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A NEW CLASSIFICATION OF CARBOHYDRATES*

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Customary classifications of carbohydrates are based upon the relations of sugars to *d*-glucose as determined by Fischer and others. The conventional Wohl-Freudenberg classification relates isomeric and homologous monosaccharides derived from each other by simple reactions on the carbon 1 side of the molecule. Thus *d*-glucose, *d*-fructose, *d*-mannose and *d*-arabinose are grouped together because the configurations of their remote atoms (on the carbon 5 side of the molecule) are identical. By methylation studies, Haworth demonstrated the relative stability of the six-membered pyranoid ring in hexoses and introduced perspective ring formulae to illustrate the spatial relations of substituent groups to the plane of this ring. However, neither conversions of homologous sugars, nor methylation studies have revealed certain dynamic aspects of carbohydrate molecules recently encountered by Everett and Sheppard[1] in quantitative studies of the oxidation of carbohydrates by bromine water. Arranging carbohydrates in order of their reactions with bromine, the cyclic cis-trans classification reproduced in Table I resulted.

The authors have compared the relative interatomic distances in Haworth zig-zag pyranoid models and also in the coplanar models of carbohydrate molecules preferred by Cox, Goodwin and Wagstaff,[2] and have found an interesting correlation between the behavior of carbohydrates in bromine water and the relative positions of oxygens 2, 3 and 4 to each other and to the cyclic oxygen 5. The average interoxygen distance between adjacent oxygens 2, 3 and 4 is greater in trans than in cis forms and decreases in the following order of isomeric types: xylose, lyxose, arabinose, ribose. Since the same order was obtained in Everett and Sheppard's oxidation experiments it appears that the determining interoxygen influences, such as hydrogen bridge formation, orient themselves in cis forms between adjacent oxygen atoms rather than towards the cyclic oxygen. This affects the stability of the ring, as shown by Ohle,[3] and causes a shift in equilibrium between furanoid, pyranoid and ε-oxide forms of any given carbohydrate in aqueous solution towards a more stable (trans) cyclic isomer. As a result, the reactions of the sugar or lactone solution are quantitatively modified.

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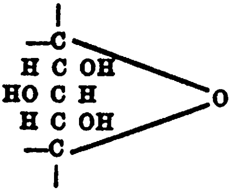
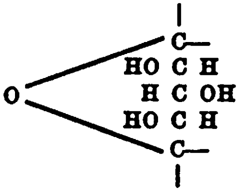
TABLE I.

CLASSIFICATION OF CARBOHYDRATES ACCORDING TO CIS-TRANS ISOMERISM OF PYRANOID FORMS



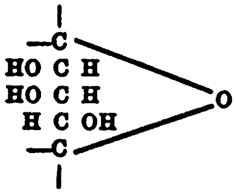
<u>*d*-XYLOSE</u>

_d_-Isorhamnose
_d_-Sorbitol
_d_-Glucose
_l_-Idose
_d_-Sorbose
_α_-_d_-Glucosan
Levoglucosan
_d_-Glucosamine
_d_-Saccharic Acid



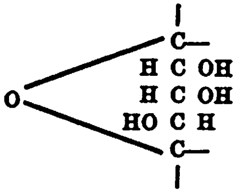
<u>*l*-XYLOSE</u>

_l_-Isorhamnose
_l_-Glucose
_d_-Idose
_l_-Sorbose



<u>*d*-LYXOSE</u>

_d_-Rhamnose
_d_-Mannitol
_l_-Gulose
_d_-Mannose
_d_-Tagatose
d-Mannosaccharic Acid
_d_-Mannoketoheptose

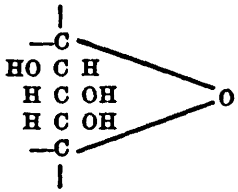


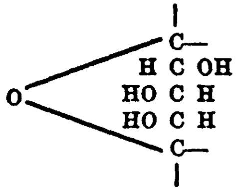
<u>*l*-LYXOSE</u>

_l_-Rhamnose
_d_-Gulose
_l_-Mannose
_l_-Tagatose
_α_-_d_-Glucoheptose

TABLE I. (*Continued*)

CLASSIFICATION OF CARBOHYDRATES ACCORDING TO CIS-TRANS ISOMERISM OF PYRANOID FORMS



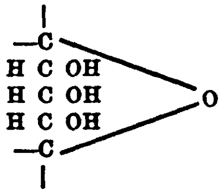


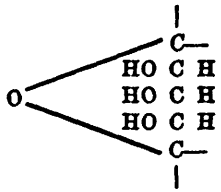
_d_-ARABINOSE

l-Fucose
d-Altrose
l-Galactose
d-Fructose

_l_-ARABINOSE

l-Arabitol
d-Fucose
Dulcitol
l-Altrose
d-Galactose
l-Fructose
Mucic Acid
Perseitol
a-*d*-Mannoheptose





_d_-RIBOSE

Adonitol
Epifucose
d-Allose
l-Talose
d-Pseudofructose
Inositol

_l_-RIBOSE

Epirhodeose
l-Allose
d-Talose
l-Pseudofructose

Everett and Sheppard found cyclic trans forms of sugars and lactones to be more rapidly oxidized than cis forms, probably because of increased stability of the trans pyranoid ring. A similar phenomenon was found for furanoid and ε-oxide forms or lactones and heptoses. In view of the stability and reactivity of the trans forms, it is not surprising that oxygen 1, whenever it can mutarotate, tends to arrange itself preponderantly in the trans position in equilibrium mixtures of α- and β- reducing sugars, as noted by Haworth and Hirst.[4] Everett and Sheppard found that when mutarotation of oxygen 1 is prevented, as in glycosides, oxidation of the β-isomer is much more rapid than oxidation of the α-isomer, regardless of cis-trans relations between oxygens 1 and 2. A somewhat similar situation characterizes the cyclic oxygen 5. During the formation of the pyranoid ring in the pentose series, oxygen 5 rotates to a distorted cis position with respect to oxygen 4, so that only strict mirror images of the pentoses appear. In hexoses, however, the cyclic oxygen is no longer free to arrange itself in this fashion and twice as many isomers appear. It is for this reason that certain sugars of the *d*- series, such as *d*-gulose, *d*-idose, etc., appear in the *l*-pentose cis-trans groups. In considering the relations of oxygens 1 and 5 to oxidation, it is important to note that both in the pentose and hexose series, *d*-isomers are oxidized by bromine more rapidly than *l*-isomers, and β-*d*-isomers more rapidly than α-*d*-isomers, regardless of whether oxygens 1 and 5 are cis or trans to oxygens 2 and 4 respectively. The preponderating directional influences of oxygens 1 and 5 are therefore referrable to the plane of the ring, rather than to adjacent oxygens.

Everett and Sheppard also found marked differences in oxidation of lactones of the pentose, hexose and methylpentose series, keturonic acid production increasing in the order named. Pyranoid pentoses and lactones naturally give large amounts of dicarboxylic lactones as the chief oxidation products. Similar dicarboxylic lactone formation occurs in the hexose series, but less extensively because ε-oxide form is less stable in the equilibrium mixtures. In the methylpentose series ε-ring formation and direct dicarboxylic lactone production become impossible.

Sugar alcohols are customarily represented by acyclic formulae, but we have included them in our classification in the positions indicated by their quantitative behavior with bromine. In these molecules the cis-trans relations of substituent groups to the plane of the unclosed ring are evidently influential factors.

The proposed cyclic cis-trans classification of carbohydrates, which represents an extension and elaboration of Ohle's principle, is therefore significant for oxidation in acid solution and may be applicable to other studies of carbohydrate dynamics in aqueous solutions.

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4. Haworth, W. N., and Hirst, E. L., J. Chem. Soc., 1221, 1928.