirring for 4 hours 15 at 40°C., adds 40 ml. methanol thereto, acidifies with conc. hydrochloric acid and separates off the organic phase. After evaporation, one thus obtains 1.5 g. which are dissolved in 30 ml. of a mixture of chloroform/ 20 methanol (1:1). After passing in trimethylamine gas for 1 hour, one after-stirs for 3 h. at 40°C. One then evaporates and stirs up the crystals with acetone. One dissolves them again in 55 ml. methanol and, after the addition of 0.4 g. silver acetate, stirs for 3 h. at room temperature. After standing overnight, one filters, 25 evaporates and purifies the end product by column chromatography, as described in Example 1. One thus obtains 0.7 g. = 40% of hygroscopic crystals which,

according to elementary analysis, contain 4.5 mole of water. M.p. 228 - 230°C., decomp.

Example 25.

2-Methyl-3-octadecylmercaptopropanol-(1)-phosphoric

5 acid monocholine ester.

To a solution of 0.12 g. sodium in 70 ml. methanol one adds 14.3 g. octadecylmercaptan and then, in an ice bath, adds dropwise 5 g. methacrylic acid methyl ester. After stirring for 1 hour at room temperature, one
10 filters off with suction the cold suspension, washes with cold methanol and dries. One thus obtains 16.3 g. of greasy crystals = 88% of thin layer chromatographic-ally uniform α -methyl- β -octadecylmercaptopropionic acid methyl ester. The reduction is carried out with 1.14 g.
15 lithium aluminium hydride in 320 ml. water-free ether and gives 14.2 g. = 94% 2-methyl-3-octadecylmercapto-propanol, m.p. 37 - 39°C.

The phosphorylation, hydrolysis and choline formation is carried out according to the procedure given in
20 Example 1. One obtains 27% of the desired product, uniform in the thin layer chromatogram, m.p. 234 - 238°C. It crystallises with 1.5 mole of water.

Example 26.

3-(2-Pentadecanesulphonylethylmercapto)-propanol-

25 (1)-phosphoric acid monocholine ester.

0.7 g. sodium are dissolved in 80 ml. methanol. There are successively added 2.4 g. mercaptoethanol and

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- 9 g. pentadecyl bromide and the mixture stirred for 3 h. at 60°C. It is then taken up in ether, separated from sodium bromide and evaporated. The residue is purified column chromatographically. Elution with
- 5 ligroin/ether 1:1, yield 8.9 g. = 97% of 2-pentadecyl-mercaptoethanol of the m.p. 44 - 46°C. 13 g. of this compound are oxidised in 310 ml. glacial acetic acid with perhydrol until a uniform spot is to be seen in the thin layer chromatogram. One thus obtains 11.1 g. = 77%
- 10 of 2-pentadecanesulphonylethanol, m.p. 64 - 66°C. From this is obtained, with phosphorus tribromide in ether in the presence of pyridine, with 49%, 2-pentadecane-sulphonylethyl bromide of m.p. 68°C., foaming, 85°C. clear melt.
- 15 The further reaction now takes place analogously to the statements made in Example 1 and leads to the following further intermediate products:
- β -(2-pentadecanesulphonylethylmercapto)-propionic acid methyl ester, used as crude product for the reduction.
- 20 3-(2-pentadecanesulphonylethylmercapto)-propanol, m.p. 73 - 75°C.

From this is subsequently obtained the desired compound with 12% yield, m.p. 54°C. sinters, 229 - 232°C. slow decomposition with brown coloration. It contains

25 2.5 mole of water.

Example 27.

3-(2-Methoxyoctadecylmercapto)-propanol-(1)-phosphoric acid monocholine ester.



This compound is obtained with 30% yield analogously to the procedure given in Example 1. According to the elementary analysis, it contains 2.5 mole of water. Because of the strongly hygroscopic behaviour, a melting point cannot be given.

Starting material is 3-(2-methoxyoctadecylmercapto)-propanol, a colourless oil which, upon standing, gradually solidifies and is obtained as follows:

α -Bromostearic acid, m.p. 47 - 51°C., obtained by bromination of stearic acid, is esterified with methanol and catalytic amounts of p-toluenesulphonic acid, the oily ester is reacted with sodium methylate to give the α -methoxystearic acid methyl ester (m.p. 33 - 36°C.) and reduced with lithium aluminium hydride to 2-methoxystearyl alcohol, m.p. 36 - 38°C. (97% yield). With phosphorus tribromide, one obtains oily 2-methoxystearyl bromide (20% yield) which is reacted with β -mercaptopropionic acid methyl ester to give the oily β -(2-methoxyoctadecylmercapto)-propionic acid methyl ester (33% yield). A renewed lithium aluminium hydride reduction gives the desired propanol with 94% yield.

Example 28.

2-(3-Octadecylmercaptopropoxyphosphorylhydroxy)-2-methylethyltrimethylammonium hydroxide.

The phosphoric acid dichloride described in Example 19 is reacted with 3-octadecylmercaptopropanol, the preparation of which is described in Example 1,

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according to the there-given procedure. One obtains with 50% yield the bromide of the desired compound. The melting point of the bromine-free compound, obtained with silver acetate, lies at 61°C. (sinters), 139°C. (melts), 200°C. (decomp.).

Example 29.

2-Methyl-3-octadecanesulphonylpropanol-(1)-phosphoric acid monocholine ester.

The oxidation of the compound described in Example 25 with 30% hydrogen peroxide in glacial acetic acid gives, with 49% yield, the sulphone of m.p. 59°C. (sinters), 227 - 234°C. (decomp.).

Example 30.

3-Tetradecylmercaptopropanol)-(1)-phosphoric acid monocholine ester.

10 g. 1-Bromotetradecane and 4 ml. β -mercapto-propionic acid methyl ester are stirred under reflux for 4 h. in a solution of 0.83 g. sodium in 110 ml. methanol. One then evaporates in a vacuum, takes up the residue in ligroin, filters and evaporates the filtrate. The residue (11 g.; m.p. 32°C.) is dissolved in 55 ml. water-free ether and rapidly added dropwise to a solution of 0.94 g. lithium aluminium hydride in 110 ml. water-free ether. After half an hour refluxing, no starting material can be detected in the thin layer chromatogram. One works up in the usual way and obtains 9.45 g. 3-tetradecylmercaptopropanol of the m.p. 34 - 38°C. which are reacted

analogously to the procedure given in Example 1. There are obtained 1.9 g. = 58% of the desired compound as monohydrate with the sinter point of 63°C. and decomposition point of 231 - 233°C.

5 Example 31.

2-Methyl-3-octadecanesulphinylpropanol-(1)-phosphoric acid monocholine ester.

2-Methyl-3-octadecylmercaptopropanol, the preparation of which is described in Example 25, is oxidised in the usual way by means of 30% hydrogen peroxide in glacial acetic acid to the sulfoxide and, after purification on a silica gel column (solvent chloroform/methanol 9:1), obtained with 55% yield. M.p. 56 - 58°C.

The phosphorylation and choline ester formation are carried out according to the procedure given in Example 1. After usual purification, one obtains 12% of crystals with 1.5 mole of water of the decomposition point 235 - 240°C.

Example 32.

20 N-[2-(3-Hexadecylmercaptopropoxyphosphoryloxyhydroxy)-ethyl]-N,N-diethylamine.

A. Analogously to the procedure given in Example 6 with the replacement of trimethylamine by diethylamine, one obtains the desired compound with 15% yield. It sinters at 66°C. and melts clearly at 104 - 110°C. It crystallises with 1/2 mole of water.

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B. In the case of the use of 1 33% solution of dimethylamine in ethanol, one obtains with 9% yield N-[2-(3-hexadecylmercaptopropoxyphosphoryloxyhydroxy)-ethyl]-N,N-dimethylamine.

5 This compound also crystallises with 1/2 mole of water, sinters at 84°C. and melts clearly at 145 - 150°C.

C. In the case of the use of a 33% solution of methylamine in ethanol, one obtains, with 19% yield

10 N-[2-(3-hexadecylmercaptopropoxyphosphoryloxyhydroxy)-ethyl]-N-methylamine.

The sinter point lies at 91°C., the substance melts clearly, upon further heating, at 194°C.

D. Finally, one obtains, in the case of the use of a concentrated, aqueous solution of ammonia, with a yield
15 of 11%

2-(3-hexadecylmercaptopropoxyphosphoryloxyhydroxy)-ethylamine.

The sinter point lies at 170°C., at 195°C. begins the melting and at 218°C. a brown melt is present. The
20 compound crystallises with 1/2 mole of water.

Example 33.

3-Hexadecylmercapto-2-methylpropanol-(1)-phosphoric acid monocholine ester.

In a way analogous to that described in Example 25
25 but with hexadecylmercaptan, there are synthesised the following compounds:

8A

α -methyl- β -hexadecylmercaptopropionic acid methyl ester;
yellow oil, 79% yield

2-methyl-3-hexadecylmercaptopropanol; white, viscous
mass, 99% yield.

- 5 The monohydrate of the desired compound sinters at
60°C. and slowly decomposes at 229 - 235°C.

Example 34.

2,2-Dimethyl-3-hexadecylmercaptopropanol-(1)-phosphoric
acid monocholine ester.

- 10 Starting from 2,2-dimethyl-1,2-propanediol, one
obtains in a way analogous to the procedure given in
Example 20, part A, 56% of the corresponding monobenzene
sulphonate as colourless oil.

In a manner analogous to that described in

- 15 Example 20, part B, one obtains, by reaction with hexa-
decylmercaptan, 2,2-dimethyl-3-hexadecylmercaptopropanol,
m.p. 25 - 28°C., with 16% yield. Finally, one phosphoryl-
ates analogously to part C in Example 20 and obtains,
after reaction with trimethylamine, the desired compound
20 with 34% yield. It contains 1.5 mole of water, sinters
at 70°C., begins to melt at 228°C. and decomposes at
235 - 238°C.

Example 35.

- 25 Cis- or trans-3-octadecylmercaptocyclohexanol-(1)-
phosphoric acid monocholine ester.

Starting from 1,3-cyclohexanediol, which is present
as cis-trans mixture, one obtains, by reaction with

benzenesulphochloride according to the method of working described in Example 20, part A, the corresponding monobenzenesulphonate, also as oily cis-trans mixture, with 62% yield.

5 The reaction with octadecylmercaptan analogously to Example 20, part B, provides, after separation of the isomer mixture on a silica gel column, 12% of each of the 3-octadecylmercaptocyclohexanol. Elution agent: ether/ligroin 1:4.

10 On the basis of the NMR spectroscopical investigation, the product with the m.p. 50 - 52°C. is indicated as cis compound (= both substituents in the 1,3-position in equatorial position), the other fraction with the m.p. 44 - 46°C. as trans compound.

15 Both substances are now phosphorylated in the usual way and reacted with trimethylamine. One thus obtains from the cis compound the above-mentioned compound with the sinter point of 51°C. and a melting point of 241 - 244°C. with decomposition, from the trans compound the
20 above-mentioned isomer with the sinter point of 45°C. and the melting point of 239 - 241°C., with decomposition.

According to the elementary analysis (C, H, N, P, S determination), both products contain 1.5 mole of water.

Example 36.

25 3-(14-Methoxytetradecylmercapto)-propanol-(1)-phosphoric acid monocholine ester.

1,14-Dibromotetradecane, m.p. 38 - 40°C. is

obtained analogously to "Org. Synth.", Coll. Vol. 1, 29, in 92% yield from the corresponding diol ("Helv.", 9, 271/1926).

3.6 g. thereof are added to a solution of 0.23 g. sodium in 40 ml. methanol + 1.1 ml. β -mercaptopropionic acid methyl ester and the suspension stirred under reflux for 4 h. One evaporates, stirs up the residue with ether, separates off the ethereal solution, evaporates it and chromatographs the residue on a silica gel column with ether/ligroin 1:10. The desired fractions are combined and, after evaporation, provide 1.6 g. = 41% β -(14-bromotetradecylmercapto)-propionic acid methyl ester of the m.p. 33 - 35°C.

The β -(14-methoxytetradecylmercapto)-propionic acid methyl ester obtained therefrom with sodium methylate solution after boiling for 15 hours must also be purified on a column. Yield: 11%, m.p. 31 - 32°C.

0.8 g. thereof are reduced in 25 ml. water-free ether with 62 mg. lithium aluminium hydride and gives 0.6 g. = 86% 3-(14-methoxytetradecylmercapto)-propanol of m.p. 35 - 37°C.

This compound is now phosphorylated analogously to Example 20, part C, and reacted to the choline ester. One thus obtains 26% of the monohydrate which sinters at 76°C. and melts with decomposition at 238 - 244°C.

Example 37.

N-[2-(3-Hexadecylmercaptopropoxyphosphoryloxyhydroxy)-ethyl]-N-methyl-N,N-diethylammonium hydroxide.

3.7 g. of the compound prepared according to Example 32, part A, are stirred in 37 ml. tetrahydrofuran, together with 4.2 g. sodium bicarbonate in 50 ml. water and 8.5 ml. methyl iodide, for 2 h. at room temperature.

5 Thereafter, in the thin layer chromatogram, the starting material spot had disappeared and a new main spot formed. After evaporation in a vacuum, it is taken up in chloroform, filtered, evaporated, the base produced with silver acetate in methanol and purified column chromatographically as described in Example 1. The yield amounts to

10 13%. The compound sinters at 40°C. and decomposes at 119°C. It contains 4.5 mole of water.

Example 38.

20-Isopropyl-3-octadecylmercaptopropanol-(1)-phosphoric

15 acid monocholine ester.

10.1 g. isopropylmalonic acid diethyl ester are reduced in 150 ml. water-free ether with 2.7 g. lithium aluminium hydride in the usual way. There are obtained 5.9 g. of an oil uniform in the TLC.

20 In a way analogous to that described in part A of Example 20, one now reacts with benzenesulphochloride to give the monobenzenesulphonate of 2-isopropylpropane-1,3-diol, which is obtained in 42% yield as colourless oil.

25 In a way analogous to that described in Example 20, part B, one obtains therefrom, in 87% yield, the 2-isopropyl-3-octadecylmercaptopropanol of m.p. 29°C.

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Finally, one phosphorylates according to part C, Example 20 and reacts further with trimethylamine to give the desired end product. One thus obtains 37% of crystals with 1.5 mole of water of the sinter point
5 55°C. and melting point 230 - 233°C., with decomposition.

Example 39.

4-Heptadecylmercapto-3-methyl-n-butanol-(1)-phosphoric acid monocholine ester.

In analogous way as above, the benzenesulphonate
10 of 1-hydroxy-2-methyl-3-butanone is obtained as oil in 30% yield. The reaction with heptadecylmercaptan gives, after column chromatographic purification, with 61% yield, the 1-heptadecylmercapto-2-methyl-3-butanone as oil. Finally, the lithium aluminium hydride reduction
15 leads, with 85% yield, to the TLC-uniform 1,2-dimethyl-3-heptadecylmercaptopropanol, m.p. 28 - 30°C. The phosphorylation thereof and choline ester formation take place in the manner given in Example 20, part C, and provides, with 13% yield, the desired compound
20 which crystallises with 1.5 mole of water. It sinters at 55°C. and melts at 230 - 233°C. with decomposition.

Example 40.

3-Octadecylmercaptobutanol-(1)-phosphoric acid monocholine ester.

25 2 g. Octadecylmercaptobutanol, m.p. 35 - 38°C., is phosphorylated in the way given in Example 20, part C, and reacted to the choline ester (1.85 g. = 59%). After

purification on a silica gel column, the crystals sinter at $58^{\circ}\text{C}.$, become discoloured above $208^{\circ}\text{C}.$ and decompose at $232^{\circ}\text{C}.$ The compound crystallises with 1.5 mole of water.

5 The starting material is obtained as follows:
1,3-butyleneglycol is reacted with acetic anhydride at room temperature to give 1,3-butanediol-1-acetate.
Yield: 63%.

10 In the presence of pyridine, it is then esterified
with benzenesulphochloride and the reaction product
eluted over a silica gel column with ether/ligroin 1:1.
Yield: 24% of a colourless oil which is reacted with
octadecanethiol sodium according to the procedure given
in Example 20, part B, and then treated with dilute
15 aqueous sodium hydroxide solution, whereby 12% octadecyl-
mercaptobutanol result, m.p. $35 - 38^{\circ}\text{C}.$

Example 41.

3-(9-Octyloxynonylmercapto)-propanol-(1)-phosphoric
acid monocholine ester.

20 One phosphorylates 3-(9-octyloxynonylmercapto)-
propanol, m.p. $29 - 32^{\circ}\text{C}.$, analogously to Example 20,
part C, and obtains, according to the method of working
there given, with 39% yield, the desired choline ester
which crystallises with 1.75 mole of water. The sinter
25 point lies at $50^{\circ}\text{C}.$, in the case of further heating
the substance decomposes at $221 - 224^{\circ}\text{C}.$

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Example 42.

3-(4-Tridecyloxybutylmercapto)-propanol-(1)-
phosphoric acid monocholine ester.

One dissolves 2.3 g. sodium in 44 ml. 1,4-butane-
5 diol by warming, adds 38 ml. 1-bromotridecane thereto
and stirs for 5 h. at 150°C. bath temperature. After
cooling, one extracts with a mixture of ether/ligroin
1:2, evaporates and purifies on a silica gel column by
elution with ligroin which is later replaced by ether/
10 ligroin 1:1. The desired fractions are collected and
evaporated. There are thus obtained 19.4 g. thin layer
chromatographically uniform 4-tridecyloxybutanol of m.p.
26 - 29°C. in 71% yield.

10 g. thereof are dissolved in 100 ml. ether,
15 0.6 ml. pyridine added thereto and 1.4 m. phosphorus
tribromide added dropwise thereto, whereby it is cooled
in an ice-bath. After standing overnight at room temp-
erature, one dilutes with ether, shakes up with ice
water, separates off the ether extract, dries and
20 evaporates it. The residue, 9.2 g. of a yellowish oil,
is applied with ether/ligroin 1:1 to a silica gel column.
The uniform fractions are combined and evaporated. One
thus obtains 5.5 g. = 45% of TLC-uniform 4-tridecyloxy-
butyl bromide as yellowish oil.

25 This bromide is stirred under reflux for 3 h. with
1.9 g. β -mercaptopropionic acid methyl ester in 75 ml.
methanol, which contains 378 mg. sodium. The solution

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is then evaporated and the residue again purified column chromatographically. Elution agent: ether/ligroin 1:10. One thus obtains 5.7 g. = 93% β -(4-tridecyloxybutyl-mercapto)-propionic acid methyl ester as yellowish oil.

5 This ester is reduced in 70 ml. ether with 0.4 g. lithium aluminium hydride. After 1 hours stirring under reflux, one decomposes in the usual way and elutes the ether evaporation residue on a silica gel column with ether/ligroin 1:1. One thus obtains 4 g. = 77% 3-(4-tridecyloxybutylmercapto)-propanol, m.p. 32 - 34°C., as
10 TLC-uniform product.

 The reaction to the desired end product is carried out analogously to the procedure given in Example 20, part C. One obtains 2.1 g. = 33% of the sinter point
15 55°C. and the decomposition point of 218°C. The product crystallises with 2.5 mole of water.

Example 43.

3-Pentadecylmercaptopropanol-(1)-phosphoric acid monocholine ester.

20 1-Bromopentadecane is reacted in the usual way with β -mercaptopropionic ester and the syrup obtained reduced with lithium aluminium hydride to the 3-pentadecylmercaptopropanol, m.p. 36 - 39°C.

 The further reaction steps are carried out
25 analogously to Example 20, part C. They lead, with 61% yield, to the desired product of the sinter point 60°C. and the decomposition point 237°C. It crystallises with 1.25 mole of water.

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Example 44.

5-Hexadecylmercaptopentanol-(1)-phosphoric acid
monocholine ester.

5-Hexadecylmercaptopentanol, m.p. 40 - 43°C.

5 (obtained from 1,5-pentanediol via the oily monobenzene-
sulphonate with hexadecylmercaptan potassium in 63% yield)
is phosphorylated in the usual way (see Example 20,
part C) and reacted to the choline ester. The yield
amounts to 41%. The water-soluble crystals have a sinter
10 point of 58°C. and decompose at 228 - 230°C. The product
crystallises with 1.5 mole of water.

Example 45.

3-(10-Butoxydecyloxyethylmercapto)-propanol-(1)-
phosphoric acid monocholine ester.

15 3-(10-n-butoxydecyloxyethylmercapto)-propanol, m.p.
23 - 27°C., is phosphorylated in the way given in
Example 20, part C, and reacted to the choline ester.
With 35% yield, there is obtained the desired compound
as water-soluble crystals of m.p. 36°C. (sinters 227 -
20 229°C. (decomp.)).

The hygroscopic crystals are present as dihydrate.

The starting material is obtained as follows: 1,10-
decanediol monosodium is reacted with n-butylbromide and
gives, with 62% yield, oily 10-n-butoxydecanol. This is
25 brominated with phosphorus tribromide in the presence of
pyridine. Yield: 37% of oil. After reaction of this
10-n-butoxydecyl bromide with ethylene glycol monosodium,

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there is obtained 36% of oily 10-n-butoxydecyloxyethanol which is further reacted with phosphorus tribromide in the presence of pyridine and gives 52% of oily 10-n-butoxydecyloxyethyl bromide. The reaction thereof with
5 β -mercaptopropionic acid methyl ester in the presence of sodium methylate provides 49% of oily β -(10-n-butoxydecyloxyethylmercapto)-propionic acid methyl ester which is reduced in known manner with lithium aluminium hydride and gives, with 90% yield, 3-(10-n-butoxydecyloxy-
10 ethylmercapto)-propanol of m.p. 23 - 27°C.

Example 46.

3-(11-Hexyloxyundecylmercapto)-propanol-(1)-phosphoric acid monocholine ester.

11-Bromo-1-undecanol, m.p. 45 - 48°C., is reacted
15 with sodium hexanolate and the syrupy product obtained is brought to reaction with phosphorus tribromide in the presence of pyridine. The structure of the oil obtained is confirmed mass spectroscopically as 11-bromoundecyloxyhexane. This bromo compound is reacted with β -mercapto-
20 propionic acid methyl ester in sodium methylate solution and the oil obtained subsequently reduced with lithium aluminium hydride to the 3-(11-hexyloxyundecylmercapto)-propanol, m.p. 27 - 29°C. The phosphorylation and choline ester formation take place analogously to
25 Example 20, part C, and give the desired product with 55% yield as monohydrate of m.p. 98°C. (sinters), 226 - 229°C. (decomp.).

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Example 47.

3-(7-Decyloxyheptylmercapto)-propanol-(1)-phosphoric acid monocholine ester.

3-(7-Decyloxyheptylmercapto)-propanol, m.p. 28 -
5 32°C., obtained by reaction of 1,7-heptanediol with 1-bromodecane to 7-decyloxyheptanol, bromination to the 7-decyloxyheptyl bromide, reaction with β -mercaptopropionic acid methyl ester to β -(7-decyloxyheptylmercapto)-propionic acid methyl ester and reduction thereof with
10 lithium aluminium hydride, is, as described in Example 20, part C, reacted with 17% yield to the desired choline ester. The water-soluble, white crystals sinter at 53°C. and melt at 224°C.

In analogous way, from 3-(3-tetradecyloxypropyl-
15 mercapto)-propanol, m.p. 38 - 41°C. (prepared from β -mercaptopropionic acid methyl ester and 1-bromo-3-tetradecylpropane in sodium methylate solution and subsequent reduction with lithium aluminium hydride), one obtains with 38% yield

20 3-(3-tetradecyloxypropylmercapto)-propanol-(1)-phosphoric acid monocholine ester

which sinters at 52°C. and melts with decomposition at 230 - 233°C.

Example 48.

25 Analogously to Example 20 C, by reaction of 3-hexadecylmercapto-2-methoxypropanol-(1) (wax-like substance) with 2-bromoethylphosphoric acid ester dichloride,

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subsequent saponification, treatment with triethylamine and silver acetate, one obtains

3-hexadecylmercapto-2-methoxypropanol-(1)-phosphoric acid monocholine ester

5 (m.p. 255 - 256°C.) in a yield of 16%. The substance contains 1 mole of water of crystallisation.

One obtains the 3-hexadecylmercapto-2-methoxypropanol-(1) used as starting material by reaction of 2-methoxy-1,3-propanediol monobenzenesulphonate (oily
10 substance) with the sodium salt of hexadecylmercaptan.
Example 49.

Analogously to Example 48, by the use of 3-heptadecylmercapto-2-methoxypropanol-(1) (wax-like substance) as starting material, one obtains

15 3-heptadecylmercapto-2-methoxypropanol-(1)-phosphoric acid monocholine ester

(m.p. 255 - 257°C.) in a yield of 11%. The substance contains 2 mole of water of crystallisation.

One obtains the 3-heptadecylmercapto-2-methoxypropanol-(1) used as starting material by reaction of
20 2-methoxy-1,3-propanediol benzenesulphonate with the sodium salt of heptadecylmercaptan.

Example 50.

Analogously to Example 48, by the use of 2-ethoxy-
25 3-heptadecylmercapto-2-methoxypropanol-(1) (wax-like substance); m.p. < 50°C.) as starting material, one obtains

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2-ethoxy-3-heptadecylmercaptopropanol-(1)-phosphoric acid monocholine ester

(m.p. 225 - 230°C.) in a yield of 18%. The substance contains 2 mole of water of crystallisation.

- 5 One obtains the 2-ethoxy-3-heptadecylmercapto-propanol-(1) used as starting material by reaction of 2-ethoxy-1,3-propanediol benzenesulphonate (oily substance) with the potassium salt of heptadecylmercaptan.

Example 51.

- 10 Analogously to Example 48, by the use of 2-methoxy-3-(trans-octadec-9-enylmercapto)-propanol-(1) (wax-like substance) as starting material, one obtains

2-methoxy-3-(trans-octadec-9-enylmercapto)-propanol-(1)-phosphoric acid monocholine ester

- 15 (wax) in a yield of 12%. The substance contains 3 moles of water of crystallisation.

- One obtains the 2-methoxy-3-(trans-octadec-9-enylmercapto)-propanol-(1) used as starting material by the reaction of 2-methoxy-1,3-propandiol monobenzenesulphonate
20 with the sodium salt of trans-octadec-9-enylmercaptan.

Example 52.

- Analogously to Example 48, by the use of 2-methoxy-3-(octadec-9,12-dienylmercapto)-propanol-(1) (wax-like substance) as starting material, one obtains

- 25 2-methoxy-3-(octadec-9,12-dienylmercapto)-propanol-(1)-phosphoric acid monocholine ester

(wax) in a yield of 11%. The substance contains 3 moles of water of crystallisation.

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One obtains the 2-methoxy-3-(octa-9,12-dienyl-mercapto)-propanol-(1) used as starting material by the reaction of 2-methoxy-1,3-propanediol monobenzene-sulphonate with the sodium salt of octadec-9,12-dienyl-mercaptan.

Example 53.

Analogously to Example 48, by the use of 2-methoxy-3-(1-methyloctadecylmercapto)-propanol-(1) (wax-like substance) as starting material, one obtains
10 2-methoxy-3-(1-methyloctadecylmercapto)-propanol-(1)-phosphoric acid monocholine ester
(m.p. 256 - 258°C.) in a yield of 34%. The substance contains 2 moles of water of crystallisation.

One obtains the 2-methoxy-3-(1-methyloctadecyl-mercapto)-propanol-(1) used as starting material by the
15 reaction of 2-methoxy-1,3-propanediol monobenzene-sulphonate with the potassium salt of 1-methyloxadecylmercaptan.

Example 54.

20 Analogously to Example 48, by the use of 3-(3-heptyldecylmercapto)-2-methoxypropanol-(1) (wax-like substance) as starting material, one obtains
3-(3-heptyldecylmercapto)-2-methoxypropanol-(1)-phosphoric acid monocholine ester
25 (wax) in a yield of 48%. The substance contains 1 mole of water of crystallisation.

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One obtains the 3-(3-heptyldecylmercapto)-2-methoxypropanol-(1) used as starting material by the reaction of 2-methoxy-1,3-propanediol monobenzenesulphonate with the potassium salt of 3-heptyldecylmercaptan.

5 Example 55.

Analogously to Example 48, by the use of 2-methoxy-3-(3-tetradecyloxypropylmercapto)-propanol-(1) (wax-like substance) as starting material, one obtains

10 2-methoxy-3-(3-tetradecyloxypropylmercapto)-propanol-(1)-phosphoric acid monocholine ester
(m.p. 242 - 244°C.) in a yield of 18%. The substance contains 2 mole of water of crystallisation.

One obtains the 2-methoxy-3-(3-tetradecyloxypropylmercapto)-propanol-(1) used as starting material by the
15 reaction of 2-methoxy-1,3-propanediol monobenzene-sulphonate with the potassium salt of 3-tetradecyloxypropylmercaptan.

Example 56.

Analogously to Example 48, by the use of 3-(5-dodecyloxypentylmercapto)-2-methoxypropanol-(1) as starting material, one obtains

20 3-(5-dodecyloxypentylmercapto)-2-methoxypropanol-(1)-phosphoric acid monocholine ester
(m.p. 245 - 247°C.) in a yield of 25%. The substance
25 contains 2 moles of water of crystallisation.

One obtains the 3-(5-dodecyloxypentylmercapto)-2-methoxypropanol-(1) used as starting material by the

reaction of 2-methoxy-1,3-propanediol monobenzene-sulphonate with the potassium salt of 5-dodecyloxy-pentyl-mercaptan.

Example 57.

- 5 Analogously to Example 48, by the use of 2-methoxy-3-(8-nonyloxyoctylmercapto)-propanol-(1) (wax-like substance) as starting material, one obtains
- 2-methoxy-3-(8-nonyloxyoctylmercapto)-propanol-(1)-
phosphoric acid monocholine ester
- 10 (wax) in a yield of 20%. The substance contains 1 mole of water of crystallisation.

One obtains the 2-methoxy-3-(8-nonyloxyoctylmercapto)-propanol-(1) used as starting material by the reaction of 2-methoxy-1,3-propanediol monobenzene-

15 sulphonate with the potassium salt of 8-nonyloxyoctylmercaptan.

Example 58.

- Analogously to Example 48, by the use of 2-ethyl-3-hexadecylmercaptopropanol-(1) (wax-like substance) as
- 20 starting material, one obtains
- 2-ethyl-3-hexadecylmercaptopropanol-(1)-phosphoric
acid monocholine ester
- (m.p. 236 - 238°C.) in a yield of 41%. The substance contains 2 mole of water of crystallisation.

25 One obtains the 2-ethyl-3-hexadecylmercapto-propanol-(1) used as starting material by the reaction of 2-ethyl-1,3-propanediol monobenzenesulphonate with the

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sodium salt of hexadecylmercaptan.

Example 59.

Analogously to Example 48, by the use of 3-hexadecylmercapto-2-propylpropanol-(1) (wax-like substance) as starting material, one obtains

3-hexadecylmercapto-2-propylpropanol-(1)-phosphoric acid monocholine ester

(m.p. 239 - 240°C.) in a yield of 13%. The substance contains 2 moles of water of crystallisation.

One obtains the 3-hexadecylmercapto-2-propylpropanol-(1) used as starting material by the reaction of 2-propyl-1,3-propanediol monobenzenesulphonate (oily substance) with the sodium salt of hexadecylmercaptan.

Example 60.

Analogously to Example 48, by the use of 2-n-butyl-3-octadecylmercapto-2-propylpropanol-(1) (wax-like substance; m.p. 36 - 40°C.) as starting material, one obtains

2-n-butyl-3-octadecylmercapto-2-propylpropanol-(1)-phosphoric acid monocholine ester

(m.p. 232 - 238°C.) in a yield of 17%. The substance contains 4 moles of water of crystallisation.

One obtains the 2-n-butyl-3-octadecylmercapto-2-propylpropanol-(1) used as starting material by the reaction of 2-n-butyl-1,3-propanediol monobenzenesulphonate (oily substance) with the sodium salt of octadecylmercaptan.

Example 61.

Analogously to Example 48, by the use of 2-

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benzyloxy-3-octadecylmercaptopropanol-(1) (wax-like substance; m.p. 39 - 42°C.) as starting material, one obtains

2-benzyloxy-3-octadecylmercaptopropanol-(1)-phosphoric

5 acid monocholine ester

(m.p. 210 - 212°C.) in a yield of 28%. The substance contains 1 mole of water of crystallisation.

One obtains the 2-benzyloxy-3-octadecylmercaptopropanol-(1) used as starting material by the reaction
10 of 2-benzyloxy-1,3-propanediol monobenzenesulphonate (oily substance) with the sodium salt of octadecylmercaptan.

Example 62.

Analogously to Example 48, by the use of 3-hexadecylmercapto-2-methoxymethylpropanol-(1) (wax-like
15 substance) as starting material, one obtains

3-hexadecylmercapto-2-methoxymethylpropanol-(1)-
phosphoric acid monocholine ester

(m.p. 243 - 245°C.) in a yield of 22%. The substance
20 contains 3 moles of water of crystallisation.

One obtains the 3-hexadecylmercapto-2-methoxymethylpropanol-(1) used as starting material by the reaction of
2-methoxymethyl-1,3-propanediol monobenzenesulphonate (oily substance) with the sodium salt of hexadecyl-
25 mercaptan.

Example 63.

Analogously to Example 48, by the use of 2-ethoxy-

methyl-3-hexadecylmercaptopropanol-(1) (wax-like substance) as starting material, one obtains
2-ethoxymethyl-3-hexadecylmercaptopropanol-(1)-
phosphoric acid monocholine ester

5 (m.p. 243 - 246°C.) in a yield of 11%. The substance contains 2.5 mole of water of crystallisation.

One obtains the 2-ethoxymethyl-3-hexadecylmercapto-
propanol-(1) used as starting material by the reaction
of 2-ethoxymethyl-1,3-propanediol monobenzenesulphonate
10 (oily substance) with the sodium salt of hexadecyl-
mercaptan.

Example 64.

Analogously to Example 48, by the use of 2,2-bis-
methoxymethyl-3-octadecylmercaptopropanol-(1) (wax-like
15 substance) as starting material, one obtains
2,2-bis-methoxymethyl-3-octadecylmercaptopropanol-(1)-
phosphoric acid monocholine ester

(m.p. 237 - 239°C.) in a yield of 26%. The substance contains 1 mole of water of crystallisation.

20 One obtains the 2,2-bis-methoxymethyl-3-octadecyl-
mercaptopropanol-(1) used as starting material by the
reaction of 2,2-bis-methoxymethyl-1,3-propanediol mono-
benzenesulphonate (oily substance) with the sodium salt
of octadecylmercaptan.

25 Example 65.

Analogously to Example 48, by the use of 3-hepta-
decylmercapto-2-methoxy-2-methylpropanol-(1) (wax-like

substance) as starting material, one obtains

3-heptadecylmercapto-2-methoxy-2-methylpropanol-(1)-
phosphoric acid monocholine ester

(m.p. 244 - 251°C.) in a yield of 19%. The substance
5 contains 2 moles of water of crystallisation.

One obtains the 3-heptadecylmercapto-2-methoxy-2-
methylpropanol-(1) used as starting material by the
reaction of 2-methylglycidic acid methyl ester with the
sodium salt of heptadecylmercaptan to give 3-heptadecyl-
10 mercapto-2-hydroxy-2-methylpropionic acid methyl ester
(m.p. 42 - 45°C.), subsequent methylation with methyl
iodide to give 3-heptadecylmercapto-2-methoxy-2-methyl-
propionic acid methyl ester (oily substance) and
reduction with lithium aluminium hydride.

15 Example 66.

Analogously to Example 48, by the use of 4-hexa-
decylmercaptobutanol-(2) (wax-like substance) as starting
material, one obtains

4-hexadecylmercaptobutanol-(2)-phosphoric acid
20 monocholine ester

(wax) in a yield of 19%. The substance contains 2.5 mole
of water of crystallisation.

One obtains the 4-hexadecylmercaptobutanol-(2) used
as starting material by the reduction of 4-hexadecyl-
25 mercaptobutanone-(2) (m.p. 45 - 47°C.) with lithium
aluminium hydride.

Example 67.

Analogously to Example 48, by the use of 4-octadecylmercaptopentanol-(2) (wax-like substance) as starting material, one obtains

5 4-octadecylmercaptopentanol-(2)-phosphoric acid
monocholine ester

(m.p. 239 - 245°C.) in a yield of 7%. The substance contains 3 moles of water of crystallisation.

One obtains the 4-octadecylmercaptopentanol-(2)
10 used as starting material by the reaction of 2,4-pentane-
diol monobenzenesulphonate (oily substance) with the
sodium salt of octadecylmercaptan.

Example 68.

Analogously to Example 48, by the use of 3-hexa-
15 decylmercaptocyclopentanol-(1) (wax-like substance; m.p.
45 - 50°C.) as starting material, one obtains

3-hexadecylmercaptocyclopentanol-(1)-phosphoric acid
monocholine ester

(m.p. 253 - 256°C.) in a yield of 33%. The substance
20 contains 2 moles of water of crystallisation.

One obtains the 3-hexadecylmercaptocyclopentanol-
(1) used as starting material by the reaction of 1,3-
cyclopentanediol monobenzenesulphonate with the sodium
salt of hexadecylmercaptan.

25 Example 69.

Analogously to Example 48, by the use of (S)-2-
methanesulphonamide-3-octadecylmercaptopropanol-(1)

(m.p. 85 - 87°C.) as starting material, one obtains
(S)-2-methanesulphonamido-3-octadecylmercaptopropanol-
(1)-monocholine ester

(m.p. 212 - 215°C.) in a yield of 14%. The substance
5 contains 1 mole of water of crystallisation.

One obtains the (S)-2-methanesulphonamido-3-octa-
decylmercaptopropanol-(1) used as starting material by
the reaction of (L)-S-octadecylcysteine ethyl ester with
methanesulphochloride to give (L)-N-methanesulphonyl-S-
10 octadecylcystein ethyl ester (m.p. 63 - 65°C.) and sub-
sequent reduction with lithium aluminium hydride.

Example 70.

Analogously to Example 48, by the use of 3-hexa-
decylmercapto-2-methoxymethylpropanethiol-(1) (oil) as
15 starting material, one obtains

thiophosphoric acid O-choline ester S-(3-hexadecyl-
mercapto-2-methoxymethylpropyl) ester

(m.p. 230 - 235°C., decomp.) in a yield of 14%. The
substance contains 3 moles of water of crystallisation.

20 One obtains the 3-hexadecylmercapto-2-methoxymethyl-
propanethiol-(1) used as starting material by the reaction
of 3-hexadecylmercapto-2-methoxymethylpropanol-(1) with
benzenesulphochloride to give 3-hexadecylmercapto-2-
methoxymethylpropanol-(1) (oily substance), reaction
25 with thiourea to give the corresponding isothiuronium
salt, subsequent hydrolysis with 10N potassium hydroxide
solution and acidification with hydrochloric acid.

Example 71.

Analogously to Example 48, by the use of 3-[2-(N-dodecylaminocarbonyl)-ethylmercapto]-2-methoxypropanol-(1) (m.p. 67 - 69°C.) as starting material, one obtains
5 3-[2-(N-dodecylaminocarbonyl)-ethylmercapto]-2-methoxypropanol-(1)-phosphoric acid monocholine ester
(wax-like substance) in a yield of 16%. The substance contains 4 mole of water of crystallisation.

One obtains the 3-[2-(N-dodecylaminocarbonyl)-ethylmercapto]-2-methoxypropanol-(1) used as starting
10 material by reaction of 2-methoxy-1,3-propanediol monobenzenesulphonate with the sodium salt of 2-(N-dodecylaminocarbonyl)-ethyl mercaptan. One obtains this
mercaptan by reaction of 3-mercaptopropionic acid ethyl
15 ester with dodecylamine.

Example 72.

Analogously to Example 48, by the use of 2-methoxy-3-(9-phenyloctadecylmercapto)-propanol-(1) (oily substance) as starting material, one obtains
20 2-methoxy-3-(9-phenyloctadecylmercapto)-propanol-(1)-phosphoric acid monocholine ester
(wax-like substance) in a yield of 10%. The substance contains 2 mole of water of crystallisation.

One obtains the 2-methoxy-3-(9-phenyloctadecylmercapto)-propanol-(1) used as starting material by
25 reaction of 2-methoxy-1,3-propanediol monobenzene-sulphonate with the sodium salt of 9-phenyloctadecylmercaptan.

Example 73.

Analogously to Example 48, by the use of 3-[11-(N-n-butylaminocarbonyl)-undecylmercapto]-2-methoxypropanol-(1) (m.p. 62 - 64°C.) as starting material, one
5 obtains

3-[11-(N-n-butylaminocarbonyl)-undecylmercapto]-2-methoxypropanol-(1)-phosphoric acid monocholine ester
(wax-like substance) in a yield of 13%. The substance
contains 3.5 moles of water of crystallisation.

10 One obtains the 3-[11-(N-n-butylaminocarbonyl)-undecylmercapto]-2-methoxypropanol-(1) used as starting material by reaction of 2-methoxy-1,3-propanediol monobenzenesulphonate with the sodium salt of 11-(N-n-butylaminocarbonyl)-undecylmercaptan.

15 Example 74.

Analogously to Example 48, by the use of 2-methoxy-3-octadecylmercaptopropanethiol-(1) (wax-like substance) as starting material, one obtains

thiophosphoric acid O-choline ester S-(2-methoxy-3-octadecylmercaptopropyl) ester
20 (m.p. 219 - 221°C., decomp.) in a yield of 7%. The substance contains 4 moles of water of crystallisation.

One obtains the 2-methoxy-3-octadecylmercapto-
propanethiol-(1) used as starting material by reaction
25 of 2-methoxy-3-octadecylmercaptopropanol-(1) with benzenesulphochloride to give 2-methoxy-3-octadecylmercapto-
propanol-(1)-benzene sulphonate (oily substance),

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reaction with thiourea to give the corresponding isothiuronium salt, subsequently hydrolysis with 10N potassium hydroxide solution and acidification with hydrochloric acid.

5 Example 75.

Analogously to Example 48, by the use of 4-octadecylmercaptopentane-1-thiol-(2) (m.p. 38 - 40°C.) as starting material, one obtains

10 thiophosphoric acid O-choline ester S-(4-octadecylmercapto-2-pentyl) ester

(m.p. 244 - 245°C., decomp.) in a yield of 9%. The substance contains 3.5 moles of water of crystallisation.

One obtains the 4-octadecylmercaptopentane-1-thiol-(2) used as starting material by reaction of 4-octadecylmercaptopentane-1-thiol-(2) with benzene sulphonyl chloride to give 4-octadecylmercaptopentane-1-thiol-(2) benzene sulphonate (oily substance), reaction with thiourea to give the corresponding isothiuronium salt, subsequently hydrolysis with 10N potassium hydroxide solution and acidification with hydrochloric acid.

Example 76.

2-Methyl-2-methoxycarbonyl-3-hexadecylmercaptopropanol-(1)-phosphoric acid monocholine ester.

2,2-Bis-hydroxymethylmonobenzene sulphonate propionic acid methyl ester, m.p. 58 - 62°C., is reacted with hexadecyl sodium mercaptide in methanol to give 2-hydroxymethyl-2-hexadecylmercaptomethylpropionic acid

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methyl ester, m.p. 25 - 27°C. The phosphorylation, hydrolysis and choline ester formation take place analogously to Example 20 C and gives, with 31% yield, the monohydrate of the desired compound with the sinter point of 65°C. and decomposition point of 238 - 240°C.

Example 77.

Thiophosphoric acid O-choline ester S-2-methyl-3-hexadecylmercaptopropyl ester.

From the 2-methyl-3-hexadecylmercaptopropanol described in Example 33, one obtains, via its benzene sulphonate, in the case of boiling with thiourea, the oily 2-methyl-3-hexadecylmercaptopropanethiol, the phosphorylation of which, hydrolysis and choline ester formation is carried out analogously to Example 20, part C, and leads, with 17% yield, to the desired product which, after sintering at 45°C., melts at 262°C. with foaming. The compound is present as trihydrate.

Example 78.

Analogously to Example 48, with the use of 3-hexadecylmercapto-2-(2-methoxyethoxy)-propanol-(1) (oily substance) as starting material, one obtains

3-hexadecylmercapto-2-(2-methoxyethoxy)-propanol-(1)-phosphoric acid monocholine ester

(m.p. 257 - 258., decomp.) in a yield of 18%. The substance contains 1 mole of water of crystallisation.

One obtains the 3-hexadecylmercapto-2-(2-methoxyethoxy)-propanol-(1) used as starting material by

reaction of 2-(2-methoxyethoxy)-1,2-propanediol mono-benzene sulphonate (oily substance) with the potassium salt of hexadecylmercaptan.

Example 79.

5 2-Hexadecyloxy-3-methylmercaptopropanol-(1)-phosphoric acid monocholine ester.

To 0.9 g. (2.6 mMole) 2-hexadecyloxy-3-methyl-mercaptopropanol-(1) in 15 ml. abs. toluene, one adds at 0°C. 0.95 g. triethylamine and dropwise a solution
10 of 0.95 g. (3.6 mMole) 2-bromoethylphosphoric acid ester dichloride in 15 ml. abs. toluene. One leaves to stir for 5 h. at 0°C. and overnight at 20°C. One again cools to 0°C., adds dropwise thereto 11 ml. 0.1N aqueous potassium chloride solution, leaves to stir vigorously
15 for 1 h. at 0°C. and for 2 h. at 20°C., separates the phases, dries the organic one and evaporates it. One dissolves the oily residue in 30 ml. abs. chloroform/
30 ml. abs. methanol, passes in dry trimethylamine for 10 min. and leaves to boil under reflux for 24 h. The
20 solvent is then stripped off, the residue dissolved in 50 ml. abs. methanol and mixed with 1 g. silver acetate. One stirs for 2 h. at room temperature, filters off with suction and evaporates the filtrate. The oily residue is purified over 100 g. silica gel (elution agent:
25 methylene chloride (65), methanol (25), water (4)).

After stripping off of the elution agent and drying, the product is reprecipitated from chloroform/



acetone. One obtains 0.24 g. $\approx$ 18% of an amorphous, chromatographically uniform product.

The 2-hexadecyloxy-3-methylmercaptopropanol-(1) used as starting material is new and was prepared in the following way:

1-Thioglycerol was methylated with methyl iodide to give 3-methylmercapto-1,2-propanediol and subsequently reacted with sodium hydride and 1-bromohexadecane to give a mixture of the two isomeric hexadecyl ethers which were separated column chromatographically (wax-like substances).

Example 80.

Analogously to Example 79, by reaction of 2-benzyl-3-hexadecylmercaptopropanol-(1) with 2-bromoethyl-phosphoric acid ester dichloride, subsequent saponification, as well as reaction with trimethylamine after treatment with silver acetate, one obtains

2-benzyl-3-hexadecylmercaptopropanol-(1)-phosphoric acid monocholine ester.

After reprecipitation from chloroform/acetone, one obtains the desired compound in a yield of 13% with a melting point of 220 - 230°C. with decomp.

The 2-benzyl-3-hexadecylmercaptopropanol-(1) used as starting material is new and was prepared in the following way:

25 Benzylmalonic acid diethyl ester is reduced with lithium aluminium hydride to 2-benzyl-1,3-propanediol (m.p. 64 - 65°C.) and esterified with the equivalent

amount of benzenesulphochloride in abs. pyridine to give 2-benzyl-1,3-propanediol monobenzenesulphonate (oily substance). Reaction with the sodium salt of hexadecanethiol in ethanol leads to the desired 2-benzyl-
5 3-hexadecylmercaptopropanol-(1) (wax-like compound).

Example 81.

Analogously to Example 79, by reaction of 3-hexadecylmercapto-2-phenylpropanol-(1) with 2-bromoethyl-phosphoric acid ester dichloride, subsequent saponification, as well as reaction with trimethylamine after
10 treatment with silver acetate, one obtains
3-hexadecylmercapto-2-phenylpropanol-(1)-phosphoric acid monocholine ester.

After reprecipitation from chloroform/acetone, one
15 obtains the desired compound in a yield of 27% with a melting point of 245°C. with decomposition.

The 3-hexadecylmercapto-2-phenylpropanol-(1) used as starting material is new and was prepared in the following way:

20 Phenylmalonic acid diethyl ester is reduced with lithium aluminium hydride to give 2-phenyl-1,3-propanediol and esterified with equimolar amounts of benzenesulphochloride in abs. pyridine to give 2-phenyl-1,3-propanediol monobenzenesulphonate (wax-like substance).
25 Reaction with the potassium salt of hexadecanethiol in ethanol leads to the desired 3-hexadecylmercapto-2-phenylpropanol-(1) (wax-like substance).

Example 82.

Analogously to Example 79, by the reaction of 2-allyl-3-hexadecylmercaptopropanol-(1) with 2-bromo-ethylphosphoric acid ester dichloride, subsequent saponification, as well as reaction with trimethylamine after treatment with silver acetate, one obtains 2-allyl-3-hexadecylmercaptopropanol-(1)-phosphoric acid monocholine ester.

After reprecipitation from chloroform/acetone, one obtains the desired compound in a yield of 23% with a melting point of 235 - 238°C., with decomposition.

The 2-allyl-3-hexadecylmercaptopropanol-(1) used as starting material is new and was prepared in the following way:

Allylmalonic acid diethyl ester is reduced with lithium aluminium hydride to give 2-allyl-1,3-propanediol (oil) and esterified with equimolar amounts of benzenesulphochloride in abs. pyridine to give 2-allyl-1,3-propanediol monobenzenesulphonate (oily substance). Reaction with the sodium salt of hexadecanethiol in ethanol leads to the desired 2-allyl-3-hexadecylmercaptopropanol-(1) (wax-like compound).

Example 83.

Analogously to Example 79, by reaction of 2-methylene-3-octadecylmercaptopropanol-(1) with 2-bromo-ethylphosphoric acid ester dichloride, subsequent saponification, as well as reaction with trimethylamine after

treatment with silver acetate, one obtains

2-methylene-3-octadecylmercaptopropanol-(1)-phosphoric acid monocholine ester.

After reprecipitation from chloroform/acetone, one
5 obtains the desired compound in a yield of 18% with a melting point of 235 - 237°C., with decomposition.

The 2-methylene-3-octadecylmercaptopropanol-(1) used as starting material is new and was prepared in the following way:

10 3-Bromo-2-methoxy-2-methylpropanol-(1) is reacted with the sodium salt of octadecanethiol in ethanol. One thereby obtains, with splitting off of methanol, 2-methylene-3-octadecylmercaptopropanol-(1) (wax-like substance).

15 Example 84.

3-Tetradecylmercaptopropanol-(1)-phosphoric acid monocholine ester.

To a solution of 0.3 g. 20chloro-2-oxo-1,3,2-dioxaphospholane and 0.8 ml. triethylamine in 10 ml. abs. methylene chloride, one adds dropwise at -5 to -10°C.
20 a solution of 0.5 g. 3-tetradecylmercaptopropanol in 10 ml. abs. methylene chloride. One stirs the clear solution for 2 h. in an ice-bath and leaves to stand overnight. One then evaporates, adds thereto 2.5 ml.
25 acetonitrile which contains 0.24 g. trimethylamine and leaves to react in an autoclave for 8 h. at 60°C.; the comparison with the product prepared according to

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Example 30 in the thin later chromatogram shows identity. The purification takes place according to the statements there made.

Example 85.

- 5 (+ or -)-2-Methyl-3-hexadecylmercaptopropanol-(1)-phosphoric acid monocholine ester (enantiomers A or B).

The racemic α -methyl- β -hexadecylmercaptopropionic acid methyl ester described in Example 33 is saponified under reflux with 2N aqueous sodium hydroxide solution.

- 10 One obtains, with 91% yield, rac. α -methyl- β -hexadecylmercaptopropionic acid, m.p. 53 - 56°C.

One esterifies this acid with N-hydroxysuccinimide in methylene chloride in the presence of dicyclohexylcarbodiimide. The activated rac. ester, m.p. 51 - 54°C.,

- 15 is obtained with 67% yield.

The reaction of this ester with R(+)-1-phenylethylamine in methylene chloride gives 88% of a mixture of both diastereomeric amides. One separates on a silica gel column with acetone/toluene 1:30 and thus obtained the

- 20 two pure diastereomers:

	yield	m.p.	$[\alpha]_D^{20} = 1, \text{CHCl}_3$
diastereomer A	17%	88-90°C.	+42.2°
diastereomer B	17%	71-73°C.	+32.8°

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Each diastereomeric amide is now separately saponified with semi-concentrated sulphuric acid. One thus obtains, with 60 and 63% yield respectively, the two enantiomeric α -methyl- β -hexadecylmercaptopropionic acids ($c = 1$, CHCl_3):

m.p. 56 - 59°C., $[\alpha]_{578}^{20} +9.7^\circ$ or

m.p. 58 - 60°C., $[\alpha]_{578}^{20} -8.7^\circ$

The reduction with lithium aluminium hydride leads to the enantiomeric 2-methyl-3-hexadecylmercaptopropanols (foamy products) which, as described in Example 1, are phosphorylated, hydrolysed and finally reacted with trimethylamine.

After the final purification on a silica gel column, one obtains the desired enantiomers.

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	yield	mole of water of crystallisation	m.p.	$[\alpha]_{578}^{20} c = 10, \text{CHCl}_3$
enantiomer A	47%	2	78°C.sinters, 241-245°C. (decomp.)	+0.9°
enantiomer B	52%	2	55°C.sinters, 236-239°C. (decomp.)	-1.2°

Experimental protocol.

The new sulphur-containing substances were investigated with regard to their cytotoxic action on tumour cells of the mouse in a screening. As target cells, on the one hand, there are used cells of a tumour induced by methylcholanthrene (Meth A), which is passed as ascites in the mouse, on the other hand, there are used Abelsen-8,1 lymphoma cells (Abls) which are kept in in vitro culture. For the screenings, 5×10^4 /ml. of these cells are cultured together for 24 h. in Dulbecco's Modified Eagle's Medium, which is enriched with 10% heat-inactivated foetal calf serum, 5×10^{-5} M mercaptoethanol, 50 U penicillin and 50 g. streptomycin/ml., and various concentrations of the new sulphur-containing phospholipids. The culturing takes place at 95% atmospheric humidity, 37°C ., 10% CO_2 in a culture cabinet. The action of the substances is determined by the comparison of the growth of the tumour cells in the medium with the new sulphur-containing phospholipids with a control culture without substance. As comparison substance, in each experiment there was also used 1-octadecyl-2-methylglycero-3-phosphorylcholine (from DE-OS No. 2619686). The growth of the Meth A cells is measured by the incorporation of ^3H -thymidine into the DNA of the cells, that of the Abls cells by the determination of the alkaline phosphatase activity of an aliquot of the cultures. For each substance, there is calculated the

concentration at which the thymidine incorporation or the alkaline phosphatase activity is reduced by 50% in comparison with an untreated tumour cell control.

In the following Table, substances are given which are superior to the simultaneously used comparison substances. The superiority of these substances is expressed by a factor which represents the ratio of the comparison substance to the individual substances of the new sulphur-containing phospholipids.

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Example No.	factor
comparison compound	1.0
Example 33	1.1
Example 42	1.4
Example 76	1.4
Example 20	1.7
Example 79	1.2
Example 55	1.5
Example 62	1.5
Example 65	1.5
Example 70	1.5
Example 63	1.2
factor = $\frac{C_{50} \text{ 41386}}{C_{50} \text{ substance}}$	

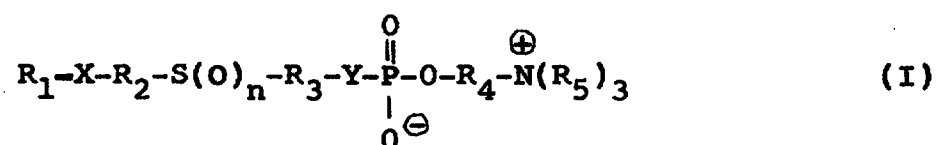


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Claims

1. Alkanol phosphoric acid monoammonium alkyl esters of the formula (I)



- 5 in which X signifies a valency bond, oxygen, sulphur, the sulphinyl or sulphonyl group, the -NHO-, -CONH- or -NHCONH- group, a C₃ to C₈ cycloalkylene or phenylene radical, Y oxygen or sulphur, R₁ hydrogen, a straight-chained or branched, saturated or unsaturated alkyl
- 10 radical with 1 to 18 carbon atoms, which is possibly substituted one or more times by aryl, halogen, a lower alkoxy, alkylmercapto, alkoxycarbonyl, alkanesulphinyl or alkanesulphonyl group, R₂ a straight-chained or branched, saturated or unsaturated alkylene chain with
- 15 1 to 18 carbon atoms, which is possibly substituted one or more times by halogen, aryl, a lower alkoxy, alkoxy-carbonyl, alkylmercapto, alkanesulphinyl or alkane-sulphonyl group, R₃ a straight-chained or branched, saturated or unsaturated alkylene chain with 2 to 8
- 20 carbon atoms, which can also be part of a cyclopentane, cyclohexane or cycloheptane ring, possibly substituted by a lower alkyl group, and is possibly substituted one or more times by hydroxyl, halogen, nitrile, a cycloalkyl, phenyl, alkoxycarbonyl, optionally alkylated carbamoyl,
- 25 alkylmercapto, alkanesulphinyl, alkanesulphonyl,



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optionally acylated amino group or by alkoxy which, in turn, can be substituted by aryl, alkylmercapto, alkane-sulphinyl, alkanesulphonyl, optionally acylated NH_2 , alkoxycarbonyl, nitrile, hydroxyl, alkoxy or optionally
5 alkylated carbamoyl, R_4 a straight-chained or branched alkylene chain with 2 to 4 carbon atoms, R_5 hydrogen or a lower alkyl group and n the numbers 0, 1 or 2, with the proviso that the group $\text{R}_1\text{-X-R}_2$, for the case in which it represents an alkyl group ($\text{X} = \text{valency}$), has up to 20
10 C-atoms, as well as their pharmacologically acceptable salts.

2. Compounds of the formula (I) according to claim 1, in which R_1 , R_2 , R_3 , Y and X have the given meaning and R_4 represents a $\text{-CH}_2\text{-CH}_2\text{-}$ chain, R_5 the methyl group and
15 n the number 0.

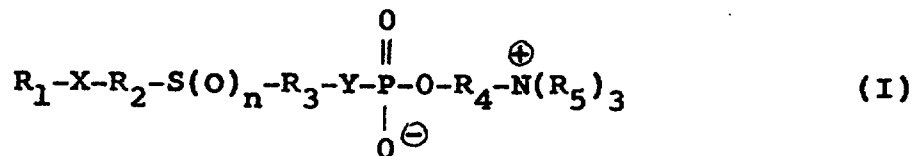
3. Compounds of the formula (I) according to claim 1, in which R_3 has the given meaning, R_4 represents a $\text{-CH}_2\text{-CH}_2\text{-}$ chain, R_5 the methyl group, Y oxygen, n the number 0 and R_1 and R_2 together have 16 to 18 C-atoms
20 and X represents a valency bond or oxygen.

4. Compounds of the formula (I) according to claim 3, in which R_1 , R_2 , R_4 , R_5 , Y, X and n have the given meaning and R_3 represents a $\text{-CH}_2\text{-CH}_2\text{-CH}_2\text{-}$ chain, the middle carbon atom of which can be substituted by hydroxyl, lower alkyl
25 or a lower alkoxy group, whereby both groups can, in turn, be substituted by alkoxy.



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5. Process for the preparation of alkanol phosphoric acid ammonium alkyl esters of the formula (I)



in which X signifies a valency bond, oxygen, sulphur, the
5 sulphinyl or sulphonyl group, the -NHCO-, -CONH- or
-NHCONH- group, a C₃ to C₈ cycloalkylene radical or
phenylene radical, Y oxygen or sulphur, R₁ hydrogen, a
straight-chained or branched, saturated or unsaturated
alkyl radical with 1 to 18 carbon atoms, which is possibly
10 substituted one or more times by aryl, halogen, a lower
alkoxy, alkylmercapto, alkoxycarbonyl, alkanesulphinyl
or alkanesulphonyl group, R₂ a straight-chained or
branched, saturated or unsaturated alkylene chain with
1 to 18 carbon atoms, which is possibly substituted one
15 or more times by halogen, aryl, a lower alkoxy, alkoxy-
carbonyl, alkylmercapto, alkanesulphinyl or alkane-
sulphonyl group, R₃ a straight-chained or branched,
saturated or unsaturated alkylene chain with 2 to 8
carbon atoms, which can also be part of a cyclopentane,
20 cyclohexane or cycloheptane ring, possibly substituted
by a lower alkyl group, and is possibly substituted one
or more times by hydroxyl, halogen, nitrile, a cycloalkyl,
phenyl, alkoxycarbonyl, optionally alkylated carbamoyl,
alkylmercapto, alkanesulphinyl, alkanesulphonyl,
25 optionally acylated amino group or by alkoxy which, in



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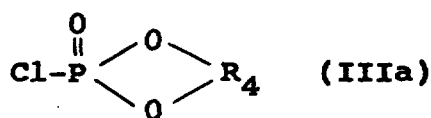
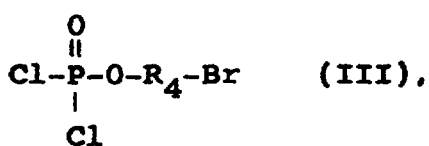
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turn, can be substituted by aryl, alkylmercapto, alkane-
sulphinyl, alkanesulphonyl, optionally acylated NH_2 ,
alkoxycarbonyl, nitrile, hydroxyl, alkoxy or optionally
alkylated carbamoyl, R_4 a straight-chained or branched
5 alkylene chain with 2 to 4 carbon atoms, R_5 hydrogen or
a lower alkyl group and n the numbers 0, 1 or 2, with
the proviso that the group $\text{R}_1\text{-X-R}_2$, for the case in which
it represents an alkyl group (X = valency), has up to 20
C-atoms, as well as of their pharmacologically acceptable
10 salts, characterised in that one reacts a compound of
the formula (II)



in which R_1 , R_2 , R_3 , X , Y and n have the above-given
meaning, either

15 a) with a compound of general formula (III) or (IIIa)



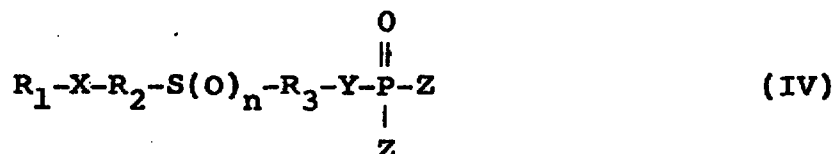
in which R_4 has the above-mentioned meaning, in the
presence of an acid-binding agent, selectively hydrolyses
the reaction product in the case of the use of a compound
20 of the formula (III) and replaces the remaining bromine
atom by an optionally alkylated ammonium group, in the
case of the use of a compound of the formula (IIIa)
treats directly with optionally alkylated ammonia, or



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b) converts into a compound of the general formula (IV)



in which R_1 , R_2 , R_3 , Y , X and n have the above-given meaning and Z signifies hydroxyl, chlorine or bromine,
5 and reacts this with a compound of the general formula (V)



in which R_4 and R_5 have the above-given meanings and Hal^- is to be chloride, bromide or iodide, in the
10 presence of an acid-binding agent or of an activating reagent, or

c) with a compound of the general formula (VI)



in which R_4 , R_5 and Z have the above-given meanings and
15 Z^- is to be chlorine or bromine, in the presence of an acid-binding agent, if desired converts the compounds obtained into the internal salt, optionally oxidises to the sulphones or sulfoxides, optionally quaternises and, if desired, converts compounds of the formula (I) into
20 pharmacologically acceptable salts.

6. Process according to claim 5, wherein a compound of the formula (II) is reacted with phosphoric acid oxyhalide in the presence of an acid-binding agent to



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give a compound of the formula (IV).

7. Medicaments containing compounds of claims 1 to 4 and conventional carrier and adjuvant materials.
8. Compounds according to claims 1 to 4 for use in
5. the combating of cancer.
9. 2-(2-Propynyl)-3-hexadecylmercaptopropanol-(1)-phosphoric acid monocholine ester.