

The Structure of α - and β -Glucose

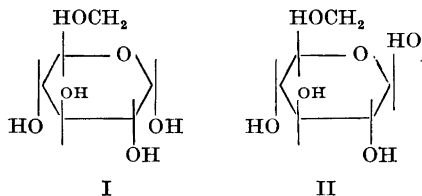
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The structures (I) and (II) are generally accepted for α - and β -D-glucose, respectively, on basis of chemical evidence (cf. e.g. Ref.¹). In the energetically favoured chair form the hydroxyl group at C₍₁₎ assumes an axial orientation in (I), and an equatorial position in (II). This picture has been conclusively confirmed by complete X-ray structure determination of α -D-glucose². A similar approach places the generally accepted structure of sucrose, representative of the α -D-glucopyranosides, beyond dispute³. Furthermore, the studies by Lemieux *et al.*⁴ of proton magnetic resonance spectra of various pyranosides are entirely consistent with the commonly accepted structures.



It hence appears surprising that Blom, in a recent communication to this journal⁵, maintains the opposite view, that in the stable chair conformation the anomeric hydroxyl group assumes an equatorial orientation in α -D-glucose and α -D-galactose, and axial positions in the β -anomers. Without invalidating the evidence for the generally accepted structures, Blom presents four arguments in support of his revised formulation with its far-reaching consequences.

It is the purpose of the present communication to redress these arguments as either irrelevant or erroneous.

1. *Melting points.* Regarding a possible relationship between melting points and molecular structures in the penta- and hexa-substituted cyclohexane series, Blom⁵ states: "eine Verbindung mit einer höheren Anzahl von *para-trans*-Substituenten hat einen höheren Schmelzpunkt als die isomere Verbindung mit einer geringeren Anzahl".* This is definitely not the case. For example, *cis*-inositol, the sole stereoisomeride with no 1,4-*trans*-pair, melts higher (390° (corr.)) than any other inositol⁶.

Blom extends the above "rule" to include the tetrahydropyran ring system and concludes, on basis of m. p. data for anomeric methyl and ethyl pyranosides of D-glucose and D-galactose, that the α -anomers contain an equatorial and the β -anomers an axial hydroxyl-group at C₍₁₎, contrary to the generally accepted structures. Unfortunately, crystalline preparations of both anomers of the methyl (and ethyl) D-aldohexopyranosides have, thus far, been recorded for only three (glucose, galactose and mannose) of the eight isomeric D-aldohexoses. However, closely analogous examples may serve to discredit Blom's suggestions. Thus, methyl β -D-xylopyranoside melts at 156–157°, the α -anomer at 91–92°, whereas the closely related methyl α -D-glucopyranoside melts at 166°, *i. e.* higher than the β -anomer (m. p. 105°).

Melting points are of course dependent upon crystal properties which are again complicated functions of molecular structure. Hence, the utmost caution is urged in all attempts to attribute structural significance to melting point data, not least where strongly hydrogen-bonded molecules are involved as in the present case.

2. *Molecular rotations.* As support for his structural revision, Blom⁵ quotes certain observed regularities between the molecular rotations of various cyclitols and formally similar glycosides. For the sake of clarity, some of Blom's examples are presented in Table 1, together with additional data pertinent for the following discussion.

On basis of the molecular rotations of the first three pairs of compounds, Blom concludes that introduction at C₍₂₎, in a C₍₂₎-

* This "rule" is presented as an extension of melting point regularities within the series of acyclic, unsaturated *cis-trans*-isomerides. It should be pointed out, however, that several examples are known of *cis*-compounds melting higher than the corresponding *trans*-isomerides within this class of compounds.

Table 1^a.

Cyclitol	Structure	Classification of substituents	MD	Methyl Glycoside	Structure	Classification of substituents	MD
Myo-inositol		aeceee	0	α -D-Glucoside		aeceee0	+309
L-Inositol		aeceee	-117	α -D-Mannoside		aeceee0	+154
Myo-2-deoxyinositol		aCeeee	-81	α -2-Deoxy-D-glucoside		aCeeee0	+246
Myo-6-deoxyinositol ^b		aeceeeC	+81	α -D-Glucoside		aeceee0	+309
Deoxy-scyllitol		eeceeeC	0	β -D-Glucoside		eeceee0	-66

^a Blom's nomenclature is employed but the generally accepted structures for the α - and β -glycosides are retained. In the schematic formulae no distinction is made between OH-, CH₂OH- and OCH₃-groupings.

^b This compound is the antipode of myo-2-deoxyinositol.

deoxy ring compound, of an equatorial hydroxyl group results in a shift to more positive values, whereas introduction of an axial substituent in the same position is accompanied by a change in rotation to more negative values. This rule is then extended to the anomeric C₍₁₎-carbon and used as an argument for reversing the generally accepted formulae for α - and β -glucose.

It should be borne in mind, however, that contributions from individual asymmetric centers to the total optical rotations are not additive. Accordingly, the C₍₂₎-rule may very well fail when the configuration of one of the asymmetric carbon atoms is changed. Extrapolation of the rule to include C₍₁₎-substituents is definitely impermissible. For example, the two last examples in Table 1 indicate that, by analogous reasoning, axial substitution at C₍₁₎ results in more positive rotations than introduction of the same substituent in an equatorial orientation, opposite to Blom's

claim. It should be emphasized, however, that the last example is not regarded as support for the accepted structures of anomeric D-glucoses, but merely as a means of disproving the validity of Blom's argumentation.

3. *Oxidation.* It is generally agreed that, within the cyclitol series, axially located hydroxyl groups are preferentially oxidized. Again, it appears a well-established fact that β -glucose is oxidized at a higher rate than the anomeric α -glucose. Blom⁵ seeks support for the proposed structural revision in these facts, apparently disregarding the semiacetalic character of the anomeric hydroxyl group in the pyranose system which may conceivably render the validity of such comparisons more than questionable. Thus, both anomers of galactose, possessing an axial group at C₍₄₎, are oxidized more readily at C₍₁₎ than at C₍₄₎. A completely satisfactory interpretation of the different oxidation rates of pyranose anomers, as well as the structur-

ally analogous cyclitols, has yet to be given, but there is evidence to indicate that different reaction mechanisms may be involved in the two ring systems (*cf. e. g.* Ref.⁷).

The frequently observed enzymic catalysis of reactions different from those favoured in non-enzymic systems renders Blom's reference to the biological glucose oxidation irrelevant in the present context.

4. *1,2-Anhydro-sugars*. Blom's argumentation on basis of the ring-opening reactions of Briegl's anhydride reflects a fatal negligence of the current, well-established stereochemical course of such reactions (*cf. e. g.* Ref.⁸) and, therefore, requires no further discussion here. In fact, the conversion of such epoxides into glycosides affords about the best chemical evidence for the correctness of the generally accepted structures.

In conclusion, the character and validity of the argumentation by Blom, balanced against the bulk of evidence in favour of the commonly accepted structures for α - and β -glucose, is insufficient to warrant any revision of the latter.

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The Synthesis of 4,4,7,7-Tetrabenzyl-1,2,3,5,6-pentathiepane

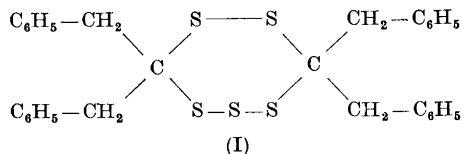
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In connection with work on duplodithioketones^{1,2}, attempts have been made to prepare these by oxidation of *gem*.dithiols. These attempts were not successful. Methanedithiol gave only polymers even when the oxidation was carried out with air in high dilution at low temperature and in the presence of ferric chloride³.

The products obtained by oxidation of *gem*.dithiols with iodine do not seem to be duplodithioketones⁴.

The synthesis of a crystalline *gem*.dithiol, 1,3-diphenyl-2,2-dimercaptopropane, has recently been reported⁵. Attempts to oxidize it to a duplodithioketone was carried out by the author, but the appropriate conditions have not yet been found. When the dithiol was treated with ammonium-polysulphide, 4,4,7,7-tetrabenzyl-1,2,3,5,6-pentathiepane (I) was obtained in 49 % yield. m.p. 130–131.5°C. (Found: C 65.52, 66.01; H 5.12, 4.96; S 29.09, 29.08; Mol.wt. 542, 550. Calc. for C₃₀H₂₆S₅: C 65.65; H 5.14; S 29.21; Mol.wt. 548.8.)



Further investigations of this reaction are in progress.

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