7. The significance of the presence or absence of the layer attached to the dispersed particles in a system has been discussed in respect of its bearing on the mechanism of well-known processes involving adhesion.

8. The reversible fugitive rigidity of plastic systems on shear has been discussed in its application to the mechanism of the "drying" of ink in the printing process.

LONDON, ENGLAND

[CONTRIBUTION FROM THE CARBOHYDRATE LABORATORY, BUREAU OF CHEMISTRY, UNITED STATES DEPARTMENT OF AGRICULTURE]

OPTICAL ROTATION AND ATOMIC DIMENSION. VI

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The preparation of crystalline fluoro-hepta-acetyl cellobiose previously reported[1] necessitated the revision of the data for the other halogen-acetyl derivatives of this sugar. A careful purification of these *biose* derivatives and measurement of their rotations as recorded in the present paper led to the conclusion that they show a *deviation* from the regular relationship observed for the corresponding derivatives of the *monose sugars* (Table I). Thus it became interesting to compare the series of halogen derivatives of other *bioses*. As only an amorphous[2] fluoro-acetyl lactose could be obtained and the fluoro derivative is a characteristic value in the relationship, other bioses were investigated. Both maltose and gentiobiose octo-acetate gave crystalline fluoro-acetyl derivatives, but no crystalline bromo or iodo derivative could be obtained from maltose. Experiments for preparing the needed derivatives of gentiobiose, as well as of melibiose, will be conducted as soon as larger amounts of the octo-acetates of these sugars have been prepared.

The further study of fluorating acetyl derivatives[3] of sugars, however,

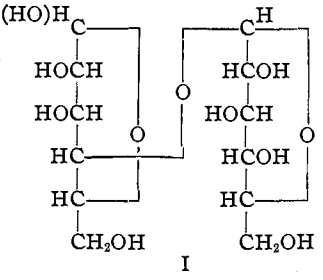
[1] Brauns, THIS JOURNAL, **45**, 834 (1923).

[2] The fluoro-acetyl derivatives of mannose and galactose also could not be obtained in a crystalline condition. Rhamnose, the only readily available monose sugar left, will be investigated in the near future.

[3] Helferich and co-workers [*Ann.*, **447**, 27 (1926)] have published an interesting synthesis of gentiobiose taking fluoro-acetyl glucose as a starting material and using particular properties of the fluoro derivatives for performing the synthesis. The possibility of splitting off the acetyl groups and preparing the fluoro sugars were known to the author when the first article of this series was written, as a saponification for analysis was first performed by shaking at 0° with 0.1 *N* sodium hydroxide solution and titration with sulfuric acid after the compound had dissolved, which showed that the acetyl groups were split off. Only traces of sodium fluoride were found to be present in the solution, however. Hence the saponification with boiling 0.25 *N* sulfuric acid was used for the analysis as has been described and it was intended to study the observed peculiarity. The author did not realize that this behavior could advantageously be used for syntheses, but thought it to be of value for the study of the structure of complicated carbohydrates.

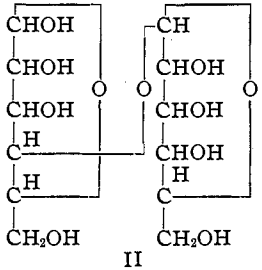
has given a method for obtaining pure, crystalline fluoro-chloro-bromo and iodo-hepta-acetyl derivatives of 4-glucosido-mannose, which was first obtained by Bergmann and Schotte[4] by an entirely different process.

Bergmann obtained this sugar by first preparing cellobial, a reduction product of cellobiose, containing a double bond between the originally reducing carbon atom and the next one. By oxidation with benzoyl-hydroperoxide the reducing carbon atom was restored and the next carbon atom obtained an hydroxyl group, but in a reversed position in comparison with the original cellobiose structure. Taking in account the latest views about the structure of cellobiose-like compounds, 4-glucosido-mannose is represented by Formula I.



I

4-Glucosido-mannose derivatives were obtained by the fluorating process by simply leaving octo-acetyl cellobiose in contact with hydrofluoric acid for a longer time (five hours) at room temperature, by which the acetyl group of the carbon atom next to the reducing carbon atom was saponified and the resulting hydroxyl group reversed, as was proved by the properties of the parent crystalline sugar, which were found to be the same as those recorded by Bergmann for 4-glucosido-mannose.



II

Lactose and cellobiose[5]

As the structure of 4-glucosido-mannose has the same type of carbon attachment as that of cellobiose and lactose, the comparison of the halogen hepta-acetyl derivatives of these sugars is particularly well adapted for our purpose. (Formula II.)

An examination of the compiled data for the specific rotations in Table I, in which the published relationship regarding the (Cl–F) and (Br–Cl) and (I–Br) ratio of the monose sugars is used for comparison, shows that the deviation from this ratio for cellobiose is *different* from that for 4-glucosido-mannose. However, if only the ratio of (Br–Cl) to (I–Br) as given in Table II (17:21 for the monose sugars) is

as the fluorating of the acetylated compounds and subsequent alkaline saponification of the acetyl groups could be followed by enzymatic hydrolysis, giving in this way an indication of replaceable acetyl groups in the original compound. The present article shows that the fluorating of acetyl derivatives of carbohydrates is not exhausted by yielding starting material for syntheses and possibly elucidating structures of available carbohydrates, but may also be used for the preparation of new bioses.

[4] Bergmann and Schotte, *Ber.*, **54**, 1564 (1921). The sugar was called by Bergmann and Schotte 5-glucosido-mannose. According to recent investigations of cellobiose it must be called 4-glucosido-mannose.

[5] Charlton, Haworth and Peat, *J. Chem. Soc.*, **1926**, p. 99. See also Irvine and MacDonald, *ibid.*, **1926**, p. 1508.

considered, we find good agreement, as the ratio of the respective cellobiose derivatives is 17:21 and that for the respective 4-glucosido-mannose derivatives also 17:21, and that for the respective lactose derivatives recently measured by Hudson and Kunz[6] is 17:20.

TABLE I

COMPARISON OF SPECIFIC ROTATIONS OF BIOSE DERIVATIVES WITH REPRESENTATIVE MONOSE DERIVATIVES (INCLUDING FLUORO DERIVATIVES)

	Derivatives of 4-Glucosido-mannose	Derivatives of Cellobiose	Respective spec. rotat. diff.		Respective spec. rotat. diff. reduced		Spec. rotat. diff. of monose sugars (glucose) reduced to Bragg's atom. diam. diff.
F	+13.6	+30.6					
			37.6	41.1	41	41	41
Cl	+51.2	+71.7					
			26.7	24.1	29	24	17
Br	+77.9	+95.8					
			33.6	29.9	37	30	21
I	+111.5	+125.7					

TABLE II

COMPARISON OF SPECIFIC ROTATIONS OF BIOSE DERIVATIVES WITH REPRESENTATIVE MONOSE DERIVATIVES (EXCLUDING FLUORO DERIVATIVES)

	Derivatives of Lactose	4-Glucosido-mannose	Cellobiose	Respective spec. rotation diff.			Resp. spec. rotat. diff. reduced			Spec. rotat. diff. of monose sugars (glucose) reduced to Bragg's atom. diam. diff.
Cl	+83.9	+51.2	+71.7							
				24.8	26.7	24.1	17	17	17	17
Br	+108.7	+77.9	+95.8							
				28.2	33.6	29.9	20	21	21	21
I	+136.9	+111.5	+125.7							

TABLE III

COMPARISON OF MOLECULAR ROTATIONS OF MONOSE AND BIOSE DERIVATIVES

	Derivatives of Glucose	Fructose	Xylose	*l*-Arabinose	4-Glucosido-mannose	Cellobiose	Respective mol. rotat. diff.					
F	+315	−316	+187	+384	+87	+195						
							294	274	317	336	248	274
Cl	+609	−590	+504	+720	+335	+469						
							204	187	214	253	210	201
Br	+813	−777	+718	+973	+545	+670						
							274	...	...	336	287	268
	+1087	...	...	+1309	+832	+938						

Taking into account the results given in the previous articles of this series, we may present the following summary and interpretation.

In the *monose* sugar derivatives we suppose that the halogens are situated at the *outer* parts of the molecule. Consequently the electronic orbits of

[6] Hudson and Kunz, THIS JOURNAL, **47**, 2052 (1925).

the halogens are not interfered with by the orbits of other atoms of the same molecule. With these derivatives the closely agreeing atomic-dimension relationship for the specific rotations is obtained (Part IV). On the other hand, we may infer that in the *bioses* the orbits of the larger halogen atoms (chlorine, bromine and iodine) are influenced in proportion to their size by atoms *which are situated in the neighborhood (as a result of the more complicated structure of the molecule)*, whereas the much smaller orbits of the fluorine atoms are not interfered with by these atoms, on account of being outside of their sphere of influence. The same interpretation seems to hold for the other class of asymmetric compounds (Part V), in which the halogens modify an asymmetric group attached to an asymmetric carbon atom and in which the *molecular* rotations have to be taken instead of the specific for comparison. In this class of compounds the observed regularity also seems to hold only if the halogens are situated at the outer parts of the molecule and are not interfered with by other atoms of the same molecule, as illustrated by the investigation of halogeno penta-acetyl salicins and halogeno acetyl-tetra-acetyl glucoses reported in Part V, whereas tetra-acetyl salicin halides prepared by Kunz[7] behave abnormally even as to the sign of rotation. In these latter derivatives the orbits of the halogens may be selectively influenced by surrounding atoms as described for the bioses. The preparation and measurement of the rotation of tetra-acetyl salicin fluoride would be of value in this connection.[8]

[7] Kunz, THIS JOURNAL, **48**, 262 (1926).

[8] It may appear that van't Hoff's superposition principle as applied by Hudson to the halogen acetyl derivatives of sugars [THIS JOURNAL, **46**, 462 (1924)] yields a satisfactory agreement between the rotations and their structure, without having to assume any additional structural property for the biose sugars, as has been made in this paper. The author believes that this impression is misleading for the following reasons: the molecular rotations of halogeno tetra-acetyl glucoses can be written according to Hudson's notations $(B_{gluc.} + A_F)$, $(B_{gluc.} + A_{Cl})$, $(B_{gluc.} + A_{Br})$, and $(B_{gluc.} + A_I)$. Hence we obtain for the differences of the molecular rotations of chloro-acetyl glucose and fluoro-acetyl glucose by subtraction $(B_{gluc.} + A_{Cl}) - (B_{gluc.} + A_F) = A_{Cl} - A_F$ (1), and in the same way for $(B_{gluc.} + A_{Br}) - (B_{gluc.} + A_{Cl}) = A_{Br} - A_{Cl}$ (2) and finally $(B_{gluc.} + A_I) - (B_{gluc.} + A_{Br}) = A_I - A_{Br}$ (3).

We find, therefore, that these differences of molecular rotations are dependent only on the A_F, A_{Cl}, A_{Br} and A_I values and, therefore, *each difference should have, according to Hudson's application of van't Hoff's superposition principle, the same value for all sugars.* Experimental data compiled in Table III are not in conformity with this deduction. The $(A_{Cl} - A_F)$ value for arabinose differs considerably from that for 4-glucosido-mannose and other sugars. If the $(A_{Cl} - A_F)$ value for arabinose were adopted, the specific rotations of the chloro compounds of 4-glucosido-mannose and fructose would have to be increased, respectively, by $+13°$ and $-17°$ to yield the same $(A_{Cl} - A_F)$ value as that for arabinose. Neither can it be said that the $(A_{Cl} - A_F)$ values are in good agreement with Hudson's application, even by excepting the arabinose value. On the other hand, we may remark that if the chloro-acetyl derivative of cellobiose had a specific rotation of $+78°$ instead of $+71.7°$ found, a difference of $6.3°$, an agreement with the atomic-diameter differences would have been obtained, as the ratio

The preparations of the 4-glucosido-mannose derivatives were as follows: by keeping octo-acetyl cellobiose in contact with anhydrous hydrofluoric acid at room temperature[9] as described in the experimental part, a sirup was obtained from which a pure, crystalline compound, found to be a fluoro-*hexa*-acetyl biose of specific rotation +20.7 could be separated. It was at first supposed to be a derivative of fluoro-hepta-acetyl cellobiose, in which one acetyl group had been saponified. Subsequent acetylation of the compound with zinc chloride and acetic anhydride, however, gave a pure, crystalline octo-acetyl biose of specific rotation +36.2 and, therefore, a compound not identical with α- or β-octo-acetyl cellobiose. On the other hand, acetylation with sodium acetate and acetic anhydride gave a pure, crystalline fluoro-hepta-acetyl *biose* with the specific rotation +13.6, whereas pure fluoro-hepta-acetyl *cellobiose* has a specific rotation[10] of +30.6. By a peculiar coincidence[11] the fluoro-hepta-acetyl derivative

of differences would have been 41:17, which is required by the relationship. A discrepancy of 6.3° from the observed regularity, however, has been rejected on the grounds that: (first) these halogeno acetyl derivatives of cellobiose and 4-glucosido-mannose have been purified and measured with the utmost care, and their specific rotations must be correct within half a degree; and (second) having established the very regular atomic-dimension relationship of the monoses, and not being hampered by any contradictory deduction, we are in the favored position of being able to derive just from these exceptional values important conclusions as to the structure of the bioses under consideration. Though Hudson's use of the superposition principle in its wide field of application has given and will undoubtedly give further interesting and important elucidation of structure, it is less accurate in relating structure to rotation than the atomic-dimension relationship in its only investigated application to the halogen derivatives. Another possibility of the application of the atomic-dimension relationship is that it makes possible the study of the magnitude of the rotation by investigating the rotations of halogen derivatives of a compound containing only one asymmetric carbon atom, yielding, therefore, the possibility of a deeper insight into the factors upon which the magnitude of the rotation of a single asymmetric carbon atom depends. These investigations will be taken up later. A systematic study of the influence of concentration, temperature, wave length, etc., also is given and it would be interesting to investigate whether the same relation for a set of halogen derivatives holds for every solvent. It is possible that a solvent forms molecular compounds or acts differently on the halogen derivatives. This would be indicated by a changed ratio. Further, the comparative x-ray analysis and the determination of the refractive indices of these sets of halogen compounds will be interesting in connection with the observed regularities.

[9] Penta-acetyl fructose, by a longer contact with hydrofluoric acid, also yields a crystalline fluoro compound different from the described derivative, as will be reported in detail later. Other sugars will also be investigated.

[10] A preliminary experiment was made by methylating fluoro-hexa-acetyl 4-glucosido-mannose with methyl iodide and silver oxide. A crystalline compound was separated, containing fluorine, of specific rotation +18.8; m. p., 101°. It seems possible, therefore, to obtain fluoro-hexa-acetyl-methyl 4-glucosido-mannose and probably a monomethyl-mannose in which the second carbon atom is methylated. Also, crystalline fluoro-mannose derivatives might be derived.

[11] This coincidence may be explained later, as our knowledge of the arrangements of the atoms in space and their rotational influence increases. A comparison of the struc-

+13.6 gives in combination with the chloro-, bromo- and iodo-hepta-acetyl cellobioses exactly the atomic dimension ratio 41: 17: 21 of the monoses. However, by treating the isomeric fluoro-hepta-acetyl derivatives of specific rotations +30.6 and +13.6 with a mixture of sulfuric acid and acetic anhydride, the former gave α-octo-acetyl cellobiose of specific rotation +41, and the latter gave the above-mentioned octo-acetyl biose of specific rotation +36.2. The fluoro-hepta-acetyl derivative of +13.6 and its octo-acetate of +36.2 are, therefore, identified as belonging to a different biose. The parent sugar was prepared in crystalline conditions and found to be identical with Bergmann's 4-glucosido-mannose. The octo-acetate of this sugar was prepared in larger amounts from the sirup obtained from fluoration, and was used as a starting material for the preparation of the crystalline chloro-, bromo- and iodo-hepta-acetyl derivatives, described in the experimental part. It is further noteworthy that bromo-hepta-acetyl cellobiose shaken with silver acetate in glacial acetic acid solution gives a very good yield of pure β-octo-acetyl cellobiose, which was formerly obtainable only in poor yield by way of the free cellobiose through a tedious recrystallization process as described by Hudson and Johnson.[12] It is intended to use this reaction for preparing the isomeric octo-acetate of 4-glucosido-mannose.

Experimental Part

General Remarks.—For all determinations of the specific rotation, chloroform U.S.P. or purified chloroform[13] was used. The volume of the solution was made up in the same flask to 24.9767 cc. at 20°, which requires multiplication by the factor 4.0038 for obtaining 100 cc. The reading was performed in the same 4dm. tube at 20° and is given in circular degrees.

Fluoro-hepta-acetyl Cellobiose.—The preparation of this compound described in Part I of this series[14] was improved by keeping the closed receiver after the distillation one and a half hours longer in ice. The reaction product was worked up in the manner already described. From 10 g. of α-cellobiose-octo-acetate[15] 5 g. (instead of 2 g.) of pure fluoro-hepta-acetyl cellobiose is obtained. The following record shows that the

ture of fluoro-hepta-acetyl cellobiose and fluoro-hepta-acetyl 4-glucosido-mannose indicates that a hydrogen atom is the selectively influencing atom.

[12] Hudson and Johnson, THIS JOURNAL, **37**, 1276 (1915). See also Hess and Salzmann, *Ann.*, **445**, 118 (1925).

[13] THIS JOURNAL, **46**, 1486 (1924).

[14] *Ibid.*, **45**, 833 (1923).

[15] For the preparation of α-cellobiose octo-acetate, which was needed in large amounts for the investigation of 4-glucosido-mannose, only the method of Klein [*Z. angew. Chem.*, **25**, 1409 (1912)] was found to give good results. The crude product which crystallizes after standing for two days, however, is not poured into water as described by Klein, but filtered on a Büchner filter with small holes containing a double layer of ordinary filter paper, washed with ether, stirred in a dish with 95% alcohol, again filtered by suction, and at last recrystallized from hot 95% alcohol, by which a pure preparation is obtained.

pure compound has a specific rotation of +30.62 (previously found, +30.03). The 8.7 g. of impure product obtained by evaporating the chloroform solution was dissolved in 250 cc. of hot 95% alcohol, the solution filtered by the aid of a hot-water funnel, and seeded for preventing gelatination. The first three fractions obtained on standing and cooling (about 5 g.) gave a specific rotation of about +30. The results of the recrystallizations of this preparation carried out in the same way (taking the first fraction) gave the following results.

Rotation. First recrystallization. Subs., 0.6158, 0.6208: α = +2.984, +3.005; $[\alpha]_D^{20}$ = +30.25, +30.22.

Second recrystallization. Subs., 0.6306, 0.6555: α = +3.091, +3.206; $[\alpha]_D^{20}$ = +30.61, +30.54.

Third recrystallization. Subs., 0.6254, 0.6178: α = +3.067, +3.029; $[\alpha]_D^{20}$ = +30.62, +30.61.

Fourth recrystallization. Subs., 0.6127: α = +3.005; $[\alpha]_D^{20}$ = +30.62. This is taken as the specific rotation of the pure substance.

Chloro-hepta-acetyl Cellobiose.—The preparation of this compound has received attention from many investigators.[16] Bodart's method, as described by Skraup and König was followed. Several preparations of the compound showed that it is well to keep the sealed tube for one week, after which it is cooled and opened and the contents are evaporated in a dish with a current of dry air under a bell jar. Different methods of recrystallization were followed, the method of Weltzien by adding ether to a chloroform solution giving the best results. The first recrystallizations are advantageously performed by quickly filtering off by suction the first separation of crystals, which contain most of the impurities. This careful study of the method of purification showed that the specific rotation is +71.70. Therefore, the higher rotations recorded by Geinsperger (+75.21 and +74.87) and by Schliemann (+73.8) are erroneous. The pure compound melts sharply at 200–201°, whereas Hardt-Stremayr reports 195°, Schliemann 186–187° and Weltzien 192°. The first recrystallization of preparations of the compound often show a rotation of about +65°. A record follows of recrystallizations of combined preparations having a purity indicated by a specific rotation of +70 to +71. The recrystallization is performed by adding ether to a concentrated chloroform solution until crystallization just starts.

Rotation. First crystallizations: first and second fractions, respectively. Subs., 0.6064, 0.6123: α = +6.931, +7.018; $[\alpha]_D^{20}$ = +71.37, +71.56.

Recrystallization of first fraction. Subs., 0.6062, 0.6067, 0.6002: α = +6.966, +6.983, +6.897; $[\alpha]_D^{20}$ = +71.75, +71.87, +71.75.

Recrystallization of the preceding fraction. Subs., 0.6019, 0.6140: α = +6.814, +7.049; $[\alpha]_D^{20}$ = +71.72, +71.68.

The average, $[\alpha]_D^{20}$ = +71.70, is taken as the specific rotation of the pure substance.

Anal. Subs., 0.2012: CO_2, 0.3501; H_2O, 0.1001. Subs., 0.2030: AgCl, 0.0445. Calcd. for $C_{26}H_{35}O_{17}Cl$: C, 47.65; H, 5.39; Cl, 5.42. Found: C, 47.46; H, 5.56; Cl, 5.42.

Bromo-hepta-acetyl Cellobiose.—This compound was prepared by the method of Fischer and Zemplén.[17] They found for two determinations of the specific rotation in chloroform +95.30 and +96.32. The successive recrystallizations made according to these authors gave the following results, using purified chloroform as a solvent.

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[16] Geinsperger, *Monatsh.*, **26**, 1415 (1905). Hardt-Stremayr, *ibid.*, **28**, 63 (1907). Schliemann, *Ann.*, **378**, 374 (1911). See also Bodart's method described by Skraup and König, *Monatsh.*, **22**, 1033 (1901). Weltzien, *Ann.*, **435**, 144 (1923).

[17] Fischer and Zemplén, *Ber.*, **43**, 2538 (1910). Zemplén, *Ber.*, **53**, 996 (1920).

Rotation. Subs., 0.6110: $\alpha = +9.316$; $[\alpha]_D^{20} = +95.20$.

Third recrystallization. Subs., 0.6041, 0.6118, 0.6089: $\alpha = +9.253, +9.340, +9.316$; $[\alpha]_D^{20} = +95.64, +95.32, +95.53$.

Fourth recrystallization. Subs., 0.6207, 0.6162: $\alpha = +9.513, +9.451$; $[\alpha]_D^{20} = +95.70, +95.77$.

Fifth recrystallization. Subs., 0.6063: $\alpha = +9.298$; $[\alpha]_D^{20} = +95.76$, which is taken as the specific rotation of the pure substance.

Iodo-hepta-acetyl Cellobiose.—This derivative was prepared according to the method of Fischer and Zemplén,[17] who found the specification rotation in chloroform to be +125.6. The following rotations were made with purified chloroform as a solvent.

Rotation. Second recrystallization. Subs., 0.7146, 0.7630: $\alpha = +14.296, +15.266$; $[\alpha]_D^{20} = +124.91, +124.93$.

Third recrystallization. Subs., 0.6148, 0.6530: $\alpha = +12.359, +13.100$; $[\alpha]_D^{20} = +125.52, +125.27$.

Fourth recrystallization. Subs., 0.6505, 0.6098, 0.6641: $\alpha = +13.083, +12.269, +13.378$; $[\alpha]_D^{20} = +125.58, +125.62, +125.78$.

The value +125.70 was taken as the specific rotation of the pure substance.

β-Octo-acetyl Cellobiose from Bromo-hepta-acetyl Cellobiose.—A solution of 3 g. of bromo-hepta-acetyl cellobiose in 50 cc. of glacial acetic acid was shaken with 4 g. of silver acetate. After one-half hour a filtered sample was found to be free from bromine. The reaction product was filtered into a large casserole and the residue on the filter washed with glacial acetic acid. The water-clear filtrate was diluted with about thrice its volume of water, nearly neutralized with sodium bicarbonate, shaken out with chloroform, and then entirely neutralized and shaken out again. The chloroform evaporated on the steam-bath with a current of air left 2.7 g. of white crystals, which were powdered and dried in a vacuum. The determination of the specific rotation gave the following results.

Rotation. Subs., 0.7719: $\alpha = -1.490$; $[\alpha]_D^{20} = -12.5$.

After a recrystallization from alcohol. Subs., 1.1959: $\alpha = -2.703$; $[\alpha]_D^{20} = -14.11$.

Hudson and Johnson[12] found for the pure compound in different concentrations −14.48 and −14.74.

Fluoro-hexa-acetyl 4-Glucosido-mannose.—After this compound had been prepared in small amounts with the aid of a platinum still, it was also prepared with approximately the same yield on a larger scale with copper apparatus. The retort contained 2 kg. of dry potassium hydrogen fluoride (KF.HF) and the receiver 200 g. of powdered octo-acetyl cellobiose. The retort condenser and receiver were connected by brass ground joints, the receiver being also connected with a copper calcium chloride tube. Ice water was used for cooling and the receiver was cooled in an ice-and-salt bath. The distillation was finished in about two hours and the tared receiver hermetically closed and weighed. The yield of hydrofluoric acid was mostly about $^1/_5$ of the used salt. After being kept for five hours at room temperature, the receiver was cooled in an ice-and-salt bath, and the contents were poured into a large separatory funnel containing water, cracked ice and chloroform. The chloroform extract was dried and concentrated in a vacuum and the chloroform-free yellow sirup poured into a beaker and stirred with methyl alcohol. The mixture solidified gradually to a thick mass of white crystals, which was separated by suction after standing overnight. The mother liquor gave another crop of crystals on standing. The total yield was more than 30 g. The mother liquor was dried in a vacuum and used as the starting substance for the preparation of the octo-acetyl 4-glucosido-mannose described below. The recrystallization of fluoro-hexa-acetyl 4-glucosido-mannose is easily accomplished from hot methyl alcohol, from which it separates in small needles on cooling. The pure compound melts at

145° (not sharp). The determination of the specific rotation in chloroform gave the following result.

Rotation. First recrystallization. Subs., 0.3729: $\alpha = +1.248$; $[\alpha]_D^{20} = +20.90$.

Second recrystallization. Subs., 0.7925: $\alpha = +2.634$; $[\alpha]_D^{20} = +20.75$.

This last value is taken as the specific rotation of the pure substance. Other preparations often gave a final rotation of about +20.0.

Anal. Subs., 0.2472: CO_2, 0.4364; H_2O, 0.1149. Subs., 0.5000: CaF_2, 0.0291. Subs., 0.6000: 106.18 cc. of 0.25 *N* H_2SO_4, 329.20 cc. of 0.1 *N* NaOH. Calcd. for $C_{12}H_{14}O_3(C_2H_3O_2)_6OHF$: C, 48.30; H, 5.58; F, 3.19; 64.95 cc. of 0.1 *N* NaOH for CH_3COOH + F. Found: C, 48.15; H, 5.20; F, 2.83; 63.75 cc. of 0.1 *N* NaOH.

Octo-acetyl 4-glucosido-mannose can be obtained by acetylating fluoro-*hexa*-acetyl 4-glucosido-mannose with zinc chloride and acetic anhydride. It is also obtained by acetylating in the same way the mother liquor of this fluoro compound. If large quantities are needed it is advantageous to acetylate directly with zinc chloride the sirup obtained from the fluorating process. The mother liquor weighed about 90 g. Five hundred and sixty cc. of acetic anhydride, in which 6 g. of zinc chloride had been dissolved, was gradually added to this sirup in a round flask and boiled for 10 minutes. The hot solution was poured into a large amount of ice water and, by stirring, the octo-acetyl derivative was soon obtained in a crystalline form. It was filtered by suction and recrystallized from hot methyl alcohol. Two recrystallizations gave about 35 g. of pure product; m. p., 202–203°. The determination of the specific rotation in chloroform gave the following results.

Rotations. First recrystallization. Subs. 0.8966: $\alpha = +5.164$; $[\alpha]_D^{20} = +35.96$.

Second recrystallization. Subs., 1.0366: $\alpha = +6.030$; $[\alpha]_D^{20} = +36.32$.

Third recrystallization. Subs., 1.3840: $\alpha = +8.023$; $[\alpha]_D^{20} = +36.20$.

Fourth recrystallization. Subs., 1.3830, 0.5789: $\alpha = +8.006, +3.362$; $[\alpha]_D^{20} = +36.15, +36.26$.

The value +36.20 was taken as the specific rotation of the pure substance. The compound which crystallizes in small needles is tasteless. It is sparingly soluble in benzene, slightly more so in alcohol, and fairly soluble in other solvents except petroleum ether and water. The saponifications were conducted by boiling the substances with 0.25 *N* sulfuric acid for three and a half and three hours in a quartz flask and titrating with 0.1 *N* sodium hydroxide solution, using phenolphthalein as indicator.

Anal. Subs., 0.2545: CO_2, 0.4627; H_2O, 0.1278. Subs. 0.5000, 0.5000: 105.95, 105.95 cc. of 0.25 *N* H_2SO_4; 323.94 of, 324.12 cc. of 0.1 *N* NaOH. Subs., 0.4715, 0.3111: C_6H_6, 100, Δf, 0.032°, 0.025°. Calcd. for $C_{28}H_{38}O_{19}$: C, 49.54; H, 5.65; 59.00 cc. of 0.1 *N* NaOH for AcOH; mol. wt., 678. Found: C, 49.58; H, 5.62; 59.1, 59.2 cc. of 0.1 *N* NaOH; mol. wt., 736, 622.

Preparation and Identification of 4-Glucosido-mannose

The parent sugar of the above-described octo-acetate of specific rotation +36.2 was prepared by the saponification method of Weltzien and Singer.[18] Six g. of octo-acetate was dissolved in 1250 cc. of methyl alcohol and the solution cooled in ice. To this solution was added the necessary amount of titrated barium methylate solution prepared according to Weltzien and Singer and the product was kept in the ice box overnight. The necessary amount of 0.25 *N* sulfuric acid was then added and the liquid filtered through an asbestos mat on a Buechner funnel. The neutral filtrate was distilled in a vacuum and at last dried in a vacuum desiccator over sodium hydroxide. The residue was dissolved in a small amount of water, the solution filtered and again dried in the

[18] Weltzien and Singer, *Ann.*, **443**, 104 (1925).

vacuum desiccator. The residue was extracted by stirring repeatedly with absolute alcohol at room temperature and filtering through a hardened filter. The alcoholic solution was allowed to evaporate in a crystallizing dish at the air. Crystals separated, which proved to be tetrahedrons when observed with a magnifying glass. The yield was about 0.8 g. of crystals. The crystalline sugar reduced Fehling's solution and was slightly sweet.

Anal. Subs., 0.1561: CO_2, 0.2265; H_2O, 0.0967. Calcd. for $C_{12}H_{22}O_{11} + H_2O$: C, 39.98; H, 6.72. Found: C, 39.64; H, 6.93.

In conformity with this result of the combustion the sugar was found to contain one molecule of crystallization water, which is given off by drying at 100° in a high vacuum; m. p. of the water-containing sugar, 139–140°; m. p. of the water-free sugar, 174–175°. The determination of the specific rotation of the sugar containing one molecule of crystallization water was determined in watery solution. The air dry substance taken was 0.4854 g.; after 15 minutes the specific rotation was found to be $[\alpha]_D^{20} = +7.3$; after 35 minutes, +6.5; after 80 minutes, +5.8; after 24 hours, the same value, +5.8, was found. For the octo-acetate prepared with acetic anhydride and sodium acetate as a catalyst, as described, $[\alpha]_D^{20} = +36.2$ was found; m. p., 202–203°.

Bergmann and Schotte[4] found for 4-glucosido-mannose that it is represented in air-dry condition by the formula $C_{12}H_{22}O_{11} + H_2O$, that it loses its water of crystallization in a high vacuum at 100°, melts in water-free condition at 175–176° (corr.), that the sugar containing water of crystallization mutarotates in water in about 10% solution from 12.4 (seven minutes) to $[\alpha]_D^{20} = +9.7$ constant, and that the octo-acetate prepared with acetic anhydride and pyridine as a catalyst gives an octo-acetate with $[\alpha]_D^{20} = +33.2$ (acetylene tetrachloride) and melting at 196–197°. The description of the crystals by the authors as "vielseitig" may be a misprint for "vierseitig." As these data agreed with those reported above (the slight disagreement found in the specific rotations of the sugar being probably due to the inaccuracy of the determination of this low-rotating sugar), the experiments which Bergmann and Schotte performed for proving that their substance yields on hydrolysis mannose and glucose were repeated with the sugar prepared from the fluorating process.

Forty-five hundredths g. of the sugar hydrolyzed with *N* hydrochloric acid and neutralized and concentrated to a small volume gave with phenylhydrazine and acetic acid 0.300 g. of phenylhydrazone (calcd., 0.340 g.). The hydrazone was recrystallized from hot water and afterwards from 60% alcohol and gave colorless crystals melting at 198° which did not change their melting point after being mixed with phenylhydrazone prepared from mannose (Bergmann and Schotte found a melting point of 197–201°) which identifies the substance as mannose phenylhydrazone. From the filtrate of the mannose phenylhydrazone 0.180 g. of glucose phenylosazone was separated in the ordinary way. The osazone was recrystallized by dissolving in hot absolute alcohol and diluting to a 30% alcoholic solution. The separated crystals were filtered off and washed with a small amount of 30% alcohol and cold acetone. The melting point was 210°, which did not change on admixture of the substance with some osazone prepared from glucose.

From these experiments is concluded that a 4-glucosido-mannose derivative is formed from cellobiose-octo-acetate by dissolving this compound in water-free hydrofluoric acid and keeping the solution for five hours at room temperature.

Fluoro-hepta-acetyl 4-Glucosido-mannose is prepared by acetylating fluoro-*hexa*-acetyl 4-glucosido-mannose with sodium acetate and acetic anhydride. To a solution of 1.5 g. of water-free sodium acetate in 24 cc. of hot acetic anhydride is added 3 g. of fluoro-*hexa*-acetyl 4-glucosido-mannose, and the mixture is boiled for ten minutes. The reduction product, poured into ice water, yields the crystalline product, which is

separated by suction and recrystallized from methyl alcohol. Two recrystallizations gave about 2 g. of pure product; m. p., 155–156°. The determination of the specific rotation in chloroform gave the following results.

Rotation. First recrystallization. Subs., 0.7071: $\alpha = +1.515$; $[\alpha]_D^{20} = +13.37$.
Second recrystallization. Subs., 1.0536: $\alpha = +2.322$; $[\alpha]_D^{20} = +13.76$.
Third recrystallization. Subs., 0.8334: $\alpha = +1.799$; $[\alpha]_D^{20} = +13.48$. Second fraction of the same. Subs., 0.6404: $\alpha = +1.400$; $[\alpha]_D^{20} = +13.65$.

The value +13.60 was taken as the specific rotation of the pure substance. The compound, which crystallizes in small needles, is tasteless. It is sparingly soluble in benzene, slightly more so in alcohol, and fairly soluble in other solvents except petroleum ether and water.

Anal. Subs., 0.2209: CO_2, 0.3959; H_2O, 0.1135. Subs., 0.5000: CaF_2, 0.0277. Subs., 0.5000: 106.18 cc. of 0.25 *N* H_2SO_4; 328.16 cc. of 0.1 *N* NaOH. Subs., 0.8606, 0.7842; C_6H_6, 100 Δf, 0.071°, 0.075°. Calcd. for $C_{26}H_{35}O_{17}F$: C, 48.88; H, 5.53; F, 2.97; 62.67 cc. of 0.1 *N* NaOH for AcOH + F; mol. wt., 638. Found: C, 48.88; H, 5.74; F, 2.69; 62.7 cc. of 0.1 *N* NaOH; mol. wt., 605, 523.

α-Octo-acetyl Cellobiose from Fluoro-hepta-acetyl Cellobiose and Octo-acetyl 4-Glucosido-mannose from Fluoro-hepta-acetyl 4-Glucosido-mannose.—These conversions are important for proving that the isomeric fluoro derivatives belong to different bioses as indicated by their preparations. A solution of 0.5 g. of the fluorine derivative of specific rotation +30.6 in 5 cc. of a mixture of 20% by weight of sulfuric acid in acetic anhydride was heated to boiling over a small flame, and directly cooled with ice. Working up the reaction product in the ordinary way made possible the separation of nearly 0.1 g. of a substance which contained no fluorine, melted at 225°, and had a specific rotation of +40, thus agreeing sufficiently with the data recorded for the pure α-octo-acetyl-cellobiose as recorded by Hudson and Johnson;[13] m. p., 229.5°; $[\alpha]_D^{20} = +41$.

The same procedure applied to 0.5 g. of fluorine derivative of specific rotation +13.6 gave a substance which did not contain fluorine, melted at 203°, and had a specific rotation of +35, thus agreeing sufficiently with the recorded data for the pure octo-acetyl pseudo-cellobiose; m. p., 202–203°; $[\alpha]_D^{20} = +36$. A mixture of each separated substance with the one with which it had been identified did not change the melting point appreciably, whereas a mixture with the other octo-acetate gave a melting point of about 197°.

Chloro-hepta-acetyl 4-Glucosido-mannose was prepared from octo-acetyl 4-glucosido-mannose, using the same procedure as for the isomeric cellobiose compound. The method of purification is, however, different. The compound was dissolved in pure ethyl acetate (alcohol-free) and petroleum ether was added until crystallization started. The first recrystallization is advantageously conducted by quickly filtering off by suction the first separation of crystals, which contain most of the impurities; m. p. of the pure substance, 172°. The determination of the specific rotation in purified chloroform gave the following results.

Rotation. First recrystallization. Subs., 0.7994: $\alpha = +6.516$; $[\alpha]_D^{20} = +50.90$.
Second recrystallization. Subs., 0.6075: $\alpha = +4.974$; $[\alpha]_D^{20} = +51.12$.
Third recrystallization. Subs., 0.6616: $\alpha = +5.406$; $[\alpha]_D^{20} = +51.02$.
Fourth recrystallization. Subs., 0.4831: $\alpha = +3.951$; $[\alpha]_D^{20} = +51.06$.

Therefore, +51.12 did not change on further recrystallization. Other preparations gave as final rotations +51.10 to 51.20. Therefore, +51.20 is taken as the specific rotation of the pure substance. The compound, which crystallizes in small needles, is tasteless. It is sparingly soluble in benzene and fairly soluble in other solvents except ether and petroleum ether and water. It seems to be changed by alcohol which colors it yellow. The saponification was performed by shaking the substance for 80 hours at 0° with 0.1 *N* sodium hydroxide solution and titrating with 0.1 *N* sulfuric acid.

Anal. Subs., 0.2398: CO_2, 0.4197; H_2O, 0.1166. Subs., 0.1954: AgCl, 0.0435. Subs. 0.6000: 190.35 cc. of 0.1 *N* NaOH; 117.20 cc. of 0.1 *N* H_2SO_4. Subs., 1.4042: C_6H_6, 100, Δf, 0.109°. Calcd. for $C_{26}H_{35}O_{17}Cl$: C, 47.65; H, 5.39; Cl, 5.41; 73.31 cc. of 0.1 *N* NaOH; mol. wt., 655. Found: C, 47.73; H, 5.44; Cl, 5.41; 73.11 cc. of 0.1 *N* NaOH; mol. wt., 644.

Bromo-hepta-acetyl 4-Glucosido-mannose was prepared from octo-acetyl 4-glucosido-mannose, using the same procedure as for the isomeric cellobiose compound. The method of purification is, however, different. The impure compound was stirred with absolute ether, filtered off by suction and washed with ether. It was dissolved in ethyl acetate (alcohol-free), the solution filtered and petroleum ether was added until crystallization started; m. p. of the pure compound, 168–169°. The determination of the specific rotation in purified chloroform gave the following results.

Rotation. First recrystallization. Subs., 0.3603: $\alpha = +5.770$; $[\alpha]_D^{20} = +77.78$.
Second recrystallization. Subs., 0.3094: $\alpha = +4.955$; $[\alpha]_D^{20} = +77.63$.
Third recrystallization. Subs., 0.6141: $\alpha = +9.835$; $[\alpha]_D^{20} = +77.88$.

The value +77.90 is taken as the specific rotation of the pure substance. The compound, which crystallizes in small needles, is tasteless and has the same general properties as those reported for the chloro compound. The saponification required 48 hours' shaking at 0° with 0.1 *N* sodium hydroxide solution.

Anal. Subs., 01.882: CO_2, 0.3087; H_2O, 0.0840. Subs., 0.1901: AgBr, 0.0512. Subs., 0.6000: 187.5 cc. of 0.1 *N* NaOH; 118.93 cc. of 0.1 *N* H_2SO_4. Subs., 0.7025, 1.4646: C_6H_6, 100; Δf, 0.055°, 0.115°. Calcd. for $C_{26}H_{35}O_{14}Br$: C, 44.62; H, 5.05; Br, 11.43; 68.65 cc. of 0.1 *N* NaOH for CH_3COOH + Br; mol. wt., 699. Found: C, 44.73; H, 4.99; Br, 11.46; 68.57 cc. of 0.1 *N* NaOH; mol. wt., 639, 637.

Iodo-hepta-acetyl 4-Glucosido-mannose.—On account of the theoretical considerations involved, the attempts to prepare this substance which had been unsuccessful using Fischer and Zemplén's[17] method and also Sloan-Mills' method[19] were resumed and finally led to preparation of the pure, crystalline substance by modifying Mills' method by working at about —15°. Eight g. of octo-acetyl 4-glucosido-mannose was dissolved in 16 cc. of methylene chloride in a large Pyrex test-tube, and cooled in an ice-and-salt bath. A slow stream of dry hydriodic acid was passed through the solution for half an hour. The solution was poured into a cold crystallizing dish and evaporated under a glass jar by means of a rapid current of dry air. The sirup left after evaporation was extracted with petroleum ether by stirring and pouring off the solution. This procedure was repeated several times. To the residue was added some ether, and by rubbing with a glass rod the sirup was brought to crystallization. The crystals were filtered off by suction, washed with ether and recrystallized by dissolving in a small amount of alcohol-free ethyl acetate, adding some ether and finally petroleum ether until turbidity appeared. Some crystals were then added and the mixture was stirred until crystallization started. The substance crystallizes in small needles grouped around a center, and melts or decomposes at 140°, a dark brown melt being formed at this temperature. It is not stable, but can be kept in pure condition in a desiccator over sodium hydroxide in the ice box. The compound is slightly bitter. It is insoluble in petroleum ether and water, slightly soluble in ether and benzene and readily soluble in chloroform and ethyl acetate. The determination of the specific rotation in purified chloroform gave the following results.

Rotation. Second recrystallization. Subs., 0.4316: $\alpha = +7.715$; $[\alpha]_D^{20} = +111.61$.
Third recrystallization. Subs., 0.4361: $\alpha = +7.784$; $[\alpha]_D^{20} = +111.45$.

Therefore +111.50 is taken as the specific rotation of the pure substance, as another preparation gave as a final rotation +111.40.

[19] Mills, *Chem. News*, **106**, 165 (1912).

Anal. Subs., 0.2354: CO_2, 0.3629; H_2O, 0.1031. Subs., 0.1517: AgI, 0.048. Calcd. for $C_{26}H_{35}O_{17}I$: C, 41.82; H, 4.73; I, 17.01. Found: C, 42.04; H, 4.94; I, 17.10.

Summary

The specific-rotational values reported in the literature for chloro-, bromo- and iodo-hepta-acetyl cellobiose have been revised. In addition to the fluoro-hexa-acetyl and octo-acetyl compounds, the fluoro, chloro-, bromo- and iodo-hepta-acetyl derivatives of 4-glucosido-mannose have been prepared and described. A comparison of the specific rotational values shows that these two sets of *biose* derivatives deviate from the regular relationship observed for the corresponding derivatives of the *monose* sugars. An agreement is, however, obtained by excluding the values for the fluoro derivatives. When studied for other bioses these deviations may lead to a more detailed knowledge of the spatial arrangement of the atoms in the bioses.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF STANFORD UNIVERSITY]

THERMAL DATA ON ORGANIC COMPOUNDS. IV. THE HEAT CAPACITIES, ENTROPIES AND FREE ENERGIES OF NORMAL PROPYL ALCOHOL, ETHYL ETHER AND DULCITOL

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In three earlier papers[1] it has been shown that the entropy and free energy of an organic compound are related to its constitution in a simple additive manner. In the present investigation, heat-capacity data for *n*-propyl alcohol, ethyl ether and dulcitol have been obtained and thereby the corresponding entropies and free energies have been calculated. These new results enable us to test further the above proposition. Moreover, the results accumulated thus far permit an interesting comparison to be made between the entropies and free energies of three sets of isomers, namely, *n*- and *iso*propyl alcohol, ether, *n*-butyl alcohol and *tert.*-butyl

TABLE I

THE ENTROPIES AND FREE ENERGIES OF SOME ISOMERS AT 298°K.

Substance		M. p., °K.	Entropy	Free energy, cal.
C_3H_8O	*n*-Propyl alcohol	147.0	51.2	−44,100
	*iso*Propyl alcohol	184.6	45.6	−47,700
$C_4H_{10}O$	Ethyl ether	156.8	67.7	−33,600
	n-Butyl alcohol	183.9	60.2	−44,100
	tert.-Butyl alcohol	298.5	47.2	−49,900
$C_6H_{14}O_6$	Mannitol	439.1	60.5	−226,200
	Dulcitol	461	59.2	−228,100

[1] Parks, THIS JOURNAL, **47**, 338 (1925). Parks and Kelley, *ibid.*, **47**, 2094 (1925). Parks and Anderson, *ibid.*, **48**, 1506 (1926).