

Carbohydrate Chemistry

Edited by
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Carbohydrate Chemistry

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Carbohydrate Chemistry

Preface

The field of carbohydrate chemistry has historically fallen into two categories based on the molecular size of the molecules concerned. From this segregation two strong lines emerged—monosaccharide chemistry, in which the emphasis has been on organic synthesis and reactions; and polysaccharide chemistry, in which the principal studies have been on primary structure, physical properties, and derivatization. Carbohydrates were regarded as uninteresting, second class citizens compared with proteins and nucleic acids.

The predominant factors which have made dramatic changes to this now historical classification have been the realization that carbohydrates are heavily involved in biologically active molecules, that carbohydrates are extensively found attached to protein, and that monosaccharide synthetic chemistry has many significant applications. Examples of these are the extensive chemical and biological understanding of the carbohydrate antibiotics, the behaviour of glycolipids as operating factors in the biosynthesis of macromolecules, the synthesis of monosaccharide derivatives and their build up into biologically active oligosaccharides, the function of carbohydrate moieties on glycoproteins, the new industrial uses of polysaccharides, including oil-well drilling aids, the finding that so many carbohydrate-containing molecules are antibiotics, the chemotherapeutic utility of nucleosides and related compounds, the involvement of gangliosides and proteoglycans in health and disease of tissues, the current emphasis on utilization of starches from different sources, the use of cellulose via enzyme conversion to valuable chemicals, the vast range of carbohydrate-directed enzymes with probably just as many again yet to be discovered, the huge extent of knowledge of the chemical reactions and derivatization of carbohydrates in the simple, and more-complicated modified forms, the synthesis of oligosaccharides for biological and medical applications, and the use of carbohydrates as supports for a number of bioactive solid-phase materials, and the involvement of carbohydrates in cells—in enzymes, structural molecules, and energy storage molecules. In fact, carbohydrate chemistry is now to be found in the fields on organic synthesis, protein and nucleic acid chemistry, enzymology, antibiotics, immunology, and biotechnology.

Carbohydrate Chemistry has been designed and edited to provide a deeply informative text which presents carbohydrates in their true context regardless of their manifestation, molecular size, or application. This text is aimed at final year graduate level options in carbohydrate chemistry and postgraduate and research levels. It is equally aimed at readers who are experts in their own field including synthesis, analysis, biochemistry, and biotechnology but need to be newly briefed in one or more aspects of carbohydrate chemistry.

I am indebted to all my authors who, in spite of being experts in various

seemingly disassociated areas of carbohydrate chemistry, have been willing to contribute to this one volume. This will make it a successful work which truly addresses carbohydrate chemistry rather than just one branch of it. I am also grateful to my personal secretary, Mrs. P. M. Sharratt, whose administrative help has been invaluable.

Birmingham

March 1988

JFK

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PART I

Chemical identification and chemical
properties of carbohydrates

1

Classification and description of monosaccharides, oligosaccharides, and polysaccharides

J. F. Kennedy and C. A. White

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1.1 Introduction

Carbohydrates, as the name implies, were originally believed to consist solely of the elements of carbon and water in a 1:1 ratio but our present understanding is that a number of other atoms and functional groups can be present in a carbohydrate and the original formula of $C_nH_{2n}O_n$ is no longer rigidly adhered to. Carbohydrates are traditionally considered in three

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groups: monosaccharides, oligosaccharides, and polysaccharides, with monosaccharides being the simple sugars which cannot be hydrolysed to smaller molecules and from which the two other groups are obtained by formation of glycosidic linkages. This simple classification system defines oligosaccharides as simple polymers of monosaccharides containing between two and 10 monosaccharide units or residues. Polysaccharides are higher molecular weight polymers of monosaccharides which contain in excess of 10 residues. Whilst the division between oligosaccharides and polysaccharides is arbitrarily set at 10 residues, nature has made the division much easier to observe since carbohydrates containing between five and 15 residues rarely exist in nature, while only a few consist of 25 to 75 residues. The majority of naturally occurring polysaccharides contain 80 to 100 residues although a few contain considerably more, with native cellulose comprising a series of polymers with an average molecular weight distribution equivalent to 3000 residues. Such polysaccharides rarely exist as a single discrete polymer of defined molecular weight but as a range of macromolecules having a distribution of molecular weights. This phenomenon is known as microheterogeneity.

1.2 Monosaccharides

Monosaccharides are classified according to the number of carbon atoms they contain. Trioses have the general formulae ($C_3H_6O_3$), tetroses ($C_4H_8O_4$), pentoses ($C_5H_{10}O_5$), and hexoses ($C_6H_{12}O_6$), etc. with subdivisions being made according to functional groups which may also be present. For example aminohexoses have the general formulae ($C_6H_{13}O_5N$), deoxyhexoses ($C_6H_{12}O_5$), and hexuronic acids ($C_6H_{10}O_7$).

1.2.1 Configuration

Each family of monosaccharides (hexoses, pentoses, etc.) was found to comprise a collection of molecular forms (stereoisomers) which have identical formulae but different three-dimensional arrangements of the respective atoms and functional groups. The number of asymmetric carbon atoms (i.e. a carbon atom to which four different atoms or groups are attached) determines the number of stereoisomers which can be formed. Where two stereoisomers are mirror images of each other they are known as enantiomers or an enantiomorph pair whilst those which are not mirror images of each other are referred to as diastereoisomers. The number of asymmetric carbon atoms, stereoisomers, and enantiomorph pairs for aldoses and ketoses up to hexoses is shown in Table 1.1.

D-Glucose is a hexose (sometimes referred to as dextrose, particularly by the sugar and related industries) which is the most common monosaccharide in nature. It occurs as the monosaccharide in the juice of fruits and as a component of honey and combined in oligosaccharides and polysaccharides,

TABLE 1.1. *The number of stereoisomers and enantiomorphic pairs for aldoses and ketoses up to the hexoses*

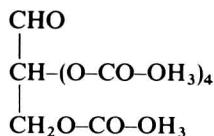
Monosaccharide	Number of asymmetric carbon atoms	Number of stereoisomers	Number of enantiomorphic pairs
Aldotrioses and ketotetroses	1	2	1
Aldotetroses and ketopentoses	2	4	2
Aldopentoses and ketohexoses	3	8	4
Aldohexoses	4	16	8

the most common of which include starch, glycogen, dextran, and cellulose. The structure of D-glucose, together with those of some other hexoses and pentoses was determined by Fischer in the early 1890s, using the stereochemistry ideas of Le Bel and van't Hoff to devise a series of chemical reactions to determine the stereochemistry of the substituents on each carbon atom. For this work Fischer was awarded the Nobel Prize for chemistry in 1907 (Freudenberg 1966).

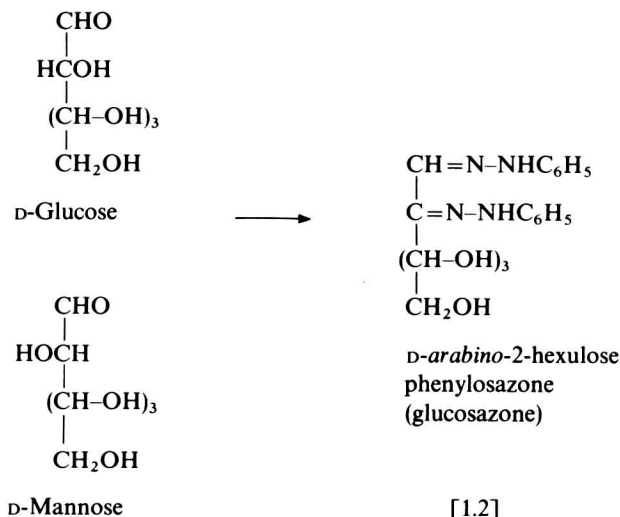
D-Glucose forms a penta-acetate [1.1], not a hexa-acetate indicating that one of the oxygen atoms is not part of a hydroxyl group, unlike the other five oxygen atoms and this single oxygen is found to be part of an aldehyde group (as shown by the ability of D-glucose to be oxidized to a monocarboxylic acid by mild reagents). Since the presence of two hydroxyl groups on a single carbon atom is a very unstable arrangement, five of the carbon atoms in D-glucose must carry a single hydroxyl group whilst the remaining carbon atom is part of the aldehyde group. Reactions which destroy stereochemistry by formation of a double bond (for example, by phenylosazone formation) at one carbon atom have shown that certain pairs of monosaccharides give the same product and therefore must possess the same orientation of hydroxyl groups (configuration) at the other carbon atoms. D-Glucose and D-mannose give the same phenylosazone [1.2] with the loss of stereochemistry at carbon atom 2 (C-2) and therefore must possess the same configuration at the other carbon atoms (Scheme 1.1); they are said to be epimeric at C-2.

By use of other similar reactions and those which add or remove a carbon atom (see Chapter 10) it can be shown that the aldoses have structures which are related as in Fig.1.1 when the configuration at the asymmetric carbon atom furthest from the aldehyde group is in the D-configuration, as defined by Rosanoff and later confirmed by Bijvoet *et al.* (1951), namely to the right when the carbon atom is at the lower end of the Fischer projection formulae. The convention used for these Fischer projection formulae is that the vertical

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[1.1] An *aldehydo*-aldohexose penta-acetate



[1.2]

Scheme 1.1

(carbon-carbon) bonds, except the one under consideration, lie behind the plane of the page. All horizontal bonds (i.e. carbon-hydrogen and carbon-oxygen) project in front of the page. For aldehydo monosaccharides, the aldehydo group (C-1) must be at the top of the structure whilst the C-2 keto group in keto sugars is always next to the top of the projection formulae. A similar series of structural relationships exists for the L-aldoses which are the mirror images of the D-aldoses. Thus, for aldoses, the configuration at C-5 determines whether it is a D- or L-aldose and, in general, the configuration at the penultimate carbon atom determines which enantiomeric form or absolute configuration a particular aldose possesses, the D-series being related to D-glyceraldehyde as shown in Fig. 1.2.

To build up to D-series of D-aldopentoses, the 'initials' RAXL give the order ribose, arabinose, xylose, and lyxose which have (see Fig. 1.1):

- C-4 hydroxyl groups all to the right;
- C-3 hydroxyl groups first pair right, second pair left;
- C-2 hydroxyl groups alternating right then left.

The mnemonic: '**All altruists gladly make gum in gallon tanks**' gives the