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RELATIONS BETWEEN ROTATORY POWER AND STRUCTURE IN THE SUGAR GROUP. XXXI. THE ALPHA AND BETA FORMS OF ETHYL-*d*-GLUCOSIDE AND THEIR TETRAACETATES¹

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According to Hudson's³ second rule of isorotation the sum of the molecular rotations of the alpha and beta derivatives of any aldose where only the end asymmetric carbon atom is affected, is equal to the sum for the alpha and beta forms of the aldose itself. Using the best data of the present time for the rotations of the α and β forms of glucose and methylglucoside, one observes that the rule is borne out very well (see Table I), the difference of the sums being less than 3° in specific rotation. In Hudson's 1909 article, similar data were quoted from E. Fischer⁴ for α -ethylglucoside and from Koenigs and Knorr⁵ for β -ethylglucoside; namely, $(\alpha)_D + 151^\circ$ and -30° , respectively, leading to $(151-30)(208) = 25,200$ as the molecular rotation sum for these substances. This value is somewhat larger (5 to 7° in specific rotation) than those mentioned, but it is to be noticed that Koenigs and Knorr's measurement is only approximate, having been obtained from an amorphous substance. Crystalline β -ethylglucoside was first prepared through enzymotic synthesis by Bourquelot and Bridel,⁶ who reported its $[\alpha]_D$ value to be -33.4° in aqueous solution, and this rotation was later revised by Bourquelot⁷ to -35.8° . For α -ethylglucoside Bourquelot⁷ reported $[\alpha]_D +150.9^\circ$, confirming Fischer's measurement. The revised data of Bourquelot lead to the sum $(150.9-35.8)(208) = 23,940$, which agrees closely with the sums for the forms of glucose and of methylglucoside. The writer has now re-prepared both α - and β -ethylglucoside by chemical synthesis in crystalline condition, and also their crystalline tetraacetates, the alpha isomer of which is a new

¹ The author has arranged with Dr. C. S. Hudson, at whose suggestion this research was carried out, that it be published in this series. No. XXX, by Dale and Hudson, was published in *THIS JOURNAL*, **52**, 2534 (1930).

² Submitted in partial fulfillment of the requirements for the Ph.D. degree in the Graduate School of the University of Pittsburgh.

³ Hudson, *THIS JOURNAL*, **31**, 66 (1909), *Scientific Papers of the Bureau of Standards*, No. 533 (1925). *Reports on Carbohydrates, Tenth Conference of the International Union of Chemistry, Liège, 1930*, p. 59.

⁴ Fischer, *Ber.*, **23**, 1154 (1895).

⁵ Koenigs and Knorr, *ibid.*, **34**, 972 (1901). In Hudson's 1909 article this reference should take the place of the one to E. F. Armstrong, for β -ethylglucoside.

⁶ Bourquelot and Bridel, *Compt. rend.*, **155**, 86 (1912); *Ann. chim. phys.*, **29**, 190 (1913).

⁷ Bourquelot, *J. pharm. chim.*, **14**, 225 (1916).

substance. As is shown in the tables, the rotations of these four substances agree closely with Hudson's second rule of isorotation.

TABLE I

CONFIRMATION OF HUDSON'S SECOND RULE OF ISOROTATION. GLUCOSE AND THE METHYL- AND ETHYLGLUCOSIDES

Substance	$[\alpha]_D$ in H ₂ O	Mol. wt.	Mol. rot.	Sum
α - <i>d</i> -Glucose ⁸	113	180	+20,340	
β - <i>d</i> -Glucose ⁸	19	180	+ 3,420	23,760
α -Methyl- <i>d</i> -glucoside ⁹	158.9	194	30,830	
β -Methyl- <i>d</i> -glucoside ⁹	-34.2	194	- 6,630	24,200
α -Ethyl- <i>d</i> -glucoside	152	208	31,620	
β -Ethyl- <i>d</i> -glucoside	-36.7	208	- 7,630	23,990

TABLE II

CONFIRMATION OF HUDSON'S SECOND RULE OF ISOROTATION. ACETATES OF THE SUBSTANCES

Substance	$[\alpha]_D$ in CHCl ₃	Mol. wt.	Mol. rot.	Sum
α - <i>d</i> -Glucose pentaacetate ¹⁰	101.6	390	39,600	
β - <i>d</i> -Glucose pentaacetate ¹⁰	3.8	390	1,500	41,100
α -Methyl- <i>d</i> -glucoside tetraacetate ¹⁰	130.6	362	47,300	
β -Methyl- <i>d</i> -glucoside tetraacetate ¹⁰	-18.3	362	- 6,600	40,700
α -Ethyl- <i>d</i> -glucoside tetraacetate	132.1	376	49,670	
β -Ethyl- <i>d</i> -glucoside tetraacetate	-22.7	376	- 8,535	41,135

The present data for the rotation of the acetates of the ethylglucosides can be used for the calculation of the rotations of the two forms of heptaacetylmaltoside by Hudson's first rule of isorotation. Hudson and Johnson¹¹ have shown from the rotational values of the alpha and beta forms of octaacetylmaltose that the value for the B part of the molecule (which concerns itself with all of the molecule excepting the aldehyde carbon atom) should be one-half the sum of the molecular rotations of the two forms or $125,400/2 = 62,700$. The value for A (the aldehyde carbon atom with the attached ethyl group) calculated as half the difference of the rotations of the alpha and beta forms of tetraacetylmaltoside is $(49,670 + 8,535)/2 = 29,102$. Combining these two values, we have for the alpha form of heptaacetyl methylmaltoside $[\alpha]_D = (29,102 + 62,700)/664 = 138^\circ$, and for the beta modification $[\alpha]_D = (-29,102 + 62,700)/664 = 50.6^\circ$, both referred to chloroform solution. From the close agreement of the latter value with that obtained by Fischer and Koegl¹² for a heptaacetylmaltoside made from acetobromomaltose in ethyl alcohol solution and silver carbonate, which gave a specific rotation in acetylene tetra-

⁸ Hudson and Yanovsky, *THIS JOURNAL*, **39**, 1013 (1917).

⁹ Riiber, *Ber.*, **57**, 1797 (1924).

¹⁰ Hudson and Dale, *THIS JOURNAL*, **37**, 1264 (1915).

¹¹ Hudson and Johnson, *ibid.*, **37**, 1277 (1915). See also Hudson, *ibid.*, **47**, 277 (1925).

¹² Fischer and Koegl, *Ann.*, **436**, 226 (1924).

chloride of 48.93°, it is evident that their compound was a beta modification, as would be expected from the method used in its synthesis. It is known that rotations in chloroform and acetylene tetrachloride are closely alike.

Experimental Part

β -Tetraacetylethylglucoside.—Twenty-five grams of pentaacetylglucose was treated with 51 g. of a solution of glacial acetic acid containing 32% by weight of dry hydrobromic acid. The mixture was allowed to stand at 28° until all the pentaacetylglucose had gone into solution and the color of the mixture had become a deep brownish red. The time required was about one hour. The mixture was then diluted with 102 cc. of cooled chloroform and poured into 150 cc. of ice water. The resulting mixture was well shaken and the layers separated. The water layer was next washed with 30 cc. of chloroform in three portions of 10 cc. each. The combined chloroform layers were washed until neutral with a solution of sodium bicarbonate. The sodium bicarbonate was removed by washing with ice water. The chloroform layer was dried over calcium chloride until clear and filtered into a distilling flask. The solution was concentrated under vacuum at 40° to a thick sirup. At this point the sirup was dissolved in 175 cc. of absolute alcohol and the solution shaken in a flask with 32 g. of freshly prepared silver carbonate, until most of the carbon dioxide had been evolved. The flask was stoppered and shaken on a machine for one-half hour until the solution gave a negative test for bromide ion with silver nitrate. The silver residues were removed by filtration and washed with ether. The neutral filtrate was evaporated to one-half volume on a water-bath, cooled and further evaporated with a stream of air until crystals began to separate. The solution was then cooled overnight in an ice box and the crystalline product filtered off. The yield corresponded to 50% of the theoretical. The compound thus prepared melted at 105°. The crude material was recrystallized from absolute alcohol to constant rotation and melting point. The pure substance melted at 106.8°.

Optical Rotation.—2.4688 g. in 25 cc. of chloroform solution in a 2-dm. tube gave $\alpha = -4.474^\circ$; $[\alpha]_D^{22.5} = -22.67^\circ$.

β -Ethylglucoside.—Koenigs and Knorr¹³ described a method for the saponification of β -tetraacetylethylglucoside, but stated that they were unable to crystallize the sirup so prepared. Their method was modified as follows. Five grams of β -tetraacetylethylglucoside was suspended in 300 cc. of distilled water, 16 g. of Ba(OH)₂·8H₂O, which had been recrystallized three times from hot water, was added and the mixture shaken on a machine for fifteen hours. The excess barium hydroxide was then precipitated with carbon dioxide and the resulting barium carbonate centrifuged and filtered. The filtrate was concentrated under reduced pressure using a bath at 45–50° until a thick sirup was obtained. This residue was extracted with absolute alcohol, the precipitated barium acetate filtered by means of a suction funnel containing filter paper covered with a layer of activated carbon, and the filtrate again concentrated *in vacuo* to a thick sirup with a bath at 35°. To this was added a few drops of dry acetone and the solution was allowed to stand in a desiccator over phosphorus pentoxide for fifteen days. At the end of this time, a small crystalline area was observed which after a few days had spread throughout the sirup in a series of radiating needles. These crystals were used thereafter for seeding purposes. All subsequent saponifications were made with sodium ethylate using the general procedure of Zemplén.¹⁴

Twenty grams of β -tetraacetylethylglucoside was dissolved in 80 cc. of absolute

¹³ Koenigs and Knorr, *Ber.*, **34**, 971 (1901).

¹⁴ Zemplén and Pacsu, *Ber.*, **62**, 1613–1614 (1929).

alcohol and 6 cc. of a solution of 0.3 g. of sodium in 25 cc. of absolute alcohol was added. The flask was tightly stoppered with a rubber stopper covered with tin foil and allowed to stand at room temperature for twenty hours. At the end of this time the solution was evaporated *in vacuo* from the original flask, at room temperature, to dryness. Ten cc. of dry acetone was then added slowly with shaking and the solution was seeded and allowed to stand stoppered overnight at room temperature. The next day the bottom was covered with a mass of needle crystals. The flask was then put in the ice box and allowed to stand for ten hours. At the end of this time the solution had solidified. This was quickly filtered on a glass Büchner funnel which was so arranged that all air passing through was previously dried by calcium chloride. The precipitate was washed with a little dry acetone and then quickly transferred to a vacuum desiccator containing phosphorus pentoxide.

On opening the flask preparatory to filtration, the solid mass became quite sticky due to absorbed water (the compound is very hygroscopic) but after desiccation changed to a white amorphous mass. This mass was then treated with a few cc. of acetone and shaken until most of the compound had gone into solution. At this point, small needles could be seen which ultimately disappeared. The solution was cooled in an ice-salt bath and dry ethyl acetate added slowly, with shaking, until the solution became turbid. It was then seeded as before, stoppered, and put away in the ice box. After a few hours, the solution had solidified to a crystalline mass. This was filtered as before, washed with dry acetone and dried in a phosphorus pentoxide vacuum desiccator. The yield was 45% of the theoretical.

Optical Rotation.—0.3575 g. in 25 cc. of water solution in a 2-dm. tube gave $\alpha = -1.05^\circ$; $[\alpha]_D^{29.5} = -36.71^\circ$.

The filtrate from the first filtration, which contained a considerable amount of sirup, was diluted with a little acetone. It was poured into a wide-mouthed flask, stoppered and cooled in an ice-salt bath. Ethyl acetate was then added, as before described, until slight turbidity was attained. After crystallization it was again treated with dry acetone, allowed to stand until only a few needle crystals could be seen and then cooled in an ice-salt bath until turbid. The solution at this point was put in the ice box, and after one day contained a mass of fine white needle crystals. These immediately became gummy during filtration, but on desiccation changed into a pure white crystalline mass.

Optical Rotation.—0.3828 g. in 25 cc. of water solution in a 2-dm. tube gave $\alpha = -1.12^\circ$; $[\alpha]_D^{31} = -36.57^\circ$.

Another batch prepared in the same manner and recrystallized three times gave a specific rotation of -36.85° . Therefore the average rotation has been given in Table I as -36.7° . The melting point was 90.4° .

α -Tetraacetyethylglucoside.—In preparing this compound from β -tetraacetyethylglucoside, titanium tetrachloride was used as described by Pacsu.¹⁶ Fourteen grams of β -tetraacetyethylglucoside dissolved in 110.7 cc. of dry chloroform was treated with 4.2 cc. of titanium tetrachloride in 74.7 cc. of absolute chloroform. A yellow solid immediately separated, which slowly dissolved upon standing. The mixture was heated on a water-bath just below the boiling point for three hours under a reflux condenser. It was then cooled, poured into ice water and stirred until the chloroform layer became clear. The layers were separated and the chloroform washed twice with distilled water, and dried over calcium chloride. It was evaporated *in vacuo* in a bath at 45° to a thick sirup. This was treated with 40 cc. of absolute alcohol, filtered through an activated carbon layer by suction, and cooled in an ice-salt bath. On scratching the sides of the beaker with the glass rod, small crystals began to separate. At the end of an hour the solution solidified. After filtering and drying, 13 g. of material melting at 58 – 59°

¹⁶ Pacsu, *Ber.*, **61**, 1511 (1928).

was obtained. The specific rotation was $+118.9^\circ$. The product was then recrystallized from absolute alcohol until it gave a constant rotation and melting point. The final melting point was 61.8° .

Optical Rotation.—0.2209 g. in 25 cc. of chloroform solution in a 2-dm. tube gave $\alpha = +2.335^\circ$; $[\alpha]_D^{30} 132.13^\circ$. The final melting point was 61.8° .

Anal. Calcd.: C, 51.03; H, 6.43; O, 42.54. Found: C, 50.54, 50.81, 50.63; H, 6.43, 6.37; O, 42.94.

α -Ethylglucoside.—This compound was prepared by the saponification of α -tetraacetyethylglucoside with sodium ethylate in the following manner.

Nine grams of α -tetraacetyethylglucoside was dissolved in 40 cc. of absolute alcohol and 2.7 cc. of a solution containing 0.3 g. of sodium in 25 cc. of absolute alcohol was added. The flask was stoppered with a rubber stopper covered with tin foil and allowed to stand for twelve hours at 33° . At the end of one-half hour, the solution had turned slightly yellow and the odor of ethyl acetate was quite strong. The solution was then filtered through an activated carbon layer to decolorize, and concentrated *in vacuo* in a bath at 40° to a thick sirup. Five cc. of absolute alcohol was then added and the mixture shaken until all of the sirup had gone into solution. It was then seeded from an impure batch of α -ethylglucoside made according to the method described by Fischer,¹⁶ and put in the ice box. After twenty-four hours, granular crystals had separated and were filtered. The yield was 60% of the theoretical. The glucoside was recrystallized from dry acetone to constant melting point and rotation. The final melting point was 114.6° .

Optical Rotation.—0.1402 g. in 25 cc. of water solution in a 2-dm. tube gave $\alpha = 1.705^\circ$; $[\alpha]_D^{23} 152.01^\circ$.

Summary

The alpha and beta forms of ethyl-*d*-glucoside and their tetraacetates have been prepared in pure condition and their rotations measured. The results closely confirm Hudson's second rule of isorotation when they are compared with other substances of the glucoside series. A test of the first rule of isorotation, made by comparing certain of them with the rotation of a substance of the maltose series (β -ethylmaltoside heptaacetate) also shows confirmation.

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¹⁶ Fischer, *Ber.*, **28**, 1154 (1895).