

# The polyhydric alcohols. Acyclic polyhydric alcohols.

By

**E. J. Bourne.**

With 1 figure.

## I. Introduction.

The polyhydric alcohols (polyols) may be divided into two classes, depending on whether or not they possess a ring structure. In this section consideration is given only to the acyclic polyols, which are known also as glykitols or sugar alcohols. The cyclic polyols (cyclitols) were reviewed fully by FLETCHER in 1948, and are discussed further in the following section of this volume<sup>1</sup>.

The present very extensive knowledge of the glykitols has been accumulating since the beginning of the nineteenth century and is based on the firm foundations laid by such early workers as BERTHELOT, BERTRAND, LOBRY DE BRUYN and EMIL FISCHER. The great interest shown in these substances stems from their wide natural distribution (in both the free and combined states), from their close relationship to the sugars, from the variety of their chemical reactions and from a growing realisation of their industrial potentialities.

With a few exceptions (*e.g.* the deoxy-derivatives), the glykitols have the molecular formula  $C_nH_{n+2}(OH)_n$  and are usually classified in groups of stereoisomers on the basis of the value of  $n$ ; these groups are named, accordingly, tetrityls, pentityls, hexityls, etc., the simplest glykitol being the triol, glycerol.

## II. Structures and properties.

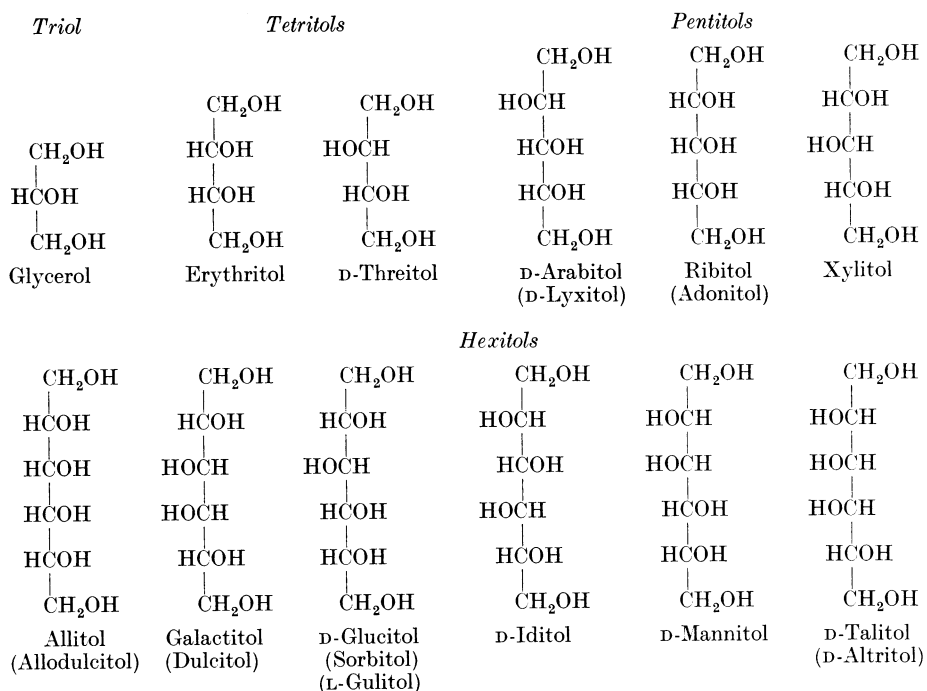
### A. Structures.

A glykitol may be prepared conveniently in the laboratory by reduction of the corresponding aldose, the potential aldehyde group of the open-chain form of the sugar being thus transformed into a primary alcohol group; this conversion may be effected by sodium amalgam, by sodium borohydride, by catalytic hydrogenation, by electrolytic reduction, by a Cannizzaro-type reaction in the presence of Raney nickel, etc. (for details see the review by LOHMAR and GOEPP 1949). Reduction of a ketose creates a new asymmetric centre and so two glykitols are formed; thus D-fructose yields D-mannitol and D-glucitol.

The structures of the hexityls and lower homologues shown on page 346 are written according to the FISCHER-ROSANOFF convention for expressing the three-dimensional structures in one plane; the historical development of this convention and its implications have been discussed recently by HUDSON (1948). The formulae are derived by laying mechanical models on the plane of the paper in such a way that the carbon atoms lie in a straight line and the hydrogen and hydroxyl attachments stand *above the plane*; projections are then taken.

<sup>1</sup> See this volume, p. 363 ff.: DANGSCHAT, G.: Inosite und verwandte Naturstoffe (Cyclite).

It will be recalled that sugars are designated D or L according as to whether they can be synthesised from D- or L-glyceraldehyde, by a conventional ascent of the series, and *not* on the basis of their specific rotations; thus the orientation of the hydrogen and hydroxyl substituents on the secondary carbon atom adjacent to the primary hydroxyl group determines whether an optical enantiomorph is designated D or L — if in the above convention the hydrogen is on the



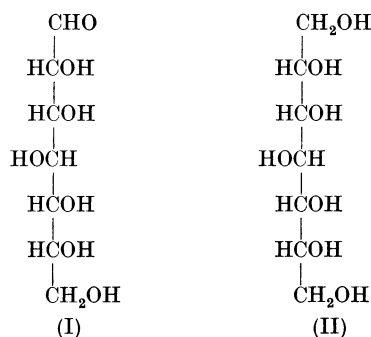
*Structures of the Glykitols according to the FISCHER-ROSANOFF Convention.*

left and the hydroxyl group on the right, the compound is assigned to the D-series. This system of nomenclature is unambiguous in the case of simple aldose sugars, but difficulties are encountered with the glykitols inasmuch as a primary hydroxyl group is present at each end of the carbon chain; for example, the compound commonly known as sorbitol could be regarded as a member of both the D- and L-series (N.B. It is permissible to turn the planar formulae only in the plane of the paper). The difficulty is surmounted by using a name indicative of the sugar from which the glykitol can be derived by reduction; in this way sorbitol is regarded as the trivial name for D-glucitol (*syn.* L-gulitol) and is used only for the natural isomer (LOHMAR and GOEPP).

It will seem from the structural formulae, which include only the D-member of each pair of optical enantiomorphs, that there is only one possible triol, three tetritols, four pentitols and ten hexitols, whereas the corresponding figures for the aldoses are two, four, eight and sixteen, respectively. This decrease in the number of possible structures is due to two reasons: (a) some of the glykitols (*e.g.* glycerol, erythritol, ribitol, xylitol, allitol and galactitol) possess a plane of symmetry and are, therefore, *meso*-compounds, and (b) the same glykitol may be obtained by reduction of two different aldoses (*e.g.* D-arabitol from D-arabinose and D-lyxose, D-glucitol from D-glucose and L-gulose, and D-talitol from D-talose

and D-altrose). Racemates of glykitols (*e.g.* DL-threitol) are known, but they usually result from chemical reactions and not from natural sources. It should be noted that a derivative of a *meso*-glykitol, in which substituents are arranged unsymmetrically, will exist in enantiomorphous forms, so that a compound of this type isolated from a natural source might well display optical activity, whereas if the compound were synthesised chemically from the *meso*-glykitol it would be obtained as a mixture of the D- and L-forms.

As the homologous series of glykitols is ascended to the heptitols and higher members the number of possible isomers continues to increase; there are sixteen theoretical structures for a heptitol and most of these compounds are now known, although only a few have yet been shown to occur naturally. The system of nomenclature follows the same pattern as that given above, the suffix "ose" in the corresponding aldose being replaced by "itol" (see Rules of Carbohydrate Nomenclature). FISCHER originally used the symbols  $\alpha$  and  $\beta$  in his nomenclature of the higher sugars, the aldose (I) which arises from D-glucose, by ascent



of the series, being called " $\alpha$ -D-glucoheptose". As the configurations of these substances were established, the need for a less arbitrary system became apparent and in 1938 HUDSON devised a new nomenclature, based on his observation that the properties of each higher aldose closely resemble those of the hexose of like configuration for carbon atoms 1 to 5 (for a review see HUDSON, 1945). Compound (I), which has the D-glucose configuration for carbon atoms 3, 4, 5, 6, and that of D-gulose for carbon atoms 2, 3, 4, 5, thus became D-gluco-D-guloheptose. Hence the alcohol (II) is gluco-gulo-heptitol; it is a *meso*-compound.

### B. Physical properties.

With the exception of the lowest member, glycerol, the glykitols are white crystalline solids with characteristic melting-points, which have been tabulated by PIGMAN and GOEPP (1948) (general), LOHMAR and GOEPP (1949) (hexitols) and HUDSON (1945) (heptitols and octitols). D-Glucitol is exceptionally difficult to crystallise (ROSE and GOEPP 1939). It does, however, form a relatively insoluble pyridine complex (STRAIN 1937), which serves to distinguish it from most of the other glykitols; 2-deoxy-D-glucitol forms a similar complex (WOLFROM, KONIGSBERG, MOODY and GOEPP 1946).

The glykitols are soluble in water and, to a smaller extent, in the lower alcohols and in acetone; they are usually crystallised from these solvents, or from mixtures of them. They are virtually insoluble in most other organic solvents. Galactitol is more readily crystallised from water than is glucitol and use is made of this fact in the separation of the two hexitols from the mixture obtained by hydrolysis and hydrogenation of lactose.

The best general methods for fractionation of mixtures of glykitols are those involving chromatographic procedures. For small-scale analysis, filter-paper chromatography is particularly useful (HOUGH 1950); the spots can be detected with alkaline silver nitrate (HOUGH), alkaline permanganate (PACSU, MORA and KENT 1949), bromocresolpurple in a borate buffer (BRADFIELD and FLOOD 1950), etc. Reducing sugars present as impurities would, of course, also be detected with these sprays, but they can be distinguished readily from the glykitols by means of their colour reaction with aniline trichloroacetate (HOUGH). Good separations can be obtained between glykitols having different molecular weights; isomeric glykitols are separated less readily. The method can be adapted for quantitative work (HIRST and JONES 1949). Larger-scale fractionations can be achieved on columns of Florex XXX (LEW, WOLFROM and GOEPP 1946), Silene EF-celite (GEORGES, BOWER and WOLFROM 1946) and cellulose (BARKER, BOURNE and CARRINGTON).

In general, glykitols have low specific optical rotations (*e.g.* D-glucitol,  $-2.0^{\circ}$ ; D-mannitol,  $-0.2^{\circ}$ ) and so, when such a compound is isolated, it is often difficult to decide whether it has a *meso*-structure, or not. The question can be solved by examination of the acetate, or of the glykitol itself in a borate buffer; in each case the optical rotatory power of an enantiomorphic glykitol is usually enhanced (BOESEKEN 1949). Other polybasic inorganic oxyacids, at suitable  $p_H$  values, may be used in the same way as boric acid; examples are molybdic acid (MERRILL, HASKINS, HANN and HUDSON 1947) and the oxides of antimony and arsenic (BADREAU 1921, HATT and HILLIS 1947).

Infra-red spectra are now proving extremely useful in the comparison of carbohydrate samples with authentic specimens (KUHN 1950) and also in structural determinations (BARKER, BOURNE, STACEY and WHIFFEN 1953, 1954, WHISTLER and HOUSE 1953). There can be little doubt that they will be used effectively in future studies of glykitols since they already facilitate the detection of impurities in certain glykitols produced commercially (BARKER, BOURNE, STEPHENS and WHIFFEN).

### C. Chemical properties.

The chemical reactions of glykitols may be divided conveniently into two classes: those in which each of the hydroxyl groups reacts as a separate entity and those in which two or more hydroxyl groups are jointly involved. The former class includes esterifications, etherifications and certain oxidation processes.

Treatment of a glykitol, under appropriate conditions, with excess of an acylating agent, such as acetic anhydride or benzoyl chloride, gives the fully esterified product, which is usually readily purified by crystallisation. Of such esters, the acetates are most commonly used for characterisations; their physical constants have been listed by PIGMAN and GOEPP (1948) (general), LOHMAR and GOEPP (1949) (hexitol acetates and other derivatives of hexitols) and HUDSON (1945) (heptitol and octitol acetates). When the appropriate acid anhydride or acid chloride is not available, it is very convenient to use trifluoroacetic anhydride to promote a direct reaction between the carboxylic acid and the glykitol (BOURNE, STACEY, TATLOW and TEDDER 1949). Preferential esterification of the primary hydroxyl groups occurs when a glykitol is treated with a deficiency (2 molecular proportions) of benzoyl chloride or tosyl chloride and di-esters, prepared in this way, are useful intermediates in the synthesis of many glykitol derivatives. However, caution should be exercised in the interpretation of any reaction in which a partially-esterified glykitol is employed, particularly if a

trace of alkali is present, because of the known tendency of ester groups to migrate from one position to another (*cf.* PACSU 1945). Tosyl esters of carbohydrates have been reviewed recently by TIPSON (1953).

Ethers of glykitols may be prepared by the general methods applicable in the case of simple aliphatic ethers, although it is often difficult to achieve complete etherification; methylation is usually accomplished with methyl iodide and silver oxide, methyl sulphate and aqueous alkali, etc. (for a review of these methods see BOURNE and PEAT 1950). Preferential etherification of the primary alcohol groups is not usually possible, except in the case of triphenylmethyl ethers (trityl ethers); trityl chloride in pyridine at room temperature reacts far more rapidly with primary alcohol groups than with secondaries, and indeed the formation of a trityl ether under these conditions has often been regarded as indicative of the presence of a primary alcohol group. Such a conclusion is not wholly justified, because cases are known of reaction occurring with secondary alcohol groups (HELFERICH 1948). A full review of the relative reactivities of hydroxyl groups of carbohydrates has been prepared by SUGIHARA (1953).

Oxidations of glykitols can be effected by a variety of methods, leading to products of different types (PIGMAN and GOEPP 1948). With nitric acid, under suitable conditions, the corresponding saccharic acids may be obtained as the principal products; thus galactosaccharic acid (mucic acid; galactaric acid) can be prepared in good yield from galactitol. However, nitric acid is not specific for the conversion of the primary alcohol groups to carboxyl groups and, in its place, the more specific oxidants, nitrogen dioxide and oxygen in the presence of a platinum catalyst, are now being used increasingly (MEHLTRETTER 1953). Other oxidation processes (*e.g.* bromine water; hydrogen peroxide in the presence of ferrous ions; electrolysis) result in the formation of aldoses and ketoses.

The chemical oxidation of secondary hydroxyl groups in preference to primaries is far more difficult to achieve and usually necessitates the use of protective substituents. An important example is the transformation of D-glucitol into L-sorbose, an intermediate in the chemical synthesis of vitamin C; this entails the conversion of the hexitol into 6-O-benzoyl-1:3-2:4-di-O-ethylidene-D-glucitol (III), oxidation with chromic acid to 1-O-benzoyl-3:5-4:6-di-O-ethylidene-*keto*-L-sorbose (IV) and removal of the substituents to give L-sorbose (V) (SULLIVAN 1945). Fortunately, biochemical oxidation provides a more direct and cheaper alternative and is of great importance industrially. Certain organisms of the *Acetobacter* species (*e.g.* *Acetobacter suboxydans*, *Acetobacter xylinum*) oxidise specifically secondary hydroxyl groups, which are adjacent to primaries in glykitols, to keto-groups, thus catalysing such conversions as D-glucitol into L-sorbose, D-mannitol into D-fructose and allitol into L-psicose. Detailed studies of the factors controlling the oxidation (*e.g.* species specificity, effect of glykitol configuration) have been made by BERTRAND and others, and have been summarised by LOHMAR and GOEPP (1949) (see also page 358).

The final oxidation process to be discussed brings us to those reactions in which two or more hydroxyl groups are involved and concerns the use of glycol-splitting reagents, of which the two most commonly encountered are lead tetraacetate and sodium metaperiodate. The former is usually employed in an organic solvent (*e.g.* glacial acetic acid) and the latter in water. One mol. of oxidant is consumed by each  $\alpha$ -glycol group, two by three contiguous hydroxyl groups, three by four contiguous hydroxyl groups, etc. As will be seen from VI and VII, the products from glykitols are aldehydes and formic acid; when a glycol group occurs at the end of a carbon chain (R=H), one of the aldehyde fragments is formaldehyde. Thus, by measuring the amount of oxidant consumed and the



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