THE RING STRUCTURE OF MANNOSE

BY HORACE S. ISBELL

NATIONAL BUREAU OF STANDARDS, WASHINGTON, D. C.

Read before the Academy September 23, 1930

For a long time the structure of the sugars has been the subject of considerable controversy. Originally the sugars were considered to be straight chain aldehydes, but they are now believed to have a cyclic or ring structure. The size of the ring may be determined experimentally by methylating the free hydroxyls and determining where the groups are located by degradation. Another method for determining ring structure has been devised by C. S. Hudson. This method depends upon the comparison of optical rotations. Those substances whose rotations conform to certain rules which he has developed are considered to have the same ring structure, while those which do not agree are considered to have different ring structures. Although there are other instances where the results from the two methods do not agree, the discussion today will be restricted to the ring structure of mannose.

The sugar mannose differs from glucose in that the hydroxyl on the second carbon atom lies to the left rather than to the right as in glucose. The difference in the molecular rotations of like forms of glucose and mannose is presumably twice the rotation of the second carbon atom, which is
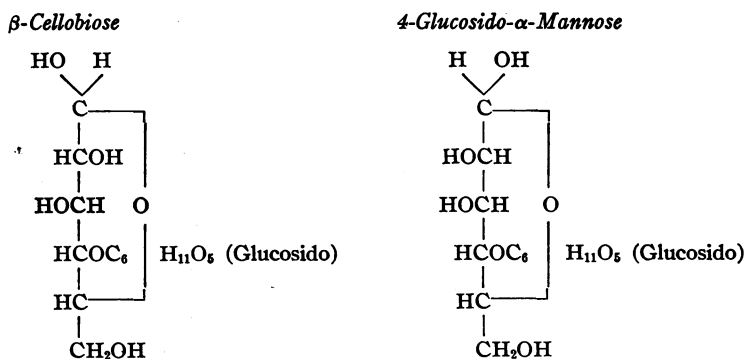
β-*Cellobiose*	4-*Glucosido-α-Mannose*

FIGURE 1

termed the epimeric difference in rotation. The value for this difference obtained from α-mannose and α-glucose is 14,900, while a value of 6500 is obtained from β-mannose and β-glucose. According to the van't Hoff theory of optical superposition the same value should be obtained from the two pairs. The question is, what difference in the structures of the compounds causes the different values. According to Hudson, the substances

differ in ring structure. He believes that α-mannose and α-methyl man-noside have the 1,4 ring, while β-mannose, α- and β-glucose and α- and β-methyl glucosides have the 1,5 ring. The 1,4 ring for α-methyl mannoside is not in agreement with the results obtained from methylation studies by Haworth and other workers. In order to decide between the two views Hudson has recently devised a very ingenious test. He states that "a decision between the rival ring classifications might be obtainable from measurements of the rotations of a pair of substances having configurations in which only one of the 1,4 and 1,5- rings could be assumed to exist." He pointed out that cellobiose and 4-glucosido-mannose are a pair of sub-stances which fulfill these requirements.

In figure 1 the structure of 4-glucosido-mannose and cellobiose are shown. It is seen that in each a glucosido group is substituted for the hydroxyl group on the fourth carbon atom; consequently the compounds cannot form a 1,4 ring.

Hudson found that the difference in the molecular rotations of the halo-gen acetyl derivatives of these two sugars (11,800) agreed with the value (11,300) which he obtained by comparison of certain acetylated derivatives of glucose and mannose. But it did not agree with the value obtained from the acetylated α-methyl glucoside and mannoside. This, he believed, proved that the values obtained according to his classification are correct and that, since the value obtained from the acetylated α-methyl mannoside and glucoside is not confirmed, there is no escape from the conclusion that Haworth's assignment of the same ring to normal methyl glucoside and mannoside must be invalid.

The importance of this conclusion demands that the evidence be con-clusive. A search of the data in the literature shows that 4-glucosido-mannose has been prepared, and although its initial rotation was not reported, the rotation of the substance 7 minutes after solution indicated that it did not support Hudson's deduction. In the light of this the writer decided to repeat the preparation of 4-glucosido-mannose and to attempt the preparation of a sufficient number of derivatives of the sugar to deter-mine whether the conclusion, that α-mannose and α-methyl mannoside have the 1,4 ring structure, is supported by the rotations of all the deriva-tives of 4-glucosido-mannose.

In 1921 Bergmann and Schotte first prepared 4-glucosido-mannose mono-hydrate by the oxidation of cellobial. Subsequently the same compound was prepared by Brauns by means of the action of anhydrous hydrogen fluoride upon cellobiose. Bergmann and Schotte gave the specific rotation of the substance 7 minutes after solution as $+15.07$, becoming constant at 10.65, while Brauns gave $+7.3$, 15 minutes after solution, becoming constant at 5.8. The writer has repeated Dr. Brauns' work. The initial rotation of the monohydrate of the sugar extrapolated to zero time was

found to be $+14.6$, with the final rotation of 5.88 in agreement with Dr. Brauns' value.

It is now possible to compare the molecular rotation of β-cellobiose and 4-glucosido-α-mannose. The difference in the molecular rotations of these substances is equal to

$$2R_2 - 2A_{OH} = 212.$$

The value of $2A_{OH}$ has been determined by Hudson and found to be about 16,700, which gives for $2R_2$ the epimeric difference 16,900. This value differs widely from the value (6700) obtained according to Hudson's classification of ring structures. However, it agrees more closely with the values (14,900 and 15,300) obtained from α-mannose and α-methyl-mannoside. Since 4-glucosido-mannose cannot form a 1,4 ring, this parallelism with α-mannose is strong evidence that neither α-mannose nor α-methyl-mannoside has the 1,4 ring structure.

TABLE 1

EPIMERIC DIFFERENCES IN MOLECULAR ROTATIONS FOR THE MANNOSE SERIES

Alpha Forms	$[\alpha]_D$	$[M]$	EPIMERIC DIFFERENCE $2R_2$
α-Glucose	$+113$	20,340	
α-Mannose	$+ 30$	5,400	14,940
α-Methyl glucoside	$+157.9$	30,630	
α-Methyl mannoside	$+ 79$	15,330	15,300
β-Cellobiose	$+ 16$	5,470	
4-Glucosido-α-mannose	$+ 14.6$	5,258	16,900 ($212 + 2A_{OH}$)
Beta Forms			
β-Glucose	$+ 19$	3,420	
β-Mannose	$- 17$	$- 3,060$	6,480
β-Cellobiose	$+ 16$	5,470	
4-Glucosido-β-mannose	$- 5$	$- 1,710$	7,180

It has just been shown that the α-forms of a pair of sugars suggested by Hudson as suitable to decide between the rival ring classifications give an epimeric difference which is in agreement with Haworth's classification of normal methyl glucoside and mannoside.

We will now consider the beta forms of the same disaccharides in order to establish a parallelism with the rotations of beta mannose. 4-Glucosido-β-mannose was not reported in the literature; accordingly it was necessary to prepare it for the first time. It was obtained by crystallization from methyl alcohol. The first product was mixed with the crystalline anhydrous alpha form which was also obtained for the first time. The separation of the two substances was difficult but the beta compound was finally obtained in what appeared to be the pure state. It separates in slender prisms which melt at $205°$ and give a specific rotation of about $-5°$.

The difference in the molecular rotations of cellobiose and 4-glucosido-β-mannose is approximately 7200. This value is in agreement with Hudson's classification, or in other words, with the value obtained from β-mannose and normal glucose. Thus it appears that 4-glucosido-α-mannose is a substituted α-mannose, while 4-glucosido-β-mannose is a substituted β-mannose. The rotations of the alpha forms give an epimeric difference of about 16,900, while those of the beta give a difference of about 7200.

The parallelism between the optical rotations of the α- and β-forms of 4-glucosido-mannose with the corresponding forms of mannose indicates that neither α- nor β-mannose has a 1,4 ring structure. We cannot definitely state at this time which form of mannose has a structure similar to the normal form of glucose. It is entirely possible that Hudson's classification of ring structures is in reality a classification of a new type of isomerism. It seems reasonable to presume that there is a difference in the structures of α- and β-mannose, the exact nature of which must remain for the future to determine.

The writer expresses his appreciation to Dr. D. H. Brauns for the loan of the apparatus with which he originally prepared 4-glucosido-α-mannose. Appreciation is also expressed to other members of the Polarimetry Section who have aided in the course of the investigation.

NON-DISJUNCTION OF THE X-CHROMOSOME IN DROSOPHILA VIRILIS[1]

BY M. DEMEREC AND J. G. FARROW

DEPARTMENT OF GENETICS, CARNEGIE INSTITUTION OF WASHINGTON. COLD SPRING HARBOR, N. Y.

An extensive series of experiments were made to test the effect of x-ray radiation on the mutability of the mutable reddish-alpha and the miniature-beta genes. These experiments were planned in such a way as to give results which could be used to determine the effect of x-rays on the mutable genes and also to study non-disjunction of the X-chromosome. The results related to the problem mentioned last will be reported in this paper.

PRIMARY NON-DISJUNCTIONS. *Frequency.*—Data on the frequency of primary non-disjunctions were obtained by breeding F_1 females from crosses involving several sex-linked characters. That precaution made it certain that these females were not non-disjunctional and to a large extent eliminated the possibility of inclusion in the results of secondary non-disjunctions. Since, however, there was practically no way of making certain that the male parents of the F_1 females were not XYY, it cannot be claimed