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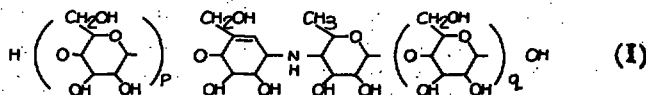
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(54) AMINO-SUGAR DERIVATIVES, PROCESSES FOR THEIR PREPARATION AND THEIR USE AS MEDICAMENTS

(71) We, BAYER AKTIENGESellschaft, a body corporate organised under the laws of Germany, of Leverkusen, Germany, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The present invention relates to new amino-sugar derivatives, several processes for their preparation and their use as medicaments, in particular as agents against diabetes, adiposity and hyperlipaemia.

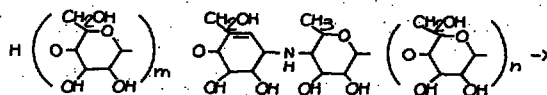
A number of Actinomycetes, especially Actinoplanaceae, form oligosaccharide-like inhibitors of α -glucosidases. The higher-molecular compounds are highly potent inhibitors of α -amylase and the low-molecular compounds are strong saccharase inhibitors with a surprisingly high inhibition of starch digestion in vivo. These inhibitors can be defined by the general formula



in which

P and q represent a number from 0 to 8 and the sum of P and q has a value of 1 to 8. (DT—OS (German Published Specification) 2,347,782 and German Patent Application P 2,614,393.1).

The present invention provides amino-sugar derivatives of the general formula



in which

n and m independently of each other represent a number from 0 to 8 and the sum $n+m$ has a value of 0 to 8, and

X designates a group —OR, —SH, —SR, —NH₂, —NHR or NRR₁, in which

R designates an alkyl, alkenyl, cycloalkyl, aralkyl, aryl or heterocyclic radical, which can be substituted, and

R₁ designates an alkyl, cycloalkyl, aralkyl or aryl radical, which can be substituted or

R and R₁, together with the nitrogen atom to which they are bonded, form a heterocyclic ring.

It has been found that the compounds of the formula (II) are highly active inhibitors for glycoside hydrolases of the digestive tract.

When R is alkyl, it is preferably straight-chain or branched alkyl with 1 to 30, especially 1 to 18, carbon atoms. Examples which may be mentioned are methyl, ethyl, n-propyl, i-propyl, n-butyl, t-butyl, n-hexyl, n-octyl, octyl-2, dodecyl, lauryl, cetyl and stearyl.

The alkyl radicals R can carry one or more, preferably 1 to 5, identical or different substituents. Examples of substituents which may be mentioned are: hydroxyl, or alkoxy with preferably 1 to 4 carbon atoms, in particular methoxy and ethoxy; amino or monoalkylamino and dialkylamino with preferably 1 to 4 carbon atoms per alkyl radical, in particular monomethylamino, monoethylamino, dimethylamino and diethylamino; mercapto or alkylthio with preferably 1 to 4 carbon atoms, in particular methylthio and ethylthio; halogen, preferably fluorine, chlorine and bromine; alkyl-carbonyl with preferably 1 to 4 carbon atoms in the alkyl radical; and carboxyl, nitro, cyano, the aldehyde group and the sulphonic acid group.

It should be mentioned that the radicals derived from sugar derivatives, such as polyalcohols or sugar acids, are of particular interest, in the scope of the present Application, for R in the meaning of a substituted alkyl radical.

When R is alkenyl, it is preferably straight-chain or branched alkenyl with 2 to 6 carbon atoms, which can carry substituents, such as hydroxyl, alkoxy with 1 to 4 carbon atoms, mercapto, alkylthio with 1 to 4 carbon atoms, halogen or nitro.

When R is cycloalkyl it is preferably a carbocyclic radical with 3 to 7 carbon atoms, which can be substituted, possible substituents being the groups and atoms mentioned above in the case of open-chain hydrocarbon radicals R.

When R is aryl it is preferably an aromatic radical with 6 to 10 carbon atoms in the aryl part, in particular phenyl, which can be substituted.

The aryl or aralkyl radicals can carry one or more, preferably 1 to 3, identical or different substituents. Examples of substituents which may be mentioned are: alkyl with 1 to 10 carbon atoms, which in turn can again be substituted, for example by chlorine, nitro or cyano; optionally substituted alkenyl radicals with 1 to 10 carbon atoms; hydroxyl or alkoxy with preferably 1 to 4 carbon atoms; amino or monoalkyl-amino and dialkylamino with preferably 1 to 4 carbon atoms per alkyl radical; mercapto or alkylthio with preferably 1 to 4 carbon atoms; and carboxyl or carbalkoxy with preferably 1 to 4 carbon atoms; the sulphonic acid group, alkylsulphonyl with preferably 1 to 4 carbon atoms and arylsulphonyl, preferably phenylsulphonyl; amino-sulphonyl or alkylaminosulphonyl and dialkylaminosulphonyl with 1 to 4 carbon atoms per alkyl group, preferably methylaminosulphonyl and dimethylaminosulphonyl; nitro, cyano or the aldehyde group; alkylcarbonylamino with preferably 1 to 4 carbon atoms; and alkylcarbonyl with 1 to 4 carbon atoms, benzoyl, benzylcarbonyl and phenylethylcarbonyl, it being possible for the last-mentioned alkyl, phenyl, benzyl and phenylethyl radicals in turn to be again substituted, for example by chlorine, nitro or hydroxyl, as well as radicals derived from sugars.

When R is alkyl it preferably has 6 to 10, especially 6, carbon atoms in the aryl part and preferably 1 to 4, especially 1 or 2, carbon atoms in the alkyl part, as for example in benzyl or phenylethyl. Possible substituents for the aryl part of the aralkyl radical are preferably those substituents mentioned for the aryl radicals R above.

When R is a heterocyclic radical, it preferably has a hetero-paraffinic, hetero-aromatic or hetero-olefinic 5-membered or 6-membered ring with preferably 1 to 3 identical or different hetero-atoms. Hetero-atoms are oxygen, sulphur or nitrogen. These ring systems can carry further substituents, for example hydroxyl, amino or C₁—C₄-alkyl groups, or benzene nuclei or further, preferably 6-membered, hetero-cyclic rings of the type mentioned can be fused to them.

In this case, the bonding of the heterocyclic radical R is effected via a carbon atom of the heterocyclic system or of the fused benzene nucleus. Particularly preferred heterocyclic radicals are derived, for example, from furane, pyrane, pyrrolidine, piperidine, pyrazole, imidazole, pyrimidine, pyridazine, pyrazine, triazine, pyrrole,

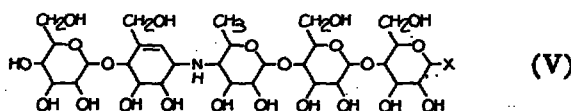
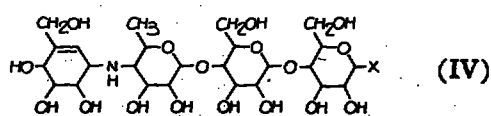
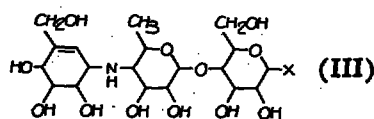
pyridine, benzimidazole, quinoline, isoquinoline or purine. Heterocyclic radicals are also to be understood as including those which are bonded via a $-\text{CH}_2-$ bridge outside the ring, for example the furfuryl radical.

R_1 preferably represents a straight-chain or branched alkyl radical with 1 to 6 carbon atoms or a benzyl or phenyl radical, it being possible for the radicals mentioned to be preferably substituted by alkoxy with 1 to 4 carbon atoms, amino, C_1-C_4 -monoalkylamino and C_1-C_4 -dialkylamino, nitro, halogen, cyano, hydroxyl, mercapto, C_1-C_4 -thioalkyl or the carboxyl or sulphonic acid group and, in the case where R_1 denotes phenyl, also by C_1-C_4 -alkyl.

As indicated above, it is also possible for R and R_1 , together and including the nitrogen atom to which they are bonded, to form a heterocyclic ring.

This ring can be saturated or unsaturated and can contain 1 to 3 further (preferably 1) oxygen atoms, sulphur atoms or nitrogen atoms and, as hetero groups, a SO_2 group or a N-alkyl group, the alkyl in the N-alkyl group preferably containing 1 to 4, in particular 1 or 2, carbon atoms. Methyl, ethyl, n- and i-propyl and n-, i- and t-butyl may be mentioned as alkyl. The heterocyclic ring contains 5 to 7, preferably 5 or 6, ring members. The 6-membered heterocyclic ring preferably contains the hetero-atom or the hetero-group in the para-position relative to the nitrogen atom. Examples of the heterocyclic ring which may be mentioned are pyrrolidine, piperidine, piperazine, hexamethyleneimine, morpholine and n-methylpiperazine.

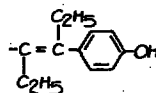
Particularly valuable inhibitors of this invention are those in which n is 1 or 2; amongst these the amino-sugar derivatives of the formulae (III), (IV), and (V) are particularly important.



X has the following particularly preferred meanings:

X denotes a $-\text{OR}$, $-\text{SH}$, $-\text{SR}$, $-\text{NH}_2$, $-\text{NHR}$ or $-\text{NRR}_1$ group, in which

R designates an alkyl radical with 1 to 18 carbon atoms, which can be substituted by, to 5 hydroxyl or C_1-C_4 -alkoxy groups; a phenyl radical which is optionally substituted by 1 to 3 C_1-C_4 -alkyl, OH, C_1-C_4 -alkoxy, amino, C_1-C_4 -alkylamino, C_1-C_4 -dialkylamino, carboxyl, methoxycarbonyl, nitro, glucopyranyl, benzoyl, p-hydroxyphenylethylcarbonyl, C_1-C_4 -alkylaminosulphonyl or C_1-C_4 -dialkylaminosulphonyl radicals or by one radical



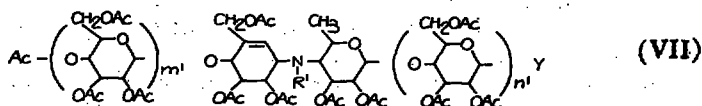
or a benzyl radical or 2-benzthiazolyl radical; and

R_1 designates C_1-C_4 -alkyl or, together with R, forms a morpholine or piperidine ring.

Surprisingly, the compounds according to the invention exhibit a higher inhibiting action for α -glucosidases than the non-derived parent substances and are thus an enrichment of the total range of available medicaments.

Furthermore, the invention provides a process for the preparation of a compound according to the invention of formula (II) in which

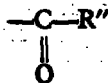
(1) an acyl halogen derivative of the formula



in which

m' and n' independently of each other represent a number from 0 to 8 and the sum $n' + m'$ has values of 0 to 8,

Ac designates a radical

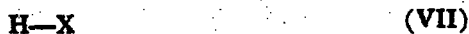


in which

"R" represents an optionally substituted alkyl, alkenyl cycloalkyl, aralkyl or aryl radical and

R' designates hydrogen or the radical Ac defined as above and

Y represents halogen (preferably chlorine or bromine), is reacted with a compound of the formula



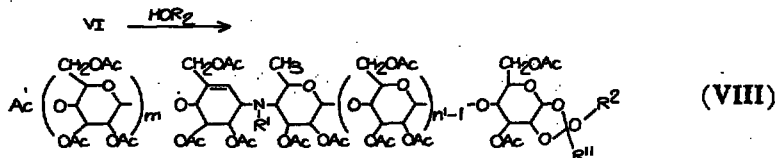
in which

X has the meaning indicated above,

(or a salt thereof in which H is replaced by a metal, preferably Na or K) optionally in the presence of an acid-binding agent;

(in this process variant an O-acyl halogen compound, that is to say a derivative of the formula (VI) in which R' is hydrogen and a derivative in which R'' is a C₁-C₆-acyl radical or an aroyl radical, preferably acetyl, is preferably employed);

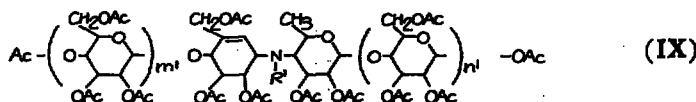
or (2) an ortho-ester of the formula (VIII) (obtainable from the acyl halogen compounds (VI) by reaction with alcohols of the formula HOR_2 , in which R_2 designates alkyl with 1 to 6 carbon atoms or phenyl, preferably methyl or t-butyl)



in which

Ac, m', n', R₂ and R'' have the meanings indicated above, is reacted with a compound of the formula (VII) (for example by the method of Kochetkov [R. L. Whistler and J. N. BeMiller, *Methods of Carbohydrate Chemistry*, volume VII, page 480, Academic Press, New York and London]);

or (3) a compound of the formula (IX), (obtainable from the acyl halogen compounds (VI) by reaction with H_2O , H_2S , NH_3 or NH_2R_1 , R_1 having the meaning indicated above)



in which

m', n', Ac and R' have the meanings indicated above and

Y' is —OH, —SH, —NH₂ or NHR₁, with the meaning for R₁ indicated above, is reacted with a compound of the formula



in which

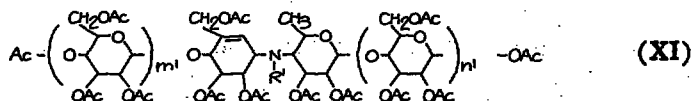
R_3 has the meaning of R indicated above or denotes aryl-N=N— and

Z designates an acid radical, preferably radical of a strong acid, such as $-\text{Cl}$, $-\text{Br}$, $-\text{I}$, $-\text{HSO}_4$ or SO_3H ; (this process variant is particularly suitable for the preparation of the thioethers);

(Note: the esters or amides, which may be obtained in process variants 1—3, of the compounds of the formula (IV) may then be converted into the compounds

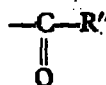
(VI) by known processes, for example with catalytic amounts of sodium in methanol [G. Zemplen, Ber. 56, 1705 (1923)] or by saponification with aqueous alkali metal hydroxide solutions);

or (4) an acyl derivative, preferably an O-acyl derivative of the formula



in which

m' , n' , Ac and R' have the meanings indicated above, is reacted with a compound of the formula (VII) and the radicals



are then removed,

or (5) a parent substance of the formula (I) is reacted with a compound of the formula (VII), with the elimination of water, optionally under acid catalysis.

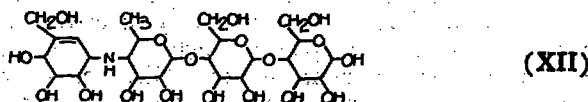
The preparation of the starting compounds of the formula (I) in which $P=O$ and $q=1-7$ is known -DT-OS (German Published Specification) 2,347,782].

The starting compounds of the formula (I) in which P and q represent a number from 0-8 and the sum of $n+m$ can assume a value of 1 to 8, are the subject of German Patent Application P 2,614,393.1. The compounds thus mentioned may be prepared by culturing strains of microorganisms of the order *Actinomycetales*, in particular of the family *Actinoplanaceae*, in a manner which is in itself known and by subsequently separating off and isolating the individual compounds, also in a manner which is in itself known.

The compounds of the formula used as starting materials have not yet hitherto been disclosed, but can be prepared by processes which are customary in sugar chemistry. For example, in order to prepare compounds of the formula (VI) with $Y=Br$, $Ac=acetyl$ and $R'=H$, the O-acetyl compounds of the formula (XI) are reacted with HBr in glacial acetic acid at temperatures between $-10^\circ C$ and room temperature, preferably at $0^\circ C$. The reaction time is 15 minutes to 4 hours, preferably about 1 hour. The reaction products are isolated by diluting the reaction mixture with chloroform, removing the acetic acid by washing with water, drying the chloroform phase and evaporating the solution to dryness under reduced pressure in a rotary evaporator. The resulting crude product, that is to say the acetobromo compound, can be used without further purification for the reactions mentioned.

The compounds of the formula (XI) are obtainable from compounds of the formula (I) by processes which are in themselves known, for example by reaction with carboxylic acid chlorides or carboxylic acid anhydrides. In the case of O-acetylation, reaction with acetic anhydride/pyridine for 12 to 48 hours at room temperature has proved suitable.

The compound of the formula (XI) in which $m'=O$ and $n'=O$ and R' denotes hydrogen or Ac and Ac represents the acetyl radical is obtainable, for example, by acetolysis of the amino-sugar derivative of the formula (XII)



In this procedure, the amino-sugar derivative (XII) is heated with acetic anhydride/glacial acetic acid (1:1) in the presence of catalytic amounts of sulphuric acid, whereupon degradation of the two glucose units and simultaneous acylation of the sugar derivative which remains occurs.

The ortho-esters of the formula (VIII) are also new. However, they can be easily prepared from the compounds of the formula (VI) and alcohols of the formula (R_2OH). The alcohols R_2OH are preferably employed in excess. The reaction can be carried out with and without diluents; nitromethane is preferably used as a diluent. 2,6-Lutidine is preferably used as an acid-binding agent. The reaction is preferably carried out at room temperature and under normal pressure.

The compounds of the formula (IX) in which Y' designates the mercapto group can be obtained by a process which is in itself known [M. Cerny, D. Zorchystalova and J. Pacak, Collection Czechoslov. Chem. Commun 26, 2206 (1961)] from the acetobromo compounds of the formula (VI) by reaction with thiourea in acetone and subsequent hydrolysis of the reaction products in a weakly alkaline medium ($\text{NaHCO}_3/\text{NaHSO}_3$ in $\text{H}_2\text{O}/\text{CHCl}_3$).

The alcohols, polyalcohols, sugar derivatives, phenols, mercaptans, thiophenols and amines of the general formula (VII) are already known. Some compounds of the formula (IV) are mentioned in detail in the following as examples:

It should be expressly emphasised that in the case of the compounds mentioned, polyfunctional compounds can optionally also be employed in the reaction in the form of suitable partially protected derivatives. The protective groups must be appropriately chosen here so that they can be removed again from the reaction product without the glucosidic bonds or the double bonds being thereby attacked.

Examples which may be mentioned of compounds of the formula VII are: methanol, ethanol, propanol, isopropanol, tert.-butanol, n-butanol, allyl alcohol, cyclopentanol, n-hexanol, n-octyl alcohol, octanol-2, lauryl alcohol, cetyl alcohol, 1-dimethylamino-propanol-2, benzyl alcohol, furfuryl alcohol, trichloroethanol, ethylene glycol, ethylene glycol monomethyl ether, butane-1,4-diol, D-glucose, D-sorbitol, mesoinositol, pehnol, p-nitrophenol, m-chlorophenol, 2,4-dichlorophenol, 6-chloro-3-hydroxy-toluene, 4-hydroxy-1-tert.butylbenzene, 3-hydroxybenzoic acid, 4-hydroxybenzoic acid, salicylic acid, resorcinol, hydroquinone, phloroglucinol, p-acetamidophenol, diethylstilbestrol, phloretin, phlorhizin, 8-hydroxy quinoline, methylmercaptan, ethylmercaptan, n-propylmercaptan, iso-propylmercaptan, n-hexylmercaptan, cyclohexylmercaptan, benzylmercaptan, 1,3-dimercaptopropane, thiophenol, m-thiocresol, p-bromothiophenol, β -thionaphthol, thiohydroquinone, methylamine, dimethylamine, ethylamine, propylamine, dipropylamine, isopropylamine, tert.-butylamine, N-ethyl-N-propylamine, n-hexylamine, dodecylamine, stearylamine, allylamine, ethylenediamine, putrescine, 3-amino-1-dimethylaminopropane, 2-aminoethanol, 2-methylaminoethanol, bis-(2-hydroxy-ethyl)-amine, ethyl 3-amino-propyl ether, 4-amino-2-butanol, cyclohexylamine, benzylamine, pyrrolidine, piperidine, morpholine, piperazine, aniline, N-methylaniline, p-toluidine, o-chloroaniline, m-anisidine, p-nitraniline, m-aminophenol, 4-chloro-3-nitroaniline, p-phenylenediamine, 3-trifluoromethylaniline, α -naphthylamine, benzidine, furfurylamine, 3-aminosulpholane, benzimidazole, hypoxanthine, adenine, uracil, cytosine and 2-desoxystreptamine.

The reaction of compounds of the formula VI with compounds of the formula VII can be carried out with and without a diluent. It is preferably carried out under the conditions of a Königs-Knorr reaction or of one of its more recent variants. Diluents which can be used are all the inert solvents, such as benzene, chloroform, ether or nitromethane, or also basic solvents, such as pyridine or quinoline. The reaction is optionally carried out in the presence of acid-binding agents, Lewis acids and drying agents. Silver salts or mercury salts and drierite are preferably used.

The reaction is generally carried out at temperatures between 0°C and 100°C , preferably at room temperature, and preferably under normal pressure.

Equimolar amounts of the compounds VI and VII and of the silver salts or mercury salts can be employed in the reaction; however, a large excess of the compounds VII is appropriately also favourable for the reaction. The reaction can also be carried out using metal salts of the compounds VII, for example the alkali metal salts of VII. Silylated derivatives of the compounds VII can also optionally be used.

However, the reaction can also optionally be carried out in protic solvents, such as alcohols, water or a water/acetone mixture. This variant is particularly suitable acetic acid or mixture of these solvents. Alkali metal carbonates or alkali metal hydroxides or alkali metal carbonates are preferably used as acid-binding agents.

If the preparation of the compounds of the formula II is carried out according to the 2nd process, when R_2 is methyl, nitromethane is preferably used as the solvent and mercury-II bromide is preferably used as the catalyst in the reaction of the ortho-ester VIII with compounds of the formula VII. If R_2 is tert.-butyl, chlorobenzene is preferably used as the solvent and 2,6-lutidinium perchlorate is preferably used as the catalyst. The reaction is preferably carried out under normal pressure and at the boiling point, and a shift of the equilibrium in the direction of the desired reaction product is effected by distilling off volatile reaction products.

If the compounds of the formula II are prepared according to the variant (3) via the intermediate products IX, the reaction of the compounds IX with compounds of the formula X can be carried out, for example, in the following solvents: acetone,

dimethylformamide, dioxane, tetrahydrofurane, alcohol, water, chloroform, benzene, acetic acid or mixture of these solvents. Alkali metal carbonates or alkali metal hydroxides are preferably used as acid-binding agents in this reaction. The reaction can be carried out with equimolar amounts of the compounds X, but also optionally with an excess of X. The reaction is carried out at temperatures between 0° and 140° C, preferably between 20° C and 80° C, and preferably under normal pressure.

The reaction of compounds of the formula XI with compounds of the formula VII can be carried out with and without a diluent. A preferred variant of this process is the reaction of XI with phenol of the formula VII, optionally with an excess of the phenol, in the melt. The reaction is catalysed by protons or Lewis acids. Preferred catalysts are p-toluenesulphonic acid or ZnCl_2 . The reaction is carried out at temperatures between 60 and 200° C, preferably between 80 and 140° C.

The reaction of amines of the formula VII, preferably of aromatic amines, with compounds of the formula XI is preferably carried out using lower alcohols as solvents with the addition of acetic acid, optionally also with an excess of the amine.

The reaction is carried out at temperatures between 20 and 80° C, preferably at room temperature, and preferably under normal pressure.

The reaction of compounds of the formula I with compounds of the formula VII can be carried out with and without diluents. A preferred variant of this process is the reaction of the compounds I with an excess of lower, anhydrous alcohols of the formula VII, catalysed by mineral acid or cation exchangers.

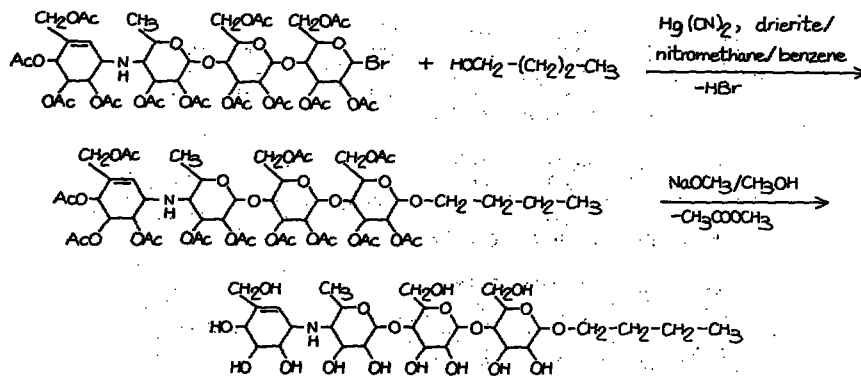
The reaction is preferably carried out at the boiling point of the alcohol, but can also optionally be carried out at a lower temperature.

If the compounds of the formula VII are amines, preferably aromatic amines, the reaction with compounds of the formula I is preferably carried out by heating the compounds in a little water, as a solvent, or in 50% strength acetic acid or in alcohols, as a solvent, at pH=3—4. The reaction can also be carried out by heating the two components without a diluent. The reaction is carried out at temperatures between 25 and 200° C, preferably between 60 and 120° C.

In most of the processes, the compounds of the formula II are first obtained as O-acyl derivatives. The splitting off of the acyl protective group is preferably carried out by transesterification under basic catalysis, for example with catalytic amounts of Na in methanol or with triethylamine in methanol, by saponification with alkali metal hydroxides in alcohol/water or by reaction with amines, for example with ammonia in methanol.

The individual procedures for the preparation of the new amino-sugar derivatives are illustrated in the following:

If n-butanol and the compound of the formula VI in which Y is Br, m' is 0, n' is 2, Ac is acetyl and R' is H, are used as the starting materials, the course of the reaction according to variant (1) can be formulated as follows (modified Koenigs-Knorr synthesis according to R. H. Whistler and J. N. BeMiller, *Methods in Carbohydrate Chemistry*, volume VI, page 474, Academic Press, New York and London).

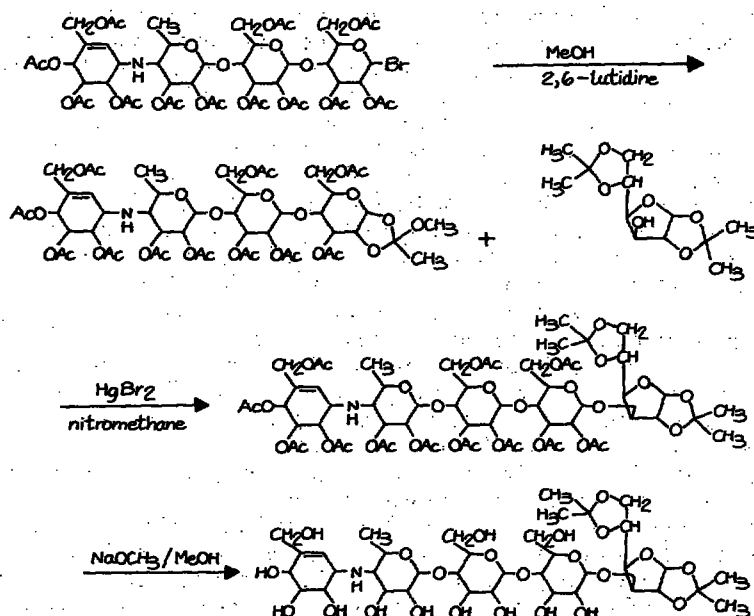


If phenol is the reactant of the formula VII, an embodiment of variant (1), in which the reaction is carried out with Ag_2O and drierite as auxiliaries and quinoline as the solvent, or an embodiment in which acetone/ H_2O is used as the reaction medium and KOH is used as the acid-binding agent, is preferred.

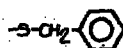
If 1,2-, 5,6-di-O-isopropylidene- α -D-glucopyranose is used as the alcohol component of the formula VII and the procedure followed is according to process variant

(P)

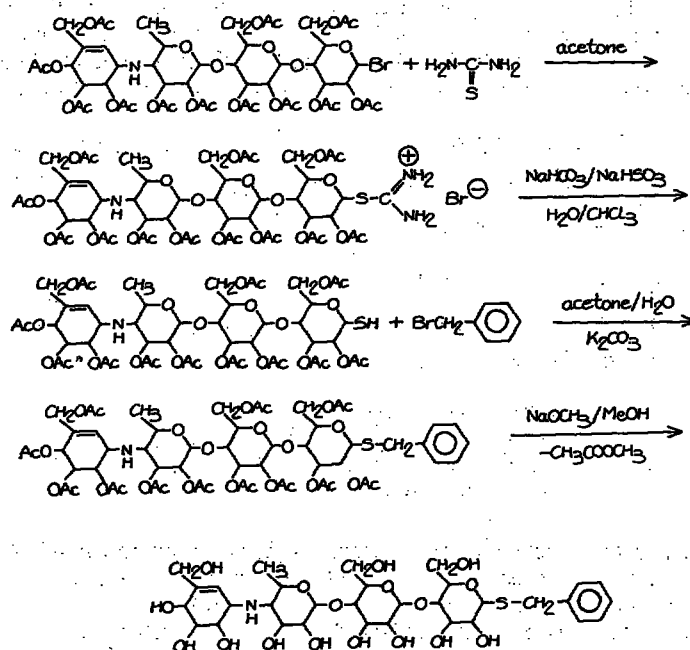
(2), the reaction is formulated, for example, as follows [Kochetkov-method according to R. L. Whistler and J. N. BeMiller, *Methods in Carbohydrate Chemistry*, volume VI, page 480, Academic Press, New York and London].



5. The preparation of a compound of the formula (II) in which —X is for example



from a compound of the formula (VI) in which, for example, Y is Br, m' is 0, n' is 2, Ac is acetyl and R' is H according to process variant (3), can be described by the following equation [Cerny method according to M. Cerny and J. Pacak, *Collection Czechoslov. Chem Commun* 24, 2566 (1959) and M. Cerny, J. Vrkoc and H. Stanek, *ibid.* 24, 64 (1959)].

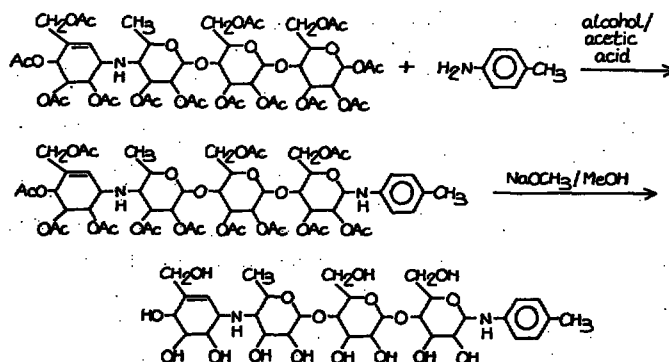


For the preparation of compounds of the formula (II) in which X is aryl, for example

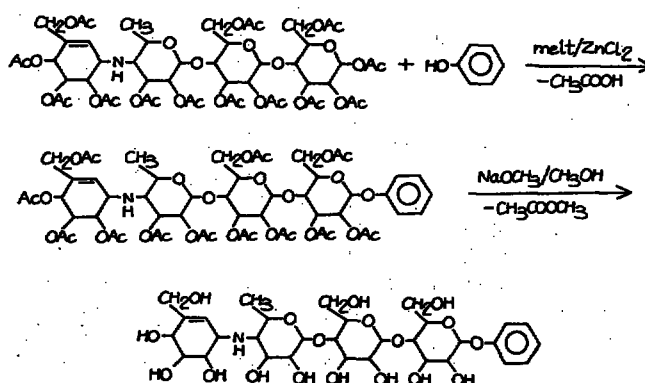


process variant (3) can be modified to the effect that in the third reaction stage the S—H compound is reacted with an aryldiazonium salt, for example with phenyldiazonium chloride, the O-acylated derivative of the formula (II) being formed with the splitting off of HCl and evolution of N₂. [Cerny method according to M. Cerny, D. Zachystalova and J. Pacak, Collection Czechoslov. Chem. Commun. 26, 2206, (1961)].

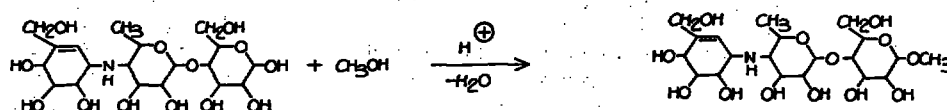
If O-acyl derivatives of the formula XI, for example the compound with m'=0, n'=2, Ac=acetyl and R'=H, and p-toluidine are employed as starting materials in the reaction for the preparation of compounds of the formula (II), the course of the reaction can be described as follows:



If phenol is the starting material of the formula (VII), the following embodiment of the reaction is preferred [Helferich method according to B. Helferich and E. Schmitz-Hillebrecht, Ber. 66, 378 (1933)].

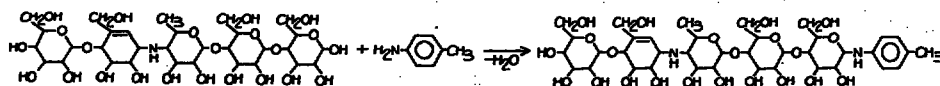


If the compounds of the formula (I) described in DT—OS (Germany Published Specification) 2,347,782, for example the compound in which m is 0 and n is 1, and, for example, MeOH are employed as starting materials in the reaction for the preparation of compounds of the formula (II), the following equation results [Fischer method according to E. Fischer, Ber. 28, 1151 (1895)].



If the compound in which m is 1 and n is 2 is chosen as the starting material of the formula I and p-toluidine is chosen as the starting material of the formula VII, the following equation results:

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The reaction is carried out between 0° C and 100° C, preferably at room temperature, and under normal pressure.

The crude active compounds of the formula II are appropriately purified by column chromatography. Chromatography on cellulose, using a butanol/ethanol/water mixture as the running agent, is preferred.

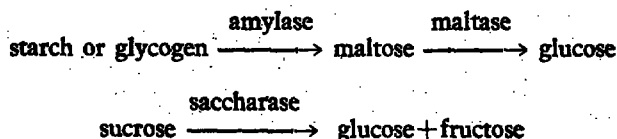
{ In detail, new active compounds which may be mentioned are the following: }
 C≡4,6 - dideoxy - 4 - [1S - (1,4,6/5) - 4,5,6 - trihydroxy - 3 - hydroxy-
 methylcyclohex - 2 - en - 1 - yl amino] - α - D - glucopyranosyl

phenyl - 4,6 - dideoxy - 4 - [1S - (1,4,6/5) - 4,5,6 - trihydroxy - 3 - hydroxy-
 methylcyclohex - 2 - en - 1 - yl amino] - β - D - glucopyranoside, phenyl - 4,6-
 dideoxy - 4 - [1S - (1,4,6/5) - 4,5,6 - trihydroxy - 3 - hydroxymethyl - cyclohex-
 2 - en - 1 - yl amino] - β - D - thioglucopyranoside, methyl - 4,6 - dideoxy - 4-
 [1S - (1,4,6/5) - 4,5,6 - trihydroxy - 3 - hydroxymethyl - cyclohex - 2 - en - 1-
 yl amino] - α - D - glucopyranoside, Ethyl - O - {C} - (1→4) - β - D - glucopyrano-
 side, methyl - O - {C} - (1→4) - α - D - glucopyranoside, benzyl - O - {C} - (1→4)-
 β - D - glucopyranoside, phenyl - O - {C} - (1→4) - β - D - glucopyranoside, p-
 nitrophenyl - O - {C} - (1→4) - β - D - thioglucopyranoside, N - p - tolyl - O -
 {C} - (1→4) - D - glucopyranosylamine, phenyl - O - {C} - (1→4) - O - α - D-
 glcp - (1→4) - β - D - glucopyranoside, p - carbomethoxyphenyl - O - {C} - (1→4)-
 O - α - D - glcp - (1→4) - β - D - glucopyranoside, p-carboxyphenyl - O - {C}-
 (1→4) - O - α - D - glcp - (1→4) - β - D - glucopyranoside, m - carbomethoxy-
 phenyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - β - D - glucopyranoside,
 m - carboxyphenyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - β - D - gluco-
 pyranoside, p-hydroxyphenyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - β -
 D - glucopyranoside, m - hydroxyphenyl - O - {C} - (1→4) - O - α - D - glcp-
 pyranoside, p - hydroxyphenyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - β -
 glcp - (1→4) - β - D - glucopyranoside, p-tert.-butylphenyl - O - {C} - (1→4) - O -
 α - D - glcp - (1→4) - β - D - glucopyranoside, methyl - O - {C} - (1→4) - O -
 α - D - glcp - (1→4) - β - D - glucopyranoside - ethyl - O - {C} - (1→4) - O - α -
 D - glcp - (1→4) - α - D - glucopyranoside, n - butyl - O - {C} - (1→4) - O - α -
 D - glcp - (1→4) - β - D - glucopyranoside, benzyl - O - {C} - (1→4) - O - α -
 D - glcp - (1→4) - β - D - glucopyranoside, n - octyl - O - {C} - (1→4) - O - α -
 D - glcp - (1→4) - β - D - glucopyranoside, n-hexadecyl - O - {C} - (1→4) - O - α -
 D - glcp - (1→4) - β - D - glucopyranoside, m - dimethylaminophenyl - O - {C}-
 (1→4) - O - α - D - glcp - (1→4) - β - D - glucopyranoside, p - dimethylamino-
 sulphonylphenyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - β - D - gluco-
 pyranoside, p - benzoylphenyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - β -
 D - glucopyranoside, phenyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - β - D-
 thioglucopyranoside, o - aminophenyl - O - {C} - (1→4) - O - α - D - glcp-
 (1→4) - β - D - thioglucopyranoside, benzyl - O - {C} - (1→4) - O - α - D - glcp-
 (1→4) - β - D - thioglucopyranoside, n - butyl - O - {C} - (1→4) - O - α - D -
 glcp - (1→4) - β - D - thioglucopyranoside, carboxymethyl - O - {C} - (1→4)-
 O - α - D - glcp - (1→4) - β - D - thioglucopyranoside, N - phenyl - O - {C}-
 (1→4) - O - α - D - glcp - (1→4) - D - glucopyranosylamine, N - p - tolyl - O -
 {C} - (1→4) - O - α - D - glcp - (1→4) - D - glucopyranoside, N - methyl - N-
 phenyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - D - glucopyranosylamine,
 N - p - hydroxyphenyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - D - gluco-
 pyranosylamine, N - propyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - D -
 glucopyranosylamine, O - {C} - (1→4) - O - α - D - glcp - (1→4) - D - gluco-
 pyranosylmorpholine, O - {C} - (1→4) - O - α - D - glcp - (1→4) - D - gluco-
 pyranosylpiperidine, p - aminophenyl - O - {C} - (1→4) - O - α - D - glcp-
 (1→4) - β - D - glucopyranoside, m - aminophenyl - O - {C} - (1→4) - O - α -
 D - glcp - (1→4) - β - D - glucopyranoside, naringenindihydrochalcone - 4' - [O -
 {C} - (1→4) - O - α - D - glcp - (1→4) - β - D - glucopyranoside], naringenindi-
 hydrochalcone - 2' - β - D - glucopyranoside - 4' - [O - {C} - (1→4) - O - α - D-
 glcp - (1→4) - β - D - glucopyranoside], diethylstilbestrol - 4' - [O - {C} - (1→4)-
 O - α - D - glcp - (1→4) - β - D - glucopyranoside], D - sorbital - 4 - [O - {C}-
 (1→4) - α - D - glucopyranoside], O - {C} - (1→4) - O - β - D - glcp - (1→6)-
 D - glucopyranose, O - {C} - (1→4) - O - α - D - glcp - (1→4) - O - β - D - glcp-

- (1→6) - D - glucopyranose, p - nitrophenyl - O - {4,6 - dideoxy - 4 - [1S - (1,4,6/5) - 4,5,6 - trihydroxy - 3 - hydroxymethyl - 4 - O - α - D - glucopyranosyl - (1→4) - cyclohex - 2 - en - 1 - yl amino] - α - D - glucopyranosyl} - (1→4) - O - α - D - glcp - (1→4) - β - D - glucopyranoside, phenyl - O - {4,6 - dideoxy - 4 - [1S - (1,4,6/5) - 4,5,6 - trihydroxy - 3 - hydroxymethyl - 4 - O - α - glucopyranosyl - (1→4) - cyclohex - 2 - en - 1 - yl amino] - α - D - glucopyranosyl} - (1→4) - O - α - D - glcp - (1→4) - β - D - thioglucopyranoside, N - p - tolyl - O - {4,6 - dideoxy - 4 - [1S - (1,4,6/5) - 4,5,6 - trihydroxy - 3 - hydroxymethyl - 4 - O - α - D - glucopyranosyl - (1→4) - cyclohex - 2 - en - 1 - yl amino] - α - D - glucopyranosyl} - (1→4) - O - α - D - glcp - (1→4) - D - glucopyranosylamine, p - nitrophenyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - O - α - D - glcp - (1→4) - β - D - glucopyranoside, phenyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - O - α - D - glcp - (1→4) - β - D - thioglucopyranoside, p - nitrophenyl - O - {4,6 - dideoxy - 4 - [1S - (1,4,6/5) - 4,5,6 - trihydroxy - 3 - hydroxymethyl - 4 - (O - α - D - glcp - (1→4) - O - α - D - glucopyranosyl) - (1→4) - cyclohex - 2 - en - 1 - yl amino] - α - D - glucopyranosyl} - (1→4) - O - α - D - glcp - (1→4) - β - D - thioglucopyranoside, p - nitrophenyl - O - {4,6 - dideoxy - 4 - [1S - (1,4,6/5) - 4,5,6 - trihydroxy - 3 - hydroxymethyl - 4 - (O - α - D - glcp - (1→4) - O - α - D - glcp - (1→4) - O - α - D - glucopyranosyl) - (1→4) - cyclohex - 2 - en - 1 - yl amino] - α - D - glucopyranosyl} - (1→4) - O - α - D - glcp - (1→4) - β - D - glucopyranoside, O - {C} - (1→4) - O - α - D - glcp - (1→4) - D - glucopyranosylamine and O - {C} - (1→4) - O - α - D - glcp - (1→4) - 1 - thio - D - glucopyranose.

The compounds according to the invention are inhibitors of glucoside hydrolases and are thus suitable for the treatment of diseases in which an inhibition of these enzymes appears desirable.

It is known that in animals and humans, after intake of carbohydrate-containing foodstuffs and beverages (for example cereal starch, potato starch, fruit, fruit juice, beer and chocolate, hyperglycaemias arise which are brought about as a result of a rapid degradation of the carbohydrates by glucoside hydrolases (for example salivary and pancreatic amylases, maltases and saccharases) according to the following equation



In the case of diabetics, these hyperglycaemias are particularly strong and of long-lasting pronounced character. In the case of adipose subjects, the alimentary hyperglycaemia frequently leads to a particularly intense insulin secretion which in turn leads to increased fat synthesis and decreased fat degradation. Following such hyperglycaemias, a hypoglycaemia frequently occurs in the case of adipose persons of sound metabolism, as a result of the insulin secretion. It is known that both hypoglycaemias and foodstuff sludge remaining in the stomach promote the production gastric juice which in turn causes, or favours, the formation of a gastritis or a gastric or duodenal ulcer.

It is also known that carbohydrates, particularly sucrose, are split in the oral cavity by micro-organisms and the formation of caries is thereby promoted.

Malabsorption of carbohydrates, for example as a result of intestinal saccharase deficiency, causes diarrhoea. Suitable doses of a glucosidase inhibitor effect a synthetic malabsorption and are thus suitable for counteracting constipation.

The inhibitors according to the invention are thus suitable for use as therapeutic agents for the following indications: adiposity, hyperlipoproteinaemia, atherosclerosis, diabetes, pre-diabetes, hypoglycaemia gastritis, constipation and caries.

In order to broaden the spectrum of activity, it can be advisable to combine inhibitors for glucoside hydrolases which complement one another in their action, the combinations being either combinations of the inhibitors according to the invention with one another or combinations of the inhibitors according to the invention with inhibitors which are already known.

In some cases, combinations of the inhibitors according to the invention with known oral antidiabetic agents (β-cytotropic sulphonylurea derivatives and/or biguanides having an action on the blood sugar) and with blood lipid-lowering active

compounds, such as, for example, clofibrat, nicotinic acid, cholestyramine and others, are also advantageous.

The compounds can be administered without dilution, for example as a powder or in a gelatine casing, or in combination with an excipient in a pharmaceutical composition.

The present invention provides a pharmaceutical composition containing as active ingredient a compound of the invention in admixture with a solid or liquefied gaseous diluent, or in admixture with a liquid diluent other than a solvent of a molecular weight less than 200 (preferably less than 350) except in the presence of a surface active agent.

The invention further provides a pharmaceutical composition containing as active ingredient a compound of the invention in the form of a sterile or isotonic aqueous solution.

The invention also provides a medicament in dosage unit form comprising a compound of the invention.

The invention also provides a medicament in the form of tablets (including lozenges and granules), dragees, capsules, pills, ampoules or suppositories comprising a compound of the invention.

"Medicament" as used in this Specification means physically discrete coherent portions suitable for medical administration. "Medicament in dosage unit form" as used in this Specification means physically discrete coherent units suitable for medical administration each containing a daily dose or a multiple (up to four times) or sub-multiple (down to a fortieth) of a daily dose of the compound of the invention in association with a carrier and/or enclosed within an envelope. Whether the medicament contains a daily dose or, for example, a half, a third, or a quarter of a daily dose will depend on whether the medicament is to be administered once or, for example, twice, three times or four times a day respectively.

The pharmaceutical compositions according to the invention may, for example, take the form of suspensions, solutions and emulsions of the active ingredient in aqueous or non-aqueous diluents, syrups, granulates or powders.

The diluents to be used in pharmaceutical compositions (e.g. granulates) adapted to be formed into tablets, dragees, capsules and pills include the following:

(a) fillers and extenders, e.g. starch, sugars, mannitol, and silicic acid; (b) binding agents, e.g. carboxymethyl cellulose and other cellulose derivatives, alginates, gelatine and polyvinyl pyrrolidone; (c) moisturizing agents, e.g. glycerol; (d) disintegrating agents, e.g. agar-agar, calcium carbonate and sodium bicarbonate; (e) agents for retarding dissolution e.g. paraffin; (f) resorption accelerators, e.g. quaternary ammonium compounds; (g) surface active agents, e.g. cetyl alcohol, glycerol monostearate; (h) adsorptive carriers, e.g. kaolin and bentonite; (i) lubricants, e.g. talc, calcium and magnesium stearate and solid polyethylene glycols.

The tablets, dragees, capsules and pills formed from the pharmaceutical compositions of the invention can have the customary coatings, envelopes and protective matrices, which may contain opacifiers. They can be so constituted that they release the active ingredient only or preferably in a particular part of the intestinal tract, possible over a period of time. The coatings, envelopes and protective matrices may be made, for example, of polymeric substances or waxes.

The ingredient can also be made up in microencapsulated form together with one or several of the above-mentioned diluents.

The diluents to be used in pharmaceutical compositions adapted to be formed into suppositories can, for example, be the usual water-soluble or water-insoluble diluents, such as polyethylene glycols and fats (e.g. cocoa oil and high esters [e.g. C_{14} -alcohol with C_{16} -fatty acid]) or mixtures of these diluents.

The pharmaceutical compositions which are solutions and emulsions can, for example, contain the customary diluents (with, of course, the above-mentioned exclusion of solvents having a molecular weight below 200 except in the presence of a surface-active agent), such as solvents, dissolving agents and emulsifiers; specific examples of such diluents are water, ethyl alcohol, isopropyl alcohol, ethyl carbonate, ethyl acetate, benzyl alcohol, benzyl benzoate, propylene glycol, 1,3-butylene glycol, dimethylformamide, oils [for example ground nut oil], glycerol, tetrahydrofurfuryl alcohol, polyethylene glycols and fatty acid esters of sorbitol or mixtures thereof.

For parenteral administration, the solutions and emulsions should be sterile, and, if appropriate, blood-isotonic.

The pharmaceutical compositions which are suspensions can contain the usual diluents, such as liquid diluents, e.g. water, ethyl alcohol, propylene glycol, surface-

active agents (e.g. ethoxylated isostearyl alcohols, polyoxyethylene sorbite and sorbitane esters), microcrystalline cellulose, aluminium metahydroxide, bentonite, agar-agar and tragacanth or mixtures thereof.

All the pharmaceutical compositions according to the invention generally contain from 0.1 to 99.5, usually from 0.5 to 95% of the active ingredient by weight of the total composition.

In addition to a compound of the invention, the pharmaceutical compositions and medicaments according to the invention can also contain other pharmaceutically active compounds. They may also contain a plurality of compounds of the invention.

Any diluent in the medicaments of the present invention may be any of those mentioned above in relation to the pharmaceutical compositions of the present invention. Such medicaments may include solvents of molecular weight less than 200 as sole diluent.

The discrete coherent portions constituting the medicament according to the invention will generally be adapted, by virtue of their shape or packaging, for medical administration and may be, for example, any of the following: tablets, (including lozenges and granulates), pills, dragees, capsules, suppositories and ampoules. Some of these forms may be made up for delayed release of the active ingredient. Some, such as capsules, include a protective envelope which renders the portions of the medicament physically discrete and coherent. The envelope is coloured.

The production of the above-mentioned pharmaceutical compositions and medicaments is carried out by any method known in the art, for example, by mixing the active ingredient(s) with the diluent(s) to form a pharmaceutical composition (e.g. a granulate) and then forming the composition into the medicament (e.g. tablets).

This invention further provides a method of combating (including prevention, relief and cure of) the above-mentioned diseases in non-human animals, which comprises administering to the animals a compound of the invention alone or in admixture with a diluent or in the form of a medicament according to the invention.

It is envisaged that these active compounds will be administered perorally, parenterally (for example intramuscularly, intraperitoneally or intravenously) or rectally. Preferred pharmaceutical compositions and medicaments are therefore those adapted for such administration.

In general it has proved advantageous to administer amounts of 30 to 3×10^6 AIU/kg and of 1 to 1×10^4 SIU/kg of body weight per day to achieve effective results. Nevertheless it can at times be necessary to deviate from those dosage rates, and in particular to do as a function of the nature and body weight of the animal subject to be treated, the individual reaction of this subject to the treatment, the type of formulation in which the active ingredient is administered and the mode in which the administration is carried out, and the point in the progress of the disease or interval at which it is to be administered. Thus it may in some case suffice to use less than the above-mentioned minimum dosage rate, whilst other cases the upper limit mentioned must be exceeded to achieve the desired results. Where larger amounts are administered it can be advisable to divide these into several individual administrations over the course of the day.

In addition to the above-mentioned examples of pharmaceutical compositions, there may be used a pharmaceutical composition in the form of a foodstuff containing these active compounds; for example sugar, bread, potato products, fruit juice, beer, chocolate and other confectionery, and preserves, such as, for example, jam, a therapeutically active amount of at least one of the inhibitors according to the invention having been added to these products.

Furthermore, the inhibitors according to the invention have the property, in animals, on influencing, to a high degree, the ratio of the proportion of undesired fat to the proportion of desired flesh of low fat content (lean flesh) in favour of the lean flesh. This is of particular importance for the rearing and keeping of agricultural stock animals, for example in the fattening of pigs, but is also of considerable importance for the rearing and keeping of other stock animals and pets. Furthermore, the use of inhibitors can lead to a considerable rationalisation of the feeding of the animals, both in respect of time, quantity and quality. Since they cause a certain delay in digestion, the residence time of the nutrients in the digestive tract is extended, whereby ad libitum feeding associated with less expense is made possible. Furthermore, in many cases a considerable saving of valuable protein feed results when the inhibitors according to the invention are used.

The active compounds can thus be used in virtually all sections of animal nutrition as agents for reducing the formation of fatty layers and for the saving of feed protein.

The activity of the active compounds here is largely independent of the nature and

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the sex of the animals. The active compounds prove particularly valuable in species of animals which generally tend to deposit relatively large amounts of fat or tend to do so during certain stages of their life.

The active compounds according to the invention are administered to the animals with which the inhibitors for reducing the formation of fatty layers and/or for saving feed protein can be employed: warm-blooded animals, such as cattle, pigs, horses, sheep, goats, cats, dogs, rabbits, fur-bearing animals, for example mink and chinchillas, and other pets, for example guinea pigs and hamsters, laboratory animals and zoo animals, for example rats, mice, monkeys and the like, poultry, for example chickens, geese, ducks, turkeys and pigeons, parrots and canaries, and cold-blooded animals, such as fish, for example carp, and reptiles, for example snakes.

Because of the favourable properties of the active compounds, the amount of active compounds administered to the animals in order to achieve the desired effect can be substantially varied. It is preferably 0.5 mg of 2.5 g/kg, in particular 10 to 100 mg/kg, of feed. The period over which the active compound is administered can be from a few hours or days to several years. The appropriate amount of active compound and the appropriate period over which it is administered are closely connected with the object of feeding. In particular, they depend on the nature, the age, the sex and the state of health of the animals and on the method of keeping the animals and can be easily determined by any person skilled in the art.

The active compounds according to the invention are administered to the animals by the customary methods. The nature of the administration depends, in particular, on the nature, the behaviour and the general condition of the animals. Thus, it is possible to carry out the administration orally once or several times daily, at regular or irregular intervals. In most cases, oral administration, in particular in the rhythm of the food and/or drink intake of the animals, is to be preferred for reasons of expediency.

The active compounds can be administered as pure substances or in the formulated form, the formulated form being understood both as a premix, that is to say mixed with non-toxic inert excipients of any desired nature, and also as part of a total ration in the form of a supplementary feed and as a constituent of the mixture of a mixed feed by itself. Administration of suitable formulations by means of the drinking water is also included.

The active compounds, optionally in the formulated form, can also be administered together with other nutrients and active compounds, for example mineral salts, trace elements, vitamins, proteins, energy carriers (for example starch, sugar or fats), dyestuffs and/or flavouring substances or other feedstuff additives, such as, for example, growth promoters, in a suitable form. The active compounds can be administered to the animals before, during or after the food intake.

Oral administration together with the feed and/or drinking water is advisable, the active compounds being added to the total amount or only to parts of the feed and/or drinking water, depending on the requirement.

The active compounds can be added to the feed and/or the drinking water according to customary methods by simple mixing as the pure substances, preferably in the finely divided form, or in the formulated form mixed with edible, non-toxic excipients, and optionally also in the form of a premix or a feed concentrate.

The feed and/or drinking water can, for example, contain the active compounds according to the invention in a concentration from 0.001 to 5.0%, in particular 0.02 to 2.0% (weight). The optimum level of the concentration of the active compound in the feed and/or drinking water depends, in particular, on the amount of feed and/or drinking water intake of the animals and can be easily determined by any expert.

The nature of the feed and its composition is not important here. It is possible to use all the usual commercially available or special feed compositions, which preferably contain the customary balance of energy substances and proteins, including vitamins and mineral substances, necessary for balanced nutrition. The feed can be composed, for example, of vegetable substances, for example shredded oilcake, shredded cereal and cereal by-products, but also of hay, silage fodder, beets, and other forage plants, of animal substances, for example meat and fish products, bonemeal, fats and vitamins, for example A, D, E, K and B-complex, as well as special sources of protein, for example yeasts and certain aminoacids, and mineral substances and trace elements, such as, for example, phosphorus and iron, zinc, manganese, copper, cobalt and iodine.

Premixes can preferably contain 0.1 to 50%, in particular 0.5 to 5.0%, (weight) of the active compounds of the formula II, in addition to any desired edible excipients and/or mineral salts, for example carbonated feed lime, and are prepared by the customary mixing methods.

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Mixed feeds preferably contain 0.001 to 5.0%, in particular 0.02 to 2.0% (weight) of the active compounds of the formula II, in addition to the customary raw material components of a mixed feed, for example shredded cereal or cereal by-products, shredded oilcake, animal protein, minerals, trace elements and vitamins. They can be prepared by the customary mixing methods.

The active compounds in premixes and mixed feed agents can preferably also be appropriately protected from air, light and/or moisture by suitable agents which cover their surface, for example with non-toxic waxes or gelatine.

The following is an example of the composition of a finished mixed feed, for poultry, containing an active compound according to the invention: 200 g of wheat, 340 g of maize, 360.3 g of coarse soya bean meal, 60 g of beef tallow, 15 g of dicalcium phosphate, 10 g of calcium carbonate, 4 g of iodinated sodium chloride, 7.5 g of a vitamin/mineral mixture and 3.2 of an active compound premix give, after careful mixing, 1 kg of feed.

The vitamin/mineral mixture consists of: 6,000 I.U. of vitamin A, 1,000 I.U. of vitamin D₃, 10 mg of vitamin E, 1 mg of vitamin K₃, 3 mg of riboflavin, 2 mg of pyridoxine, 20 mg of vitamin B₁₂, 5 mg of calcium pantothenate, 30 mg of nicotinic acid, 200 mg of choline chloride, 200 mg of MnSO₄ · H₂O, 140 mg of ZnSO₄ · 7H₂O, 100 mg of FeSO₄ · 7H₂O and 20 mg of CuSO₄ · 5H₂O.

The active compound premix contains, for example, the active compound from Example 1, 8 in the desired amount, for example 1,600 mg, and in addition 1 g of DL-methionine and enough soya bean flour to form 3.2 g of premix.

The following is an example of the composition of a mixed feed, for pigs, which contains an active compound of the formula II: 630 g of shredded cereal feed (composed of 200 g of shredded maize, 150 g of shredded barley, 150 g of shredded oats and 130 g of shredded wheat), 80 g of fishmeal, 60 g of coarse soya bean meal, 58.8 g of tapioca flour, 38 g of brewer's yeast, 50 g of a vitamin/mineral mixture for pigs (composition, for example, as in the chicken feed), 30 g of linseed cake meal, 30 g of maize gluten feed, 10 g of soya bean oil, 10 g of cane sugar molasses and 2 g of active compound premix (composition, for example, as in the chicken feed) give, after careful mixing, 1 kg of feed.

The feed mixtures indicated are intended, preferably, for rearing and fattening chicken or pigs respectively, however, they can also be used, in an identical or similar composition, for rearing and fattening other animals.

In vitro α-amylase inhibition test.

The in vitro α-amylase inhibition test makes it possible to determine the enzymic inhibitory activity of the sample by comparing the activity of commercially obtainable α-amylase from the pig's pancreas in the presence of the inhibitor with its activity in the absence (so-called 100% value) of the inhibitor. For this, soluble starch is used as the substrate; the enzyme activity determination is based on the colorimetric determination of reducing groups by means of dinitrosalicylic acid.

An amylase inhibitory unit (AIU) is defined as that inhibitory activity which reduces a given amylolytic activity in a defined test batch by one unit (amylase unit = AU); the amylase unit is defined here as that enzyme activity which in one minute under given conditions splits one μmol of glucosidic bonds and thus leads to the formation of one μmol of reducing groups.

200 μl of a solution of α-amylase from the pig's pancreas (crystal suspension "BOEHRINGER") in 20 mM sodium glycerophosphate buffer of pH 6.9, of 1 mM strength in CaCl₂ are added to 10 μl of a sample solution which is diluted so that it contains 0.05—0.15 AIU in the said aliquot and the mixture is pre-incubated for 10 minutes at 37° C. The amylase solution is to be adjusted to an activity of 2.0—2.5 AU/ml. The amylolytic reaction is then started by adding 200 μl of a 5% strength solution of starch ("MERCK 1257") in sodium glycerophosphate buffer of pH 6.9, of 1 mM strength in CaCl₂ and after an incubation period of 5 minutes at 37° C is stopped by adding 0.5 ml of dinitrosalicylic acid reagent (S. P. COLOWICK + N. O. KAPLAN, editors: Meth. Enzymol 1 (1955) 149). In order to develop the colour, the mixture is heated to 100° C for 5 minutes, after which it is diluted with 2.5 ml of H₂O and measured photometrically at 540 nm against a reagent blank (without enzyme).

In order to calculate the enzyme activities in the presence and in the absence of the inhibitor, standards are set up with 1 and 2 μmols of maltose in 400 μl of sodium glycerophosphate buffer; the extinction for 1 μmol of reducing groups is obtained from the extinction difference between the two standards. This value is used in a known manner in the calculation of the enzyme activities (in amylase units). The

specific inhibitory activity of the inhibitor, expressed in amylase inhibitory units per gramm (AIU/g) is obtained from the activity difference between the uninhibited and inhibited batch, taking into account the amounts of inhibitor employed.

In vitro saccharase inhibition test.

The in vitro saccharase inhibition test makes it possible to determine the enzyme inhibitory activity of a sample by comparing the activity of the solubilised intestinal disaccharidase complex in the presence of the inhibitor with its activity in the absence (so-called 100% value) of the inhibitor. A virtually glucose-free (<100 ppm) saccharose is used here as the substrate, which determines the specificity of the inhibition test; the enzyme activity determination is based on the colorimetric determination of liberated glucose by means of glucoseoxydase, peroxydase and 2,2-azino-di-[3-ethyl-benzthiazoline-6-sulphonate] (=ABTS) as the chromogen.

A saccharase inhibitor unit (SIU) is defined as that inhibitory activity which reduces a given saccharolytic activity in a defined test batch by one unit (saccharase unit=SU); the saccharase unit is defined here as that enzyme activity which, under given conditions, in one minute splits 1 μ mol of sucrose and thus leads to the liberation of 1 μ mol of glucose, which is determined in the test, and fructose, which is not detected in the test.

The intestinal disaccharidase complex is obtained from pig's small intestine mucosa by trypsin digestion, precipitation from 66% ethanol at -20° C, taking up of the precipitate in 100 mM phosphate buffer of pH 7.0 and concluding dialysis against the same buffer.

100 μ l of a dilution of the intestinal disaccharidase complex in 0.1 M maleate buffer of pH 6.25 are added to 10 μ l of a sample solution which is diluted so that the extinction of the test batch is at least 10%, but not more than 25%, below that of the 100% value, and the mixture is pre-incubated for 10 minutes at 37° C. The dilution of the disaccharidase complex is to be adjusted to an activity of 0.05 SU/ml. The saccharolytic action is then started by adding 100 μ l of a 0.4 M solution of sucrose ("SERVA 35579") in 0.1 M maleate buffer of pH 6.25 and after an incubation period of 20 minutes at 37° C is stopped by adding 1 ml of GOD/POD/ABTS reagent (50 mg of GOD, degree of purity II, "BOEHRINGER" + 30 mg of POD, degree of purity II "BOEHRINGER" + 2 g. of ABTS, "BOEHRINGER" in 1,000 ml of 0.5 M tris buffer at pH 7.0). In order to develop the colour, the mixture is incubated for 30 minutes at 37° C, after which it is diluted with 2 ml of tris buffer and measured photometrically at 420 nm against a reagent blank (with enzyme but without sucrose).

The calculation of the inhibitory activity of inhibitors is made more difficult by the fact that even slight alterations in the test system, for example a 100% value which varies slightly from determination to determination, have an influence on the test results which can no longer be disregarded. These difficulties are avoided by simultaneously running a standard in each determination; the compound of the formula I (page 2) with m=0 and n=2, which has a specific inhibitory activity of 68,000 SIU/g and, when amounts of 5 and 10 mg are employed, leads to an inhibition in the test of the order of size specified above, is used as the standard. When the difference in the extinctions at 420 nm between the 100% value and the batch inhibited by the standard is known, the specific inhibitory activity of the inhibitor, expressed in saccharase inhibitor units per gram (SIU/g) can be calculated in a known manner from the extinction difference between the 100% value and the batch inhibited by the sample solution, taking into account the amount of inhibitor employed.

In vitro method for the inhibition of glucose absorption:

The inhibition of glucose absorption by the compounds according to the invention were demonstrated in a modified experimental arrangement according to Crane and Mandelstam [Biochem. Biophys. Acta 45 (1960) 460-476].

The upper part of the small intestine of fasting male Wistar rats is folded over and cut into rings about 3 mm wide. 10 of these rings (~150 mg moist weight) are incubated for 2 minutes at 37° C in 5 ml of Krebs-Ringer bicarbonate buffer (pH 7.4) with D-glucose-¹⁴C (U) (10 mg/ml, 0.2 μ Ci/ml), with the addition of the active compounds. The washed and dried-off intestine rings are weighed, dissolved in 5 ml of Digestin (Merck)/isopropanol (1:1) and the radioactivity absorbed in the tissue is determined in a liquid scintillation counter. All values are corrected using the radioactivity absorbed in the tissue as D-mannitol-1-¹⁴C.

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Results:

In vitro inhibitions of the glucose absorption by some selected compounds (10 mg/ml):

Table I.

Number of the compound in the Preparation Examples	Inhibition ^{*)}
Example 1, 8	+
Example 1, 7	+
Example 1, 9	++
Example 1, 5	++
Example 4, 18	++

^{*)} Inhibition 25—50% of the control value +
Inhibition > 50% of the control value ++

- 5 The in vivo activity of the compound was tested on some examples using the experimental arrangement described in the following text. 5
- 10 Oral administration of starch or sucrose causes a rise in the blood sugar in humans and animals, provided that the carbohydrates are enzymatically degraded in the small intestine to monosaccharides. The inhibition of their enzymatic hydrolysis by glycosidase inhibitors causes a reduced rise in the blood sugar. 10
- 15 In order to detect the action of glucosidase inhibitors, 6 fasting rats receive perorally, 1 g of boiled starch or 2.5 g of sucrose/kg in the form of an aqueous suspension or in the form of an aqueous solution (starch and sucrose control respectively). An equal number of rats receive the glucosidase inhibitor in the dose indicated, together with the same amount of the carbohydrate concerned. An equal volume of physiological sodium chloride solution is administered orally to a further six rats (control). After administration of the carbohydrate concerned ± glucosidase inhibitor, the post-prandial change in blood sugar is measured, at the times indicated, in blood from the postorbital venous plexus in an auto-analyser according to the method of W. S. Hoffmann [J. biol. Chem. 120, 51 (1937)]. 15
- 20 It was shown here that the active compounds according to the invention are highly active inhibitors of starch and sucrose digestion and in low doses already have a high activity and long-lasting period of action. 20
- 25 Table II contains the results of the starch feeding test and Table III shows those of the sucrose feeding test. 25

22

TABLE II

Blood sugar in mg/dl $\pm$ standard deviation

Dose/kg perorally	15	30	45	60 minutes
Fasting control	82 $\pm$ 12	72 $\pm$ 10	102 $\pm$ 6.7	88 $\pm$ 7.4
Starch	146 $\pm$ 19	144 $\pm$ 8.9	120 $\pm$ 7.9	118 $\pm$ 6.9
+ 10 mg of 2	102 $\pm$ 10	73 $\pm$ 9.1	100 $\pm$ 6.5	108 $\pm$ 9.3
+ 10 mg of 20	87 $\pm$ 12	83 $\pm$ 13	99 $\pm$ 17	111 $\pm$ 5.6
+ 10 mg of 13	70 $\pm$ 8.3	40 $\pm$ 6.8	89 $\pm$ 9.0	100 $\pm$ 4.6
Fasting control	60 $\pm$ 4.2	62 $\pm$ 3.4		
Starch	131 $\pm$ 7.2	113 $\pm$ 9.2		
+ 0.78 mg of 6	110 $\pm$ 6.1	105 $\pm$ 10		
+ 0.65 mg of 8	112 $\pm$ 9.9	109 $\pm$ 12		
+ 0.92 mg of 3	89 $\pm$ 8.0	97 $\pm$ 13		
+ 0.86 mg of 1	93 $\pm$ 6.4	84 $\pm$ 12		
+ 1.56 mg of 4	99 $\pm$ 8.1	97 $\pm$ 10		
+ 0.92 mg of 7	121 $\pm$ 7.7	112 $\pm$ 4.3		

--- probability <0.05 ——— probability <0.01 === probability <0.001 compared with the corresponding starch control

TABLE III

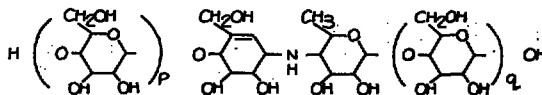
Blood sugar in mg/dl $\pm$ standard deviation

Dose/kg perorally	15	30	45	60 minutes
Fasting control	61 $\pm$ 13	65 $\pm$ 3.9	66 $\pm$ 6.9	76 $\pm$ 3.7
Sucrose	113 $\pm$ 6.5	116 $\pm$ 9.2	104 $\pm$ 12	123 $\pm$ 8.1
" + 10 mg of 2	79 $\pm$ 4.1	86 $\pm$ 10	74 $\pm$ 7.2	71 $\pm$ 15
" + 10 mg of 20	83 $\pm$ 20	85 $\pm$ 8.3	73 $\pm$ 8.5	69 $\pm$ 9.3
" + 10 mg of 13	79 $\pm$ 6.8	80 $\pm$ 5.4	85 $\pm$ 16	86 $\pm$ 2.0
" + 10 mg of 15	80 $\pm$ 6.1	83 $\pm$ 9.4	87 $\pm$ 4.8	94 $\pm$ 13
Fasting control	60 $\pm$ 4.6	64 $\pm$ 3.7	73 $\pm$ 7.1	66 $\pm$ 4.2
Sucrose	128 $\pm$ 8.0	133 $\pm$ 8.7	134 $\pm$ 6.1	119 $\pm$ 10
" + 0.78 mg of 6	96 $\pm$ 15	100 $\pm$ 3.4	106 $\pm$ 18	117 $\pm$ 6.5
" + 0.65 mg of 8	112 $\pm$ 3.1	114 $\pm$ 6.3	119 $\pm$ 9.4	112 $\pm$ 4.3
" + 0.92 mg of 3	97 $\pm$ 10	108 $\pm$ 4.2	112 $\pm$ 15	111 $\pm$ 11
" + 0.86 mg of 1	103 $\pm$ 6.4	110 $\pm$ 10	108 $\pm$ 13	107 $\pm$ 11
" + 1.56 mg of 4	95 $\pm$ 7.0	112 $\pm$ 5.5	104 $\pm$ 6.7	115 $\pm$ 7.0
" + 0.92 mg of 7	110 $\pm$ 3.4	118 $\pm$ 14	112 $\pm$ 10	117 $\pm$ 9.0
Fasting control	71 $\pm$ 3.7	70 $\pm$ 5.3	77 $\pm$ 5.5	78 $\pm$ 7.3
Sucrose	134 $\pm$ 13	116 $\pm$ 20	125 $\pm$ 8.6	112 $\pm$ 15
" + 3.0 mg of 9	85 $\pm$ 4.8	83 $\pm$ 7.9	88 $\pm$ 3.4	92 $\pm$ 9.4
" + 1.54 mg of 22	80 $\pm$ 3.7	79 $\pm$ 5.2	86 $\pm$ 4.5	86 $\pm$ 11

--- probability 0.05 ——— probability 0.01 ===== probability 0.001 compared with the corresponding sucrose control

19

On the preparation of the starting compounds.



A column with a diameter of 1.5 cm is filled with 30 g (moist weight) of "Dowex" (Trade Mark) 50 W $\times$ 4, (H⁺), 200—400 mesh, in 0.001 N HCl. 500 ml of mixed desorbed products (400,000 SIU/l, pH 2.5, 60% acetone), obtained according to Example 10, Table, consecutive No. 7, of DT—OS (German Published Specification) 2,347,782, are then pumped through the column in about 1 hour and the column is then rinsed with 500 ml of 0.001 N HCl. Under these conditions, activity is eluted only in traces. Subsequently, the product was desorbed with 0.0125 N HCl and the conductivity or the refractive index of the column eluate was recorded. In addition, the SIU content of the eluate was tested. The active fractions 74—100 were combined and neutralised by adding Amberlite IRA 410 OH⁻, and then concentrated to 5 ml and digested with 5 ml of methanol and the product was precipitated by adding the mixture dropwise to 200 ml of acetone. After washing with acetone and ether, the product was dried in vacuo.

Yield: 1 g of the compound with $p+q=2$, containing 65,000 SIU/g.

The compounds with $p+q=3$ to 8 glucose units are obtained from the runnings and the active preliminary fractions.

In contrast to alkaline desorption, this process of acid desorption thus makes fractionation of the individual amino-sugar derivatives of this series possible.

In order to separate the isomeric compounds with three glucose units, 10 g of an isomer mixture, dissolved in water, were washed with water, on a column filled with Dowex ² 50 W $\times$ 4 (H⁺), until the eluate was neutral and then eluted with 0.025 N hydrochloric acid. Fractions of 3 ml each were collected and examined by thin layer chromatography. The thin layer chromatography was carried out on silanised silica gel plates (MERCK, Germany) using 100:60:40:2 ethyl acetate+methanol+water+25% strength ammonia, with three-fold development. The compound with $p=0$ and $q=3$ runs a greater distance from the starting compound than the compound with $p=1$ and $q=2$. Fractions 215 to 272, containing 6 g of isomer with $p=1$ and $q=2$, and fractions 288 to 294, containing 600 mg of isomer with $p=0$ and $q=3$, were combined, neutralised with "Amberlite" (Trade Mark) IRA—410 (OH⁻) and concentrated.

The in vitro sucrose inhibitory activity of the isomers with $p=0$ and $q=3$, isolated by this process, is 19,000 SIU/g.

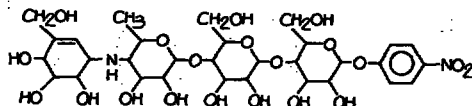
The preparation of further starting compounds is described in Examples 8, 23; 8, 24; 8, 25; 9, 26; 9, 27 and 9, 28.

Preparation Examples for the amino-sugar derivatives according to the invention.

Example 1.

p - Nitrophenyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - β - D - glucopyranoside.

C $\equiv$ 4,6- Dideoxy - 4 - [1S - (1,4,6/5) - 4,5,6 - trihydroxy - 3 - hydroxymethylcyclohex - 2 - en - 1 - yl amino] - α - D - glucopyranosyl.



5 g of drierite, 1.2 g (8.6 mmols) of p-nitrophenol and 1 g (4.3 mmols) of silver oxide are added to 40 ml of absolute quinoline and the mixture is stirred for 30 minutes, with the exclusion of moisture. 10 g of compound 26 from Example 9 are then added and the mixture is allowed to come to room temperature slowly, whilst stirring vigorously.

The reaction mixture is stirred for a further 12 hours at room temperature, 300 ml of chloroform are added and the insoluble residue is separated off. The chloroform solution is washed, whilst cooling with ice, first with 5% strength hydrochloric acid, then with sodium carbonate solution and finally with water and is then dried. The

residue is added to a solution of 400 mg of sodium in 100 ml of absolute methanol and the mixture is stirred for 2 hours at room temperature. It is then diluted with 100 ml of water and neutralised with a weakly acid ion exchanger (H^+ form), the exchanger is separated off and the solution is evaporated to dryness on a rotary evaporator. The residue is taken up in a little dimethylformamide/water and discharged onto a column (length: 70 cm; $\varnothing$: 2.6 cm) filled with cellulose (Avicel, Merck).

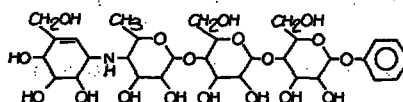
The column is eluted with butanol which is saturated with water and the individual fractions are examined by thin layer chromatography. 3 g of the non-crystalline compound 1 with an optical rotation value $\alpha_D = 88.8^\circ$ (H_2O ; $c=1\%$) are obtained.

For further characterisation, a small amount of the compound is acetylated in acetic anhydride/pyridine at room temperature and a mass spectrum of the resulting dodecaacetate of the compound 1 is recorded.

Molecular weight determined by mass spectrometry: 1,270 ($C_{55}H_{72}N_2O_{32}$).

The following compounds were prepared in an analogous way:

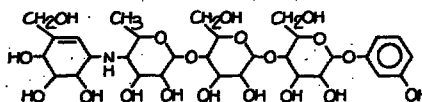
- 15 2 Phenyl - O - {C} - (1 $\rightarrow$ 4) - O - α - D - glcp - (1 $\rightarrow$ 4) - β - D - glucopyranoside. 15



$\alpha_D = 101.6^\circ$ (H_2O ; $c=1\%$).

The mass spectrum of the acetylated compound and the H^1 -NMR and C^{13} -NMR spectra were measured.

- 20 3 m - Hydroxyphenyl - O - {C} - (1 $\rightarrow$ 4) - O - α - D - glcp - (1 $\rightarrow$ 4) - β - D - glucopyranoside. 20

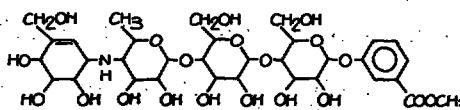


(O - Acetylresorcinol was employed as the starting compound).

$\alpha_D = 100.2^\circ$ (H_2O ; $c=1\%$).

- 25 Molecular weight of the acetylated compound, determined by mass spectrometry: 1,283 ($C_{57}H_{73}NO_{32}$). 25

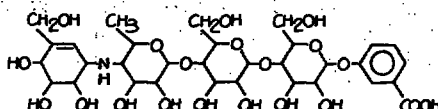
- 4 m - Carbomethoxyphenyl - O - {C} - (1 $\rightarrow$ 4) - O - α - D - glcp - (1 $\rightarrow$ 4) - β - D - glucopyranoside.



$\alpha_D = 71.0^\circ$ (H_2O ; $c=1\%$).

- 30 Molecular weight of the acetylated compound, determined by mass spectrometry: 1,283 ($C_{57}H_{73}NO_{32}$). 30

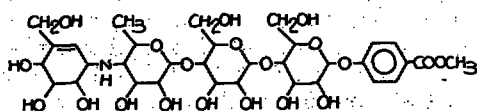
- 5 m - Carboxyphenyl - O - {C} - (1 $\rightarrow$ 4) - O - α - D - glcp - (1 $\rightarrow$ 4) - β - D - glucopyranoside.



5 was prepared by saponifying 4 with 10% strength sodium hydroxide solution at room temperature.

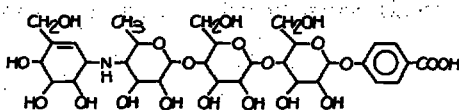
$\alpha_D = 91.7^\circ$ (H_2O ; $c=1\%$).

- 6 p - Carbomethoxyphenyl - O - {C} - (1→4) - O - α - D - glcp - (1→5) - β - D - glucopyranoside.



Molecular weight of the acetylated compound, determined by mass spectrometry: 1,283 ($C_{57}H_{73}NO_{31}$).

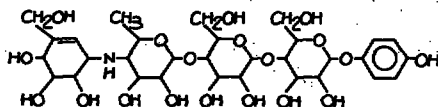
- 7 p - Carboxyphenyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - β - D - glucopyranoside.



7 was prepared by saponifying 6 with 10% strength sodium hydroxide solution at room temperature.

$\alpha_D = 85.9^\circ$ (H_2O ; $c=1\%$).

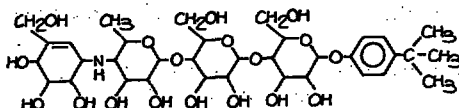
- 8 p - Hydroxyphenyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - β - D - glucopyranoside.



(O-Benzoyl-hydroquinone was employed as the starting compound).

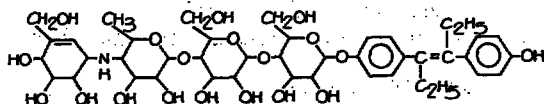
Molecular weight of the acetylated compound, determined by mass spectrometry: 1,283 ($C_{57}H_{73}NO_{32}$).

- 9 p - tert. - Butylphenyl - O - {C} - 1(→4) - O - α - D - glcp - (1→4) - β - D - glucopyranoside.



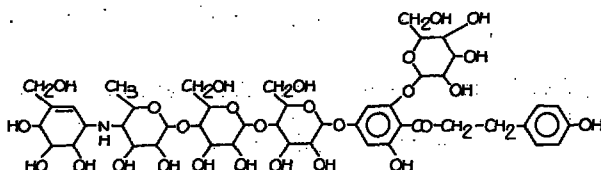
Molecular weight of the acetylated compound, determined by mass spectrometry: 1,281 ($C_{59}H_{79}NO_{30}$).

- 10 Diethylstilbostrol - 4' - [O - {C} - (1→4) - O - α - D - glcp - (1→4) - β - D - glucopyranoside].



After acetylation, the compound was characterised by mass spectrometry.

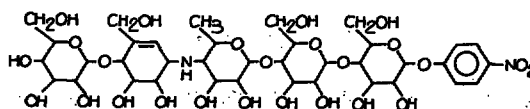
- 11 Naringeninidihydrochalcone - 2' - β - glucopyranoside - 4' - [O - {C} - (1→4) - O - α - D - glcp - (1→4) - β - D - glucopyranoside].



(Phlorhizin was employed as the starting compound) $C_{46}H_{45}NO_{27}$ (1,064.0).

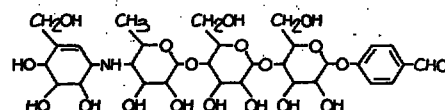
Found: C 51.6 H 7.1 N 0.8 O 38.5

- 5



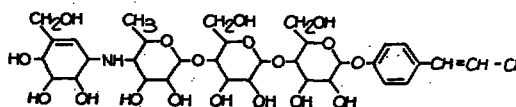
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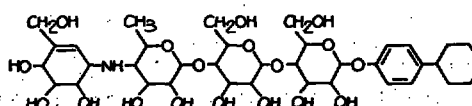


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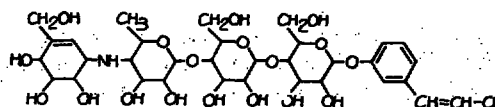
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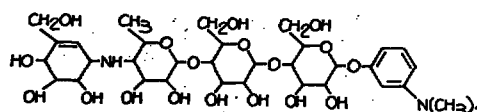


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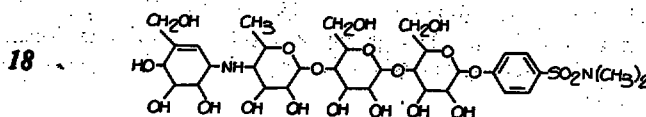
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1,556,345

24

4 - Dimethylaminosulphonyl - phenyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - β - D - glucopyranoside



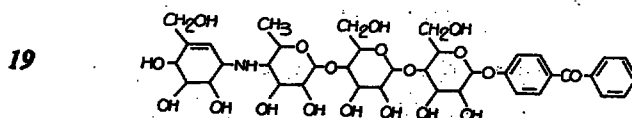
$\alpha_D = 85.4^\circ$ (H_2O ; $C=1$)

5

Molecular weight of the acetylated compound, determined by mass spectrometry: 1,332 ($C_{37}H_{76}N_2O_{22}S$).

5

4 - Benzoyl - phenyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - β - D - glucopyranoside



$\alpha_D = 75.46^\circ$ (H_2O ; $C=1\%$)

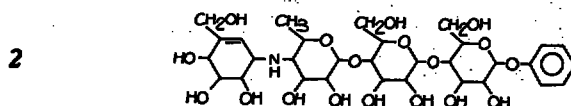
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10

Molecular weight of the acetylated compound, determined by mass spectrometry: 1,329 ($C_{62}H_{75}NO_{31}$).

Example 2.

Phenyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - β - D - glucopyranoside



15

15

8.8 g (7.3 mmols) of the compound 26 from Example 9 in 22 ml of acetone were added, at room temperature, to a solution of 3.2 g (34 mmols) of phenol and 1.08 g (19.3 mmols) of KOH in 14 ml of H_2O . The mixture was stirred overnight and then diluted with 50 ml of benzene. The organic phase was separated off and concentrated in a rotary evaporator. The residue was taken up in 200 ml of benzene and the benzene solution was extracted by shaking first with 20 ml of water, then with 40 ml of 2 N NaOH and finally 3 times with 80 ml of water each time. The benzene phase was dried, filtered and concentrated. Residue: 6.4 g.

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The residue was stirred overnight in a solution of 50 mg of Na in 50 ml of MeOH. The mixture was then diluted with water and neutralised with Amberlite IRC 50 (H^+ form). After filtration, the solution was evaporated to dryness in a rotary evaporator. Residue: 3.2 g.

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25

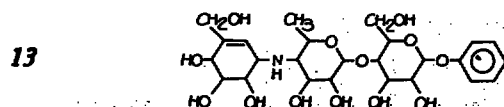
The residue was discharged onto a column (50 cm long, Ø: 2.4 cm) filled with cellulose (Merck: "Avicel" (Trade Mark)). Butanol saturated with water was used as the eluting agent. The dropping rate was 15 drops/minute; fractions of 400 drops each were collected. Fractions 36—57 gave 1.5 g of non-crystalline 2.

30

30

The following compound was prepared in an analogous way:

Phenyl - O - C - (1→4) - β - D - glucopyranoside



35

The product was characterised by a proton resonance spectrum of 220 MHz, a ^{13}C -NMR spectrum and a mass spectrum of the acetylated compound.

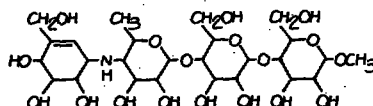
35

34

Example 3.

Methyl - O - C - (1→4) - O - α - D - glcp - (1→4) - β - D - glucopyranoside

14



1.3 g of yellow mercury-II oxide, 0.1 g of mercury-II bromide and 2.0 g of drierite are stirred in 20 ml of absolute methanol and 20 ml of pure chloroform for half an hour at room temperature. 3.0 g of the compound 26 from Example 9 are then added and the mixture is stirred overnight. The insoluble residue is filtered off and the filtrate is evaporated to dryness in a rotary evaporator. The residue is taken up in chloroform and the solution is once more clarified by filtration and then concentrated again.

The residue is stirred overnight with 75 ml of a 0.1% strength solution of sodium methanolate in methanol at room temperature. The mixture is then diluted with water to 400 ml and neutralised with a weakly acid ion exchanger (H⁺ form). The solvent is removed in a rotary evaporator and the residue is discharged onto a column (length: 70 cm; Ø: 2.4 cm) filled with cellulose ("Avicel", Merck). The column is eluted with butanol/ethanol/water 3:1:1.

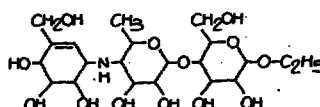
Fractions of about 8 ml are collected and the individual fractions are examined by thin layer chromatography. Fractions 60—92 contain 500 mg of the compound 14.

After acetylation with acetic anhydride/pyridine, a mass spectrum of the compound was measured. Molecular weight determined by mass spectrometry: 1,163 (C₂₅H₃₉NO₁₃).

The following compound was prepared in an analogous way:

Ethyl - O - {C} - (1→4) - β - D - glucopyranoside

15

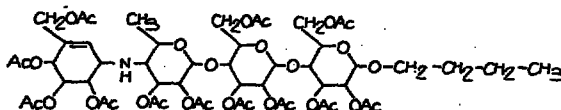


Molecular weight of the acetylated compound, determined by mass spectrometry: 889 (C₃₉H₅₃NO₂₂).

Example 4.

n - Butyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - β - D - glucopyranoside

16



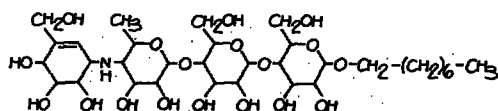
20 ml of liquid are distilled off from a mixture of 40 ml of nitromethane and 40 ml of benzene, with the exclusion of moisture. After cooling, 1 ml of n-butanol and 1 g of drierite are added and the mixture is stirred for 30 minutes at 40°C. 0.5 g of mercury-II cyanide and 2.4 g of the compound 26 from Example 9 are then added and the mixture is warmed to 40 to 50°C for a further 24 hours. The reaction mixture is then diluted with benzene and the benzene solution is washed first with water, then with a sodium bicarbonate solution and finally with water again.

After drying, the solution is evaporated to dryness on a rotary evaporator. The residue is de-acetylated overnight at room temperature with 50 ml of a 0.1% strength solution of sodium methanolate in methanol. The mixture is diluted with water and neutralised with a weakly acid ion exchanger. The solution is concentrated in a rotary evaporator and the residue is discharged onto a column filled with cellulose. The column is eluted with butanol which is saturated with water. The individual fractions are examined by thin layer chromatography. 500 mg of the non-crystalline compound 16 are obtained. Molecular weight of the acetylated compound, determined by mass spectrometry: 1,205 (C₃₃H₄₇NO₂₀).

The following compounds were prepared in an analogous way:

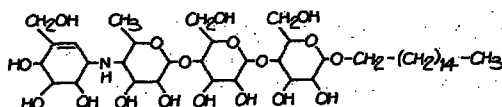
n - Octyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - β - D - glucopyranoside

17



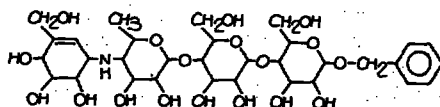
n - Hexadecyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - β - D - glucopyranoside

18



Benzyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - β - D - glucopyranoside

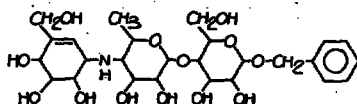
19



Molecular weight of the acetylated compound, determined by mass spectrometry: 1,239 ($C_{56}H_{78}NO_{30}$).

Benzyl - O - {C} - (1→4) - β - D - glucopyranoside

20

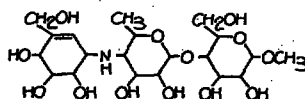


Molecular weight of the acetylated compound, determined by mass spectrometry: 951 ($C_{44}H_{57}NO_{22}$).

Example 5.

Methyl - O - {C} - (1→4) - α - D - glucopyranoside

21



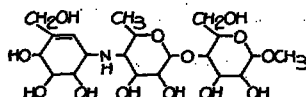
1 g of O - {C} - (1→4) - α - D - glcp - (1→4) - D - glucopyranose was heated under reflux in 100 ml of absolute methanol and 2 ml of concentrated sulphuric acid for 10 hours. After cooling, the mixture was diluted with 100 ml of water and the solution was neutralised with $NaCO_3$. The mixture was filtered and the filtrate was concentrated in a rotary evaporator. The residue was dissolved in a little water and discharged onto a column filled with a strongly acid ion exchanger (Dowex 50 WX4, H^+ form). The column was eluted first with water and then with 0.025 N HCl. The individual fractions were investigated by thin layer chromatography. Fractions 44—60 gave 360 mg of 21. Molecular weight of the acetylated compound, determined by mass spectrometry: 875 ($C_{38}H_{53}NO_{22}$).

The α-configuration of the glucoside is demonstrated by a proton resonance spectrum at 100 MHz.

Example 6.

Methyl - O - {C} - (1→4) - α - D - glucopyranoside

21



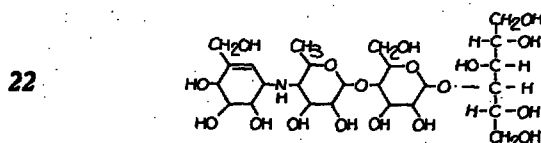
1 g of O - {C} - (1→4) - D - glucopyranose was warmed to 60°C in 100 ml of

1% strength methanolic hydrochloric acid for 24 hours. The solution was then evaporated to dryness on a rotary evaporator.

The residue was taken up in water and the solution was then neutralised with a basic ion exchanger (OH^- form). The aqueous solution was discharged onto a column filled with a strongly acid ion exchanger (Dowex 50 WX4, H^+ form). The further procedure was as described under Example 5. Yield: 500 mg of 21.

Example 7.

D - Sorbitol - 4 - [O - C - (1 $\rightarrow$ 4) - α - D - glucopyranoside]



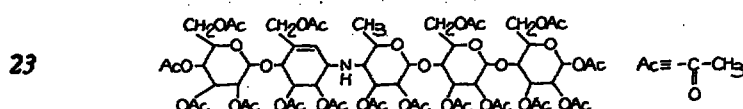
1 g of O - {C} - (1 $\rightarrow$ 4) - O - α - D - glcp - (1 $\rightarrow$ 4) - D - glucopyranose was dissolved in 50 ml of distilled water. The solution was adjusted to pH 10 with 1% strength sodium hydroxide solution. 100 mg of NaBH_4 were then added and the mixture was stirred for 48 hours at room temperature. It was neutralised with a weakly acid ion exchanger and the aqueous solution was discharged onto a column filled with a strongly acid ion exchanger (Dowex WX4, H^+ form). The column was eluted first with water and then 0.05 N hydrochloric acid. 370 mg of 22 were obtained.

$n_D^{20} = 96.8^\circ$ (H_2O ; $c = 1\%$).

Molecular weight of the acetylated compound, determined by mass spectrometry: 1,235 ($\text{C}_{53}\text{H}_{78}\text{NO}_{31}$).

Example 8.

Trideca - O - acetyl - O - {C} - (1 $\rightarrow$ 4) - O - β - D - glcp - (1 $\rightarrow$ 4) - D - glucopyranose

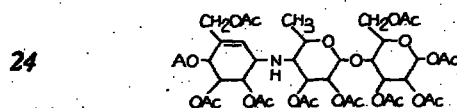


3.8 g of O - {C} - (1 $\rightarrow$ 4) - O - α - D - glcp - (1 $\rightarrow$ 4) - D - glucopyranose were stirred for 48 hours in 50 ml of acetic anhydride and 50 ml of pyridine at room temperature. The mixture was then concentrated in a rotary evaporator, the residue was taken up in chloroform and the chloroform solution was extracted by shaking three times with water and dried with Na_2SO_4 . After removing the solvent, 6.2 g of non-crystalline 23 were obtained.

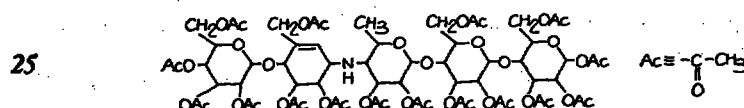
The molecular weight of the compound, determined by mass spectrometry, is 1,191 ($\text{C}_{51}\text{H}_{76}\text{NO}_{31}$).

The following compounds were prepared analogously:

Deca - O - acetyl - O - {C} - (1 $\rightarrow$ 4) - D - glucopyranose

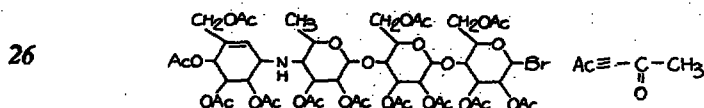


Hexadeca - O - acetyl - O - {4,6 - dideoxy - 4 - [1S - (1,4,6/5) - 4,5,6 - trihydroxy - 3 - hydroxymethyl - 4 - O - α - D - glucopyranosyl - (1 $\rightarrow$ 4) - cyclohex - 2 - en - 1 - yl amino] - α - D - glucopyranosyl} - (1 $\rightarrow$ 4) - O - α - D - glcp - (1 $\rightarrow$ 4) - D - glucopyranose



Example 9.

Dodeca - O - acetyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - α - D - glucopyranosyl bromide



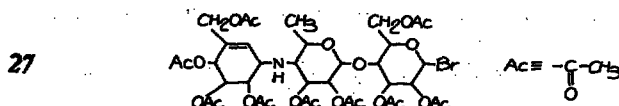
5 g of 23 were dissolved in 15 ml of glacial acetic acid. 10 ml of a saturated solution of hydrogen bromide in glacial acetic acid were added to the ice-cooled solution. The mixture was then stirred for 1 hour, whilst cooling with an ice bath. It was then diluted with chloroform and the chloroform solution was extracted by shaking with ice-water, until the wash water was neutral.

The chloroform solution was dried with Na_2SO_4 , filtered and evaporated. Yield: 4.6 g of 26.

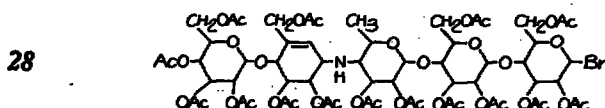
The non-crystalline crude product is used without further purification for the preparation of the glucoside.

The following compounds were prepared in an analogous way:

Nona - O - acetyl - O - {C} - (1→4) - α - D - glucopyranosyl bromide

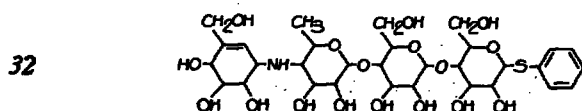


Pentadeca - O - acetyl - O - 4,6 - dideoxy - 4 - [IS - (1,4,6/5) - 4,5,6 - trihydroxy - 3 - hydroxymethyl - 4 - O - α - D - glucopyranosyl - (1→4) - cyclohex - 2 - en - 1 - yl amino] - α - D - glucopyranosyl - (1→4) - O - α - D - glcp - (1→4) - α - D - glucopyranosyl bromide



Example 10.

Phenyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - β - D - thioglucopyranoside



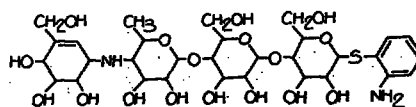
2.424 g of compound 26 from Example 9 is added to an ice-cold solution of 0.264 g (2 mmols) of sodium thiophenolate in 10 ml of absolute dimethylformamide and the mixture is stirred for 24 hours at room temperature, with the exclusion of moisture. It is concentrated to dryness in vacuo. The evaporation residue is taken up in chloroform/water, the phases are separated and the chloroform phase is washed 2 × with water, dried and evaporated in vacuo. The resulting residue is stirred for 1 hour in an ice-bath with a solution of 100 mg of sodium in 25 ml of absolute methanol and the resulting suspension is rendered neutral with absolute glacial acetic acid and concentrated in a rotary evaporator. The residue is taken up in a little dimethylformamide/water/butanol and discharged onto a column (length: 65 cm; Ø: 3 cm) filled with cellulose (Avicel, Merck). The column is eluted with butanol which is saturated with water and the individual fractions are examined by thin layer chromatography. 670 mg of the non-crystalline compound 32 with an optical rotation value $\alpha_D = +106.7^\circ$ (H_2O ; $C=1\%$) are obtained.

Molecular weight of the acetylated compound, determined by mass spectrometry: 1,241 ($\text{C}_{55}\text{H}_{71}\text{NO}_{29}\text{S}$).

The following compounds were prepared analogously:

2 - Aminophenyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - β - D - thiogluco-
pyranoside

33



α_D 71.7° (H₂O; C=1%)

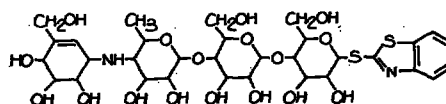
5

Molecular weight of the acetylated compound, determined by mass spectrometry:
1,298 (C₃₇H₇₄N₂O₁₀S).

5

2 - Benzthiazolyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - β - D - thiogluco-
pyranoside

34



10

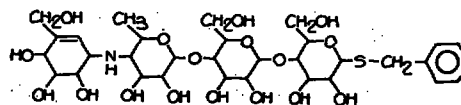
α_D = 66.9° (H₂O; C=1%).

The mass spectrum of the acetylated compound was measured.

10

Benzyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - β - D - thiogluco-
pyranoside

35

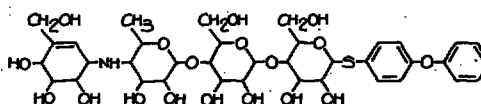


15

Molecular weight of the acetylated compound, determined by mass spectrometry:
1,255 (C₃₆H₇₃NO₁₀S).

15

36 4 - Phenoxy - phenyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - β - D -
thiogluco-
pyranoside

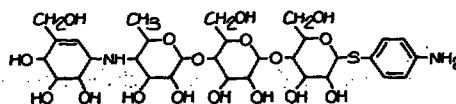


20

Molecular weight of the acetylated compound, determined by mass spectrometry:
1,333 (C₆₁H₇₅NO₁₀S) α_D 107.5° (C=1; H₂O).

20

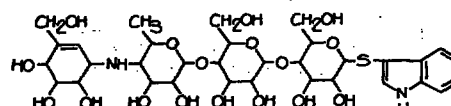
37 4 - Aminophenyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - β - D - thio-
gluco-
pyranoside



25

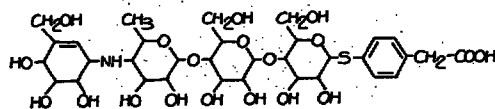
38 Indolyl - 3 - O - {C} - (1→4) - O - α - D - glcp - (1→4) - β - D - gluco-
pyranoside

25



4 - Carboxymethyl - phenyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - β - D - thioglycopyranoside

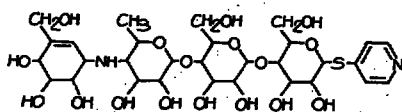
39



Molecular weight of the acetylated compound, determined by mass spectrometry: 1,299 ($C_{37}H_{78}NO_{21}S$). $\alpha_D = 101.3^\circ$ (H_2O ; $C=1$)

Pyridyl - 4 - O - {C} - (1→4) - O - α - D - glcp - (1→4) - D - glucopyranoside

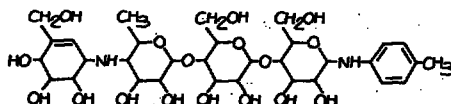
40



Example 11.

N - p - Tolyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - D - glucopyranosylamine

36



A solution of 1 g of p-toluidine in 4.8 ml of absolute ethanol is added to a solution of 1 g of compound I ($m=0$) ($n=2$) in 2 ml of 0.001 N sulphuric acid. The mixture is stirred for 3 days at room temperature, 400 mg of barium carbonate are added, the mixture is filtered and the filtrate is concentrated in a rotary evaporator. The evaporation residue is dried in a desiccator, triturated with ether, filtered off and washed with ether. The resulting crude product (1.1 g) is dissolved in a little methanol and discharged onto a column (length: 70 cm; Ø: 2.6 cm) filled with cellulose (Avicel, Merck). The column is eluted with a 4:1 methanol/ethanol mixture and the individual fractions are examined by thin layer chromatography.

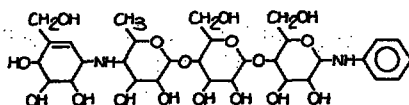
330 mg of a non-crystalline compound with an optical rotation value $\alpha_D = 109.1^\circ$ (H_2O ; $C=1\%$) are obtained.

The molecular weight of the acetyl compound, determined by mass spectrometry, is 1,238 ($C_{36}H_{74}N_2O_{29}$).

The following compounds were prepared analogously:

N - Phenyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - D - glucopyranosylamine

37

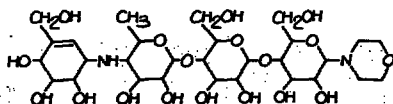


$\alpha_D = 97.6^\circ$ (H_2O ; $C=1$)

Molecular weight of the acetylated compound, determined by mass spectrometry: 1,224 ($C_{35}H_{72}N_2O_{29}$)

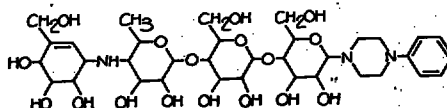
O - {C} - (1→4) - O - α - D - glcp - (1→4) - D - glucopyranosylmorpholine

38



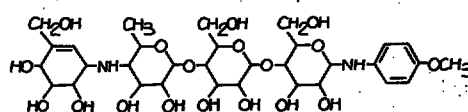
Molecular weight of the acetylated compound, determined by mass spectrometry: 1,218 ($C_{33}H_{74}N_2O_{30}$).

39 O - {C} - (1→4) - O - α - D - glcp - (1→4) - D - glucopyranosyl - N' - phenyl-piperazine



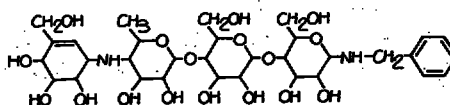
5 Molecular weight of the acetylated compound, determined by mass spectrometry: 1,293 ($C_{59}H_{74}N_2O_{29}$) $\alpha_D = 127.1$ (H_2O ; $C=1$)

40 N - (p - Methoxy - phenyl) - O - {C} - (1→4) - O - α - D - glcp - (1→4) - D - glucopyranosylamine



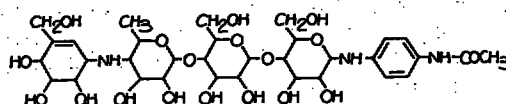
10 Molecular weight of the acetylated compound, determined by mass spectrometry: 1,254 ($C_{56}H_{74}N_2O_{28}$) $\alpha_D = 133.5$ (H_2O ; $C=1$)

41 N - Benzyl - O - {C} - (1→4) - O - α - D - glcp - (1→4) - D - glucopyranosylamine



15 Molecular weight of the acetylated compound, determined by mass spectrometry: 1,280 ($C_{58}H_{76}N_2O_{29}$) $\alpha_D = 144.1$ (H_2O ; $C=1$)

42 N - (p - Acetyl amino - phenyl) - O - {C} - (1→4) - O - α - D - glcp - (1→4) - D - glucopyranosylamine

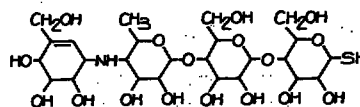


20 Molecular weight of the acetylated compound, determined by mass spectrometry: 1,281 ($C_{57}H_{75}N_2O_{29}$) $\alpha_D = 122.2$ (H_2O ; $C=1$)

Example 12.

O - {C} - (1→4) - O - α - D - glcp - (1→4) - 1 - thio - D - glucopyranose

39



25 A) 22.24 g (20 mmols) of compound 26 from Example 9 are added to a suspension of 1.56 g (20 mmols) of thiourea in 20 ml acetone and the mixture is stirred for 15 minutes under reflux, with the exclusion of moisture. It is concentrated to dryness in vacuo. The crude product is used for the further reaction.

30 B) 25.76 g (20 mmols) of dodeca - O - C - (1→4) - β - D - glucopyranosyl-isothiuronium bromide and 30 ml of carbon tetrachloride are added to a solution, heated to 85°C, of 3.41 g (17.9 mmols) of sodium pyrosulphite in 20 ml of water and the mixture is stirred for 10 minutes at 85°C. After cooling, it is diluted with chloroform, the phases are separated and the chloroform phase is washed 2 times with ice-water, dried and concentrated in vacuo. The residue is taken up in a little chloroform and discharged onto a column (length: 90cm; Ø: 4cm) filled with silica gel 60 (Merck). The column is eluted with chloroform/ethyl acetate 2:1 and the individual

35

35

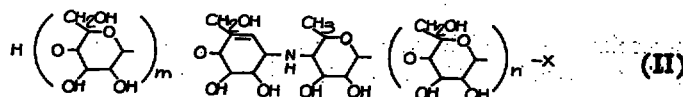
Empirical formula: $C_{49}H_{67}NO_{29}S$

Thin layer chromatography: finished silica gel 60 F 254 plates (Merck)

$R_{f,rel} = 0.854$ (relative to compound 26 from Example 9, $R_{f,rel} = 1.0$)

For de-acetylation, the compound is stirred with a solution of 1 g of sodium in 250 ml of absolute methanol in an ice bath for 2 hours, 100 ml of water are added to the resulting suspension and the mixture is rendered neutral with a weakly acid ion exchanger, that is to say Amberlite IRC 50 (Serva) and filtered and the filtrate is evaporated in vacuo. The residue is dissolved in a little water and the solution is freeze-dried. 6 g of a non-crystalline compound with an optical rotation $\alpha_D = +125.0^\circ$ (H_2O ; $C=1$) are obtained.

1. Amino-sugar derivatives of the formula



n and m independently of each other represent a number from 0 to 8 and the value of the sum $n + m$ is a number from 0 to 8 and

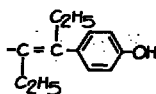
R_1 represents an alkyl, cycloalkyl, aralkyl or aryl radical, which can be substituted.

R and R₁, together with the nitrogen atom, form a heterocyclic ring.

2. Amino-sugar derivatives of the formula (II) in which

X represents a —OR, —SH, —SR, —NH₂, —NHR or NRR₁ group in which

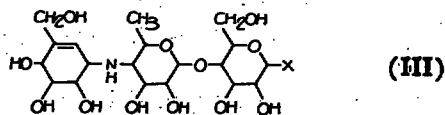
R represents an alkyl radical with 1 to 18 carbon atoms, which can be substituted by 1 to 5 hydroxyl or C₁—C₄ alkoxy group, or represents a phenyl radical which is optionally substituted by 1 to 3 C₁—C₄ alkyl, OH, C₁—C₄ alkoxy, amino, C₁—C₄ alkylamino, di-C₁—C₄ alkylamino, carboxyl, methoxycarbonyl, nitro, glucopyranyl, benzoyl, p-hydroxyphenylethylcarbonyl, C₁—C₄ alkylaminosulphonyl or C₁—C₄ dialkylaminosulphonyl radicals or by a radical



or represents a benzyl radical or a 2-benzthizolyl radical; and

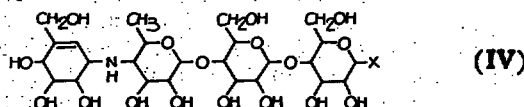
R_1 designates C_1-C_4 alkyl or, together with R, forms a morpholine or piperidine ring.

3. Amino-sugar derivatives of the formula



X has the meaning given in claim 1 or 2.

4. Amino-sugar derivatives of the formula



X has the meaning given in claim 1 or 2.



fractions are examined by thin layer chromatography. 10.6 g of a non-crystalline compound are obtained.

Empirical formula: $C_{49}H_{67}NO_{29}S$

Mass spectrum: $m/e=1,131$ (corresponds to $M-H_2S$)

Thin layer chromatography: finished silica gel 60 F 254 plates (Merck)

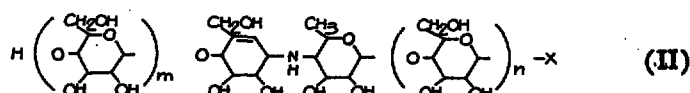
Running agent: chloroform/ethyl acetate 1:2

$R_{f,rel}=0.854$ (relative to compound 26 from Example 9, $R_f=1.0$)

For de-acetylation, the compound is stirred with a solution of 1 g of sodium in 250 ml of absolute methanol in an ice bath for 2 hours, 100 ml of water are added to the resulting suspension and the mixture is rendered neutral with a weakly acid ion exchanger, that is to say Amberlite IRC 50 (Serva) and filtered and the filtrate is evaporated in vacuo. The residue is dissolved in a little water and the solution is freeze-dried. 6 g of a non-crystalline compound with an optical rotation $\alpha_D=+125.0^\circ$ (H_2O ; $C=1$) are obtained.

WHAT WE CLAIM IS:—

1. Amino-sugar derivatives of the formula



in which

n and m independently of each other represent a number from 0 to 8 and the value of the sum $n+m$ is a number from 0 to 8 and

X represents a group $-OR$, $-SH$, $-SR$, $-NH_2$, $-NHR$ or NRR_1 , in which

R represents an alkyl, alkenyl, cycloalkyl, aralkyl, aryl or heterocyclic radical, which can be substituted, and

R_1 represents an alkyl, cycloalkyl, aralkyl or aryl radical, which can be substituted,

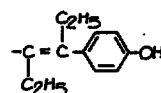
or

R and R_1 , together with the nitrogen atom, form a heterocyclic ring.

2. Amino-sugar derivatives of the formula (II) in which

X represents a $-OR$, $-SH$, $-SR$, $-NH_2$, $-NHR$ or NRR_1 group in which

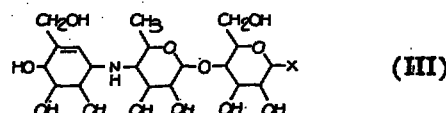
R represents an alkyl radical with 1 to 18 carbon atoms, which can be substituted by 1 to 5 hydroxyl or C_1-C_4 alkoxy group, or represents a phenyl radical which is optionally substituted by 1 to 3 C_1-C_4 alkyl, OH, C_1-C_4 alkoxy, amino, C_1-C_4 alkylamino, di- C_1-C_4 alkylamino, carboxyl, methoxycarbonyl, nitro, glucopyranyl, benzoyl, p-hydroxyphenylethylcarbonyl, C_1-C_4 alkylaminosulphonyl or C_1-C_4 di-alkylaminosulphonyl radicals or by a radical



or represents a benzyl radical or a 2-benzthiazolyl radical; and

R_1 designates C_1-C_4 alkyl or, together with R, forms a morpholine or piperidine ring.

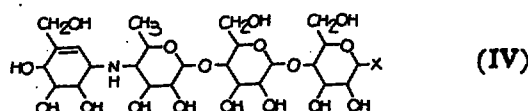
3. Amino-sugar derivatives of the formula



in which

X has the meaning given in claim 1 or 2.

4. Amino-sugar derivatives of the formula



in which

X has the meaning given in claim 1 or 2.



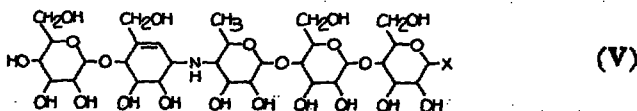
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5. Amino-sugar derivatives of the formula

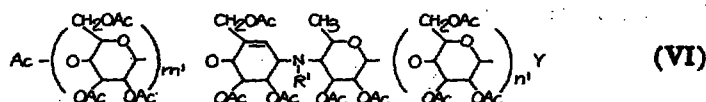


in which

X has the meaning given in claim 1 or 2.

6. Each of the amino-sugar derivatives according to claim 1 which are hereinbefore specifically identified in Example 1, compounds 1—12; Example 2, compounds 2, 13; Example 3, compounds 14, 15; Example 4, compounds 16—20; Examples 5 and 6, compounds 21; Example 7, compound 22; Example 10, compounds 32—35; Example 11, compounds 36—38.

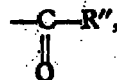
7. A process for the production of an amino-sugar derivative according to any of claims 1 to 6 in which (I) an aryl halogen derivative of the formula



in which

m' and n' independently of each other represent a number from 0 to 8 and the sum n' + m' has values of 0 to 8,

Ac designates a radical



in which

R'' represents an optionally substituted alkyl, alkenyl, cycloalkyl, aralkyl or aryl radical and

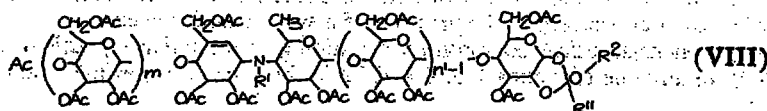
R' designates hydrogen or the radical Ac defined as above and

Y represents halogen, is reacted with a compound of the formula



in which

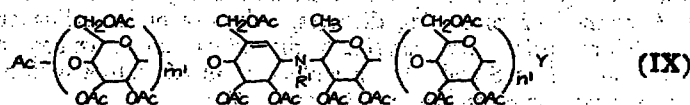
X has the meaning given in claim 1, (or a salt thereof in which H is replaced by a metal), or (2) an orthoester of the formula



in which

Ac, m', n', R', and R'' have the meanings indicated above, is reacted with a compound of the formula (VII);

(3) a compound of the formula



in which

m', n', Ac and R' have the meanings indicated above and Y' designates —OH, —SH, —NH₂ or —NHR₁, with the meaning for R₁ indicated above,

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is reacted with a compound of the formula

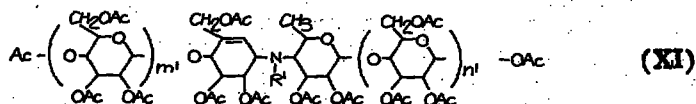


in which

R_2 has the meaning of R indicated above or designates aryl—N=N—, and

Z designates an acid radical, or

(4) a compound of the formula

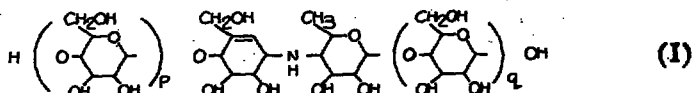


in which

m' , n' , Ac and R' have the meanings indicated above,

is reacted with a compound of the formula (VII); or

(5) a compound of the formula



in which

P and q represent a number from 0 to 8 and the sum of $P+q$ has a value of 1 to 8, is reacted with a compound of the formula (VII):

and, in the case of the reaction products from process variants (1)–(4), the Ac protective groups are removed by processes which are in themselves known and the amino-sugar derivatives are isolated.

8. A process according to claim 7 (1) in which Y denotes a chlorine or bromine atom.

9. A process according to claim 7 (1) or 8 in which the compound of the formula (VII) is used in the form of a salt thereof in which H is replaced by Na or K .

10. A process according to claim 7 (3) in which, in the compound of the formula (X), R_2 designates phenyl—N=N— and Z designates —Cl, —Br, —I, —HSO₃ or —SO₃H.

11. A process for the production of a compound according to claim 1 substantially as hereinbefore described in any of Examples 1 to 7, 10 and 11.

12. A compound according to claim 1 whenever prepared by a process according to any of claims 7–11.

13. A pharmaceutical composition containing as an active ingredient a compound according to any one of claims 1 to 6 and 12 in admixture with a solid or liquefied gaseous diluent or in admixture with a liquid diluent other than a solvent of a molecular weight less than 200 except in the presence of a surface-active agent.

14. A pharmaceutical composition containing as an active ingredient a compound according to any one of claims 1 to 6 and 12 in the form of a sterile or isotonic aqueous solution.

15. A composition according to claim 13 or 14 containing from 0.5 to 95% by weight of the said active ingredient.

16. A medicament in dosage unit form comprising a compound according to any one of claims 1 to 6 and 12.

17. A medicament in the form of tablets, pills, dragees, capsules, ampoules, or suppositories comprising a compound according to any one of claims 1 to 6 and 12.

18. A method of combating diabetes, adiposity or hyperlipaemia in non-human animals which comprises administering to the animals an active compound according to any one of claims 1 to 6 and 12 either alone or in admixture with a diluent or in the form of a medicament according to claim 16 or 17.

19. A method according to claim 18 in which the active compound is administered in an amount of 30 to 3×10^5 AIU per kg body weight per day.

20. A method according to claim 18 or 19 in which the active compound is administered orally.

21. A method for the treatment of adiposity and/or atherosclerosis and/or diabetes and/or pre-diabetes and/or hypoglycaemia and/or gastritis and/or constipation and/or caries, characterised in that an active compound according to any of claims 1 to 6 and 12 are administered to non-human animals suffering from these diseases.



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22. A method for preventing an undesired formation of fatty layers and for achieving an increased build-up of flesh, as well as for better food utilisation in non-human animals, characterised in that an active compound according to any of claims 1 to 6 and 12 is administered to said animals.

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23. Each of the amino-sugar derivatives according to claim 1 which are hereinbefore specifically identified in any of Examples 1, 10, 11 and 12 (other than those claimed in claim 6).

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24. A composition or medicament according to any of claims 13—17 in which the active compound is according to claim 23.

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25. A method according to any of claims 18—22 in which the active compound is according to claim 23.

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