PATENT SPECIFICATION

NO DRAWINGS

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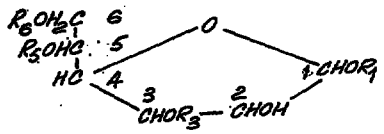
International Classification:—A61k. C07d.

COMPLETE SPECIFICATION

New Sugar Derivatives, a process for their manufacture and Pharmaceutical preparations containing them

We, CIBA LIMITED, a body corporate organised according to the laws of Switzerland, of Basle, Switzerland, 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 provides a D-glucofuranoside of the formula



in which R_1, R_3, R_5 and R_6 each represents the organic radical of an alcohol and R_3, R_5 and R_6 may also each represent an acyl radical of an aromatic or heterocyclic carboxylic acid, and in which R_1 contains at least 2 carbon atoms, and the 2-O-substituted derivatives in which the 2-substituent is a substituted or unsubstituted aliphatic, alicyclic, alicyclic-substituted aliphatic, araliphatic or heterocyclyl-aliphatic hydrocarbon radical or an acyl radical of a carboxylic or sulphonic acid.

The acyl substituents in the 2-position are advantageously those derived from aliphatic carboxylic acids, for example fatty acids, for example formic acid, acetic acid, propionic acid or butyric acid, or from higher alkane- or alkene-carboxylic acids, alicyclic carboxylic acids, for example cyclopentyl-carboxylic acid, alicyclic-substituted aliphatic carboxylic acids, araliphatic or aromatic carboxylic acids, for example phenylacetic acids or benzoic acids in which the phenyl radicals may be substituted, for example by lower alkoxy, alkyl or trifluoromethyl groups or halogen atoms, heterocyclic carboxylic acids, or from organic sulphonic acids, especially from benzenesulphonic acids, for example toluene-sulphonic acids.

In this Specification the term "lower" when used in connection with an alkyl, alkenyl, alkinyl or alkoxy group specifies the presence of a maximum of 6 carbon atoms.

The invention relates more particularly to compounds of the formula shown above and their 2-O-substituted derivatives defined above, in which R_1, R_3, R_5 and R_6 each represents a substituted or unsubstituted aliphatic, alicyclic, alicyclic - substituted aliphatic, araliphatic hydrocarbon or heterocyclyl-aliphatic radical, and in which R_1 contains at least 2 carbon atoms, or R_3, R_5 and R_6 may also each represent an acyl radical of a substituted or unsubstituted carbocyclic aromatic or heterocyclic carboxylic acid.

The aliphatic hydrocarbon radical R_1 advantageously represents an alkyl radical containing 2 to 6 carbon ~~atoms~~, for example the ethyl, propyl or butyl radical, an alkenyl radical containing 2 to 6 carbon atoms, for example the allyl radical, or an alkinyl radical, for example the propinyl radical. The aliphatic hydrocarbon radicals R_3, R_5 and R_6 and in the 2-position are advantageously lower alkyl radicals, for example the methyl, ethyl, propyl or butyl radical, lower alkenyl radicals, for example the allyl radical or lower alkinyl radicals, for example the propinyl r[illegible]lical. As substituents of these r[illegible]dicals there come into

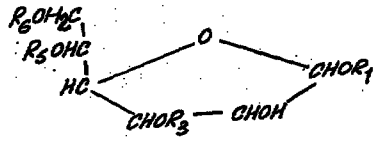
consideration particularly free or substituted amino, hydroxyl or mercapto groups, for example lower mono- or di-alkyl, alkenyl, cycloalkyl, cycloalkenyl amino groups, alkyleneamino-, oxa- or aza-alkyleneamino groups, for example dimethylamino- diethylamino, pyrrolidino, piperidino, morpholino or piperazino groups, alkoxy or alkylmercapto groups, for example methoxy or ethoxy groups, free or functionally converted carboxyl groups, for example lower carbalkoxy, carbamyl or nitrile groups, or halogen atoms, for example chlorine, bromine or fluorine atoms. The alicyclic hydrocarbon radicals R_1, R_3, R_5, R_6 and in the 2-position are advantageously cycloalkyl or cycloalkenyl radicals, for example cyclopentyl, cyclohexyl, cyclopentenyl or cyclohexenyl radicals which may be substituted, for example by a lower alkyl radical. As alicyclic aliphatic hydrocarbon radicals in the positions named there may be mentioned more particularly cycloalkyl or cycloalkenyl-alkyl radicals, for example cyclopentyl-methyl radicals. Araliphatic hydrocarbon radicals in the 1-, 2-, 3-, 5- and 6-positions are especially phenylalkyl or phenylalkenyl radicals, for example benzyl or phenylethyl radicals. As substituents of the aryl radicals there come into consideration especially lower alkoxy groups, for example methoxy, ethoxy or propoxy or methylene-dioxy groups, halogen atoms, for example chlorine or bromine atoms, alkyl radicals, for example methyl, ethyl, propyl or butyl or trifluoromethyl radicals. As heterocyclyl-aliphatic radicals in the 1-, 2-, 3-, 5- and 6-position there may be particularly mentioned the radicals of mononuclear heterocyclic substituted methanols, for example thienyl, furyl or pyridyl-carbinols, for example thienyl or furfuryl alcohol.

The acyl radicals R_3, R_5 and R_6 are advantageously derived from benzoic acids which may be substituted, for example, in the same way as the aromatic radicals mentioned above, or from mononuclear heterocyclic carboxylic acids, for example pyridine, thiophene, furane, pyrrole, pyrazole, pyridazine, pyrazine or pyrimidine carboxylic acids, for example pyridine-2-, 3- or 4-carboxylic acid.

The new compounds have valuable pharmacological and biological properties. They increase the resistance of animal organisms to bacterial and virus infections and enhance the therapeutic effect of chemotherapeutics, for example sulphonamides, in infections. They can therefore be used alone or in combination with other medicaments, such as sulphonamides, for prophylaxis or therapy in infections. In addition, they have an antiendotoxin activity. They inhibit anaphylactic shock and inflammatory processes. They can consequently be used as medicaments.

Finally, the new compounds are also valuable intermediates. They can be converted into O-unsubstituted D-glucofuranosides, for example by hydrolysis or hydrogenolysis, by elimination of the radicals R_3, R_5, R_6 and the radicals in the 2-position.

Especially valuable in view of the above pharmacological or biological effects are the compounds of the given formula and their 2-O-acyl or substituted or unsubstituted alkyl derivatives as defined above in which R_1 represents an alkyl or alkenyl radical containing 2 to 6 carbon atoms, for example the ethyl, propyl or butyl radical, a cycloalkyl radical or a benzyl radical, and R_3, R_5 and R_6 represent lower alkyl radicals containing at most 6 carbon atoms, for example methyl, ethyl, propyl or butyl radicals, lower alkenyl radicals containing at most 6 carbon atoms, for example allyl radicals, cycloalkyl radicals, for example cyclopentyl or cyclohexyl radicals, unsubstituted benzyl radicals or benzyl radicals substituted as shown above, or R_3, R_5 and R_6 may, though less advantageously, also represent unsubstituted benzoyl radicals or benzoyl radicals substituted as shown above. Examples of these compounds are the D-glucofuranosides of the formula



and their 2-O-acyl or substituted or unsubstituted alkyl derivatives, in which R_1 represents an alkyl or alkenyl radical containing 2 to 6 carbon atoms, a cycloalkyl radical or a benzyl radical and R_3, R_5 and R_6 each represents a benzyl or benzoyl radical, a lower alkyl, a lower alkenyl or a cycloalkyl radical.

Of this group the alkyl-3:5:6-benzyl-D-glucofuranosides in which the alkyl radical contains at least 2 carbon atoms, particularly ethyl-3:5:6-tribenzyl-D-glucofuranoside, are outstanding.

The new compounds are obtained by etherifying a D-glucofuranose whose hydroxyl groups in the 1- and 2-positions are substituted by a methylidene group, preferably the isopropylidene group, and those in the 3-, 5- and 6-positions are substituted by the radicals R_3, R_5 and R_6, with an alcohol containing at least 2 carbon atoms in the presence of a Lewis acid.

Etherification is carried out in the manner customary in sugar chemistry, Lewis acids, for example hydrochloric acid, sulphuric acid or glacial acetic acid, if desired in admixture with hydrochloric acid, toluenesulphonic acid or salts having the ~~chacracter~~ character of a Lewis acid, being used as acids.

The resulting 2-unsubstituted compounds can be substituted in the 2-position in the manner known in the literature on sugar chemistry, for example with a reactive ester

of an alcohol, for example an alkanol, with a strong inorganic or organic acid, for example hydrochloric acid, sulphuric acid or a benzenesulphonic acid, or with a carboxylic acid halide or anhydrides or a sulphonic acid halide, preferably in the presence of an acid-binding condensing agent, for example a tertiary base or sodium acetate.

The starting materials are known or can be obtained by methods known *per se*.

When the new compounds contain basic or acid groups, for example amino or carboxyl groups, salts may be prepared therefrom. Free bases can be converted, for example, into their salts with acids, particularly those which form therapeutically useful salts, such as hydrohalic acids, sulphuric acid, phosphoric acid, nitric acid, perchloric acid; aliphatic, alicyclic, aromatic or heterocyclic carboxylic or sulphonic acids, for example formic, acetic, propionic, oxalic, succinic, glycollic, lactic, malic, tartaric, citric, ascorbic, hydroxymaleic dihydroxymaleic or pyruvic acids; phenylacetic, benzoic, para-aminobenzoic, anthranilic, parahydroxybenzoic, salicylic or para-aminosalicylic acid; methanesulphonic, ethanesulphonic, hydroxyethanesulphonic, ethylenesulphonic acid; toluenesulphonic, naphthalenesulphonic acids or sulphanilic acid. Free acids can be converted, for example into metal salts, for example alkali metal or alkaline earth metal salts, or ammonium salts. The salts can be converted into the free bases in the customary manner.

The new compounds or their salts can be used as medicaments, for example in the form of pharmaceutical preparations. Thus, the present invention also provides a pharmaceutical preparation which comprises one or more of the new compounds in admixture or conjunction with a pharmaceutical, organic or inorganic, solid or liquid carrier suitable for enteral, parenteral or topical administration. To make up these preparations such substances are concerned as do not react with the new compound, such as for example water, gelatine, lactose, starches, magnesium stearate, talc, vegetable oils, benzyl alcohols, gums, polyalkylene glycols or other known carrier. The pharmaceutical preparations can be for example in the form of tablets, dragees, or in liquid form as solutions, suspensions or emulsions. They may also be sterilized and/or contain auxiliary substances, such as preserving, stabilising, wetting or emulsifying agents, salts for regulating the osmotic pressure or buffers. They may also contain other therapeutically useful substances. The preparations are obtained by customary methods.

The following Examples illustrate the invention:

EXAMPLE 1

9.8 Grams of 3:5:6 - tribenzyl - 1:2-isopropylidene - D - glucofuranose are kept overnight at room temperature with 200 cc of N-ethanolic hydrochloric acid. Evaporation under vacuum at below 50° C. is then carried out and the residue taken up in 300 cc of chloroform. The chloroform solution is thoroughly washed with sodium bicarbonate solution, dried with calcined sodium sulphate and evaporated under vacuum. The oily residue is now distilled under vacuum with a free flame. In this manner there is obtained ethyl - 3:5:6 - tribenzyl - D - glucofuranoside of b.p. 270—280° C. under 1.2 mm pressure and $[\alpha]_D^{26}$ in chloroform = +8°.

The D-glucofuranose used as starting material is obtained as follows:

8.8 Grams of 1:2 - isopropylidene - D-glucofuranose and 50.6 grams of benzyl chloride are treated with a total of 28 grams of potassium hydroxide in portions with cooling and stirring. The mixture is then stirred for 3 hours at 80—90° C. Working up from chloroform solution and distillation at 250—260° C. under 0.1 mm pressure give 8.9 grams of 1:2 - isopropylidene - 3:5:6 - tribenzyl-D - glucofuranose ($[\alpha]_D^{22}$ in chloroform = −28°).

EXAMPLE 2

5.33 Grams of 3:5:6 - tribenzoyl - 1:2-isopropylidene - D - glucofuranose are shaken for 1/2 hour with 30 cc of saturated ethanolic hydrochloric acid and 30 cc of glacial acetic acid. The mixture is worked up as in Example 1. There is thus obtained ethyl - 3:5:6-tribenzoyl - D - glucofuranoside of b.p. 310—330° C. under 2.1 mm pressure and $[\alpha]_D^{27}$ in pyridine = −34°.

EXAMPLE 3

9.8 Grams of 3:5:6 - tribenzyl - 1:2-isopropylidene - D - glucofuranose are shaken for 24 hours in 200 cc of N - propanolic hydrochloric acid. The mixture is then evaporated under reduced pressure and the residue taken up in chloroform. The chloroform solution is washed with saturated sodium bicarbonate solution and dried with sodium sulphate. The chloroform is removed in a water-jet vacuum and the residue distilled in a high vacuum. There is obtained propyl - 3:5:6-tribenzyl - D - glucofuranoside as an oil boiling at 270—280° C. under 0.2 mm of pressure.

EXAMPLE 4

4.78 Grams of ethyl - 3:5:6 - tribenzyl-D - glucofuranoside are kept for 24 hours at room temperature in 10 cc of pyridine with 4.7 cc of acetic acid anhydride. The mixture is worked up with the use of ether and yields ethyl - 3:5:6 - tribenzyl - 2 - acetyl - D-glucofuranoside as an oil.

EXAMPLE 5

10. 5 Grams of 3:5:6 - trimethyl - 1:2-isopropylidene - D - glucofuranose are shaken overnight with 105 cc of N-ethanolic hydrochloric acid. The mixture is then evaporated under reduced pressure and the product purified by extraction with chloroform and distil-

lation in a high vacuum. There is obtained ethyl - 3:5:6 - trimethyl - D - glucofuranoside in the form of a thinly liquid oil boiling at 98—105° C. under 0.05 mm of pressure; optical rotation $[\alpha]_D^{28} = +3.0°$ (in chloroform). By fractional distillation a fraction with enriched α-form ($[\alpha]_D^{29} = 38.2°$ in chloroform) and β-form ($[\alpha]_D^{29} = -7.7°$ in chloroform) is obtained.

The starting material is obtained as follows:

127.8 cc of 9.4 N-sodium hydroxide solution are added dropwise with stirring to 33 grams of monoacetone glucose, 120 cc of carbon tetrachloride and 57 cc of dimethyl sulphate. The temperature rises during the course of one hour from 26° to 60° C. The carbon tetrachloride is then distilled off. 127.8 cc of 9.4 N-sodium hydroxide solution are then added and 57 cc of dimethyl sulphate are added dropwise during the course of one hour with stirring. The mixture is heated at 80 to 90° C. for 45 minutes with stirring; extraction is carried out with chloroform, the chloroform removed under reduced pressure and the residue methylated once more in the last-mentioned manner. Isolation of the reaction product by extraction with chloroform and distillation in a high vacuum yield 29 grams of 3:5:6 - trimethyl - 1:2 - isopropylidene-D - glucofuranose boiling at 102° C.—110° C. under 0.03 mm of pressure.

EXAMPLE 6

9.8 Grams of 3:5:6 - tribenzyl - 1:2-isopropylidene - D - glucofuranose are shaken for 24 hours with 200 cc of N-benzyl alcoholic hydrochloric acid. The mixture is worked up as described in Example 3. There is obtained 1:3:5:6 - tetrabenzyl - D - glucofuranoside in the form of an oil boiling at 250—260° C. under 0.2 mm of pressure.

EXAMPLE 7

9.8 Grams of 3:5:6 - tribenzyl - 1:2-isopropylidene - D - glucofuranose are shaken for 24 hours with 200 cc of N-cyclohexanolic hydrochloric acid and the reaction product worked up as described in Example 3. There is obtained cyclohexyl - 3:5:6 - tribenzyl-D - glucofuranoside in the form of an oil boiling at 240—260° C. under 0.4 mm of pressure.

EXAMPLE 8

6.8 Grams of 3:5:6 - triallyl - 1:2-isopropylidene - D - glucofuranose are shaken for 24 hours with 200 cc of N-ethanolic hydrochloric acid. After working up in the manner described in Example 3, there is obtained ethyl - 3:5:6 - triallyl - D - glucofuranoside as a thinly liquid oil boiling at 180—190° C. under 0.06 mm of pressure.

The starting material is obtained as follows:

25.1 cc of allyl bromide are added dropwise to 11 grams of monoacetone glucose, 50 cc of dioxane and 16.8 grams of potassium hydroxide. The mixture is then stirred for 1½ hours at 90° C., cooled and 25.1 cc of allyl bromide are again added, 16.8 grams of potassium hydroxide are added in portions and the mixture stirred for 2 hours at 80 to 90° C. Isolation by extraction with chloroform and distillation in a high vacuum yield 10.8 grams of 3:5:6 - triallyl - 1:2 - isopropylidene - D - glucofuranose as a thinly liquid oil boiling at 165—180° C. under 0.4 mm of pressure.

EXAMPLE 9

9.8 Grams of 3:5:6 - tribenzyl - 1:2-isopropylidene - D - glucofuranose are shaken for 24 hours with 200 cc of a solution of N-hydrochloric acid in ethylene glycol. After working up in the same manner as described in Example 3 there is obtained hydroxyethyl-3:5:6 - tribenzyl - D - glucofuranoside as an oil boiling at 240—260° C. under 0.1 mm of pressure.

EXAMPLE 10

13.6 Grams of 3:5:6 - triallyl - 1:2-isopropylidene - D - glucofuranose are shaken for 24 hours with 400 cc of a solution of hydrochloric acid in ethylene glycol. After working up in the manner described in Example 3 there is obtained hydroxyethyl-3:5:6 - triallyl - D - glucofuranoside as a thinly liquid oil boiling at 190—205° C. under 0.04 mm of pressure.

EXAMPLE 11

12.8 Grams of 9.4 N-aqueous sodium hydroxide solution are added to 3.28 grams of ethyl - 3:5:6 - triallyl - D - glucofuranoside; 5.7 cc of dimethyl sulphate are then added dropwise during the course of 2 hours at 80—90° C. bath temperature with stirring. The mixture is then stirred for 5 hours at 80 to 90° C. and then worked up with chloroform. The evaporation residue is distilled in a high vacuum. There are obtained 2.7 grams of ethyl - 2 - methyl - 3:5:6 - triallyl - D-glucofuranoside boiling at 125—135° C. under 0.02 mm of pressure.

EXAMPLE 12

9.8 Grams of 1:2 - isopropylidene - 3:5:6 - tribenzyl - D - glucofuranose are shaken for 1½ hours with 60 cc of glycerine saturated with hydrogen chloride and 60 cc of glacial acetic acid. The solution is then poured into ice water, extracted with chloroform, the chloroform extract evaporated under reduced pressure and the residue distilled in a high vacuum. There is obtained $\beta:\gamma$ - dihydroxypropyl - 3:5:6 - tribenzyl - D - glucofuranoside boiling at 260—280° C. under 0.03 mm of pressure.

EXAMPLE 13

3.28 Grams of ethyl - 3:5:6 - triallyl - D-glucofuranoside, 20 cc of pyridine and 10 cc of acetic anhydride are kept for 12 hours at room temperature. After working up from chloroform and distillation in a high vacuum there is obtained ethyl - 2 - acetyl - 3:5:6-

triallyl - D - glucofuranoside boiling at 150—155° C. under 0.04 mm of pressure.

EXAMPLE 14

2.5 Grams of ethyl - 3:5:6 - trimethyl - D - glucofuranoside, 20 cc of pyridine and 1 cc of acetic anhydride are kept for 12 hours at room temperature. After working up from chloroform and distillation in a high vacuum there is obtained ethyl - 2 - acetyl - 3:5:6 - trimethyl - D - glucofuranoside boiling at 130—135° C. under 0.05 mm of pressure.

EXAMPLE 15

To 5 grams of ethyl - 3:5:6 - trimethyl - D - glucofuranoside there are added 20 cc of N-sodium methylate solution. The solution is evaporated and the residue stirred for 12 hours at 70—80° C. with 4.95 grams of sodium monochloro-acetate, 0.8 grams of sodium hydroxide and 50 cc of dioxane. The reaction mixture is dissolved in water and then the water is acidified to pH 1 and extracted with chloroform. The chloroform extract is washed with ice water, dried with sodium sulphate and evaporated under reduced pressure. The residue distils at 150—170° C. under 0.02 mm of pressure. There is obtained ethyl - 2-carboxymethyl - 3:5:6 - trimethyl - D-glucofuranoside.

EXAMPLE 16

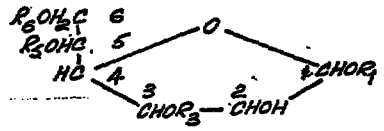
9.8 Grams of 3:5:6 - triallyl - 1:2 - isopropylidene - D - glucofuranose are shaken for 2 hours with 60 cc of glycerine (saturated with hydrochloric acid gas) and with 60 cc of glacial acetic acid. The reaction mixture is then worked up from chloroform as described in Example 12. There is obtained $\beta:\gamma$-dihydroxy - propyl - 3:5:6 - triallyl - D-glucofuranoside boiling at 200—220° C. under 0.05 mm of pressure.

EXAMPLE 17

5.6 Grams of potassium hydroxide and 50 cc of xylene are added to 5 grams of ethyl-3:5:6 - trimethyl - D - glucofuranoside, and 7.2 grams of β-dimethylaminoethyl chloride hydrochloride are added in portions at 80—90° C. with stirring. After stirring for 12 hours at 80—90° C., the mixture is suction-filtered, evaporated under reduced pressure, and the residue distilled in a high vacuum. There is obtained ethyl - 2 - (β - dimethyl-amino - ethyl) - 3:5:6 - trimethyl - D-glucofuranoside boiling at 110—135° C. under 0.15 mm of pressure. It can be converted into its salts, for example with hydrochloric acid, sulphuric acid, phosphoric acid, nitric acid, tartaric acid, malic acid, maleic and other acids, in the customary manner.

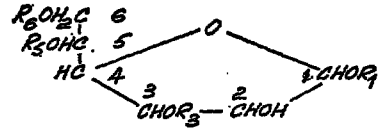
WHAT WE CLAIM IS:—

1. A D-glucofuranoside of the formula



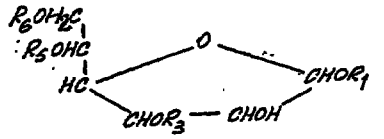
in which R_1, R_3, R_5 and R_6 each represents the organic radical of an alcohol and R_3, R_5 and R_6 may also each represent an acyl radical of an aromatic or heterocyclic carboxylic acid, and in which R_1 contains at least 2 carbon atoms, or a 2-O-substituted derivative thereof in which the 2-substituent is a substituted or unsubstituted aliphatic, alicyclic, alicyclic-substituted aliphatic, araliphatic or heterocyclyl-aliphatic hydrocarbon radical or an acyl radical of a carboxylic or sulphonic acid.

2. A D-glucofuranoside of the formula



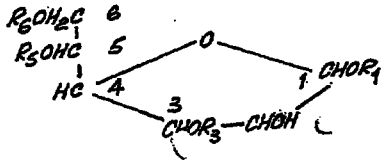
or a 2-O-substituted derivative thereof in which R_1, R_3, R_5 and R_6 each represents a substituted or unsubstituted aliphatic, alicyclic, alicyclic - substituted aliphatic, araliphatic hydrocarbon or heterocyclylaliphatic radical, in which R_1 contains at least 2 carbon atoms, or R_3, R_5 and R_6 may also each represent an acyl radical ~~or~~ a substituted or unsubstituted carbocyclic ~~aromatic~~ or heterocyclic carboxylic acid, and the 2-substituent is a substituted or unsubstituted aliphatic, alicyclic, alicyclic-substituted aliphatic, araliphatic or heterocyclyl-aliphatic hydrocarbon radical, or the acyl radical of an aliphatic, alicyclic, alicyclic-substituted aliphatic, araliphatic, aromatic or heterocyclic carboxylic acid or of an organic sulphonic acid.

3. A D-glucofuranoside of the formula



in which R_1 represents an alkyl radical containing 2 to 6 carbon atoms, and R_3, R_5 and R_6 each represents a benzoyl radical.

4. A D-glucofuranoside of the formula



triallyl - D - glucofuranoside boiling at 150—155° C. under 0.04 mm of pressure.

EXAMPLE 14

2.5 Grams of ethyl - 3:5:6 - trimethyl - D - glucofuranoside, 20 cc of pyridine and 9 cc of acetic anhydride are kept for 12 hours at room temperature. After working up from chloroform and distillation in a high vacuum there is obtained ethyl - 2 - acetyl - 3:5:6 - trimethyl - D - glucofuranoside boiling at 130—135° C. under 0.05 mm of pressure.

EXAMPLE 15

To 5 grams of ethyl - 3:5:6 - trimethyl - D - glucofuranoside there are added 20 cc of N-sodium methylate solution. The solution is evaporated and the residue stirred for 12 hours at 70—80° C. with 4.95 grams of sodium monochloro-acetate, 0.8 grams of sodium hydroxide and 50 cc of dioxane. The reaction mixture is dissolved in water and then the water is acidified to pH 1 and extracted with chloroform. The chloroform extract is washed with ice water, dried with sodium sulphate and evaporated under reduced pressure. The residue distils at 150—170° C. under 0.02 mm of pressure. There is obtained ethyl - 2-carboxymethyl - 3:5:6 - trimethyl - D-glucofuranoside.

EXAMPLE 16

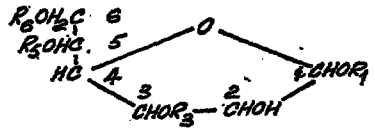
9.8 Grams of 3:5:6 - triallyl - 1:2 - isopropylidene - D - glucofuranose are shaken for 2 hours with 60 cc of glycerine (saturated with hydrochloric acid gas) and with 60 cc of glacial acetic acid. The reaction mixture is then worked up from chloroform as described in Example 12. There is obtained β:γ-dihydroxy - propyl - 3:5:6 - triallyl - D-glucofuranoside boiling at 200—220° C. under 0.05 mm of pressure.

EXAMPLE 17

5.6 Grams of potassium hydroxide and 50 cc of xylene are added to 5 grams of ethyl-3:5:6 - trimethyl - D - glucofuranoside, and 7.2 grams of β-dimethylaminoethyl chloride hydrochloride are added in portions at 80—90° C. with stirring. After stirring for 12 hours at 80—90° C., the mixture is suction-filtered, evaporated under reduced pressure, and the residue distilled in a high vacuum. There is obtained ethyl - 2 - (β - dimethyl-amino - ethyl) - 3:5:6 - trimethyl - D-glucofuranoside boiling at 110—135° C. under 0.15 mm of pressure. It can be converted into its salts, for example with hydrochloric acid, sulphuric acid, phosphoric acid, nitric acid, tartaric acid, malic acid, maleic and other acids, in the customary manner.

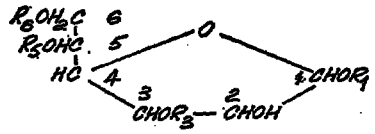
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1. A D-glucofuranoside of the formula



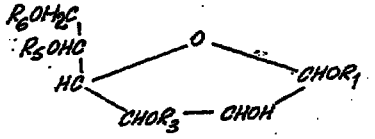
in which R_1, R_3, R_5 and R_6 each represents the organic radical of an alcohol and R_3, R_5 and R_6 may also each represent an acyl radical of an aromatic or heterocyclic carboxylic acid, and in which R_1 contains at least 2 carbon atoms, or a 2-O-substituted derivative thereof in which the 2-substituent is a substituted or unsubstituted aliphatic, alicyclic, alicyclic-substituted aliphatic, araliphatic or heterocyclyl-aliphatic hydrocarbon radical or an acyl radical of a carboxylic or sulphonic acid.

2. A D-glucofuranoside of the formula



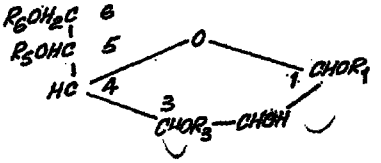
or a 2-O-substituted derivative thereof in which R_1, R_3, R_5 and R_6 each represents a substituted or unsubstituted aliphatic, alicyclic, alicyclic-substituted aliphatic, araliphatic hydrocarbon or heterocyclylaliphatic radical, in which R_1 contains at least 2 carbon atoms, or R_3, R_5 and R_6 may also each represent an acyl radical or a substituted or unsubstituted carbocyclic ~~aromtic~~ aromatic or heterocyclic carboxylic acid, and the 2-substituent is a substituted or unsubstituted aliphatic, alicyclic, alicyclic-substituted aliphatic, araliphatic or heterocyclyl-aliphatic hydrocarbon radical, or the acyl radical of an aliphatic, alicyclic, alicyclic-substituted aliphatic, araliphatic, aromatic or heterocyclic carboxylic acid or of an organic sulphonic acid.

3. A D-glucofuranoside of the formula



in which R_1 represents an alkyl radical containing 2 to 6 carbon atoms, and R_3, R_5 and R_6 each represents a benzoyl radical.

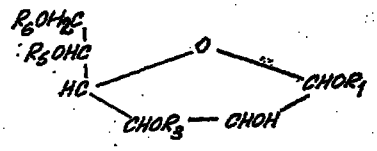
4. A D-glucofuranoside of the formula



in which R_1 represents an alkyl radical containing 2 to 6 carbon atoms and R_3, R_5 and R_6 each represents a benzyl radical.

5. A derivative of a compound as claimed in claim 3 or 4, which is O-substituted in the 2-hydroxyl group by an acyl group of a carboxylic or sulphonic acid or a substituted or unsubstituted alkyl radical.

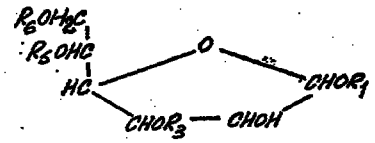
6. A D-glucofuranoside of the formula



in which R_1 represents an alkenyl radical containing 2 to 6 carbon atoms, and R_3, R_5 and R_6 each represents a benzoyl or benzyl radical.

7. A derivative of a compound as claimed in claim 6, which is O-substituted in the 2-hydroxyl group by an acyl group of a carboxylic or sulphonic acid or a substituted or unsubstituted alkyl radical.

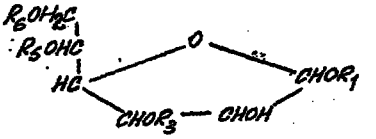
8. A D-glucofuranoside of the formula



in which R_1 represents a cycloalkyl radical, and R_3, R_5 and R_6 each represents a benzoyl or benzyl radical.

9. A derivative of a compound as claimed in claim 8, which is O-substituted in the 2-hydroxyl group by an acyl group of a carboxylic or sulphonic acid or a substituted or unsubstituted alkyl radical.

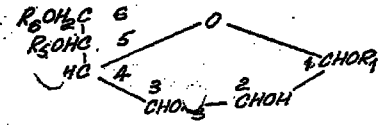
10. A D-glucofuranoside of the formula



in which R_1 represents a benzyl radical, and R_3, R_5 and R_6 each represents a benzoyl or benzyl radical.

11. A derivative of a compound as claimed in claim 10, which is O-substituted in the 2-hydroxyl group by an acyl group of a carboxylic or sulphonic acid or a substituted or unsubstituted alkyl radical.

12. A D-glucofuranoside of the formula



in which R_1 represents an alkyl or alkenyl radical containing 2 to 6 carbon atoms, a cycloalkyl radical or a benzyl radical, and R_3, R_5 and R_6 each represents a lower alkyl, lower alkenyl or cycloalkyl radical.

13. A derivative of a compound as claimed in claim 12, which is O-substituted in the hydroxyl group by an acyl group of a carboxylic or sulphonic acid or a substituted or unsubstituted alkyl radical.

14. Ethyl - 3:5:6 - tribenzyl - D - glucofuranoside.

15. Ethyl - 3:5:6 - tribenzoyl - D - glucofuranoside.

16. Propyl - 3:5:6 - tribenzyl - D - glucofuranoside.

17. Ethyl - 3:5:6 - tribenzyl - 2 - acetyl-D - glucofuranoside.

18. Ethyl - 3:5:6 - trimethyl - D - glucofuranoside.

19. 1:3:5:6 - Tetrabenzyl - D - glucofuranoside.

20. Cyclohexyl - 3:5:6 - tribenzyl - D-glucofuranoside.

21. Ethyl - 3:5:6 - triallyl - D - ~~furanoside~~ glucofuranoside.

22. Hydroxyethyl - 3:5:6 - tribenzyl - D-glucofuranoside.

23. Hydroxyethyl - 3:5:6 - triallyl - D-glucofuranoside.

24. Ethyl - 2 - methyl - 3:5:6 - triallyl-D - glucofuranoside.

25. $\beta:\gamma$ - Dihydroxy - propyl - 3:5:6-tribenzyl - D - glucofuranoside.

26. Ethyl - 2 - carboxymethyl - 3:5:6-trimethyl - D - glucofuranoside.

27. β - γ - Dihydroxypropyl - 3:5:6-triallyl - D - glucofuranoside.

28. Ethyl - 2 - (β - dimethylaminoethyl)-3:5:6 - trimethyl - D - glucofuranoside.

29. Ethyl - 2 - acetyl - 3:5:6 - triallyl-D - glucofuranoside.

30. Ethyl - 2 - acetyl - 3:5:6 - trimethyl-D - glucofuranoside.

31. A salt of a compound as claimed in any one of claims 1—13, as far as it contains an acid or basic group.

32. A D-glucofuranoside as claimed in claim 1 and described in any one of the Examples herein.

33. A pharmaceutical preparation which comprises a compound as claimed in any one of claims 1—13 and 31, or a mixture containing two or more such compounds in admixture or conjunction with a pharmaceutical carrier suitable for enteral, parenteral or topical administration.

34. A pharmaceutical preparation which comprises a compound as claimed in claim 14 or 15 in admixture or conjunction with a pharmaceutical carrier suitable for enteral, parenteral or topical administration.

35. A pharmaceutical preparation which comprises a compound as claimed in any one

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of claims 16 to 25 in admixture or conjunction with a pharmaceutical carrier suitable for enteral, parenteral or topical administration.

36. A pharmaceutical preparation which comprises a compound as claimed in any one of claims 26 to 30 in admixture or conjunction with a pharmaceutical carrier suitable for enteral, parenteral or topical administration.

37. A process for the manufacture of a D-glucofuranoside, wherein a D-glucofuranose whose hydroxyl groups in the 1- and 2-position are together substituted by a methylidene group and those in the 3-, 5- and 6-position by the radicals R_3, R_5 and R_6, in which R_3, R_5 and R_6 each represents the organic radical of an alcohol or the acyl radical of an aromatic or heterocyclic carboxylic acid, is etherified with an alcohol containing at least 2 carbon atoms in the presence of a Lewis acid.

38. A process for the manufacture of a D-glucofuranoside as claimed in claim 1, conducted substantially as described in either of Examples 1 and 2 herein.

39. A process for the manufacture of a D-glucofuranoside as claimed in claim 1, conducted substantially as described in any one of Examples 3—12 herein.

40. A process for the manufacture of a D-glucofuranoside as claimed in claim 1, conducted substantially as described in any one of Examples 13—17 herein.

41. A D-glucofuranoside when made by the process claimed in any one of claims 37 to 40.

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