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 $\beta$ -*D*-TALOSE AND *D*-TALOSE ACETATES AND ORTHOESTERS<sup>1</sup>

By William Ward Pigman and Horace S. Isbell

## ABSTRACT

Mutarotation and oxidation measurements are given for the new sugar,  $\beta$ -*D*-talose. The difference between the molecular rotations of  $\alpha$ - and  $\beta$ -*D*-talose, called by Hudson  $\Delta A$ , is shown to be 9,870. This value is similar to that for *D*-mannose, which resembles talose in the configuration of carbons 2 and 3. Crystalline  $\alpha$ -penta-acetyl talose,  $\alpha$ -tetra-acetyl talose, 1-bromo-tetra-acetyl talose, and an orthoester derivative, triacetyl talose 1,2-orthomethylacetate, are reported. The conditions necessary for orthoester formation are discussed. A new crystalline monobenzoyl talose is described. This substance is produced in small yields along with the sugars when galactal is oxidized with perbenzoic acid. Evidence is presented which indicates that the monobenzoyl talose has an orthobenzoic acid structure and the properties of orthoester derivatives are contrasted with those to be expected of orthoacid derivatives.

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## I. INTRODUCTION

The elucidation of the chemistry and properties of talose and its derivatives is of particular importance since this sugar represents a fundamental pyranose type, concerning which very little has been

<sup>1</sup> A part of the material in this paper was presented as a thesis by William Ward Pigman, of this Bureau, in May 1936 to the Faculty of the Graduate School of the University of Maryland, represented by Dr. Nathan L. Drake, in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

previously reported. Earlier workers have succeeded in preparing in the crystalline state only a few derivatives of *d*-talose, namely, talonic acid and its lactones [1, 2],<sup>2</sup> several hydrazones [3, 4], and certain acetone derivatives [2]. The sugar was known only in an amorphous state until the relatively recent crystallization of  $\alpha$ -*d*-talose by Levene and Tipson [4]. Shortly after this work was reported we succeeded independently in obtaining the crystalline  $\alpha$ -*d*-talose, and later reported data showing that the mutarotation was complex in character and that solutions of talose contain at least three isomers in dynamic equilibrium [5, 6].

In this paper, crystalline  $\beta$ -*d*-talose,  $\alpha$ -penta-acetyl-*d*-talose, tetra-acetyl-*d*-talose, 1-bromo-tetra-acetyl-*d*-talose, triacetyl-*d*-talose or orthomethylacetate, and a monobenzoyl talose (obtained from the glycol synthesis and probably having an orthobenzoic acid structure) are reported. These new substances may be used for the separation and identification of talose, for the preparation of other derivatives, and for assistance in the correlation of the properties of the sugars with their configurations and structures.

## II. $\alpha$ - AND $\beta$ -*d*-TALOSE

Crystalline  $\beta$ -*d*-talose (I, p. 198) was prepared for the first time by crystallization from methyl alcoholic solution. It is difficult to obtain, since the alpha form under all of the conditions studied crystallizes the more readily when seed of both are present.

The mutarotation of  $\beta$ -*d*-talose is complex and, as with the alpha isomer, equations having two exponential terms are required to express the change of optical rotation. The equations developed for  $\beta$ -*d*-talose at 20° C and 0.1° C are

$$[\alpha]_D^{20} = -17.5 \times 10^{-.0262t} + 9.7 \times 10^{-.101t} + 21.0 \quad (1)$$

$$[\alpha]_D^{0.1} = -17.6 \times 10^{-.00339t} + 5.5 \times 10^{-.0241t} + 25.2 \quad (2)$$

The corresponding expressions for  $\alpha$ -*d*-talose were given by Isbell and Pigman [5, 6] as

$$[\alpha]_D^{20} = 9.3 \times 10^{-.0263t} + 37.9 \times 10^{-.126t} + 20.8 \quad (3)$$

$$[\alpha]_D^{0.1} = 9.8 \times 10^{-.00362t} + 27.5 \times 10^{-.0255t} + 25.2 \quad (4)^3$$

The data upon which equations 1 and 2 are based are given in tables 1 and 2 and are illustrated in figure 1. The curves constructed of alternate dots and dashes represent first-order reactions with reaction constants having the same value as those calculated for the latter part of the mutarotations. Since the mutarotation curve for  $\beta$ -*d*-talose exhibits a maximum value which cannot be explained by a simple beta-alpha interconversion, two or more reactions involving three or more substances must take place during the establishment of the equilibrium.

<sup>2</sup> Figures in brackets here and elsewhere in the text correspond to the numbered literature references at the end of this paper.

<sup>3</sup> On page 159 of reference [6], the exponent  $-.00362t$  for  $\alpha$ -*d*-talose at 0.1° C was printed incorrectly as 0.00632t.

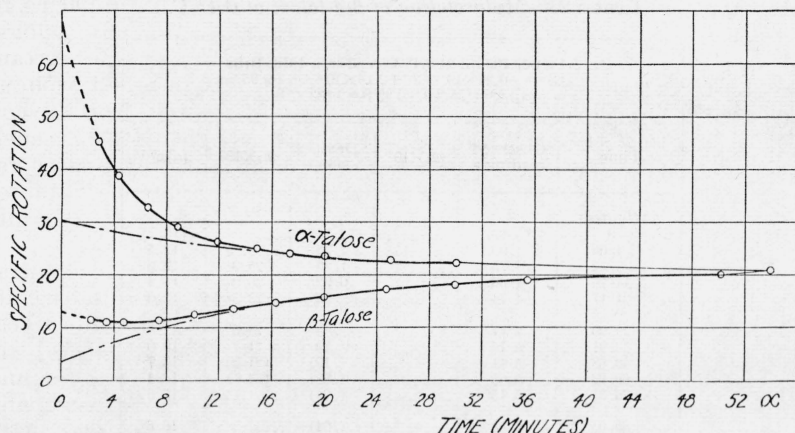


FIGURE 1.—Mutarotation of  $\alpha$ - and  $\beta$ -D-talose at 20° C.

TABLE 1.—Mutarotation of  $\beta$ -D-talose at 20° C.

4.0 g per 100 ml at 20.0° C read in a 2-dm tube $^{\circ}\text{S} = -4.04 \times 10^{-5} t + 2.25 \times 10^{-5} t^2 + 4.85$ $[\alpha]_D^{20} = (21.0/4.85) \times ^{\circ}\text{S} = 4.330 \times ^{\circ}\text{S}$					
Time <sup>a</sup>	Observed reading <sup>b</sup>	$m_1 \times 10^3$	Deviation	$m_2 \times 10^3$	$[\alpha]_D^{20}$
Minutes	$^{\circ}\text{S}$				
0	(3.06)	-----	(2.25)	-----	(13.2)
2.27	2.66	-----	1.33	-----	11.5
3.52	2.58	-----	1.00	99	11.2
4.76	2.55	-----	0.73	105	11.0
7.43	2.64	-----	.37	108	11.4
10.20	2.89	-----	.22	99	12.5
13.13	3.14	-----	.12	96	13.6
16.31	3.40	-----	.06	96	14.7
19.99	3.64	-----	-----	-----	15.8
24.79	3.94	25.8	-----	-----	17.1
30.01	4.21	27.6	-----	-----	18.2
35.45	4.38	26.6	-----	-----	19.0
40.03	4.47	25.1	-----	-----	19.4
50.18	4.65	25.9	-----	-----	20.1
59.90	4.74	26.1	-----	-----	20.5
$\infty$	4.85	-----	-----	-----	21.0
Average	-----	26.2	-----	101	-----

<sup>a</sup> The equations representing the optical rotations are calculated according to the method of T. M. Lowry and G. F. Smith, J. Phys. Chem. **33**, 9 (1929), as modified by H. S. Isbell and W. W. Pigman, J. Research NBS **18**, 156 (1937) RP699. The equations were developed for reactions of the type  $x \rightleftharpoons y \rightleftharpoons z$ , where one set of reactions is much more rapid than the other. As a first approximation, the sum of the velocity constants for the slow change may then be considered empirically to be  $m_1$ , while that for the rapid change may be considered to be  $m_2$ . The "deviation" represents the difference between the observed rotation and the rotation obtained by extrapolation of the slow mutarotation to the same time.

<sup>b</sup> Averages of consecutive readings.

TABLE 2.—Mutarotation of  $\beta$ -*d*-talose at 0.1° C.

3.4 g per 100 ml at 0.1° C read in a 4-dm tube $^{\circ}\text{S} = -6.96 \times 10^{-4} + 2.18 \times 10^{-4} t + 9.95$ $[\alpha]_D^{0.1} = (25.2/9.95) \times ^{\circ}\text{S} = 2.533 \times ^{\circ}\text{S}$					
Time	Observed reading <sup>b</sup>	$m_1 \times 10^3$	Deviation	$m_2 \times 10^3$	$[\alpha]_D^{0.1}$
<i>Minutes</i>	$^{\circ}\text{S}$				
0	(5.17)	-----	(2.14)	-----	(13.1)
4.00	4.95	-----	1.75	-----	12.5
9.12	4.75	-----	1.29	25.9	12.0
14.76	4.66	-----	0.92	26.0	11.8
21.17	4.74	-----	.69	23.5	12.0
29.90	4.87	-----	.43	23.5	12.3
39.91	5.14	-----	.29	21.7	13.0
49.58	5.41	-----	(.19)	(21.2)	13.7
60.27	5.68	-----	(.08)	(23.8)	14.4
76.31	6.15	-----	(.04)	-----	15.6
89.95	6.54	-----	(.04)	-----	16.6
119.96	7.22	-----	-----	-----	18.3
156.31	7.88	3.31	-----	-----	20.0
180.19	8.23	3.33	-----	-----	20.8
240.67	8.86	3.30	-----	-----	22.4
303.57	9.33	3.51	-----	-----	23.6
360.27	9.56	3.52	-----	-----	24.2
23.5 hr	9.95	-----	-----	-----	25.2
Average..	-----	3.39	-----	24.1	-----

<sup>a</sup> See footnote b, table 1.<sup>b</sup> Averages of 10 consecutive readings.

The initial rotations calculated from the equations representing the optical rotations are  $[\alpha]_D^{20} = +13.2$  and  $[\alpha]_D^{0.1} = 13.1$  for the  $\beta$ -*d*-talose, and  $[\alpha]_D^{20} = +68.0$  and  $[\alpha]_D^{0.1} = +62.5$  for the  $\alpha$ -*d*-talose. The molecular-rotation difference ( $\Delta$ ) is then  $(68.0 - 13.2) 180.1 = 9,870$  at 20° C, and  $(62.5 - 13.1) 180.1 = 8,900$  at 0.1° C. The corresponding value for *d*-glucose according to our measurements [6] is 16,840 and for *d*-mannose is 8,340 at 20° C. The value for *d*-talose (9,870) resembles that for *d*-mannose (8,340), as might be anticipated since the two sugars have the same configuration for the adjacent carbon atoms 2 and 3. The agreement of these values can be considered as evidence that the new modification of talose is the pure beta pyranose modification. Further evidence that the compound is pure was obtained by the oxidation of the sugar with bromine water according to the method described in previous publications [6, 7, 8], in which it is shown that the oxidation of a mixture of alpha and beta isomers of a sugar proceeds rapidly at first and then more slowly as the less readily oxidizable modification continues to be oxidized.

The oxidation data for  $\beta$ -*d*-talose are given in table 3. The reaction takes place at a rapid and uniform rate. When the oxidation is 92.1 percent complete, the velocity constant has a value  $(747 \times 10^{-3})$ , which is close to the average of the values for the earlier times, and, therefore, the  $\beta$ -*d*-talose sample is essentially homogeneous. If the sample had contained appreciable quantities of the alpha isomer (5 percent or more), the reaction constants for the latter part of the oxidation would have had a much smaller value than that found. Heretofore there has not been any direct method for determining the homogeneity of the alpha and beta forms of the sugars. The oxidation method, however, provides a direct means for the determination of



alpha and beta isomers in the presence of one another. The purity of alpha isomers (slowly oxidizable sugars) is easily obtained by graphic extrapolation of the oxidation data to zero time [7, page 529], while the purity of beta isomers (rapidly oxidizable sugars) is obtained with more difficulty by a comparison of the reaction constants for the later part of the oxidation with those at earlier times. The error of the determination, which depends upon the difference between the rates of oxidation, should not exceed 5 percent for most sugars.

TABLE 3.—Bromine oxidation of  $\beta$ -*d*-talose

Time after beginning oxidation	Unoxidized sugar	Oxidation	Temperature	Bromide (Br <sup>-</sup> )	Bromine (Br <sub>2</sub> )	Free bromine (a)	Velocity constants	
							$ak = \frac{1}{t} \log \frac{A}{A-X}$	
							$ak \times 10^3$	$k \times 10^3$
Minutes	mg	Percent	°C (+0.5)	Moles/liter (0.360)	Moles/liter (0.368)	Moles/liter		
0.....	180.0	0						
1.1.....	158.5	11.9		.367	.364	0.085	50.2	591
10.0.....	51.7	71.3		.403	.346	.070	54.2	774
25.0.....	14.2	92.1		.423	.323	.059	44.1	747
Average.....								704

Data have been previously given [6] for the bromine oxidation of  $\alpha$ -*d*-talose. The velocity constant for the bromine oxidation of the beta form is approximately nine times that of the alpha. Thus the rates of oxidation for  $\alpha$ - and  $\beta$ -*d*-talose are in accord with the generalization previously presented [6, 7] that the beta sugars, when named according to Isbell's nomenclature [9], are more rapidly oxidized by bromine water than the alpha isomers. The oxidation of a solution of *d*-talose in equilibrium at 0° revealed the presence of 56 percent of less reactive sugar (supposedly largely  $\alpha$ -*d*-talose) and 44 percent of the more reactive modification (supposedly largely  $\beta$ -*d*-talose) [6].

A calculation of the relative amounts of the alpha and beta forms in the equilibrium solution, made by use of the optical rotations of the two isomers and of the equilibrium solution, and on the assumption that only two isomers exist in solution, gives 25 percent of alpha and 75 percent of beta. The discrepancy between the proportions calculated from the rotations and those derived from the oxidation data is probably due to the presence of more than two modifications in the equilibrium solution. This interpretation is also supported by the complex mutarotations of both  $\alpha$ - and  $\beta$ -*d*-talose and by the changes in optical rotation which follow an alteration in the temperature [5, 6].

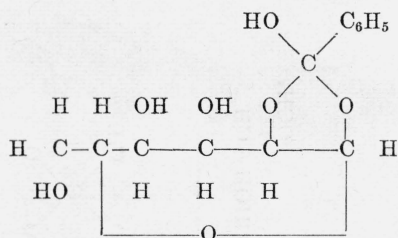
From the data given in tables 1 and 2 the heats of activation for the mutarotation reaction may be calculated by application of the Arrhenius equation. The values obtained are  $Q_1=16,300$  calories for the slow reaction, and  $Q_2=11,500$  calories for the rapid reaction; the corresponding values previously given for  $\alpha$ -*d*-talose [6] are  $Q_1=15,900$  and  $Q_2=12,800$ , while those for the averages of a number of sugars were given as  $Q_1=16,900$ , and  $Q_2=13,200$ . The temperature coefficient, which is the ratio of the rates of mutarotation at 35° C to that at 25° C, is 2.4 for the slow reaction and only 1.9 for the rapid reaction.

If the ring structure of the two crystalline isomeric taloses be assumed as pyranoid, it will be observed that these substances follow the lactone rule [10] since the ring lies to the right and the rotation of a solution containing equal proportions of the alpha and beta isomers [11] would be  $1/2 (68.0 + 13.2) = +40.6$ .

### III. MONOBENZOYL TALOSE AND ITS RELATIONSHIP TO THE GLYCAL SYNTHESIS

The talose needed for this investigation was prepared by the action of perbenzoic acid on galactal according to the method of Bergmann and Schotte [13] as applied to the preparation of talose by Levene and Tipson [4]. The glycal synthesis is of importance and is superior to the older methods for the preparation of certain rare sugars. However there are several problems connected with its application which hitherto have not been explained. Thus the rotation of anhydrous 4-glucosido-mannose, prepared by application of the glycal synthesis to cellobiose, is reported by Bergmann and Schotte [13] to be  $[\alpha]_D^{16} = 10.65$ , and by Haworth, Hirst, Streight, Thomas, and Webb [14] to be  $[\alpha]_D^{18} = 12.5$  at equilibrium. On the other hand, Brauns [15] and Isbell [16], working with material prepared by the action of hydrogen fluoride on cellulose octa-acetate, reported the values  $[\alpha]_D^{20} = +5.8$  and  $[\alpha]_D^{20} = +5.88$ , respectively, for the monohydrate. Also, Watters and Hudson [17] reported that a third substance of unknown composition was present with the lactose and 4-galactosido-mannose produced by the action of perbenzoic acid on lactal. We have now succeeded in separating from the products from the action of perbenzoic acid on 150 g of galactal, 5 g of a crystalline difficultly soluble substance which was identified as monobenzoyl talose. It seems probable that similar substances are responsible for the discrepancies in the rotations reported for 4-glucosido-mannose and for other sugars prepared by the glycal synthesis.

The crystalline compound obtained in the synthesis of talose gives a positive color test for benzoic acid only after acid hydrolysis, and, therefore, it is not a molecular compound of talose and benzoic acid. The method used for the preparation of monobenzoyl talose eliminates any position for the benzoyl residue other than carbons 1 and 2, but the properties of the monobenzoate are different from those which might be anticipated for a normal 1- or 2-monobenzoyl talose. Thus the  $\beta$ -1-monobenzoyl glucose of Zervas [18] is stable in hot methyl alcohol solution, does not mutarotate in water, and has a sharp melting point. In contradistinction to these properties, the monobenzoyl talose reacts with cold methyl alcohol, is decomposed by alkali (and even distilled water over a long period of time), and does not have a distinct melting point. The lack of mutarotation in acid solution does not correspond with properties to be expected of 2-monobenzoyl talose. These and other data which are presented in the next section are best explained by an orthoester structure and for the present the monobenzoyl talose is assigned the following formula:

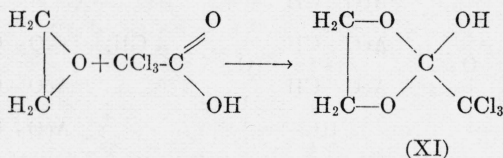


The monobenzoate probably is produced by the addition of benzoic acid to an intermediate ethylene oxide derivative [12] (formed by the action of perbenzoic acid on galactal) in a manner analogous to the formation of sugars and glycosides from glycals [13]. These reactions are illustrated as follows:





This mechanism is supported by the analogous reaction of trichloroacetic acid and ethylene oxide which, according to Hibbert and Greig [20], give 2-hydroxy-2'-trichloromethyl 1,3-dioxolane (XI).



In the glycol synthesis, however, the conditions are more complex because several competing reactions take place. Ordinarily water is present in large excess, and consequently the sugars are the principal products. When large quantities of benzoic acid are present, mixtures are obtained which contain benzoic acid but which do not yield crystalline products until after hydrolysis.

In contrast to the talose derivative, Levene and Tipson [4] obtained a 1-monobenzoyl-triacetyl galactose by the action of perbenzoic acid on an anhydrous solution of triacetyl galactal. The production of a galactose derivative in one case and a talose in the other is in harmony with their observation that the perbenzoic acid oxidation of triacetyl galactal gives principally galactose derivatives, while galactal gives talose predominantly [4]. Our monobenzoyl talose differs from the acetylated monobenzoyl galactose in that it is probably an orthoacid derivative.

In the next section the properties of the new monobenzoyl talose will be compared with the properties of other compounds which presumably have orthoacid structures.

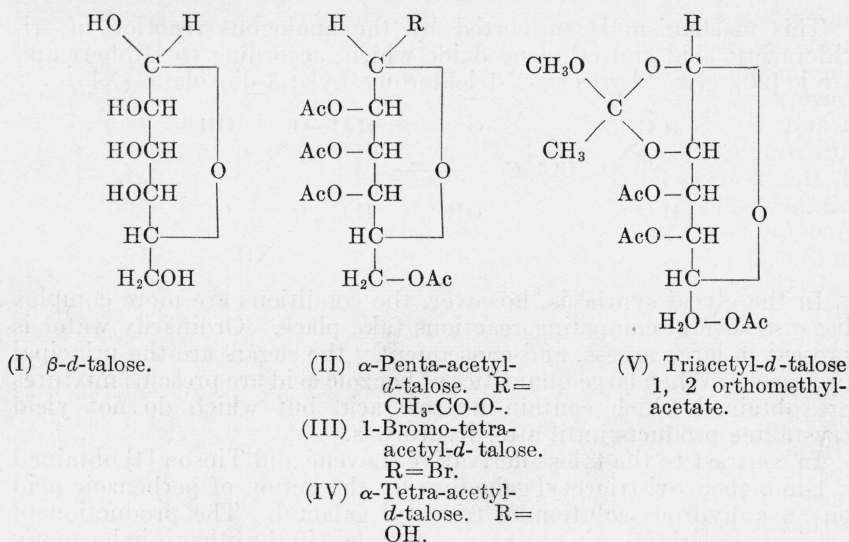
#### IV. ACETYLATED DERIVATIVES OF *d*-TALOSE

##### 1. $\alpha$ -PENTA-ACETYL-*d*-TALOSE AND DERIVATIVES

Upon acetylation with acetic anhydride at 0° C in the presence of pyridine,  $\alpha$ -*d*-talose yields crystalline  $\alpha$ -penta-acetyl-*d*-talose (II, p. 198) with  $[\alpha]_D^{20} = +70.2$  in chloroform.  $\beta$ -*d*-talose under similar conditions gives a second penta-acetate which has not yet crystallized.

Crystalline  $\alpha$ -1-bromo-tetra-acetyl-*d*-talose (III, p. 198), with  $[\alpha]_D^{20} = 165.6$  in chloroform, is prepared by the action of glacial acetic acid solution of hydrogen bromide on  $\alpha$ -penta-acetyl-*d*-talose.

Bromo-tetra-acetyl-*d*-talose reacts with moist silver salts to give crystalline tetra-acetyl-*d*-talose (IV, p. 198). This new substance mutarotates from a dextrorotation in pyridine solution at a rate corresponding to that for a first-order reaction ( $k_1 + k_2 = 0.0029$  at 20° C). The mutarotation reaction appears to be a simple reversible conversion of alpha and beta isomers because tetra-acetyl-*d*-talose may be recovered from the equilibrium solution. Since the optical rotation changes from a dextro to a less dextro rotation, the substance is called  $\alpha$ -tetra-acetyl-*d*-talose. This classification is supported by the formation of  $\alpha$ -penta-acetyl-*d*-talose when the tetra-acetate is acetylated at 0° C.



## 2. TRIACETYL-*D*-TALOSE 1,2-ORTHOMETHYLACETATE

The bromo-tetra-acetyl-*D*-talose reacts with methyl alcohol in the presence of silver carbonate to give a compound (V, p. 198) with the same empirical formula as a tetra-acetyl methyl taloside but which has only three acetyl groups which are hydrolyzable by alkali. The new substance is a derivative of orthoacetic acid similar to the so-called " $\gamma$ '-triacetyl methyl rhamnoside" of Fischer, Bergmann, and Rabe [21].

Such substances have been variously described as orthoacetates, " $\gamma$ "-glycosides, and  $\alpha$ -methoxy-ethylidenes, etc. Since they are derivatives of orthoacetic acid [22, 23] and have unique reactions which may be associated with such a structure, it seems advisable when naming compounds of this type that the orthoacid nature be emphasized. Haworth, Hirst, and Stacey [24] have named their derivative of  $\alpha$ -glucoheptose as tetra-acetyl-( $\alpha$ -glucoheptose) 1,2-orthomethylacetate. This method seems satisfactory as it may be applied to other known orthoacetates as well as to new types. The new talose derivative is then called triacetyl-*D*-talose 1,2-orthomethylacetate. Similarly the monobenzoyl-*D*-talose, which is probably a derivative of orthobenzoic acid with one acid hydroxyl not esterified, is named *D*-talose 1,2-orthobenzoic acid.

Previously orthomethylacetates have been reported for mannose [25], lyxose [26], rhamnose [21], 4-glucosido-mannose [28], ribose [27], *D*- $\alpha$ -glucoheptose [24], fructose [19], turanose [29], and maltose [30, 31], while in this paper the orthomethylacetate of talose is reported. The first four of these sugars have the mannose configuration, ribose has the talose configuration, and *D*- $\alpha$ -glucoheptose has the gulose configuration. Fructose and turanose are ketoses which have the galactose configuration, while maltose is a substituted glucose.

An examination of the configurations of the halogeno-acetyl sugars which have been converted to orthoesters reveals that many of these have the acetyl groups on carbons 2 and 3 in a *cis* position in a definite relation to the configuration of carbon 1. Thus when the two *cis*

acetyl residues are directed away from the ring-oxygen, orthomethylacetates are given by  $\alpha$ -halogeno-acetyl sugars, as for example, by the mannose and talose derivatives. When these groups are directed toward the ring, the orthoesters are produced from  $\beta$ -halogeno-acetyl sugars, such as  $\beta$ -bromo-penta-acetyl-*d*- $\alpha$ -glucoheptose. The directing influence is probably exercised by the acetyl group on carbon 3, the oxygen of which supposedly repels the corresponding oxygen of the acetyl group on carbon 3 and directs it toward carbon 1. According to this conception the unknown  $\beta$ -bromo-tetra-acetyl derivatives of gulose and allose should yield orthomethylacetates.

Orthoacetate formation, however, is not limited to these favorable structures and other factors are responsible for the formation of this type of derivative by the halogeno-acetyl derivatives of fructose, turanose, and maltose. The position of the orthomethylacetate group for the fructose and turanose derivatives is not definitely established. The group is supposed to be attached to carbons 2 and 3 [19, 29], but since a 1,2 position is possible the interpretation of the formation of these derivatives must await a determination of the position of the orthomethylacetate group. In any case, the fructose structure must be considered as representing another favorable configuration. Three chloro-acetyl derivatives of maltose, supposedly the normal  $\alpha$  and  $\beta$  derivatives, and an orthoacetyl chloride are known. Since of the three only the hexa-acetyl maltose 1,2-orthoacetyl chloride will form the corresponding orthomethylacetate [44, 30], the formation of the maltose derivative is not comparable to that of mannose and talose. Probably orthomethylacetates could be prepared for all of the sugars if the corresponding orthoacetyl chloride derivatives were known.

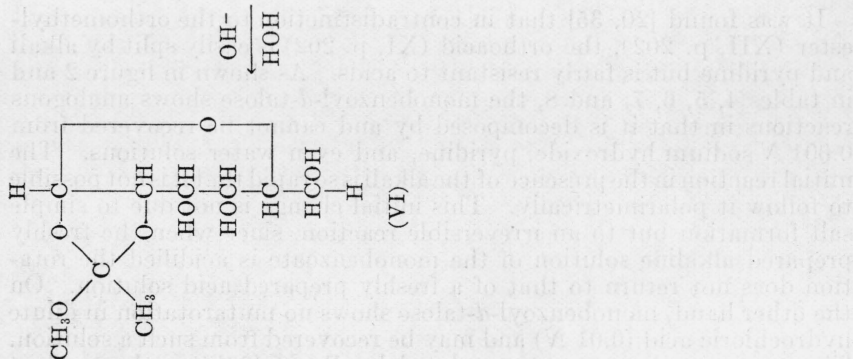
Heretofore the importance of temperature on the reaction of the halogen acetyl derivatives with methyl alcohol to form orthoesters has not been emphasized sufficiently. Miss Harriet Frush and one of the authors (Isbell) found that good yields of triacetylmannose orthomethylacetate are obtained from bromo-acetyl mannose and silver carbonate in methyl alcohol when the reaction is conducted at low temperatures (0° C). At room temperatures and above only small quantities of the orthoester could be separated. The effect of temperature on this reaction may account for some of the conflicting results which have been obtained in this field.

### 3. REACTIONS OF ACETYL SUGAR ORTHOMETHYLACETATES

Since only a small quantity of the triacetyl-*d*-talose 1,2-orthomethylacetate (V, p. 198) has been prepared, the study of its reactions has not been completed. However, several reactions typical for the orthomethylacetates have been carried out. Thus hydroxyl ions hydrolyze only three of the four acetyl groups and give talose 1,2-orthomethylacetate (VI, p. 201), which was not isolated in the crystalline state. The presence of an acetyl group resistant to alkaline hydrolysis is characteristic of the orthomethylesters [21, 25]. Another typical reaction is the conversion of the orthomethylesters to normal chloro-acetyl sugars by hydrogen chloride in chloroform solution [28]. Triacetyl-*d*-talose orthomethylacetate under these conditions reacts so rapidly that the rate of change could not be measured polarimetrically. Thus the specific rotation of triacetyl-*d*-talose orthomethylacetate in purified chloroform is  $[\alpha]_D^{20} = +3.7$ , while in chloro-

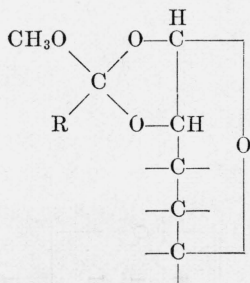
form containing hydrogen chloride the specific rotation was  $[\alpha]_D^{21} = +73$ , 3 minutes after dissolution. After evaporation of the solution, crystals were obtained which are probably chloro-triacetyl talose (VII, p. 201). The triacetyl-*d*-talose orthomethylacetate was also found to be quite unstable since upon recrystallization from warm water the substance decomposed to give considerable quantities of tetra-acetyl talose (VIII, p. 201). This substance is also obtained by treating triacetyl-*d*-talose orthomethylacetate with aqueous alcoholic hydrogen chloride. Apparently triacetyl-*d*-talose orthomethylacetate is hydrolyzed more readily than hexa-acetyl-4-glucosido-mannose orthomethylacetate [28] and it resembles hexa-acetyl turanose orthomethylacetate, which hydrolyzes readily to give a normal hepta-acetate [29b].



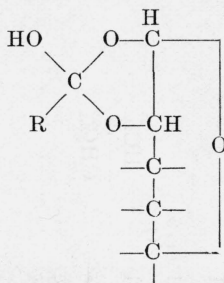


## 4. REACTIONS OF SUGAR ORTHOACIDS

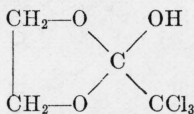
Several sugar derivatives have been postulated by Haworth, Hirst, and Teece [32], Pacsu [29], and Richtmeyer and Hudson [33] as having orthoacid structures (X, p. 202), but at the present time there is very little information concerning such structures. The hexaacetyl and hepta-acetyl 4-glucosido-mannose of Isbell [28], as well as the monobenzoyl-*d*-talose reported in this paper, also seem to belong to this class of compounds. The 2-hydroxy-2'-trichloromethyl 1,3-dioxolane (XI, p. 202) prepared by Hibbert and Greig [20] and Meerwein and Hinz [34] has an orthoacid structure in one of its tautomeric forms [36, 37] and hence may provide some information as to the properties of such substances. As might be expected, the orthoacids which have a free acidic hydroxyl appear to have strikingly different properties from the orthomethylacetates (IX and XII, p. 202)



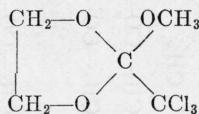
(IX)



(X)



(XI)



(XII)

It was found [20, 35] that in contradistinction to the orthomethyl-ester (XII, p. 202), the orthoacid (XI, p. 202) is easily split by alkali and pyridine but is fairly resistant to acids. As shown in figure 2 and in tables 4, 5, 6, 7, and 8, the monobenzoyl-*d*-talose shows analogous reactions in that it is decomposed by and cannot be recovered from 0.001 *N* sodium hydroxide, pyridine, and even water solutions. The initial reaction in the presence of the alkali is so rapid that it is not possible to follow it polarimetrically. This initial change is not due to simple salt formation but to an irreversible reaction, since when the freshly prepared alkaline solution of the monobenzoate is acidified the rotation does not return to that of a freshly prepared acid solution. On the other hand, monobenzoyl-*d*-talose shows no mutarotation in dilute hydrochloric acid (0.01 *N*) and may be recovered from such a solution. The monoacetyl turanose postulated by Pacsu [29b] as the product resulting from the action of acid upon turanose orthomethylacetate exhibits a similar stability to dilute acid and instability to dilute alkali.

Since, according to Meerwein, Hinz, and Sönke, the orthoacid reacts with diazomethane to give the methylester [34, 35, 36], it was hoped that this reaction might be used as a criterion for orthoacid structures. However, none of the compounds tried (monobenzoyl-*d*-talose, hexa-acetyl-4-glucosido-mannose, hepta-acetyl-4-glucosido-mannose, and chloro-hepta-acetyl-lactose) reacted appreciably, during an hour at 0° C, with an ether solution of diazomethane. As, however 2-hydroxy-2'-methyl-1, 3-dioxolane reacts much less readily [36] with diazomethane than the 2-hydroxy-2'-trichloromethyl-1, 3-dioxolane the negative results obtained with the sugar derivatives are not surprising. The use of catalysts [34] may provide a means for effecting this reaction, which is being studied further.

The action of pyridine upon the orthoacid derivatives may provide a means for detecting this type of structure. Thus the monobenzoyl-*d*-talose (table 8) shows a slow complex change of rotation when dissolved in this solvent. The hepta-acetyl-4-glucosido-mannose [28] exhibits no change of rotation in chloroform or methyl

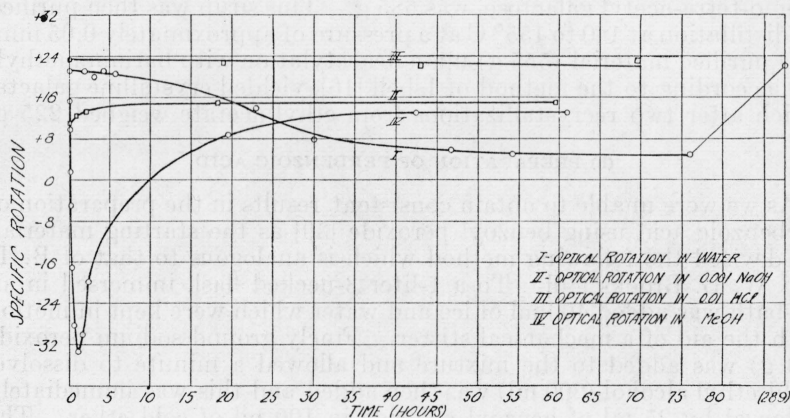


FIGURE 2.—Optical rotation measurements made on monobenzoyl talose at 20° C.

alcohol, while in pyridine an upward mutarotation occurs, although acetylation gives chiefly  $\alpha$ -octa-acetyl-4-glucosido-mannose.

As shown by its sensitivity toward very dilute alkali and by the complex and rapid reaction with methyl alcohol (fig. 2), monobenzoyl-*d*-talose is a very reactive substance and does not have the properties characteristic of normal acyl derivatives. These properties are at the present time best explained by the postulation of an orthoacid structure and hence monobenzoyl-*d*-talose is named talose 1, 2-ortho-benzoic acid. Possibly hepta- and hexa-acetyl-4-glucosido-mannose may have similar 1, 2- and 1, 6-orthoacetic acid structures, respectively.

## V. EXPERIMENTAL PROCEDURE

### I. PREPARATION OF *d*-TALOSE

The *d*-talose used in this investigation was prepared by the oxidation of galactal with perbenzoic acid according to the general method used by Levene and Tipson [4] and T. Kumoda [38].

## (a) PREPARATION OF GALACTAL

The galactal was prepared from bromo-tetra-acetyl galactose by reduction with zinc dust in 50-percent acetic acid solution according to the following procedure: To a 12-liter flask surrounded by an ice-salt bath there was added 1,000 ml of  $H_2O$ , 500 ml of glacial acetic acid, and 100 g of zinc dust which was kept in suspension by the aid of a mechanical stirrer. During a period of three hours ten 75-g portions of finely powdered bromo-tetra-acetyl galactose dissolved in 300 ml of warm glacial acetic acid were added. Water, in quantities to keep the composition at approximately 50-percent acid, and 600 g of zinc dust were also added at intervals during this period. The mixture, the temperature of which was allowed to rise slowly to room temperature over a period of 18 hours, was filtered and the filtered solution was extracted four times with a total of about 11 liters of benzene. The washed extracts were evaporated at a pressure of 14 mm to a thick sirup. The weight of the sirup, obtained by the combination of two such preparations from a total of 1,370 g of the bromo-tetra-acetyl galactose, was 685 g. This sirup was then purified by distillation at 140 to 155° C at a pressure of approximately 0.05 mm. The purified material (555 g) upon deacetylation with barium methylate, according to the method of Isbell [16], yielded crystalline galactal which after two recrystallizations from ethyl acetate weighed 225 g.

## (b) PREPARATION OF PERBENZOIC ACID

As we were unable to obtain consistent results in the preparation of perbenzoic acid using benzoyl peroxide [39] as the starting material, we devised the following method which is analogous to that of B. T. and W. B. Brooks [40]. To a 1-liter 3-necked flask immersed in an ice bath was added 400 ml of ice and water which were kept in motion with the aid of a mechanical stirrer. Finely ground sodium peroxide (30 g) was added to the mixture and allowed a minute to dissolve. Cold ethyl alcohol (200 ml) was then added and this was immediately followed by 25 ml of benzoyl chloride in 100 ml of cold ether. The mixture was stirred for several minutes and was then filtered through a large Büchner funnel. The filtrate, after acidification with 700 ml of normal sulphuric acid, was extracted with four 150-ml portions of ether. The solutions were kept as cold as possible until after the final acidification. This procedure gives consistently about 20 g of perbenzoic acid.

## (c) OXIDATION OF GALACTAL

The galactal was converted to a mixture of galactose, talose, and monobenzoyl talose in the following manner: An aqueous solution of galactal (50 g in 500 ml of water) was cooled to 0° C and then a cold solution of 58 g of perbenzoic acid in 305 ml of ether was added. The mixture was stirred at 0° C for 4 hours, and then stirred for an additional 14 hours, during which time the temperature rose slowly to 25° C. The aqueous phase was separated and extracted three times with ether and three times with chloroform. The resulting solution contained 53.4 g of reducing sugar (as galactose).

The oxidation mixture from 150 g of galactal was boiled down to about 60-percent sirup and allowed to stand overnight. A small crop of crystals appeared which were separated (weight 1.45 g). The solution was evaporated again to about a 70-percent solution and



allowed to crystallize. After five days 4.15 g of difficultly soluble crystals was separated. These crystals and the first crop proved to be talose monobenzoate.

#### (d) SEPARATION OF GALACTOSE AND TALOSE

The separation of the galactose and talose was accomplished in two ways, (1) fractional crystallization and (2) extraction of the mixture with methyl alcohol. Both methods will be described. The oxidation mixture from 100 g of galactal after removal of the monobenzoyl talose was evaporated to a thin sirup (about 70 percent) and diluted with an equal volume of methyl alcohol. Alpha talose seed was added and crystallization was allowed to take place for 24 hours. A crop weighing 37 g was separated, for which  $[\alpha]_D^{20}=33.1$ , at equilibrium. This corresponds to 79 percent of talose. The mother liquors upon evaporation and dilution with methyl alcohol in a similar manner gave, after seeding with galactose, 25 g of material,  $[\alpha]_D^{20}=74.1$ , at equilibrium (corresponding to 90 percent of galactose). Upon recrystallization of the crude talose ( $[\alpha]_D^{20}=33.1$ ) 18.5 g of material ( $[\alpha]_D^{20}=22.1$ ) was obtained. This, combined with another crop of crude talose (weight 9.7 g;  $[\alpha]_D^{20}=23.6$ ), gave 23 g of pure  $\alpha$ -*d*-talose ( $[\alpha]_D^{20}=20.8$ ). From 100 g of galactal about 40 g of pure talose was obtained. The more readily obtained isomer is the alpha which crystallizes in truncated rectangular prisms. The melting point is 133 to 134° C, and the equilibrium rotation is  $[\alpha]_D^{20}=20.8$ . These values are in approximate agreement with the values 130 to 135° C and  $[\alpha]_D^{27}=19.7$ , reported by Levene and Tipson [4].

The easiest method for separating talose and galactose is to extract a dry mixture with methyl alcohol. Thus 25 g of a mixture ( $[\alpha]_D^{20}=+40$ , at equilibrium) was heated on a steam bath for 60 minutes with 200 ml of methyl alcohol and the residue was separated by filtration. The material remaining, which was almost pure galactose, weighed 5.5 g and gave an equilibrium rotation of  $[\alpha]_D^{20}=79.8$ . The filtrate upon evaporation gave 14.0 g of material which had an equilibrium rotation ( $[\alpha]_D^{20}=25.9$ ) corresponding to 91 percent of talose.

The mother liquor from the oxidation of 100 g of galactal which remained after all of the galactose and talose which would crystallize had been separated, was hydrolyzed with 0.5 *N* sulphuric acid for 7 hours at the boiling point. When the solution had cooled, crystals appeared which were separated, recrystallized from petroleum ether, and identified by a melting-point determination as benzoic acid. The weight of the recrystallized benzoic acid was 1.0 g. The neutral filtered solution crystallized after evaporation and 4 g of sugar was separated. Since the equilibrium solution had a rotation of  $[\alpha]_D^{20}=+64$ , the sugar consisted of approximately 73 percent of galactose and 27 percent of talose. It is therefore apparent that benzoyl esters of both galactose and talose are produced in addition to the free sugars by the action of perbenzoic acid on galactal.

#### 2. $\beta$ -*d*-TALOSE

A number of small crops of crude  $\beta$ -*d*-talose were obtained by crystallization from methyl alcohol. Recrystallization was performed as follows: Finely ground sugar (6.3 g) was dissolved completely in 17 ml of ice-cold water and then induced to crystallize by the addition

of 24 ml of cold absolute ethyl alcohol. After 60 minutes the resulting crystals were separated, washed with alcohol, and dried in vacuo (weight 2.5 g). The crystals usually form hexagonal prisms which have the appearance of square plates. The melting point is 120 to 121° C and the mutarotation is given in tables 1 and 2.

The oxidation data given in table 3 were obtained by the bromine oxidation method previously reported [8] as modified for use with small amounts of sugar [7]. *Analysis.* Calculated for  $C_6H_{12}O_6$ : C, 39.98; H, 6.72. Found: C<sup>5</sup> (micro), 40.09; H, 6.83.

### 3. PROPERTIES AND IDENTIFICATION OF MONOBENZOYL-D-TALOSE

The 5.6 g of crystals, obtained by the oxidation of galactal with perbenzoic acid, as previously described, was recrystallized from hot water. The crystals separate as long slender needles. A description of some of the properties of this material and of the methods used for identifying it follows.

*Solubility.*—The bitter crystals are difficultly soluble in cold water, chloroform, benzene, ether, and alcohol. Pyridine, hot alcohol, and hot water dissolve them readily but the first two solvents cause decomposition. At 20° C the solubility in water is approximately 0.5 g per 100 ml. *Melting point.*—The material melts between 150 and 170° C, apparently with decomposition, to give a brown liquid. *Reducing power.*—A 20.3-mg sample after heating with Benedict's solution was equivalent to 10.25 ml of 0.04 *N* iodine solution. Under the same conditions glucose requires 18.44 ml of the iodine solution. Therefore the ratio of reducing power to that of glucose is 0.556. The corresponding ratio to that of galactose is 0.626. Since the ratio of the molecular weight of the hexose to that of a hexose monobenzoate is 0.634, the reducing value agrees with that to be expected of an easily hydrolyzable galactose or talose derivative. The reducing power after acid hydrolysis with 0.506 *N* HCl for 2¼ hours at 100° C was found to have decreased slightly so that the ratio to that of glucose was 0.502. *Identification of benzoic acid.*—After acid hydrolysis with 0.506 *N* hydrochloric acid for 2¼ hours at the boiling point, a positive color test for benzoic acid was obtained [41] and benzoic acid was isolated from the hydrolysate. *Optical rotatory power.*—The changes in optical rotatory power observed in distilled water, aqueous hydrochloric acid (0.01 *N*), aqueous sodium hydroxide (0.001 *N*), methyl alcohol, and pyridine solutions are shown in tables 4, 5, 6, 7, and 8. Each of the recorded values is the average of five or more consecutive readings.

<sup>5</sup> The microdeterminations of hydrogen and carbon reported in this paper were carried out by Dr. J. R. Spies and Dr. W. G. Rose, of the U. S. Department of Agriculture.

TABLE 4.—*Rotation of monobenzoyl talose in water at 20° C*

(0.1062 g made up to 25 ml and read in a 4-dm tube)

Time	Observed rotation	Specific rotation	Time	Observed rotation	Specific rotation
<i>Hours</i>	°S	$[\alpha]_{D^{20}}$	<i>Hours</i>	°S	$[\alpha]_{D^{20}}$
0.08	1.04	21.2	47	0.28	5.7
.49	1.03	21.0	54	.25	5.1
1.06	1.03	21.0	76	.24	4.9
1.9	1.04	21.2	143	.74	15.1
3.1	0.97	19.8	192	.93	18.9
4.2	1.04	21.2	241	1.04	21.2
5.7	1.01	20.6	289	1.09	22.2
23.	0.68	13.9	648	1.19	24.2
30.	.38	7.7			

TABLE 5.—*Rotation of monobenzoyl talose in 0.01 N HCl at 20° C*

(0.0498 g made up to 10 ml with 0.01 N HCl and read in a 2-dm tube)

Time	Observed rotation	Specific rotation
<i>Hours</i>	°S	$[\alpha]_{D^{20}}$
0.08	0.67	23.3
19.0	.65	22.6
43.0	.64	22.2
69.5*	.65	22.6

\* After this reading the solution was evaporated and 0.045 g of monobenzoyl talose was recovered.

TABLE 6.—*Rotation of monobenzoyl talose in 0.001 N NaOH at 20° C*

(0.0508 g made up to 10 ml and read in a 2-dm tube)

Time	Observed rotation	Specific rotation
<i>Hours</i>	°S	$[\alpha]_{D^{20}}$
0.07	0.32	10.9
.83	.37	12.6
2.1	.39	13.3
19.5	.44	15.0
68.	.44	15.0
92.	.44	15.0

TABLE 7.—*Rotation of monobenzoyl talose in methyl alcohol at 19° C*

(0.0551 g made up to 10 ml and read in a 2-dm tube)

Time	Observed rotation	Specific rotation	Time	Observed rotation	Specific rotation
<i>Minutes</i>	°S	$[\alpha]_{D^{19}}$	<i>Minutes</i>	°S	$[\alpha]_{D^{19}}$
2.96	+0.49	+15.4	29.9	-0.67	-21.1
4.26	+ .43	+13.5	40.0	- .90	-28.3
6.34	+ .31	+9.7	50.8	-1.01	-31.7
8.52	+ .27	+8.5	60.1	-1.06	-33.3
10.65	+ .05	+1.6	91.0	- .96	-30.2
13.52	- .08	-2.5	144.9	- .63	-19.8
15.16	- .16	-5.0	1170.	+ .28	+8.8
20.04	- .36	-11.3	2550.	+ .35	+11.0
25.1	- .54	-17.0	3960.	+ .35	+11.0

TABLE 8.—*Optical rotation of monobenzoyl talose in pyridine at 20° C*

(0.1932 g made up to 10 ml and read in a 2-dm tube)

Time	Observed rotation	Specific rotation	Time	Observed rotation	Specific rotation
<i>Hours</i>	$^{\circ}\text{S}$	$[\alpha]_D^{20}$	<i>Hours</i>	$^{\circ}\text{S}$	$[\alpha]_D^{20}$
0.1	+1.84	+16.5	166.7	-1.32	-11.8
.3	+1.81	+16.2	191.3	-1.39	-12.5
1.5	+1.74	+15.6	214.3	-1.32	-11.8
5.9	+1.59	+14.2	263.0	-1.04	-9.3
22.6	+1.09	+9.8	286.7	-0.85	-7.6
46.2	+0.42	+3.8	310.7	-.59	-5.3
94.2	-.53	-4.7	359.0	-.16	-1.4
118.3	-.88	-7.9	383.5	+.09	+0.8
143.0	-1.17	-10.5	430.5	+.54	+4.8

*Proof that the monobenzoate is a derivative of d-talose.*—A 0.1524-g sample of the crystals was made up to a volume of 25 ml with 0.050 *N* sulphuric acid and kept at  $57 \pm 2^{\circ}\text{C}$  for 8 days. The optical rotation was measured at intervals as recorded in table 9. The resulting solution was extracted with ether and neutralized with barium carbonate. The precipitate of barium sulphate was removed by filtration and the salt-free solution evaporated in a vacuum desiccator to a thick sirup. Upon dilution with ethyl alcohol and seeding with a minute amount of talose, crystallization occurred. The crystals were of the truncated prism type characteristics of  $\alpha$ -d-talose. The solvent was removed in a high vacuum and the sugar converted to the penta-acetate by cooling to  $0^{\circ}\text{C}$ , adding 2 ml of pyridine and 1 ml of acetic anhydride, and keeping at  $0^{\circ}$  for 3 days. After this time, the solution was poured into ice water and the whole extracted with chloroform. Upon evaporating the chloroform and taking up with ethyl alcohol, crystallization occurred spontaneously. These crystals had a melting point of 105 to  $106^{\circ}\text{C}$  and after recrystallization from ethyl alcohol melted at 106 to  $107^{\circ}\text{C}$ . A mixture of this material and known talose penta-acetate melted at 106.5 to  $107^{\circ}\text{C}$ , which is the same as that for the pure product.

TABLE 9.—*Hydrolysis of benzoyl talose at  $57 \pm 2^{\circ}\text{C}$* (0.1524 g made up to 25 ml with 0.05 *N*  $\text{H}_2\text{SO}_4$  and read in a 2-dm tube)

	Observed rotation	Specific rotation		Observed rotation	Specific rotation
<i>Minutes</i>	$^{\circ}\text{S}^a$	$[\alpha]_D^{56}$	<i>Minutes</i>	$^{\circ}\text{S}^a$	$[\alpha]_D^{56}$
5.8	0.66	18.7	304.8	0.62	17.6
15.9	.62	17.6	1,620.	.29	8.2
30.0	.60	17.0	2,900.	.16	4.5
60.6	.60	17.0	<sup>b</sup> 10,290.	.19	5.4
124.5	.60	17.0			

<sup>a</sup> Averages of 10 readings.<sup>b</sup> The temperature was raised to  $80^{\circ}\text{C}$  during the last 24 hours.

*Analysis.*—Calculated for  $\text{C}_6\text{H}_{11}\text{O}_6$  ( $\text{COC}_6\text{H}_5$ ): C, 54.90; H, 5.68; benzoyl, 8.05 ml of 0.02224 *N* NaOH per 51.2 mg. Found: C (micro), 54.76, 54.78; H (micro), 5.61, 5.57; benzoyl by alkaline saponification at  $20^{\circ}\text{C}$  for 24 hours, 7.84 ml. Under the conditions employed for



the molecular weight determination by the Rast method, the material decomposes.

*Preparation of talose and galactose monobenzoates.*—Attempts were made to combine galactal with perbenzoic acid in anhydrous solutions in order to increase the yield of talose monobenzoate. Using dioxane and ethyl formate as solvents small quantities of talose monobenzoate were prepared. The method used is illustrated in the following typical experiment.

A solution of 5 g of galactal in 150 ml of dioxane and 10 ml of acetone was prepared and cooled to 0° C. A solution of 6 g of perbenzoic acid in 10 ml of dioxane was added along with 4 g of benzoic acid and the mixture was left in a refrigerator for 3 days. The solution was then evaporated to a sirup which was extracted with ether and taken up with water. The aqueous solution after several ether extractions was evaporated and extracted with ethyl acetate. The ethyl acetate extractions after evaporation to a sirup were taken up with water and from the solution 0.13 g of talose monobenzoate crystallized. No other crystalline material was obtained from the preparation. When pyridine or acetic acid was used as the solvent instead of acetone-dioxane, crystalline material could be obtained only after acid hydrolysis, as described in the next paragraph.

The sirupy material from several such preparations (corresponding to 25 g of galactal) was combined and hydrolyzed with acid in a manner similar to that used for the talose mother liquors. After recrystallization from petroleum ether, the benzoic acid weighed 1.5 g. The sugar obtained weighed 4 g, had an equilibrium rotation of  $[\alpha]_D^{20} = +34$ , and hence consisted of 77 percent of talose and 23 percent of galactose.

#### 4. $\alpha$ -PENTA-ACETYL-*D*-TALOSE

Five grams of powdered talose, dissolved in a cold mixture of 35 ml of pyridine and 23 ml of acetic anhydride, was allowed to remain in a refrigerator at 0° C for 3 days. The mixture was then poured into 125 ml of ice water and the resulting emulsion crystallized during the course of an hour of stirring. The crystals, which characteristically appear as truncated prisms, were separated by filtration and dried. They weighed 7 g, and 1 g additional was obtained by extraction of the filtrate with benzene, evaporation of the benzene solution, and crystallization. Several grams of sirupy material remained, probably consisting of isomeric penta-acetates, which could not be induced to crystallize. The penta-acetate upon recrystallization from hot ethyl alcohol had a melting point of 106 to 107° C. In chloroform (cp) the specific rotation was  $[\alpha]_D^{20} = 69.5$  (0.3541 g made up to a volume of 10 ml, read 14.21° S in a 2-dm tube). A second recrystallization from ethyl alcohol raised the melting point slightly to 106.5 to 107° C and the rotation to  $[\alpha]_D^{20} = 70.2$  (0.3617 g made up to 10 ml with chloroform (cp) read 14.67° S in a 2-dm tube).

The action of the acetic anhydride-sulphuric acid isomerizing agent [43] on the  $\alpha$ -penta-acetate was studied and it was found that since 75 percent of the alpha form was recoverable, the equilibrium lies in favor of the alpha isomer. Crystalline  $\beta$ -penta-acetyl talose was obtained neither by this method nor by the action of the acetic anhydride and sodium acetate on alpha talose. *Analysis.*—Calculated for  $C_6H_7O_6(COCH_3)_5$ : C, 49.21; H, 5.68; acetyl, 12.81 ml

of 0.1 *N* Ba (OH)<sub>2</sub> per 100 mg. Found: C (micro), 49.64; H (micro), 5.77; acetyl (by alkaline saponification for 3 hours at 20° C), 13.13 ml.

#### 5. 1-BROMO-TETRA-ACETYL-*d*-TALOSE

A mixture of 10 g of penta-acetyl talose, 50 ml of glacial acetic acid containing 38 percent of HBr, and 2 ml of acetic anhydride was prepared at 0° C. Solution took place in about an hour, after which the liquid was kept at room temperature for 2½ hours more. Chloroform (60 ml) was then added and the bromo-acetyl talose solution was poured into ice water and extracted with chloroform. The extracts (three in all with a total of 180 ml of solvent) were washed twice with ice water, twice with cold sodium bicarbonate solution, and once again with ice water. The chloroform solution, after being dried with anhydrous sodium sulphate, was evaporated to a thin sirup, and after dilution with toluene was evaporated again to remove the last of the chloroform. Upon taking up the residue with ether, crystallization commenced immediately. After several hours 7 g was separated and an additional 0.5 g was obtained from the mother liquors. The crystals appeared as poorly defined long rectangular prisms with one pointed end. The material, after one recrystallization from ether, had a melting point of 84 to 84.5° C, although a slight sintering occurred at 83° C. A preliminary optical rotation measurement showed that ordinary chemically pure chloroform causes decomposition. Thus 0.4499 g made up to 10 ml with chemically pure chloroform read 42.57° S in a 2-dm tube 5 minutes after solution, but at 180 minutes this had dropped to 38.02° S. Therefore, the chloroform was washed with water, dried, and distilled just before using. A measurement of the rotatory power in this purified chloroform gave  $[\alpha]_D^{20} = 165.6$ , (0.4058 g made up to 10 ml, read 38.82° S in a 2-dm tube). This value was not changed appreciably after 60 minutes. *Analysis*.—Calculated for C<sub>6</sub>H<sub>7</sub>O<sub>5</sub>Br(COCH<sub>3</sub>)<sub>4</sub>: C, 40.87; H, 4.66; Br, 19.44; acetyl, 9.73 ml of 0.1 *N* NaOH per 100 mg. Found: C (micro), 40.76; H (micro), 4.78; Br [42], 19.51; acetyl [42], 9.82 ml.

#### 6. TRIACETYL-*d*-TALOSE 1, 2 ORTHOMETHYLACETATE

A solution of 3.6 g of bromo-tetra-acetyl talose in 36 ml of dry methyl alcohol was shaken with 3.5 g of silver carbonate for 1¼ hours in an ice bath. The solution was treated with decolorizing carbon, filtered, evaporated, and diluted with water. Crystals appeared and after separation weighed 0.77 g. Ethyl alcohol and hot water were found to decompose the material. From the alcohol, however, the crystals appear as irregular hexagonal and pentagonal plates. Benzene was found to be the best medium for recrystallization.

After one recrystallization from benzene the melting point was 91.5 to 92.5° C and the values of the optical rotation as measured in chloroform are given in table 10.

TABLE 10.—Optical rotation of triacetyl-*d*-talose 1,2-orthomethylacetate in chloroform

Time	Observed rotation <sup>a</sup>	Specific rotation <sup>b</sup>
	°S <sup>a</sup>	[α] <sub>D</sub> <sup>20</sup>
15.5 min.....	0.18	3.7
156. min.....	.11	2.2
19. hr.....	.11	2.2

<sup>a</sup> Average of 10 or more readings.<sup>b</sup> 32.0 mg of material made up to a volume of 0.9321 ml and read in a 0.5-dm tube.

**Acetyl analysis.**—A 0.0323-g sample was hydrolyzed at 0° C with 20 ml of 0.025 *N* barium hydroxide solution during a period of 24 hours (blanks containing only barium hydroxide solution were run under the same conditions). The solution was then titrated with 0.0291 *N* hydrochloric acid (carbon dioxide-free). Found: Acetyl 9.12 ml of 0.0291 *N* Ba(OH)<sub>2</sub> per 32.3 mg. Calculated for three acetyl groups: 9.19 ml.

**Analysis by microcombustion.**—Calculated for C<sub>15</sub>H<sub>22</sub>O<sub>10</sub>: C, 49.70; H, 6.12. Found: C (micro), 49.89; H (micro), 6.12.

7. α-TETRA-ACETYL-*d*-TALOSE

To 2.2 g of silver benzoate suspended in 25 ml of moist acetone and cooled to -4° C there was added 2 g of bromo-tetra-acetyl talose. After shaking for 1½ hours the suspension was filtered through charcoal. The filtrate which showed a negative Beilstein test for halogen was evaporated. The sirup was taken up with benzene and allowed to crystallize. A total of 0.8 g of crystalline material was obtained, which appeared as hexagonal prisms. From the mother liquors there was separated by extraction with hot petroleum ether 0.1 g of benzoic acid, mp 122° C.

After one recrystallization of the material from hot water, the melting point was 112 to 113° C and the initial rotation in purified chloroform (cp) was [α]<sub>D</sub><sup>20</sup>=42.8 (0.2016 g made up to 10 ml read 4.98° S in a 2-dm tube). The mutarotation in pyridine is given in table 11. This substance crystallizes very readily and was obtained

TABLE 11.—Mutarotation of tetra-acetyl-*d*-talose in pyridine

(0.1888 g made up to 10 ml and read in a 2-dm tube)

Time	Observed rotation	Specific rotation	<sup>a</sup> k <sub>1</sub> +k <sub>2</sub>
<i>Minutes</i>	°S <sup>b</sup>	[α] <sub>D</sub> <sup>20</sup>	
4.8	7.16	65.6	(0.0062)
9.8	7.11	65.2	
30.6	7.06	64.7	
61.4	6.91	63.4	
88.4	6.84	62.7	
239.7	6.60	60.5	(.0029)
319.5	6.52	59.8	
∞	6.43	59.0	
Average.....			0.0029

<sup>a</sup> Calculated from the first-order equation:

$$k_1 + k_2 = \frac{1}{t} \log \frac{r_0 - r_\infty}{r_t - r_\infty}$$

<sup>b</sup> Average of 5 or more readings.

in several other ways. It was separated (1) from mother liquors of bromo-tetra-acetyl talose which had decomposed; (2) from the products of reaction of silver acetate and bromo-tetra-acetyl talose in glacial acetic acid; and (3) from mother liquors of the triacetyl-*d*-talose 1,2-orthomethylacetate preparation and recrystallization. *Analysis*.—Calculated for  $C_6H_8O_6(COCH_3)_4$ : C, 48.25; H, 5.79; acetyl, 6.87 ml of 0.05 *N* NaOH per 29.9 mg. Found: C (micro), 48.15; H (micro), 5.79; acetyl (after hydrolysis with 0.05 *N* NaOH for 4½ hours at 20° C), 7.02 ml.

### 8. METHYL TALOSIDES

A solution of 5 g of talose in 75 ml of absolute methyl alcohol containing 1.52 percent of hydrogen chloride was refluxed for 8 hours. After the hydrogen chloride had been removed with the aid of silver carbonate, the solution was treated with Norit, filtered, and evaporated but it did not crystallize.

The mixture was then acetylated at 0° C with acetic anhydride in the presence of pyridine. The sirup was distilled in a high vacuum (about 0.01 mm); practically all of it volatilized at 100 to 115° C and appeared in the distillate. The colorless purified material did not crystallize.

## VI. SUMMARY

The preparation and properties of the new crystalline sugar,  $\beta$ -*d*-talose, is reported. It is shown that *d*-talose resembles mannose in that the value of Hudson's  $2A$  is 9,870 and in that it forms orthoester derivatives. The mutarotation, however, is similar to that of galactose since  $\beta$ -*d*-talose mutarotates at a rate initially slower and  $\alpha$ -*d*-talose initially faster than that for a first-order reaction. Bromine oxidation data show that  $\beta$ -*d*-talose is oxidized more rapidly than  $\alpha$ -*d*-talose and that the new beta isomer is a homogeneous substance.

A crystalline monobenzoyl talose has been separated from the products obtained by the oxidation of galactal with perbenzoic acid. The unusual properties of this substance indicate that it may have an orthobenzoic acid structure.

Crystalline  $\alpha$ -penta-acetyl-*d*-talose, tetra-acetyl-*d*-talose, and 1-bromo-tetra-acetyl-*d*-talose are reported. The 1-bromo-tetra-acetyl-*d*-talose reacts with methyl alcohol in the presence of silver carbonate to give an orthoester derivative, triacetyl-*d*-talose 1, 2-orthomethylacetate. The properties of this substance are compared with those of other orthoesters and the factors responsible for this type of isomerism are discussed.

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