

Conformational Analysis of Polysaccharides: Stereochemical Significance of Different Linkage Positions in β -Linked Polysaccharides

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Summary For homopolysaccharides in which the glycosidic oxygen is equatorial to both sugar rings, computer model building suggests that linkage positions have the following stereochemical and biological significance: 1,4-linkages lead to stiff ribbon-like chains; 1,3-linkages to stiff helices likely to combine in multiply stranded ropes; 1,6-linkages form loosely jointed chains with high flexibility and solubility; 1,2-linkages lead to stiff contorted chains unlikely to form stable tertiary structures.

We report the use of mathematical model building in the computer to investigate whether any simple rules can be formulated to predict the preferred conformations of polysaccharide chains. The principle of the method¹ is to explore all conformations systematically and exhaustively, rejecting those which involve steric compression. For many polysaccharides²⁻⁴ this leads to a single zone of allowed conformations. It has already been shown³ that replacement of glucose residues in a polysaccharide by other pyranose types, if ring conformations and the configurations at each carbon bonded to glycosidic oxygen are unchanged, almost always causes an increase in chain flexibility to an extent which is proportional to the number of new equatorial hydrogen atoms and may further "loosen" the chain by diminished inter-residue hydrogen bonding. We now describe calculations for β -glucans with different positions of linkage and, by using the earlier rules, relate the results to other polysaccharides as well. The methods were similar to those described before.³

chitin, and mannan, are established by experiment for the solid state⁶ and solution,⁷ and previously explained by conformational analysis.^{2,4,8} Any bending or folding involves steric compression.⁴ In contrast, steric effects cause the β -1,3-glucan to describe a wide helix; the shapes (Figure and Table) resemble the states of extension of a wire spring. If diequatorially β -1,3-linked polysaccharides are to have ordered tertiary structures, space filling requirements would therefore demand that they be inclusion complexes or multiply-stranded helices.† The only known polysaccharide conformations which contain diequatorial 1,3-linkages are indeed a triple helix⁹ and a double helix.¹⁰ The β -1,2-chain has seriously bad contacts between alternate residues leading to severe cramping and contortion, as has been shown before⁴ with different methods, and shown here by the severely buckled chain (Figure and Table).

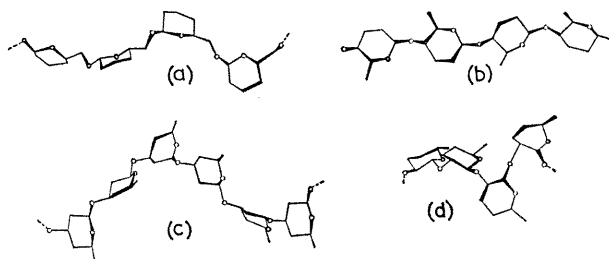


FIGURE. Regular glucan conformations, in projection, to correspond to "average conformations" deduced from the computer output: (a) β -1,6, (b) β -1,4, (c) β -1,3, (d) β -1,2.

Ranges of geometrical properties which are possible for regular conformations, without steric compression

	β -1,2-Glucan	β -1,3-Glucan	β -1,4-Glucan	β -1,6-Glucan
n	2 — 3.5	± 3.5 — ± 12.5	2 — ± 3.5	2 — ± 7
h (Å)	2.5 — 3.0	0.5 — 4.5	5.0 — 5.5	0.5 — 6.0

For this comparison, an "average conformation" was computed for each polysaccharide on the basis of the angles of rotation and geometrical properties of those regular conformations which were sterically possible. The extent of likely deviation was then characterised in terms of the ranges of h (projected residue length with respect to the chain direction) and n (number of residues per twist of the chain). Differences are immediately obvious between the polysaccharides (Figure and Table). Except in a very qualitative and pictorial way, the results do not represent statistical conformations in solution; different methods must be applied for this purpose,⁵ as will be described elsewhere.

Steric constraints which cause the cellulose chain to be kept ribbon-like are reflected in the low values for n and by h values close to the O-1...O-4 intra-residue distance of 5.42 Å (Table). Such conformations for β -1,4-glucan (cellulose) and related polysaccharides such as xylan,

This has implications for chemical reactivity and optical rotation which have already been noted.⁴ For biological purposes, there would seem little possibility of ordered tertiary structures with favourable and space-saving contacts between chains. It is not surprising that these polymers are rare in Nature because polysaccharide functions, like those of other natural polymers, seem often to depend on tertiary structure.¹⁰⁻¹³

The differences we have described are not caused by different contacts across the glycosidic bridge because the local stereochemistry is very similar for β -1,2-, β -1,3-, and β -1,4-linkages.^{3,4} The reason is rather the simple geometrical one that the aglycone bond† makes a very different angle with the glycosidic bond within each type of residue. On the other hand, the β -1,6-polysaccharide is quite different from the others because the residues are separated by three bonds rather than two. If the angles of rotation at the bridge are varied in steps of 10°, there are 36° = 46,656

† The extent to which our conclusions resemble those reached by considering intramolecular hydrogen bonding⁸ will be discussed elsewhere.

‡ This is O-C-4, O-C-3, or O-C-2, respectively

conformations to examine instead of merely $36^2 = 1296$. Of this larger number, calculation shows that a higher proportion is free from steric compression, 8.5%, compared with about 3% for linkages to secondary positions. This means that the outstanding property of the β -1,6-linkage is its flexibility, which is reflected in the large range of possible shapes indicated in the Table. The choice of a typical conformation for the Figure is correspondingly arbitrary. With an increase by two orders of magnitude in the number of accessible conformations compared with the other polysaccharides, there must be a bigger entropy

change in favour of passing from the ordered solid state to solution. The β -1,6-linkage is a typical component of polysaccharide gums of many types,¹⁴ including wood arabinogalactans, *Acacia* gums, gum ghatti, and mesquite gum. We suggest that the flexibility of the 1,6-linkages, which often occur as outer chains in these bushy molecules, is important for the characteristic solubility and viscosity properties.

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