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ALPHA AND BETA METHYL LYXOSIDES, MANNOSIDES, GULOSIDES, AND HEPTOSIDES OF LIKE CONFIGURATION[1]

By Horace S. Isbell and Harriet L. Frush

ABSTRACT

Eleven new sugar derivatives and numerous optical rotation and hydrolysis measurements are reported. A comparison of the alpha and beta methyl glucosides, mannosides, galactosides, and gulosides shows that the configurations of all of the asymmetric carbons in the pyranose ring affect the rate of hydrolysis, and that there is no fixed relationship between the configuration of the glycosidic carbon and the relative rates for the hydrolysis of the alpha and beta modifications. The configuration of carbon 3 appears to influence markedly the relative rates for the hydrolysis of the alpha and beta modifications. Aldo-pyranosides having *trans* configurations for carbons 1 and 3 are hydrolyzed more slowly than the corresponding modifications having *cis* configurations for carbons 1 and 3. This unexpectedly large influence of carbon 3, and the close resemblance of each pentose to the corresponding hexose which has the *trans* configuration for carbons 3 and 5 are discussed in relation to the spacial arrangement of the whole molecule. The similarity of the methyl gulosides and α-glucoheptosides on the one hand, and the methyl lyxosides, mannosides, and α-galaheptosides on the other hand, furnishes a substantial basis for the allocation of lyxose to the mannose series.

CONTENTS

[1] This paper was read before the Division of Sugar Chemistry and Technology of the American Chemical Society at Baltimore, Md., April 1939.

I. STRUCTURAL AND CONFIGURATIONAL RELATIONSHIPS FOR THE PENTOSES, HEXOSES, AND HEPTOSES

In previous publications [1, 2, 3],[2] the similarity of substances which have like configurations for the five carbons comprising the pyranose ring has been stressed. The object of the present investigation was to provide additional information to correlate sugars having like configuration for atoms comprising the pyranose ring and to determine to what extent the properties of the glycosides depend on the configurations of the several asymmetric carbons of the pyranose ring. In the pyranose series, the different configurations for the first carbon give rise to the alpha and beta isomers, while the different configurations for carbons 2, 3, 4, and 5 give rise to the various sugars. These sugars may be considered in eight groups, according to whether their ring configuration corresponds to that of glucose, mannose, galactose, talose, gulose, idose, allose, or altrose. The heptoses and higher sugars differ from the hexoses merely in the number and in the stereoisomeric arrangement of the atoms in the side chain, while the pentoses differ from the hexoses in that the CH_2OH group is replaced by hydrogen. Since the fifth carbon is not asymmetric in the pentose series, each pentose is configurationally related to two hexoses, which differ in the arrangement of the groups attached to carbon 5. Thus *d*-xylose is related to *d*-glucose and *l*-idose; *l*-arabinose is related to *d*-galactose and *l*-altrose; *d*-lyxose is related to *d*-mannose and *l*-gulose; and *l*-ribose is related to *d*-talose and *l*-allose. These relationships are illustrated by the accompanying projectional formulas. The marked resemblance in the properties of xylose and arabinose to those of glucose and galactose, respectively, has been shown by much experimental work and noted by numerous investigators. In order to account for this resemblance, one of us suggested that the pentose molecule as a whole is dissymmetric, and that the pyranose ring in *l*-arabinose for some reason takes a form which resembles a *d*-galactose ring [1, 2], and that the pyranose rings of *d*-xylose, *d*-lyxose, and *l*-ribose, respectively resemble the rings of *d*-glucose, *d*-mannose, and *d*-talose more closely than they resemble the rings of *l*-idose, *l*-gulose, and *l*-allose. The classification of *l*-arabinose with *d*-galactose and of *d*-xylose with *d*-glucose is supported by considerable experimental work, but since relatively few data were available for lyxose and ribose, an investigation of substances configurationally related to lyxose and ribose was begun in this laboratory.

A survey of the literature concerning the methyl glycopyranosides of the lyxose, mannose, and gulose series reveals that the glycosides configurationally related to α-methyl *d*-lyxoside (or the mirror images in the case of the heptosides and gulosides) have been crystallized and their properties studied, while the glycosides configurationally related to β-methyl *d*-lyxoside, with the exception of α-methyl *d*-guloside, have not been crystallized. Inasmuch as some of these compounds have been considered key substances in the problems of sugar structure, their crystallization has been attempted by a number of previous workers, but without success. In the course of this investigation we have prepared a series of methyl glycosides having the methyl lyxoside structure so that we have for comparison the α- and β-methyl *d*-lyxosides, *d*-mannosides, *d*-gulosides, *d*-α-galaheptosides, and *d*-α-gluco-

[2] Figures in brackets indicate the literature references at the end of this paper.

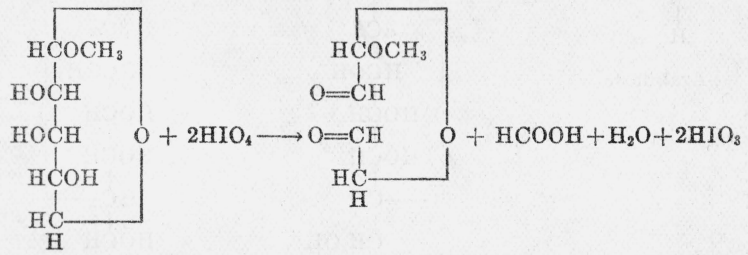
heptosides. Nine of these compounds were obtained in the crystalline state, while β-methyl *d*-α-galaheptoside was prepared as a pure sirup. The heretofore unknown β-methyl *d*-lyxoside was crystallized from the mother liquor which remained after the preparation of α-methyl *d*-lyxoside by Fischer's hydrogen chloride method. β-Methyl *d*-mannoside was obtained as a crystalline isopropyl alcoholate, while α-methyl *d*-α-glucoheptoside was crystallized through the intermediate use of a crystalline calcium compound by the process originated by Isbell [4] for the preparation of the methyl gulosides. The tendency of the members of the lyxose, mannose, and gulose series to form crystalline calcium chloride compounds was shown further by the preparation of crystalline calcium chloride compounds of α-methyl *d*-lyxoside, β-methyl *d*-α-glucoheptoside, and β-methyl *d*-mannoside. Several of the glycosides were separated as acetates, which were deacetylated by Isbell's barium methylate method [5]. The new compounds are listed in table 1.

TABLE 1.—*New compounds prepared in this investigation*

Substance	Experimental results		Solvent	Concentration	Formula
	Melting point	Specific rotation $[\alpha]_D^{20}$			
	°C			Percent	
β-Methyl *d*-lyxopyranoside	118	−128.1	H_2O	2.5	$C_6H_{12}O_5$
β-Methyl triacetyl-*d*-lyxopyranoside	88 to 89	−109.5	$CHCl_3$	4.5	$C_{12}H_{18}O_8$
β-Methyl *d*-mannopyranoside	(a)	−69.8	H_2O	3	$C_7H_{14}O_6$
β-Methyl *d*-mannopyranoside.C_3H_8O	74 to 75	−53.3	H_2O	4	$C_{10}H_{22}O_7$
α-Methyl *d*-α-glucoheptopyranoside	106 to 107	+111.5	H_2O	4	$C_8H_{16}O_7$
α-Methyl penta-acetyl-*d*-α-glucoheptopyranoside.	174 to 175	+107.4	$CHCl_3$	1	$C_{18}H_{26}O_{12}$
β-Methyl *d*-α-galaheptopyranoside	(a)	+74	H_2O	2.8	$C_8H_{16}O_7$
β-Methyl penta-acetyl-*d*-α-galaheptopyranoside.	171 to 173	+77.6	$CHCl_3$	4	$C_{18}H_{26}O_{12}$
α-Methyl *d*-β-galaheptopyranoside	154 to 155	−108	H_2O	4	$C_8H_{16}O_7$
α-Methyl *d*-lyxopyranoside.$CaCl_2$.$2H_2O$.		+31.2	H_2O	5	$C_6H_{12}O_5.CaCl_2.2H_2O$
α-Methyl *d*-α-glucoheptopyranoside.$CaCl_2.H_2O$.		+69.1	H_2O	4	$C_8H_{16}O_7.CaCl_2.H_2O$
(β-Methyl *d*-α-glucoheptopyranoside)$_2$.$CaCl_2.2H_2O$.		−56.1	H_2O	4	$(C_8H_{16}O_7)_2.CaCl_2.2H_2O$

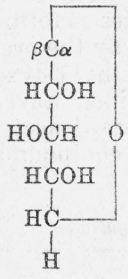
[a] Sirup.

The structure of our new β-methyl *d*-lyxoside was determined by the application of the periodic oxidation method of Jackson and Hudson [6]. As shown by Maclay and Hudson [7], α-methyl *d*-lyxopyranoside is oxidized by periodic acid according to the following equation:

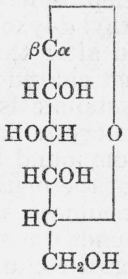


α-Methyl *d*-lyxopyranoside *d*-Methoxy-diglycolic aldehyde

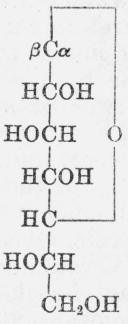
FORMULAS FOR CONFIGURATIONALLY RELATED SUBSTANCES [2]



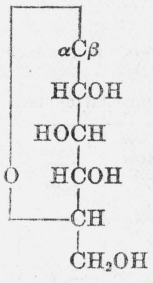
d-Xylose



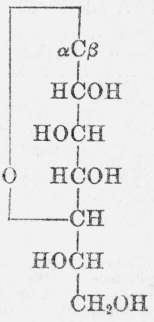
d-Glucose



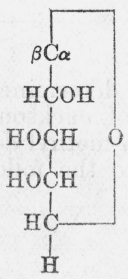
l-β-Galaheptose



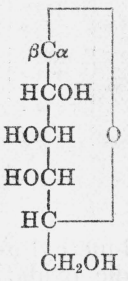
l-Idose



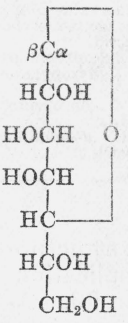
l-β-Glucoheptose



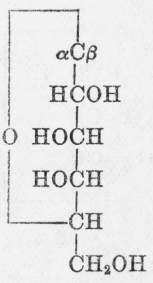
l-Arabinose



d-Galactose



d-α-Mannoheptose

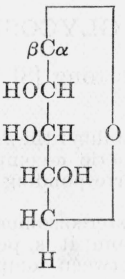


l-Altrose

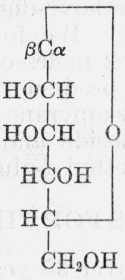
d-β-Guloheptose

[2] In the alpha modification the functional group (OH, CH_2O, etc.) lies in the position represented by alpha, with a hydrogen atom saturating the remaining valence of the carbon atom. In the beta modification, the functional group lies in the position represented by beta.

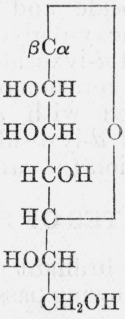
FORMULAS FOR CONFIGURATIONALLY RELATED SUBSTANCES—Continued



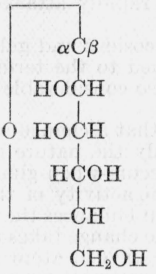
d-Lyxose



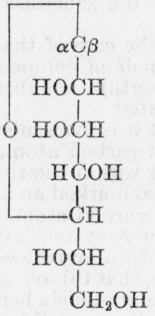
d-Mannose



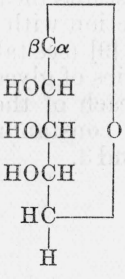
l-α-Galaheptose



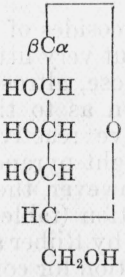
l-Gulose



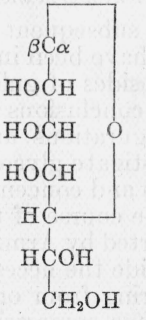
l-α-Glucoheptose



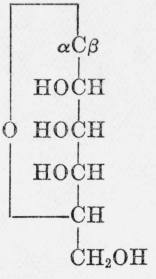
l-Ribose



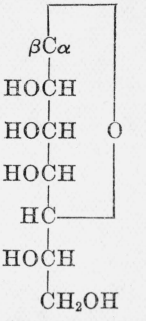
d-Talose



d-β-Mannoheptose



l-Allose



l-α-Guloheptose

From the results reported by Jackson and Hudson, one would expect β-methyl *d*-lyxoside to follow the same course as α-methyl *d*-lyxopyranoside and to give *l*-methoxy-diglycolic aldehyde instead of *d*-methoxy-diglycolic aldehyde. We found experimentally that β-methyl *d*-lyxoside reacts with 2 moles of periodic acid, and that the optical rotation of the reaction product differs merely in sign from that obtained with α-methyl *d*-lyxopyranoside. This proves that β-methyl *d*-lyxoside is a pyranoside and that it has the same configuration for carbon 1 as β-methyl *d*-glucopyranoside.

II. RATES OF HYDROLYSIS FOR THE METHYL GLYCOSIDES

In a brilliant contribution over 35 years ago, Armstrong [8] wrote the following passage:

> It will be noticed that the various hexosides vary widely in stability: the β-glucosides undergoing hydrolysis more rapidly than the stereoisomeric α-compounds whilst the galactosides are more rapidly attacked than the corresponding glucosides.
>
> In the case of the α- and β-glucosides and galactosides, the stereoisomerism in each pair of compounds is confined to the terminal carbon atom; it is, perhaps, noteworthy that there should be so considerable a difference between compounds so related.
>
> But it is even more surprising that a change in the general configuration at the fourth carbon atom, affecting only the nature of the attachment of the oxygen atoms within the ring, such as occurs when glucose passes into galactose, should have so marked an influence on the activity of the group associated with the terminal carbon atom. Such a result enhances the probability of the conclusion that the active system within which the change takes place is formed by the association of acid-water molecules with the oxygen atom in the pentaphane ring; in other words, that this oxygen atom is the attractive center.
>
> The argument here made use of renders it desirable that the behavior of the isomeric mannosides towards acids should also be studied in order that it may be possible eventually to define more or less accurately the functions of the different oxygen atoms in the molecule.

In subsequent years the glycosides of glucose, mannose, and galactose have been investigated, but very little work has been done on the glycosides of gulose, idose, allose, altrose, and talose. Before extensive conclusions can be drawn as to the relationships between the configurations and the relative reactivity, it will be necessary to investigate glycosides of all eight pyranose types at several temperatures and concentrations. However, the velocity constants measured in the course of this investigation (table 2) in conjunction with those reported by Armstrong [8] and by Riiber and Sørensen [9] (see table 3) provide the necessary information for comparing a series of glycosides differing from one another in the configurations of each of the five carbons comprising the pyranose ring. The velocity constants used for the comparisons which follow are given in tables 2 and 3.

TABLE 2.—*Velocity constants*

Substance	0.05 *N* HCl at 98° C	0.5 *N* HCl [1] at 75° C
α-Methyl *d*-lyxopyranoside	0. 00374	0. 00286
β-Methyl *d*-lyxopyranoside	. 0135	
α-Methyl *d*-mannopyranoside	. 00069	. 000471
β-Methyl *d*-mannopyranoside (isopropyl alcoholate)	. 00167	. 00113
α-Methyl *d*-gulopyranoside (hydrate)	. 0125	. 0115
β-Methyl *d*-gulopyranoside	. 00576	. 00377
α-Methyl *d*-α-glucoheptopyranoside	. 00486	. 00417
β-Methyl *d*-α-glucoheptopyranoside	. 00219	. 00132
α-Methyl *d*-α-galaheptopyranoside	. 000381	
β-Methyl *d*-α-galaheptopyranoside	. 000860	
α-Methyl *d*-β-galaheptopyranoside	. 000166	

[1] The measurements were made as described on page 149. The velocity constants were calculated from the equation for a first-order reaction and are expressed in Briggs logarithms and in minutes.

TABLE 3.—*Velocity constants reported by Riiber and Sørensen [11]*

Substance	Velocity constants [1]		Reference
	0.01 *N* HCl at 100° C	0.5 *N* HCl at 75° C	
α-Methyl glucopyranoside	0. 000066	0. 000198	[8]
β-Methyl glucopyranoside	. 000137	. 000379	[8]
α-Methyl xylopyranoside		. 00090	[9]
β-Methyl xylopyranoside		. 0018	[9]
α-Methyl galactopyranoside		. 00104	[8]
β-Methyl galactopyranoside		. 00183	[8]
α-Methyl arabinopyranoside		. 0018	[9]
β-Methyl arabinopyranoside		. 0026	[9]
α-Methyl rhamnopyranoside	. 00055		[9]
β-Methyl rhamnopyranoside	. 00125		[9]
α-Methyl mannopyranoside	. 000137		[9]
β-Methyl mannopyranoside	. 00021		[10]

[1] The velocity constants were calculated from the equation for a first-order reaction and are expressed in Briggs logarithms and in minutes.

TABLE 4.—*Effect of configuration on rate of hydrolysis of the hexopyranosides*

[0.5 *N* HCl at 75° C]

Substances differing on—	Substances	*k*/*k*′
Carbon 1	β-Methyl *d*-glucoside:α-methyl *d*-glucoside	1. 91
	β-Methyl *d*-mannoside:α-methyl *d*-mannoside	2. 40
	β-Methyl *d*-galactoside:α-methyl *d*-galactoside	1. 76
	β-Methyl *d*-guloside:α-methyl *d*-guloside	0. 33
Carbon 2	α-Methyl *d*-mannoside:α-methyl *d*-glucoside	2. 38
	β-Methyl *d*-mannoside:β-methyl *d*-glucoside	2. 98
Carbon 3	α-Methyl *d*-guloside:α-methyl *d*-galactoside	11. 06
	β-Methyl *d*-guloside:β-methyl *d*-galactoside	2. 06
Carbon 4	α-Methyl *d*-galactoside:α-methyl *d*-glucoside	5. 25
	β-Methyl *d*-galactoside:β-methyl *d*-glucoside	4. 83
Carbon 5	α-Methyl *l*-guloside [1]:β-methyl *d*-mannoside	10. 18
	β-Methyl *l*-guloside [1]:α-methyl *d*-mannoside	8. 00

[1] Measurement made on enantiomorphic substance.

TABLE 5.—*Effect of the configuration of carbon 3 on the rates of hydrolysis of the alpha and beta modifications of the methyl glycopyranosides*

Substance	Velocity constants (0.05 *N* HCl at 98° to 100° C)		$\frac{k_{trans}}{k_{cis}}$	Velocity constants (0.5 *N* HCl at 75° C)		$\frac{k_{trans}}{k_{cis}}$
	Cis modification on carbons 1 and 3	*Trans* modification on carbons 1 and 3		*Cis* modification on carbons 1 and 3	*Trans* modification on carbons 1 and 3	
Methyl *d*-glucopyranosides				0.000379	0.000198	0.52
Methyl *d*-xylopyranosides				.0018	.00090	.50
Methyl *d*-galactopyranosides				.00183	.00104	.57
Methyl *l*-arabinopyranosides				.0026	.0018	.69
Methyl *d*-mannopyranosides	0.00167	0.00069	0.41	.00113	.000471	.42
Methyl *d*-lyxopyranosides	.0135	.00374	.28			
Methyl *d*-α-galaheptopyranosides	.000860	.000381	.44			
Methyl *d*-gulopyranosides	.0125	.00576	.46	.0115	.00377	.33
Methyl *d*-α-glucoheptopyranosides	.00486	.00219	.45	.00417	.00132	.32

Previous investigators have shown that the beta methyl *d*-glucosides, *d*-mannosides, *d*-galactosides, *d*-xylosides, and *l*-arabinosides are hydrolyzed slightly more rapidly than the corresponding alpha isomers. From these results the concept arose that all beta glycosides are hydrolyzed more rapidly than the corresponding alpha glycosides, although the earlier work was based on only three of the eight pyranose types (glucose, galactose, and mannose). In this investigation we have extended the work to include the gulose pyranose type. Much to our surprise, α-methyl *d*-guloside and α-methyl *d*-α-glucoheptoside, which has the α-methyl *d*-guloside structure, were found to be hydrolyzed more rapidly than the corresponding beta isomers. It may be observed from the ratios given in table 4 that the alpha and beta glycosides of the same sugar usually differ less in rate of hydrolysis than do the glycosides of the separate sugars. In other words, the configuration of the first carbon is not the principal factor for determining the rate of hydrolysis. This is in marked contrast to the results obtained by the oxidation of the free sugars with bromine water, in which process the configuration of the first carbon is the predominating factor for determining the rate of the reaction [1, 2]. Since the mannosides differ from the glucosides in the configuration of carbon 2, the effect of the configuration of this carbon on the rates of hydrolysis is shown by comparing the methyl *d*-mannosides with the methyl *d*-glucosides. Likewise, the effect of the configurations of carbons 3, 4, and 5 is shown by comparing the methyl *d*-gulosides with the *d*-galactosides, methyl *d*-galactosides with the *d*-glucosides, and the methyl *l*-gulosides with the *d*-mannosides. The results of such comparisons clearly show that the configurations of carbons 2, 3, 4, and 5 separately and jointly affect the rate of hydrolysis. The configuration of carbon 5 appears to be particularly important in relation to the rate of hydrolysis. Also, the relationship between the configuration of carbon 3 and the rates of hydrolysis for the alpha and beta modifications is noteworthy. As may be observed by comparison of the projectional formulas with the relative rates of hydrolysis given in table 5, the modifications of the methyl pyranosides which have *trans* configurations for carbons 1 and 3 are hydrolyzed more

slowly than the corresponding modifications which have *cis* configurations.[3] That is, reversing the configuration of carbon 3 in the galactose series to give substances in the gulose series results in a change in the relative stability of the alpha and beta isomers towards acid hydrolysis. As may be noted from a space model, carbon 3 lies opposite the oxygen of the ring and its attached groups appear to be in a particularly favorable position to influence the conformation of the ring. Perhaps this accounts for the unexpectedly large influence of the configuration of carbon 3 on the relative reactivities of the alpha and beta modifications. Another observation, which may depend on the effect of the configuration of carbon 3, is that in the pentose series where the ring-forming carbon is not asymmetric, each pentose resembles the hexose in which carbons 3 and 5 have opposite configurations.

TABLE 6.—*Effect of the group R, attached to carbon 5, on the rates of hydrolysis for methyl pyranosides* [1]

Substance	Heptoside		Hexoside		Methyl pentoside		Pentoside	
	R=CH(OH)CH_2OH	Relative rate [2]	R=CH_2OH	Relative rate [2]	R=CH_3	Relative rate [2]	R=H	Relative rate [2]
α-Methyl	α-Galaheptoside*	0.55	Mannoside	1	Rhamnoside*	4.01	Lyxoside	6.07
β-Methyl	do.*	.51	do	1	do.*	5.95	do.*	8.08
α-Methyl	β-Galaheptoside*	3.50	Glucoside	1			Xyloside	4.55
β-Methyl			do	1			do	4.75
α-Methyl			Galactoside	1			Arabinoside	1.73
β-Methyl			do	1			do	1.42
α-Methyl	α-Glucoheptoside	.36	Guloside	1			Lyxoside [4*]	1.08
β-Methyl	do	.35	do	1			do.[5*]	0.65

[1] The results are based on comparable measurements at 75° C with the exception of those marked with an asterisk, which are based on comparable measurements at either 98° or 100° C.
[2] The velocity constant for the hydrolysis of the glycoside divided by the velocity constant of the configurationally related hexosides under like conditions.
[3] Since the measurements for α-methyl *d*-glucoside and α-methyl *d*-β-galaheptoside were made in 0.01 *N* and in 0.05 *N* HCl, respectively, the velocity constants were reduced to a comparable basis by use of the relative activity of the two solutions as estimated from the rates of hydrolysis of α-methyl *d*-mannoside.
[4] β-Methyl lyxoside is compared with α-methyl guloside, to which it is configurationally related.
[5] α-Methyl lyxoside is compared with β-methyl guloside, to which it is configurationally related.

As noted by Riiber and Sørensen [9], the methyl pentosides are hydrolyzed more rapidly than the methyl hexosides. Our comparisons, given in table 6, show that the methyl arabinosides are hydrolyzed about 1½ times as rapidly as the methyl galactosides and that the xylosides are hydrolyzed about 5 times as rapidly as the glucosides. Judging from these values, one would expect the lyxosides to be hydrolyzed considerably more rapidly than the configurationally related hexosides. Our experimental results reveal that the lyxosides are hydrolyzed on the average about 7 times as rapidly as the mannosides and only eight-tenths as rapidly as the gulosides. Since the rhamnosides are hydrolyzed about 5 times as rapidly as the configurationally related mannosides, the comparisons clearly indicate that the lyxosides should be classified in the mannose series. The classification of the lyxosides in the mannose series is supported by their optical rotations, which are discussed in the next section of this paper.

[3] This generalization is based on data which include four of the eight pyranose types. Obviously, it would be of interest to ascertain whether this relationship between rate of hydrolysis and configuration also applies to glycosides having the allose, altrose, idose, and talose configurations.

III. COMPARISON OF MOLECULAR ROTATIONS

1. ROTATIONAL DIFFERENCE FOR THE ALPHA AND BETA ISOMERS

The optical rotations of our new compounds, in conjunction with values to be found in the literature, provide data for many interesting comparisons. In making the comparisons which follow, the numerical values for the optical rotations recorded in table 7 were used.

A comparison of the optical rotations provides a simple and convenient method for the correlation of the alpha and beta methyl pentosides with the configurationally related methyl hexosides. If the molecular rotations of the alpha and beta modifications be considered as $+A+B$ and $-A+B$. the difference in the molecular rotations is Hudson's $2A$ [4] [11]. As may be observed from the data given in table 8, the difference in the molecular rotations of the α- and β-methyl *d*-lyxosides (+30,800) agrees more closely with the differences found for the methyl *d*-mannosides (+28,900) and *d*-α-galaheptosides (+32,300) than with the differences found for the methyl *d*-gulosides (+39,400) and *d*-α-glucoheptosides (+41,800). A similar relationship is apparent in the differences for the corresponding acetylated glycosides. As pointed out more fully on page 147, the α-methyl penta-acetyl-*d*-α-glucoheptoside prepared by us differs in optical rotation and melting point from that prepared by Haworth, Hirst, and Stacey [12]. Possibly one of the compounds is not pure, but it is noteworthy that the value of $2A$ (+53,600) for the acetylated *d*-α-glucoheptosides obtained by using the rotation of our α-methyl penta-acetyl-*d*-α-glucoheptoside agrees with the values obtained for the acetylated methyl *d*-glucosides (+53,900), *d*-xylosides (+52,400), and *d*-galactosides (+53,100). The value (+46,500) obtained by using the rotation of Haworth, Hirst, and Stacey's α-methyl penta-acetyl-*d*-α-glucoheptoside agrees with the value obtained from the acetylated methyl *d*-gulosides (+46,900). Probably the agreements in the values just noted are accidental, but possibly the two α-methyl penta-acetyl-*d*-α-glucoheptosides are definite compounds which differ in the conformation of the ring, or in some other unknown manner. One of these compounds may be structurally analogous to the acetylated methyl *d*-glucoside, while the other may be analogous to the acetylated methyl *d*-guloside. These compounds may comprise a pair of substances differing in ring conformation, such as the strainless ring isomers first mentioned by Haworth in 1929 [13], and suggested by Isbell in 1937 [1] as an explanation for the differences in the optical rotational relationships in the mannose and glucose series. More recently other investigators have recognized the possibility of different ring conformations for the pyranoid ring [14, 15].

[4] If the value of $2A$ is obtained by subtracting the molecular rotation of the glycoside having the methoxyl group on the left (in the Fischer projectional formula) from the rotation of the modification which differs by having the glycosidic methoxyl on the right, the value of $2A$ is positive for all known alpha-beta pairs.

TABLE 7.—*Optical rotations used for the comparison of the molecular rotations*

	α-Modification			β-Modification		
	$[\alpha]_D^{20}$	$[M]$ Initial	Reference	$[\alpha]_D^{20}$	$[M]$ Initial	Reference
SUGARS						
l-Arabinose	+190.6	+28,610	[2]	[1]+34.7	+11,560	[2]
l-Ribose				+20.3	+3,050	[2]
d-Xylose	+93.6	+14,050	[2]	−20	−3,000	[16]
d-Lyxose	+5.6	+840	[2]	−72.6	−10,900	[2]
d-Glucose	+112.2	+20,210	[2]	+18.7	+3,370	[2]
d-Mannose	+29.3	+5,280	[2]	−17.0	−3,060	[2]
d-Galactose	+150.7	+27,150	[2]	+52.8	+9,510	[2]
d-Talose	+68.0	+12,250	[2, 17]	+13.2	+2,380	[2, 17]
l-Allose				−1.90	−350	[18]
l-Altrose				−28.75	−5,180	[18]
d-Gulose	+61.6	+11,100	[19]			
d-α-Glucoheptose				−28.7	−6,030	[1]
d-β-Glucoheptose				−0.1	−20	[1, 20]
d-α-Galaheptose	[2]−25.2	−5,750	[1]			
d-β-Galaheptose				−19.2	−4,040	[1]
d-α-Mannoheptose	[2]+120.0	+27,380	[1]			
d-β-Mannoheptose	[2]+45.7	+10,430	[21]			
d-α-Guloheptose	−45.7	−9,600	[22]			
d-β-Guloheptose	−120.5	−25,330	[1]			
GLYCOSIDES						
Methyl *l*-arabinosides	+245.5	+40,300	[23]	+17.3	+2,840	[23]
Methyl *d*-xylosides	+153.9	+25,260	[23]	−65.5	−10,750	[23]
Methyl *d*-lyxosides	+59.4	+9,750	[24]	−128.1	−21,030	[New]
Methyl *d*-glucosides	+158.9	+30,860	[25]	−34.2	−6,640	[25]
Methyl *d*-mannosides	+79.2	+15,380	[26]	[3]−53.3	−13,550	[New]
Methyl *d*-galactosides	+196.6	+38,180	[27]	0	0	[28]
Methyl *d*-gulosides	[2]+109.4	+23,210	[4]	−83.3	−16,180	[4]
Methyl *d*-α-glucoheptosides	+111.5	+25,000	[New]	−74.9	−16,800	[28]
Methyl *d*-α-galaheptosides	−70.2	−15,700	[29]	[4]+74	+16,600	[New]
Methyl *d*-β-galaheptosides	−108	−24,200	[New]	+36.0	+8,100	[30]
ACETYLATED GLYCOSIDES						
Methyl triacetyl-*d*-xylosides	+119.6	+34,720	[31]	−60.8	−17,650	[32]
Methyl triacetyl-*d*-lyxosides	+30.1	+8,740	[33]	−109.5	−31,780	[New]
Methyl tetra-acetyl-*d*-glucosides	+130.5	+47,280	[34]	−18.2	−6,590	[34]
Methyl tetra-acetyl-*d*-mannosides	+49.1	+17,790	[35]	−50.4	−18,260	[35]
Methyl tetra-acetyl-*d*-galactosides	+132.5	+48,000	[36]	−14.0	−5,070	[37]
Methyl tetra-acetyl-*d*-gulosides	+97.3	+35,250	[4]	−32.1	−11,630	[4]
Methyl penta-acetyl-*d*-α-glucoheptosides	+107.4	+46,650	[New]	−16	−6,950	[12]
Methyl penta-acetyl-*d*-α-glucoheptoside (Haworth)	+91	+39,500	[14]			
Methyl penta-acetyl-*d*-α-galaheptosides	−20.4	−8,860	[29]	+77.6	+33,700	[New]

[1] Rotation of β-*l*-arabinose.$CaCl_2.4H_2O$.
[2] Rotation of hydrate.
[3] Rotation of β-methyl *d*-mannoside isopropyl alcoholate.
[4] Rotation of sirup.

TABLE 8.—*Difference in the molecular rotations of the alpha and beta isomers*

Substance	Differences in the molecular rotations $(+A+B)-(-A+B)=2A$					
	Sugars		Methyl glycosides		Acetylated glycosides	
	$2A$	Reference [1]	$2A$	Reference [1]	$2A$	Reference [1]
d-Lyxose	+11,700	[38]	[2]+30,800		[2]+40,500	
d-Mannose	+8,300	[10]	[2]+28,900		+36,100	[39]
d-α-Galaheptose			[2]+32,300		[2]+42,600	
d-Gulose			+39,400	[4]	+46,900	[4]
d-α-Glucoheptose			[2]+41,800		+53,600	
d-α-Glucoheptose (Haworth, Hirst, and Stacey)					+46,500	[12]
d-Glucose	+16,800	[11]	+37,500	[11]	+53,900	[31]
d-Xylose			+36,000	[11]	+52,400	[31]
d-Galactose	+17,600	[11]	+38,200	[11]	+53,100	[31]

[1] Some of the values given in this table are based on more recent optical measurements (table 7) than the original values given in the references cited.
[2] Values calculated for the first time from optical rotations of new compounds reported in this paper.

2. COMPARISONS OF THE MOLECULAR ROTATIONS OF EPIMERIC SUBSTANCES

If the molecular rotations of two epimeric substances are $(B+R_2)$ and $(B-R_2)$, the difference in the molecular rotations is $2R_2$, which Hudson has called the "epimeric difference" [40]. The value of $2R_2$ is obtained by subtracting the molecular rotation of the substance having the hydroxyl of the second carbon on the left (in the Fischer projectional formula) from the molecular rotation of the substance which differs by having the hydroxyl of the second carbon on the right. The value for the rotation at carbon 2 is influenced by the configurations of the adjacent carbon atoms [41]. There are four possible arrangements for the adjacent carbon atoms 1 and 3:

Group 1. Hydroxyl of carbon 3 *trans* to an α hydroxyl on carbon 1.
Group 2. Hydroxyl of carbon 3 *cis* to a β hydroxyl on carbon 1.
Group 3. Hydroxyl of carbon 3 *trans* to a β hydroxyl on carbon 1.
Group 4. Hydroxyl of carbon 3 *cis* to an α hydroxyl on carbon 1.

As shown by comparisons in table 9, the members of group 1 give epimeric differences of approximately +1,500; the members of group 2 give about +8,000; and the members of group 3 give about +5,000. Data are not available for calculating epimeric differences for substances of group 4. This group would be represented by α-allose and α-altrose, or by α-gulose and α-idose. The epimeric differences for the glycosides do not differ greatly from those for the free sugars, but differ considerably from the epimeric differences found for the acetylated glycosides.

TABLE 9.—*Differences in the molecular rotations of epimeric sugars, glycosides and acetylated methyl glycosides* [1]

Epimeric differences. $(B+R_2)-(B-R_2)=2R_2$	Sugars. $2R_2$	Methyl glycosides. $2R_2$	Acetylated methyl glycosides. $2R_2$
GROUP 1			
α-*d*-Glucose—α-*d*-mannose	+14,900	+15,500	+29,500
α-*d*-Galactose—α-*d*-talose	+14,900		
α-*d*-Xylose—α-*d*-lyxose	+13,200	+15,500	+26,000
α-*d*-α-Mannoheptose—α-*d*-β-mannoheptose	+17,000		
α-*d*-α-Guloheptose—α-*d*-β-guloheptose	+15,700		
GROUP 2			
β-*d*-Glucose—β-*d*-mannose	+6,400	+6,900	+11,700
β-*d*-Galactose—β-*d*-talose	+7,100		
β-*d*-Xylose—β-*d*-lyxose	+7,900	+10,300	+14,100
β-*d*-α-Galaheptose—β-*d*-β-galaheptose		+8,500	
β-*l*-Arabinose—β-*l*-ribose	+8,500		
GROUP 3			
β-*d*-α-Glucoheptose—β-*d*-β-glucoheptose	−6,000		
β-*l*-Altrose—β-*l*-allose	−4,800		

[1] Calculated from the data given in table 7.

The relationships between the configurations and the epimeric differences just noted can be used for the classification of configurationally related substances. The similarity of the epimeric difference (+13,200) obtained from the rotations of α-*d*-xylose and α-*d*-lyxose to the epimeric difference (+14,900) obtained from α-*d*-glucose and α-*d*-mannose is evidence that α-*d*-xylose and α-*d*-lyxose differ in the same manner as α-*d*-glucose and α-*d*-mannose. The similarity of the epimeric difference (+7,900) from β-*d*-xylose and β-*d*-lyxose to the epimeric difference (+6,400) from β-*d*-glucose and β-*d*-mannose is evidence that β-*d*-xylose and β-*d*-lyxose differ in the same manner as β-*d*-glucose, and β-*d*-mannose. The similarity of the epimeric difference (+8,500) from β-*l*-arabinose and β-*l*-ribose to the epimeric difference (+7,100) from β-*d*-galactose and β-*d*-talose is evidence that β-*l*-arabinose and β-*l*-ribose differ in the same manner as β-*d*-galactose and β-*d*-talose. That is, the epimeric differences for *d*-xylose and *d*-lyxose, and for *l*-arabinose and *l*-ribose show a correlation with the epimeric differences for *d*-glucose and *d*-mannose, and for *d*-galactose and *d*-talose. It is of further interest to compare the epimeric differences obtained for the pentoses with those obtained for substances having the opposite configuration for carbon 5. As may be observed from the formulas, *l*-idose, *l*-altrose, *l*-gulose, and *l*-allose differ in the configuration of carbon 5 from the previously compared hexoses, *d*-glucose, *d*-galactose, *d*-mannose, and *d*-talose. Thus the epimeric pair, *l*-gulose and *l*-idose differ from the glucose mannose pair only in the configuration of carbon 5. Unfortunately the optical rotations of *l*-idose and *l*-gulose are not known, but the optical rotations of the configurationally related epimeric heptoses (β-*l*-β-glucoheptose and β-*l*-α-glucoheptose) are known. The epimeric difference (−6,000) obtained from the optical rotations of β-*l*-β-glucoheptose and β-*l*-α-

glucoheptose differs widely from the epimeric difference (+13,200) obtained from the optical rotations of α-*d*-xylose and α-*d*-lyxose. Hence the optical rotations of these substances having the *l*-gulose and *l*-idose configurations do not appear to be in harmony with the optical rotations in the α-*d*-xylose and α-*d*-lyxose series. The epimeric difference (−4,800) obtained from the molecular rotations of β-*l*-altrose and β-*l*-allose may be compared with the epimeric difference for α-*l*-arabinose and α-*l*-ribose. The molecular rotation of α-*l*-arabinose is +28,610. The molecular rotation of α-*l*-ribose is not known, but it can be estimated from the molecular rotation of β-*l*-ribose.[5] By using the calculated value (+12,500) the epimeric difference for α-*l*-arabinose and α-*l*-ribose is found to be+16,110. This value is in accord with the epimeric difference (+14,900) for α-*d*-galactose and α-*d*-talose but differs widely from the value (−4,800) obtained for β-*l*-altrose and β-*l*-allose. The comparisons which have been cited show that the epimeric differences for *d*-xylose and *d*-lyxose resemble those for *d*-glucose and *d*-mannose rather than those for *l*-idose and *l*-gulose, and that the epimeric differences for *l*-arabinose and *l*-ribose resemble those for *d*-galactose and *d*-talose rather than those for *l*-altrose and *l*-allose.

3. COMPARISONS OF THE MOLECULAR ROTATIONS OF SUBSTANCES DIFFERING IN THE CONFIGURATION OF CARBON 3

If the induced dissymmetry at carbon 5 is neglected, *d*-lyxose and *d*-arabinose differ merely in the configuration of carbon 3 and the difference in their molecular rotations is $2R_3$. α-*d*-Lyxose has the same configuration for the glycosidic carbon as β-*d*-arabinose, and β-*d*-lyxose has the same configuration for the glycosidic carbon as α-*d*-arabinose. A comparison of the value of $2R_3$ (table 10) from α-*d*-lyxose and β-*d*-arabinose with the value of $2R_3$ from β-*d*-lyxose and α-*l*-arabinose shows a larger variation (−12,400 and −17,710) than might be anticipated for substances differing merely in the configuration of a single carbon and having like configurations of adjacent carbon atoms. The difference in the values suggests that another factor influences the rotations. If the ring-forming carbons in the pentoses are dissymmetric and if *d*-lyxose resembles *d*-mannose and *d*-arabinose resembles *l*-galactose, the comparison cited involves not only carbon 3 but also carbon 5, which in turn influences the rotation at carbon 1. Thus the difference in the values appears to be in harmony with a dissymmetric structure for the pyranose ring in the pentose series. Seemingly the configuration of carbon 3 plays an important role in this dissymmetry.

[5] According to Hudson's rule of isorotation, the rotation of α-*l*-ribose is equal to the molecular rotation of β-*l*-ribose (+3,050) plus $2A$ (the difference in the molecular rotations of a pair of alpha and beta sugars having similar configurations. Ribose, mannose, lyxose, rhamnose, and talose presumably have similar configurations for carbons 2 and 5. The values of $2A$ obtained from mannose, lyxose, rhamnose, and talose are 8,300, 11,700, 7,900, and 9,900, respectively. By using the average of these figures for $2A$, the molecular rotation of α-*l*-ribose is calculated to be 3,050+9,450=+12,500.

TABLE 10.—*Differences in the molecular rotations for carbon 3*

Rotational difference. $(B+R_3)-(B-R_3)=2R_3$	Sugars. $2R_3$	Methyl glycosides. $2R_3$
β-*d*-Arabinose—α-*d*-lyxose	−12,400	−12,590
α-*d*-Arabinose—β-*d*-lyxose	−17,710	−19,270
α-*d*-Gulose—α-*d*-galactose	−16,050	−14,970
β-*d*-Gulose—β-*d*-galactose		−16,180

IV. NOMENCLATURE OF THE HIGHER SUGARS AND THEIR DERIVATIVES

Several of the new compounds prepared in the course of this investigation belong to the heptose series. Because of the confusion[6] which exists with respect to the nomenclature of the higher sugars, the several systems of nomenclature in current use will be considered, and our compounds will be named in accordance with each system.

Naming the heptoses and their derivatives involves:

1. Classification in the *d* or *l* configurational series.
2. Classification of the alpha and beta modifications.
3. Selection of specific names.

The terms *d* and *l* frequently have been used to represent both configuration and direction of optical rotation. In the carbohydrate field the *d* and *l* prefixes ordinarily refer to configuration; in other fields they usually relate to the direction of the optical rotation. Some workers prefer to use *D* and *L* to indicate configuration, and to use the small letters to indicate optical rotation, but in this paper the small letters are used to indicate configuration. The substances are classified in the *d* series when the terminal asymmetric carbon has the same configuration as in *d*-glyceric aldehyde [42, 43]; otherwise they are classified in the *l* series.

The alpha and beta prefixes are used to distinguish between the two modifications of a single ring form. Thus the two pyranose modifications of glucose are known as α-*d*-glucose and β-*d*-glucose. The enantiomorph of α-*d*-glucose is called α-*l*-glucose. In other words, the mirror image of the α-*d*-sugar is the α-*l*-sugar. As a consequence of this system the alpha-beta nomenclature does not refer to the absolute configuration. According to the nomenclature originated by Hudson [11] the alpha and beta prefixes are assigned from the relative optical rotations of the alpha and beta isomers. If the substance belongs in the *d*-configurational series, the more dextrorotatory member of the alpha-beta pair is called alpha. If the substance belongs in the *l*-configurational series, the more dextrorotatory member is called beta. According to this system, the name of each isomer depends on its optical rotation and on whether it belongs in the *d* or *l* series. Since in the heptoses and higher sugars the asymmetric carbon which determines the classification in the *d* or *l*-configurational series is not part of the pyranose ring, and has no direct bearing on the configuration of the glycosidic carbon, this alpha-beta nomenclature for the higher sugars does not always group substances of like configuration.

[6] The Divisions of Biological Chemistry, Chemical Education, and Sugar Chemistry and Technology of the American Chemical Society have organized a committee to investigate the nomenclature of the sugars and their derivatives, and to make recommendations for obtaining a more uniform practice.

In order to correlate substances of like configuration for the pyranose ring, Isbell [3] suggested basing the alpha and beta nomenclature on the configuration of the glycosidic carbon in relation to the configuration of the ring-forming carbon. According to this proposal, which is followed in this paper, *substances which have like configurations for the glycosidic and ring-forming carbons are called alpha, and substances which have unlike configurations for the glycosidic and ring-forming carbons are called beta.* This results in the classification of substances having like configurations for the five carbons of the pyranose ring in the same alpha or beta group regardless of the configuration of the groups in the side chain of carbon 5. In case the ring-forming carbon is not asymmetric, as in the pentose series, it is necessary to name the isomers arbitrarily. In this publication the names for the alpha and beta modifications of *d*-xylose, *d*-lyxose, *l*-arabinose, and *l*-ribose correspond to the names for the alpha and beta modifications of the configurationally related hexoses, *d*-glucose, *d*-mannose, *d*-galactose, and *d*-talose, respectively.

The terms *alpha* and *beta* have been used not only to differentiate between the two modifications of a single sugar but also as part of the specific names for the higher sugars. Emil Fischer [44] called the higher sugars heptoses, octoses, and nonoses, according to the number of carbon atoms and distinguished between the two epimeric heptoses obtained from a single hexose by the prefixes α and β. The α and β symbols were given *empirically*, the first isomer to be prepared being called alpha and the next beta. The octoses and higher sugars were named in the same manner by merely increasing the number of alpha and beta terms. For example, the first octose obtained from the first heptose to be prepared from *d*-glucose was called *d*-α-α-gluco-octose [45]. With the preparation of many of the higher sugars, the multiple use of alpha and beta in the same name without structural significance becomes objectionable and it appears to be the consensus of opinion that Fischer's nomenclature should be changed. A comparison of the structures of the heptoses with their names reveals a very interesting coincidence: The six heptoses prepared by Emil Fischer show a correlation between the configuration of the second carbon and the name. In the gluco-, manno-, and galacto-heptoses, designated as alpha, the configuration of the second carbon is like that of the terminal asymmetric carbon; in those designated as beta the configuration is opposite. This correlation is accidental because the configurations were not known when the substances were named. Subsequently the guloheptoses were prepared by LaForge [46] and named according to the order in which they were isolated. It so happened that their configurations did not fit in with the relationship noted for the other heptoses. Later Isbell [1, 22] reinvestigated LaForge's guloheptoses and suggested that their names be changed so as to follow the configurational relationships noted for the heptoses prepared by Fischer. According to Isbell's suggestion, the designation of the heptoses as alpha or beta depends upon whether the configuration of the second carbon is the same as, or different from the configuration of the terminal asymmetric carbon. The suggestion was made as the simplest means for remedying a bad condition. The proposal would not affect the names for the other heptoses, would result in a saving of the labor necessary for memorizing the names and configurations, and would

not materially change the position of the reference in the various indexes through the literature. Extension of the same principle to the octoses and higher sugars would also facilitate remembering their structures, but would call for the revision of several names.

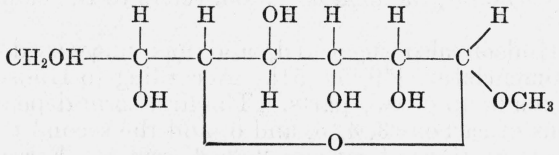
In 1938 Votoček suggested, and has since employed, a system of nomenclature in which he uses the terms *d* and *l* in place of alpha and beta in the specific names of the higher sugars [47, 48]. According to Votoček's proposal, the new methyl *d*-α-galaheptoside which we have prepared would be called α-methyl *d*-gala-*d*-heptopyranoside. The first *d* symbol in the name refers to the configuration of the terminal asymmetric carbon 6; the next *d* symbol refers to the configuration of carbon 2.

In 1938 Hudson also suggested, and has since used, a different system of nomenclature [49, 50, 51]. According to Hudson's system, the name is made up of two parts. The first term depends upon the configurations of carbons 3, 4, 5, and 6, and the second term depends upon the configurations of carbons 2, 3, 4, and 5. For example, the new methyl *d*-α-galaheptoside which we have prepared would be called α-methyl *D*-gala-*L*-mannoheptoside by Hudson. The prefix "*D*-gala" shows that the heptose was derived from *d*-galactose. The second term, "*L*-manno", represents the configurations of carbons 2, 3, 4, and 5 and shows that the substance is configurationally related to *l*-mannose. Each name has two *D* or *L* symbols. The first of these symbols represents the configuration of the terminal asymmetric carbon, and the second represents the configuration of the fifth or pyranose ring-forming carbon. As a basis for naming the alpha and beta isomers, Hudson chooses to use the first *D* or *L* term. If the second *D* or *L* term of his name were to be used as a basis for naming the alpha and beta isomers, the alpha-beta designations which Isbell proposed for the pyranose modifications of the higher sugars would result (see page 140). The methyl *d*-α-galaheptoside designated by Hudson as α-methyl-*D*-gala-*L*-mannoheptoside has the same structure and configuration for the first five carbons as β-methyl *l*-mannoside, and it resembles β-methyl *l*-mannoside very closely. In naming the higher sugars, Hudson takes into consideration the configuration of carbons 2, 3, 4, and 5, but in naming the alpha and beta modifications thereof he abandons the structural and configurational parallelism and bases his names on the terminal asymmetric carbon which lies in the side chain and has no direct bearing on the configuration of the glycosidic carbon. One feature of this system is the overlapping of the groups represented by the prefixes. In this it departs from the established principle of organic chemical nomenclature that such prefixes represent substituent groups. For example, ethylbenzene signifies a benzene molecule with an ethyl group substituted for a hydrogen. Likewise, glucosido-mannose signifies a mannose molecule with a glucosido group substituted for a hydrogen.

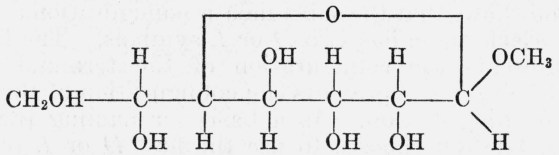
At the meeting of the American Chemical Society in Milwaukee in 1938, C. D. Hurd suggested dropping the first term in Hudson's proposed names and substituting a series of letters to represent the configurations of the higher carbons, beginning with the terminal asymmetric carbon. If the letters *d* and *l* are used to represent the configurations, *d*-α-glucoheptose would be called *d*-*d*-guloheptose. In this name the first symbol represents the configuration of carbon 6, and the second that of carbon 5. The term "*d*-gulo" shows that the sugar

has the *d*-gulose configuration. By naming the alpha and beta isomers according to the configuration of the glycosidic carbon in relation to carbon 5, names result which correlate the alpha and beta modifications of the higher sugars with the alpha and beta modifications of the configurationally related hexoses. As already pointed out, this is advantageous because the reactions and properties of the sugars depend in large measure upon the configurations of the five carbon atoms which comprise the pyranose ring.

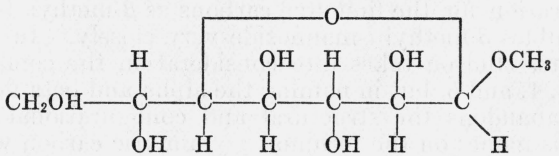
In summary it might be noted that the new heptosides which we have prepared might be represented by the following names:



α-Methyl *d*-α-glucoheptopyranoside [7] (Hudson, 1909; Isbell, 1935)
α-Methyl *D*-gluco-*D*-guloheptopyranoside (Hudson, 1938).
α-Methyl *d*-gluco-*d*-heptopyranoside (Votoček, 1938).
α-Methyl *d*-*d*-guloheptopyranoside (Hurd, 1938).



α-Methyl *d*-α-galaheptopyranoside (Isbell, 1935).
β-Methyl *d*-α-galaheptopyranoside (Hudson, 1909).
β-Methyl *D*-gala-*L*-mannoheptopyranoside (Hudson, 1938).
β-Methyl *d*-gala-*d*-heptopyranoside (Votoček, 1938).
α-Methyl *d*-*l*-mannoheptopyranoside (Hurd, 1938).



α-Methyl *d*-β-galaheptopyranoside (Isbell, 1935).
β-Methyl *d*-β-galaheptopyranoside (Hudson, 1909).
β-Methyl *D*-gala-*L*-glucoheptopyranoside (Hudson, 1938).
β-Methyl *d*-gala-*l*-heptopyranoside (Votoček, 1938).
α-Methyl *d*-*l*-glucoheptopyranoside (Hurd, 1938).

V. EXPERIMENTAL DETAILS

1. PREPARATION METHODS

(a) PREPARATION OF α-METHYL *d*-LYXOPYRANOSIDE

Fifty grams of *d*-lyxose was refluxed for 4 hours with 700 ml of absolute methyl alcohol containing 1.5 percent of hydrogen chloride. A Fehling's test at this time showed the absence of reducing sugar. The solution was cooled and neutralized with silver carbonate. A small quantity of decolorizing carbon was added and after filtration

[7] The term "-pyranoside" was originated by W .N. Haworth.

the solution was concentrated in vacuo to a sirup of about 75 percent total solids. The sirup was warmed with 75 ml of isopropyl alcohol and allowed to stand overnight in the refrigerator. The α-methyl *d*-lyxopyranoside which crystallized was collected on a filter and washed with isopropyl alcohol. The yield was 28 g and a second crop of 8 g separated from the mother liquor. Recrystallization was accomplished by dissolving the crude product in water and concentrating the solution to a sirup (75 percent total solids). After the addition of a threefold quantity of isopropyl alcohol, the mixture was seeded with crystalline α-methyl *d*-lyxopyranoside and allowed to stand. After several hours the crystals were collected on a filter and washed with isopropyl alcohol. The melting point, 108° C, and the specific rotation, $[\alpha]_D^{20} = +59.4$ (water; *c*, 4), agree with the constants reported by Phelps and Hudson [24].

(b) PREPARATION OF β-METHYL *d*-LYXOPYRANOSIDE

The mother liquor from the preparation of α-methyl *d*-lyxopyranoside was concentrated and allowed to stand in a desiccator for several weeks, whereupon crystallization occurred spontaneously. The crystals (5.5 g) were separated and found to be a mixture of the alpha and beta isomers with a specific rotation of −15°. The mixture was recrystallized by dissolving it in a minimum quantity of hot isopropyl alcohol (about sixfold), treating with activated carbon, filtering, and cooling. Fractional recrystallization yielded about 1 g of pure crystalline β-methyl *d*-lyxopyranoside and a crystalline mixture of the isomers which has not been separated. β-Methyl *d*-lyxopyranoside crystallizes in slender prisms (fig. 1,*A*), which melt at 118° C, and give $[\alpha]_D^{20} = -128.1$ (water; *c*, 2.5). When pure, the substance crystallizes readily from water, as well as from isopropyl alcohol. *Analysis:* Calculated for $C_6H_{12}O_5$: C, 43.90; H, 7.37. Found: C, 44.19; H, 7.25. The new substance was shown to be a pyranoside by periodic oxidation. A sample (0.164 g) was dissolved in 11 ml of 0.2 *M* periodic acid and the solution held at 20° C. The optical rotation was read and after about 1 hour became nearly constant at −8.67° S in a 2-dm tube. The observed rotation reduced to the basis of the dialdehyde corresponds to $[\alpha]_D^{20} = -125.5°$. This value is approximately equal in magnitude but is of opposite sign to that found by Maclay and Hudson [7] for the product from α-methyl *d*-lyxopyranoside. The residual periodic acid was determined by titration with sodium arsenite. The titration showed that periodic acid had been used in the ratio of 2.06 moles per mole of β-methyl *d*-lyxopyranoside.

(c) PREPARATION OF β-METHYL TRIACETYL-*d*-LYXOPYRANOSIDE

Four-tenths gram of pure crystalline β-methyl *d*-lyxopyranoside was warmed slightly with 5 ml of acetic anhydride and 0.5 g of fused and powdered sodium acetate. The reaction mixture, after standing overnight, was poured into cracked ice, extracted with chloroform, and the chloroform removed by evaporation in vacuo. After the addition of a little water, the new substance crystallized. The crude acetate (0.66 g) was recrystallized from water, in which it is difficultly soluble. β-Methyl triacetyl-*d*-lyxopyranoside crystallizes in large truncated prisms (fig. 1,*B*), which melt at 88 to 89° C, and give $[\alpha]_D^{20} = -109.5$ (chloroform; *c*, 4.5). *Analysis:* Calculated for $C_{12}H_{18}O_8$: C, 49.65; H, 6.25. Found: C, 50.10; H, 6.49.

(d) PREPARATION OF β-METHYL TETRA-ACETYL-*d*-MANNOPYRANOSIDE

β-Methyl tetra-acetyl-*d*-mannopyranoside was prepared in small quantity from triacetyl *d*-mannose 1,2-methyl orthoacetic ester by the method originally used by Dale [39]. Since the yield by this method was extremely small, the dimethyl sulfate method previously used by Schlubach [52] for the preparation of β-methyl *d*-glucopyranoside was adopted. The preparation was conducted in the following manner: 18 g of *d*-mannose was dissolved in 100 ml of water at 0° C; dimethyl sulfate was added dropwise to the cold solution over a period of about 3 hours while the mixture was maintained alkaline to acyl blue (pH 12) by the dropwise addition of a 30-percent solution of sodium hydroxide. A total of 20 to 22 ml of alkali was added in the course of 8 hours. After standing overnight at room temperature, the solution was neutralized, treated with activated carbon, filtered, and concentrated in vacuo to a volume of approximately 30 ml. The sirup was mixed with 60 ml of dioxane and the evaporation was repeated to facilitate dehydration. The resulting thick sirup was dissolved in 60 ml of pyridine and acetylated by the addition of 60 ml of acetic anhydride. After standing overnight at room temperature, the solution was poured into cracked ice and the gummy precipitate extracted with chloroform. The extract was washed successively with solutions of sodium bicarbonate, copper sulfate (until free from pyridine) and water. The chloroform solution was dried, treated with decolorizing carbon, filtered and evaporated to a thin sirup. One hundred milliliters of ethyl alcohol was added and the solution concentrated to a sirup which crystallized spontaneously. The material was removed from the flask with 100 ml of ether. Petroleum ether was then added to saturation. After the solution had stood for a day at 0° C, the crystals were collected on a filter and washed with a mixture of ether and petroleum ether. The yield of the mixed α- and β-methyl tetra-acetyl-*d*-mannopyranoside was about 18 g. The crude product was stirred with 100 ml of ether and filtered. The residue, about 6 g, was fairly pure β-methyl tetra-acetyl-*d*-mannopyranoside. The compound after recrystallization from 1.5 parts of 95-percent ethyl alcohol was substantially pure and gave a melting point of 159° to 160° C, and a specific rotation of −47.8°, in agreement with the constants reported by Dale [39]. Several prior investigators have deacetylated β-methyl tetra-acetyl-*d*-mannopyranoside to give β-methyl-*d*-mannopyranoside in the form of a sirup [53, 54]. In the early stages of the present investigation, a crystalline calcium chloride compound of β-methyl *d*-mannopyranoside was separated, and it was planned to use this compound for the purification of the glycoside in the manner which one of us has found useful for purifying the α- and β-methyl *d*-gulopyranosides, but before this plan was completed a crystalline methyl mannopyranoside containing isopropyl alcohol of crystallization was obtained.

(e) PREPARATION OF β-METHYL *d*-MANNOPYRANOSIDE ISOPROPYL ALCOHOLATE

Twenty-five grams of β-methyl tetra-acetyl-*d*-mannopyranoside was deacetylated with a small quantity of barium methylate [5], using 500 ml of absolute methyl alcohol and 10 ml of water-free barium methylate solution (about 0.6 *N*). After the barium methylate had been decomposed by an equivalent quantity of sulfuric acid and the barium sulfate separated by filtration, the filtrate was evaporated in

vacuo to a thin sirup (about 15 ml). Forty milliliters of isopropyl alcohol was added and the methyl mannoside containing isopropyl alcohol of crystallization ($C_7H_{14}O_6.C_3H_8O$) separated in large thin plates (fig. 1, *D*). The yield was almost quantitative. To recrystallize, the substance was dissolved in 15 parts of boiling isopropyl alcohol and allowed to stand overnight at 0° C. The crystals were collected on a filter, washed with cold isopropyl alcohol, and dried for 24 hours over calcium chloride. β-Methyl *d*-mannopyranoside isopropyl alcoholate melts at 74° to 75° C and gives $[\alpha]_D^{20} = -53.3$ (water; *c*, 4). This value is equivalent to a specific rotation of −69.8 for β-methyl *d*-mannopyranoside. The crystals have a slight odor of isopropyl alcohol and decompose on standing in an open container. They are stable in the presence of isopropyl alcohol vapor. A sample heated at 105° C in vacuo came to constant weight in 12 hours. Loss calculated for 1 molecule of isopropyl alcohol: 23.45 percent. Found: 23.21 percent. The colorless glassy residue would not crystallize from other solvents, but crystallized readily upon addition of more isopropyl alcohol. A sample of β-methyl *d*-mannopyranoside isopropyl alcoholate was placed in a combustion tube and heated at 77° C in a current of dry oxygen. Under the conditions of the experiment, 70.0 percent of the isopropyl alcohol was volatilized and analyzed. Calculated for C_3H_8O: C, 59.96; H, 13.42. Found: C, 58.56; H, 12.78. The residue was analyzed separately. Calculated for 30.0 percent β-methyl *d*-mannopyranoside isopropyl alcoholate and 70 percent β-methyl *d*-mannopyranoside: C, 44.35; H, 7.68. Found: C, 44.77; H, 8.17.

(f) PREPARATION OF α-METHYL *d*-GALAHEPTOPYRANOSIDE

The methyl heptoside which has the α-methyl *d*-mannopyranoside structure was prepared first by Hann, Merrill, and Hudson [29]. They called the substance β-methyl *d*-α-galaheptopyranoside. In accordance with nomenclature used in this article, we shall designate it as α-methyl *d*-α-galaheptopyranoside. We repeated the preparation of this compound and found its properties to be in substantial agreement with those reported by Hann, Merrill, and Hudson.

(g) PREPARATION OF β-METHYL PENTA-ACETYL-*d*-α-GALAHEPTOPYRANOSIDE

The methyl heptoside having the β-methyl *d*-mannopyranoside configuration (β-methyl *d*-α-galaheptopyranoside) resembles β-methyl *d*-mannopyranoside in that it does not crystallize under the conditions which usually give crystalline products. Using the dimethyl sulfate method followed by acetylation, as in the case of mannose, we obtained the glycoside in the form of a crystalline acetate.

d-α-Galaheptose hydrate (22.8 g) was methylated with dimethyl sulfate in alkaline solution and acetylated as described for the preparation of β-methyl tetra-acetyl-*d*-mannopyranoside. The chloroform solution containing the acetylated product was evaporated in vacuo to a thin sirup, which was taken up in ethyl alcohol. The alcoholic mixture was then evaporated again and the resulting sirup taken up in 40 ml of ether. The ether solution was saturated with petroleum ether and was allowed to stand overnight at 0° C. The crystals which formed were collected on a filter and washed with a mixture of absolute alcohol and petroleum ether. The yield was 4.1 g. A second crop of 2.5 g was obtained from the mother liquor. The

compound was recrystallized from 4 or 5 parts of boiling 95-percent ethyl alcohol. β-Methyl penta-acetyl-*d*-α-galaheptopyranoside separates in slender prisms (fig. 1, *E*) which melt at 171° to 173° C and give $[\alpha]_D^{20}=+77.6$ (chloroform; *c*, 4). *Analysis:* Calculated for $C_{18}H_{26}O_{12}$: C, 49.77; H, 6.03. Found: C, 49.67; H, 5.94.

(h) PREPARATION OF β-METHYL *d*-α-GALAHEPTOPYRANOSIDE

Five and one-half grams of pure β-methyl penta-acetyl-*d*-α-galaheptopyranoside was suspended in 110 ml of absolute methyl alcohol, cooled to 0° C, and deacetylated by treatment with 5 ml of water-free barium methylate solution, as in the preparation of β-methyl tetra-acetyl mannopyranoside. After removal of the barium, and concentration, a sirup was obtained which could not be brought to crystallization. The rate of hydrolysis and the optical properties of the amorphous product, however, were studied. The dry weight was determined on an aliquot part of the sirup by heating it in vacuo at 105° C after a preliminary evaporation of the solvent at a lower temperature (60° C). The sirup lost weight rapidly during 1 hour at 105° C, and afterwards there was a small gradual loss, apparently due to volatilization of the glycoside. Based upon the weight of the substance dried for 1 hour at 105° C, $[\alpha]_D^{20}=+74$.

(i) PREPARATION OF β-METHYL *d*-α-GLUCOHEPTOPYRANOSIDE

β-Methyl *d*-α-glucoheptopyranoside was prepared by the method of Fischer [28]. Forty grams of *d*-α-glucoheptose was refluxed for 6 hours with 400 ml of absolute methyl alcohol containing 1.5 percent of hydrogen chloride. After neutralization with silver carbonate, the solution was treated with activated carbon, filtered, and evaporated to a sirup of about 85 percent total solids. This was dissolved in 25 ml of ethyl alcohol, and after the addition of 25 ml of isopropyl alcohol, the solution was allowed to stand overnight at 0° C. The crystals of β-methyl *d*-α-glucoheptopyranoside which formed were collected on a filter and washed with a mixture of ethyl alcohol and isopropyl alcohol (1:1). The yield was 23.5 g. The crude product was recrystallized from a sixteenfold quantity of boiling 95-percent ethyl alcohol. The substance melted at 170° C and gave $[\alpha]_D^{20}=-74.7$, in substantial agreement with the properties reported by Fischer.

(j) PREPARATION OF α-METHYL *d*-α-GLUCOHEPTOPYRANOSIDE.$CaCl_2.H_2O$

The usual methods for the preparation of crystalline methyl glycosides have not been successful for the preparation of crystalline α-methyl *d*-α-glucoheptopyranoside. However, we anticipated that the procedure which had proved successful for the preparation of the configurationally related guloside [4] would be suitable for obtaining this heptoside. This proved to be the case and a crystalline calcium chloride compound of α-methyl *d*-α-glucoheptopyranoside was separated, from which crystalline α-methyl *d*-α-glucoheptopyranoside was obtained after removal of the calcium chloride with silver sulfate.

The mother liquor from the preparation of β-methyl *d*-α-glucoheptopyranoside just described was concentrated to a sirup of about 85 percent total solids. The amount of calcium chloride molecularly equivalent to the glycoside in the mother liquor was calculated from the difference between the theoretical amount of glycoside formed on

methylation and the weight of the crystalline β-methyl glycoside removed. In the preparation reported, 12.6 g of $CaCl_2.2H_2O$ was added to the mother liquor of the β-methyl *d*-α-glucoheptopyranoside. The mixture was concentrated to a thick sirup, which crystallized spontaneously. The crystals of the calcium chloride compound of α-methyl *d*-α-glucoheptopyranoside were collected on a filter and washed with 95 percent ethyl alcohol. The yield was 12.5 g. To recrystallize, the compound was dissolved in water and concentrated in vacuo to a sirup of about 75 percent total solids. A small amount of alcohol was added and the sirup was seeded and rotated during crystallization. The crystals were separated and washed with alcohol. The calcium chloride compound of α-methyl *d*-α-glucoheptopyranoside crystallizes in large colorless hexagonal plates (fig. 1, *F*) and gives $[\alpha]_D^{20} = +69.1$ (water; *c*, 4). *Analysis:* Calculated for $C_8H_{16}O_7.CaCl_2.H_2O$: C, 27.20; H, 5.14; Ca, 11.45; Cl, 19.90. Found: C, 27.17; H, 5.14; Ca, 11.35; Cl, 20.08.

(k) PREPARATION OF α-METHYL *d*-α-GLUCOHEPTOPYRANOSIDE

Ten grams of pure α-methyl *d*-α-glucoheptopyranoside.$CaCl_2.H_2O$ was dissolved in 25 ml of water and the solution shaken with an excess of silver sulfate until a test for chloride was negative. After the addition of decolorizing carbon, the mixture was filtered and the filtrate evaporated in vacuo to a heavy sirup, which was then taken up in a small amount of isopropyl alcohol and allowed to stand in a desiccator. α-Methyl *d*-α-glucoheptopyranoside crystallized in nearly quantitative yield. The crude glycoside was dissolved in a minimum quantity of boiling absolute ethyl alcohol and the sirup diluted with one-third its volume of isopropyl alcohol. The solution was cooled and allowed to stand in a desiccator overnight. The crystals were separated on a filter and washed several times with a mixture of 9 parts of absolute alcohol and 1 part of isopropyl alcohol. By the crystallization of additional crops from the mother liquor, practically all of the glycoside was recovered. α-Methyl *d*-α-glucoheptopyranoside crystallizes in rectangular prisms, many of them truncated (fig. 1, *H*). It melts at 106° to 107° C and gives $[\alpha]_D^{20} = +111.5$ (water; c, 4). *Analysis:* Calculated for $C_8H_{16}O_7$: C, 42.85; H, 7.19. Found: C, 42.75; H, 7.12.

(l) PREPARATION OF α-METHYL PENTA-ACETYL-*d*-α-GLUCOHEPTOPYRANOSIDE

One-half gram of α-methyl *d*-α-glucoheptopyranoside was treated with 5 ml of acetic anhydride and 0.5 g of freshly fused and powdered sodium acetate. The reaction mixture was warmed slightly and then allowed to stand at room temperature for several hours, after which it was poured into ice water. α-Methyl penta-acetyl-*d*-α-glucoheptopyranoside crystallized from the water mixture. The crystals (fig. 1, *I*) were collected on a filter and dried in vacuo. The compound was recrystallized from 25 ml of boiling 95 percent ethyl alcohol. It melts at 174° to 175° C and gives $[\alpha]_D^{20} = +107.4$ (chloroform; *c*, 4). *Analysis:* Calculated for $C_{18}H_{26}O_{12}$: C, 49.77; H, 6.03. Found: C, 49.67; H, 5.94. Our compound appears to differ from the product of Haworth, Hirst, and Stacey [12], which is reported to melt at 169° C and to give $[\alpha]_D^{20} = +91°$. Further investigation is necessary to show wherein the two products differ.

(m) PREPARATION OF (β-METHYL *d*-α-GLUCOHEPTOPYRANOSIDE)$_2$.CaCl$_2$.2H$_2$O

Pure β-methyl *d*-α-glucoheptopyranoside (7.7 g) was mixed with an equimolecular quantity of calcium chloride (5.1 g of $CaCl_2.2H_2O$) and the mixture dissolved in 15 ml of water. The solution was filtered, diluted with 2 volumes of ethyl alcohol, and allowed to stand for several days in a desiccator. The slender prismatic crystals (fig. 1, *G*) which formed almost quantitatively were separated on a filter and washed with 95-percent ethyl alcohol. The compound was recrystallized from a large volume of boiling 95-percent ethyl alcohol and dried for 24 hours over calcium chloride in a vacuum desiccator. *Analysis:* Calculated for $(C_8H_{16}O_7)_2.CaCl_2.2H_2O$: C, 32.27; H, 6.09; Ca, 6.73; Cl, 11.91. Found: C, 32.27; H, 6.00; Ca, 6.67; Cl, 11.88. The new product gave $[\alpha]_D^{20}=-56.1$ (water; *c*, 4).

(n) PREPARATION OF α-METHYL *d*-LYXOPYRANOSIDE.CaCl$_2$.2H$_2$O

Pure α-methyl *d*-lyxopyranoside (3.3 g) was dissolved with an equivalent quantity of calcium chloride (3 g of $CaCl_2.2H_2O$) in 5 ml of water. The solution was filtered and evaporated in a desiccator to a thick sirup, which was taken up in a few drops of isoamyl alcohol. After this had stood for several days in a desiccator, α-methyl *d*-lyxopyranoside-calcium chloride crystallized in slender rectangular plates (fig. 1, *C*), which were separated and washed with isoamyl alcohol. The product was recrystallized by dissolving it in water, evaporating the solution in a desiccator, and adding isoamyl alcohol. The recrystallized product was slightly hygroscopic, but stable in dry air. For analysis, it was dried at room temperature for several days over calcium chloride. It gives $[\alpha]_D^{20}=+31.3$ (water; *c*, 2). *Analysis:* Calculated for $C_6H_{12}O_5.CaCl_2.2H_2O$: Ca, 12.88; Cl, 22.79. Found: Ca, 12.87; Cl, 22.75.

(o) PREPARATION OF α-METHYL *d*-β-GALAHEPTOPYRANOSIDE

Five grams of *d*-β-galaheptose was refluxed for 6 hours with 100 ml of methyl alcohol containing 1.5 g of hydrogen chloride. The solution was cooled and neutralized with silver carbonate. The resulting silver chloride was separated, and the solution was evaporated under reduced pressure to a heavy sirup, which crystallized spontaneously. The semisolid crystalline mass was mixed with 30 ml of isopropyl alcohol. After the mixture had stood for several hours, the crystals were separated by filtration and washed with isopropyl alcohol. The crystalline product weighed 45 g, melted at 150° C, and gave $[\alpha]_D^{20}=-86$ (water; *c*, 4). It proved to be a mixture containing a more highly levorotatory product. Upon recrystallization from a mixture of ethyl and isopropyl alcohols, the more difficultly soluble fractions gave a specific rotation of −48 to −80, while the crystals obtained from the mother liquors gave specific rotations from −80 to −107.8. The optical rotation of the product, $[\alpha]_D^{20}=-108$ (water; *c*, 4), did not change on further recrystallization, and hence it is believed that it is a pure compound. The clusters of needle-like crystals (fig. 1, *J*) melt at 154° to 155° C and give the following analysis: Calculated for $C_8H_{16}O_7$: C, 42.85; H, 7.19. Found: C, 42.97; H, 7.34.

Our product, which resembles α-methyl *l*-glucopyranoside is the second methyl glycoside of *d*-β-galaheptose to be prepared. The heretofore known methyl *d*-β-galaheptopyranoside prepared by Hann

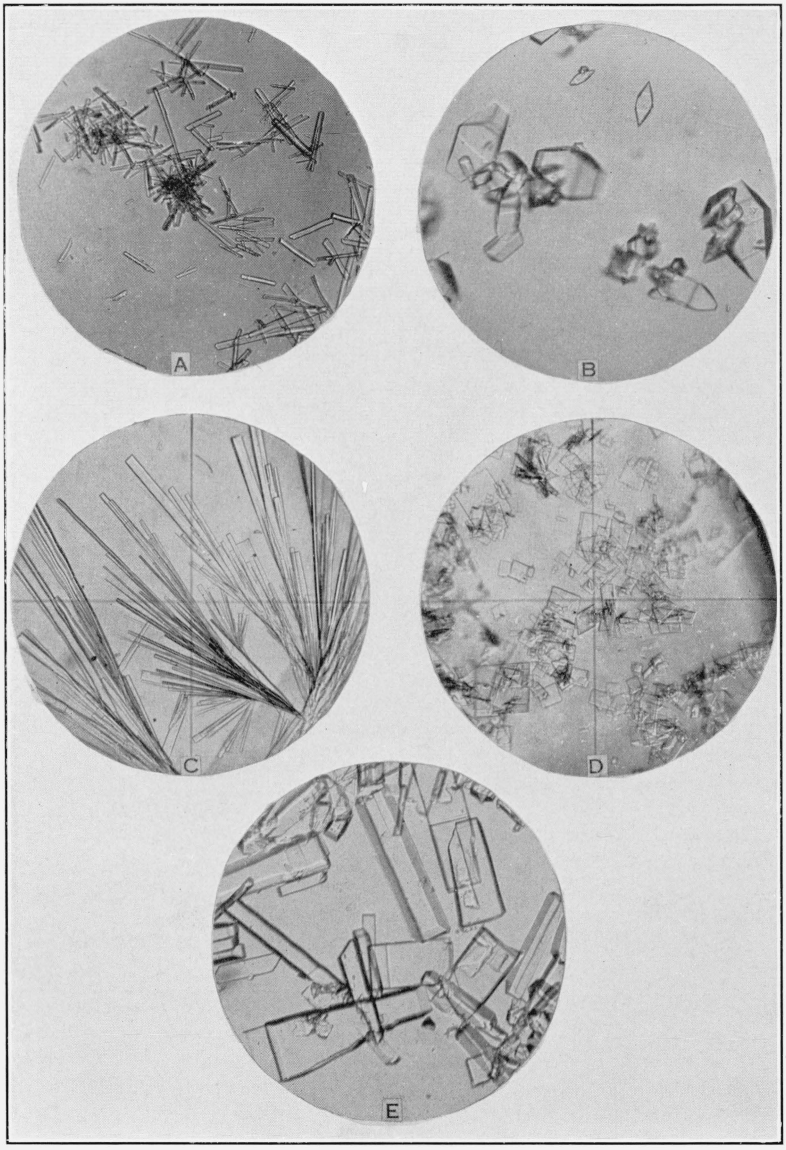


FIGURE 1.—*Photomicrographs of new glycosides.*

A—*β-Methyl d-lyxopyranoside.*
B—*β-Methyl triacetyl-d-lyxopyranoside.*
C—*α-Methyl d-lyxopyranoside.*$CaCl_2.2H_2O$.
D—*β-Methyl d-mannopyranoside isopropyl alcoholate.*
E—*β-Methyl penta-acetyl d-α-galaheptopyranoside.*

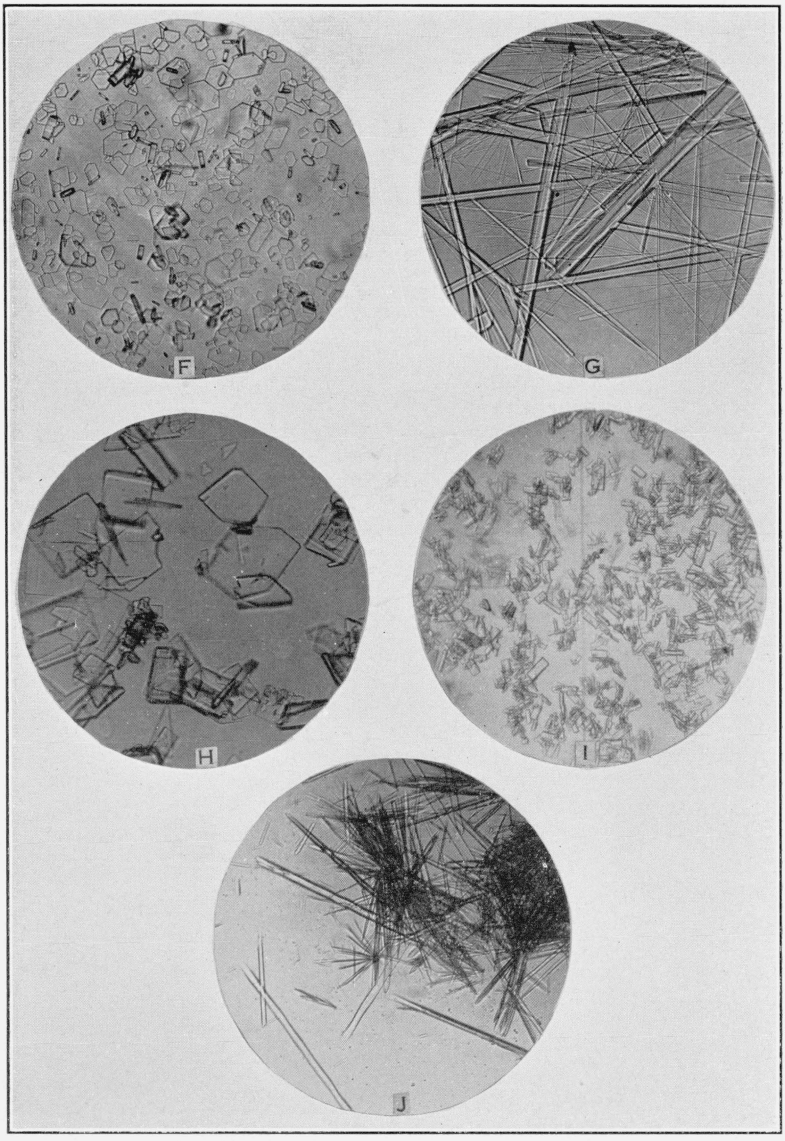


FIGURE 1 (Continued).—*Photomicrographs of new glycosides.*

F—*α-Methyl d-α-glucoheptopyranoside.* $CaCl_2.H_2O$.
G—*(β-Methyl d-α-glucoheptopyranoside)*$_2$.$CaCl_2.2H_2O$.
H—*α-Methyl d-α-glucoheptopyranoside.*
I—*α-Methyl penta-acetyl d-α-glucoheptopyranoside.*
J—*α-Methyl d-β-galaheptopyranoside.*

and Hudson [30] gives a specific rotation of +36 and is closely related to β-methyl *l*-glucopyranoside. Since the glycosidic and ring-forming carbons have like configurations in our product, we have named it α-methyl *d*-β-galaheptopyranoside. According to Hudson's alpha-beta nomenclature, it would be named β-methyl *d*-β-galaheptopyranoside.

2. MEASUREMENT OF RATES OF HYDROLYSIS

The measurements at 98° C were conducted in the following manner: The crystalline glycoside (usually 0.4 g) was dissolved in 10 ml of 0.05 *N* HCl. The optical rotation was read at 20° C, and then the polariscope tube containing the solution was immersed in a bath of boiling water. Time was measured beginning with the immersion of the tube. The polariscope tube was closed by a stopper carrying a thermometer which dipped into the solution. After a suitable time interval, the tube was removed from the bath and plunged into a mixture of ice and water. After 45 seconds the temperature dropped to approximately 20° C, and the tube was then removed from the ice bath and the optical rotation read at 20° C. The tube was then inserted in the boiling water bath and heated again. The process was repeated a number of times, thereby furnishing check values for the velocity constant. It required about 5 minutes to cool the tube and make the polariscope readings. Since the reaction at 20° C is slow in comparison with the reaction at 98° C, the time that the sample was held at the lower temperature was not included in calculating the velocity constants. The velocity constants were calculated from the usual equation:

$$k=\frac{1}{t}\log\frac{r_0-r_\infty}{r_t-r_\infty},$$

where r_0 is the rotation of the solution at the beginning of the hydrolysis, r_∞ the rotation when hydrolysis is complete, and r_t the rotation at the time, t. Inasmuch as some of the hydrolyses were very slow, the value of r_∞ was calculated from the specific rotations of the methyl glycosides and the sugar formed by hydrolysis.

The measurements at 75° C were conducted in the following manner: A freshly prepared solution of the glycoside in 0.5 *N* HCl at 75° C was placed in a water-jacketed polariscope tube, which was maintained at the desired temperature by circulating water. From time to time, the optical rotations were read and recorded. The velocity constants, as given in table 2, were calculated from the usual equation.

VI. SUMMARY

Velocity constants are given for the hydrolysis of the α- and β-methyl *d*-lyxopyranosides, *d*-mannopyranosides, *d*-gulopyranosides, *d*-α-galaheptopyranosides, *d*-β-galaheptopyranosides, and *d*-α-glucoheptopyranosides. The configurations of all of the carbons comprising the pyranose ring affect the rate of hydrolysis. Aldopyranosides having *trans* configurations for carbons 1 and 3 are hydrolyzed more slowly than the corresponding modifications having *cis* configurations for carbons 1 and 3. The molecular rotations of the methyl glycopyranosides are compared according to the configurations of carbons 1, 2, and 3, and certain relationships have been found to support the classification of the methyl lyxopyranosides in the *d*-mannose series rather than in the *l*-gulose series.

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The preparation and properties of the following new compounds given:

β-Methyl d-lyxopyranoside and β-methyl triacetyl-d-lyxopyranoside.—The mother liquor of α-methyl *d*-lyxopyranoside prepared by Fischer's hydrogen chloride method yields a small amount of crystalline β-methyl *d*-lyxopyranoside, mp 118°C, $[\alpha]_D^{20}=-128.1$ (water; *c*, 2.5). Acetylation of β-methyl *d*-lyxopyranoside with acetic anhydride and sodium acetate yields crystalline β-methyl triacetyl-*d*-lyxopyranoside, mp 88° to 89°C, $[\alpha]_D^{20}=-109.5$ (chloroform; *c*, 4.5). Addition of calcium chloride to α-methyl *d*-lyxopyranoside gives α-methyl *d*-lyxopyranoside.$CaCl_2.2H_2O$, $[\alpha]_D^{20}=+31.3$ (water; *c*, 2).

β-Methyl d-mannopyranoside isopropyl alcoholate.—Treatment of *d*-mannose with 1 equivalent of dimethyl sulfate and alkali, followed by the acetylation of the product, gives β-methyl tetra-acetyl *d*-mannopyranoside (6 g from 18 g of mannose). Deacetylation with barium methylate in methyl alcoholic solution and subsequent evaporation of the methyl alcohol and addition of isopropyl alcohol gives crystalline β-methyl *d*-mannopyranoside isopropyl alcoholate. This compound loses isopropyl alcohol readily, mp 74° to 75°C, $[\alpha]_D^{20}=-53.3$ (water; *c*, 4).

β-Methyl d-α-galaheptopyranoside and β-methyl penta-acetyl-d-α-galaheptopyranoside.—Treatment of *d*-α-galaheptose with 1 equivalent of dimethyl sulfate and alkali, followed by acetylation of the product, gives a new crystalline methyl penta-acetyl-*d*-α-galaheptopyranoside, mp 171° to 173°C, $[\alpha]_D^{20}=+77.6$ (chloroform; *c*, 4). Deacetylation with barium methylate in methyl alcoholic solution gives a new methyl *d*-α-galaheptopyranoside which could not be brought to crystallization, $[\alpha]_D^{20}=+74$.

α-Methyl d-α-glucoheptopyranoside.$CaCl_2.H_2O$ *and* (*β-methyl d-α-glucoheptopyranoside*)$_2$.$CaCl_2.2H_2O$.—Treatment of *d*-α-glucoheptose with methyl alcohol containing 1.5 percent of hydrogen chloride gives β-methyl *d*-α-glucoheptopyranoside in 55-percent yield; the mother liquor by treatment with calcium chloride yields crystalline α-methyl *d*-α-glucoheptopyranoside.$CaCl_2.H_2O$, $[\alpha]_D^{20}=+69.1$ (water; *c*, 4). Crystalline (β-methyl *d*-α-glucoheptopyranoside)$_2$.$CaCl_2.2H_2O$ prepared from the glycoside and calcium chloride gives $[\alpha]_D^{20}=-56.1$ (water; *c*, 4).

α-Methyl d-α-glucoheptopyranoside and α-methyl penta-acetyl-d-α-glucoheptopyranoside.—Removal of the calcium chloride from α-methyl *d*-α-glucoheptopyranoside.$CaCl_2.H_2O$ with silver sulfate gives crystalline α-methyl *d*-α-glucoheptopyranoside, mp 106° to 107° C, $[\alpha]_D^{20}=+111.5$ (water; *c*, 4). Acetylation with acetic anhydride and sodium acetate yields crystalline α-methyl penta-acetyl-*d*-α-glucoheptopyranoside, mp 174° to 175° C, $[\alpha]_D^{20}=+107.4$ (chloroform; *c*, 4). This acetate differs from the product described by Haworth, Hirst, and Stacey.

α-Methyl d-β-galaheptopyranoside.—Treatment of *d*-β-galaheptose with methyl alcohol containing hydrogen chloride gives crystalline methyl *d*-β-galaheptopyranoside, mp 154° to 155° C, $[\alpha]_D^{20}=-108$ (water; *c*, 4) in addition to a mixed product, $[\alpha]_D^{20}=-48$.

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VII. REFERENCES

[1] H. S. Isbell, J. Research NBS **18,** 505 (1937) RP990.
[2] H. S. Isbell and W. W. Pigman, J. Research NBS **18,** 141 (1937) RP969.
[3] H. S. Isbell, J. Chem. Education **12,** 96 (1935).
[4] H. S. Isbell, BS J. Research **8,** 1 (1932) RP396.
[5] H. S. Isbell, BS J. Research **5,** 1185 (1930) RP253.
[6] E. L. Jackson and C. S. Hudson, J. Am. Chem. Soc. **59,** 994 (1937).
[7] W. P. Maclay and C. S. Hudson, J. Am. Chem. Soc. **60,** 2059 (1938).
[8] E. F. Armstrong, Proc. Roy. Soc. (London) **74,** 192 (1904).
[9] C. N. Riiber and N. A. Sørensen, Det. Kgl. Norske Videnskab Selskabs Skrifter, no. 1, p. 1 (1938).
[10] W. N. Haworth and E. L. Hirst, J. Chem. Soc. **1930,** 2615.
[11] C. S. Hudson, J. Am. Chem. Soc. **31,** 66 (1909).
[12] W. N. Haworth, E. L. Hirst, and M. Stacey, J. Chem. Soc. **1931,** 2864.
[13] W. N. Haworth, The Constitution of Sugars, p. 91 (Edward Arnold & Co., London, 1929).
[14] E. Pacsu, J. Am. Chem. Soc. **61,** 2669 (1939).
[15] C. S. Hudson, J. Am. Chem. Soc. **61,** 2972 (1939).
[16] C. S. Hudson and E. Yanovsky, J. Am. Chem. Soc. **39,** 1013 (1917).
[17] W. W. Pigman and H. S. Isbell, J. Research NBS **19,** 189 (1937) RP1021.
[18] W. C. Austin and F. L. Humoller, J. Am. Chem. Soc. **55,** 2167 (1933); **56,** 1153 (1934).
[19] H. S. Isbell, BS J. Research **5,** 741 (1930) RP226.
[20] H. S. Isbell, J. Am. Chem. Soc. **56,** 2789 (1934).
[21] H. S. Isbell, J. Research NBS **20,** 97 (1938) RP1069.
[22] H. S. Isbell, J. Research NBS **19,** 639 (1937) RP1052.
[23] C. S. Hudson, J. Am. Chem. Soc. **47,** 265 (1925).
[24] F. P. Phelps and C. S. Hudson, J. Am. Chem. Soc. **48,** 503 (1926).
[25] C. N. Riiber, Ber. deut. chem. Ges. **57,** 1797 (1924).
[26] E. Fischer and L. Beensch, Ber. deut. chem. Ges. **29,** 2927 (1896).
[27] C. N. Riiber, J. Minsaas, and R. T. Lyche, J. Chem. Soc. **1929,** 2173.
[28] E. Fischer, Ber. deut. chem. Ges. **28,** 1145 (1895).
[29] R. M. Hann, A. T. Merrill, and C. S. Hudson, J. Am. Chem. Soc. **57,** 2100 (1935).
[30] R. M. Hann and C. S. Hudson, J. Am. Chem. Soc. **59,** 548 (1937).
[31] C. S. Hudson and J. K. Dale, J. Am. Chem. Soc. **40,** 997 (1918).
[32] J. K. Dale, J. Am. Chem. Soc. **37,** 2745 (1915).
[33] F. P. Phelps and C. S. Hudson, J. Am. Chem. Soc. **50,** 2049 (1928).
[34] C. S. Hudson and J. K. Dale, J. Am. Chem. Soc. **37,** 1264 (1915).
[35] T. L. Harris, E. L. Hirst, and C. E. Wood, J. Chem. Soc. **1932,** 2108.
[36] F. Micheel and O. Littmann, Liebigs Ann. Chem. **466,** 115 (1928).
[37] J. K. Dale and C. S. Hudson, J. Am. Chem. Soc. **52,** 2534 (1930).
[38] W. N. Haworth and E. L. Hirst, J. Chem. Soc. **1928,** 1221.
[39] J. K. Dale, J. Am. Chem. Soc. **46,** 1046 (1924).
[40] C. S. Hudson, J. Am. Chem. Soc. **48,** 1434 (1926).
[41] K. Freudenberg and R. Kuhn, Ber. deut. chem. Ges. **64,** 703 (1931).
[42] M. Rosanoff, J. Am. Chem. Soc. **28,** 525 (1906).
[43] A. Wohl and K. Freudenberg, Ber. deut. chem. Ges. **56,** 309 (1923); **58,** 451 (1925).
[44] E. Fischer, Ber. deut. chem. Ges. **23,** 934 (1890).
[45] E. Fischer, Liebigs Ann. Chem. **270,** 92 (1892).
[46] F. B. LaForge, J. Biol. Chem. **41,** 251 (1920).
[47] E. Votoček, Collection Czechoslov. Chem. Communications **10,** 264 (1938).
[48] E. Votoček, Collection Czechoslov. Chem. Communications **10,** 273 (1938).
[49] C. S. Hudson, J. Am. Chem. Soc. **60,** 1537 (1938).
[50] R. M. Hann, W. D. Maclay, A. E. Knauf, and C. S. Hudson, J. Am. Chem. Soc. **61,** 1268 (1939).
[51] R. M. Hann, W. D. Maclay, and C. S. Hudson, J. Am. Chem. Soc. **61,** 1270 (1939).
[52] H. H. Schlubach and K. Maurer, Ber. deut. chem. Ges. **57,** 1686 (1924).
[53] E. L. Jackson and C. S. Hudson, J. Am. Chem. Soc. **61,** 959 (1939).
[54] F. Klages and R. Maurenbrecher, Liebigs Ann. Chem. **535,** 182 (1938).

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