enhancement of the moment with respect to the dielectric constant effect of the media.

The ethyl acetate–hydroxide ion reaction thus conforms with theory with respect to the effect of ionic strength upon the rate. With respect to the effect upon the rate of the dielectric constant of the media, theory merely reveals an abnormally large influence, the actual cause of which is obscure. With respect to the extrapolation to higher dielectric constant, it might be added that where reasonable enhanced moments have been found from dielectric effects, extrapolation to ionic strength equal to zero for ionic strength effects and to higher dielectric constants for dielectric constant effects have resulted in quite similar k' constants being obtained for the two extrapolations. In this instance the k' constants from the dielectric extrapolation were much larger (4 to 7 times) than from the ionic strength extrapolation. Thus the values of k' extrapolated from dielectric constant data were 3.80, 8.91 and 12.0 at 0.00, 9.80 and 20.0°, respectively, as compared to the $k_{\kappa=0}$ values at the same three temperatures and listed in Table II.

Acknowledgement.—The authors want to thank Professor George Jaffee, who has contributed much to the theory of this paper. The authors wish to express their appreciation of the advice and assistance given by Dean A. R. Choppin and Dr. Edgar L. Compere during the extended absence of one of them (E. S. A.).

Summary

1. The rate of the alkaline hydrolysis of ethyl acetate was studied both as a function of ionic strength and of the dielectric constant of the media at 0.00, 9.80 and 19.10°.

2. The ionic strength dependence of the rate was found to conform to the predictions of the ion–dipolar molecule rate theory proposed by Amis and Jaffe.

3. The dielectric constant influenced the rate of hydrolysis in the direction predicted by the ion–dipolar molecule theory, but the magnitude of the effect was very much greater than was expected from the standpoint of theory.

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[A CONTRIBUTION FROM THE SOUTHERN REGIONAL RESEARCH LABORATORY[1]]

Cuprammonium–Glycoside Complexes. V. The Conformation of the Pyranose Ring in Some D-Hexose<1,5>β<1,6>Anhydrides

BY RICHARD E. REEVES

The hexosans of the levoglucosan type offer a particular opportunity for the study of pyranose ring conformations because only two of the eight theoretically possible Sachse strainless ring conformations satisfy the steric requirements of the hexosan rings. Thus, in order to make a definite assignment of ring conformation for substances of this type it is only necessary to choose between two possible ring forms.

Consideration of the properties of a large number of D-glucopyranosides[2] and D-galactopyranosides[3] has led to the observation that the existing data are in accord with assignment of a single one of the eight Sachse ring conformations to all of these simple pyranosides. This is the chair form designated C1, in which the ring oxygen atom and carbon atom 6 project on the same side of the plane of carbon atoms 1, 2, 4 and 5. However, it would be sterically impossible for a D-hexose anhydride of the levoglucosan type to possess this ring form.

The two pyranose conformations which, in the D-hexoses, are capable of forming hexosans of the <1,5>β<1,6> type are those designated 1C and 3B in an earlier communication.[2] These two ring forms are shown diagrammatically in Fig. 1. There are apparently valid theoretical arguments favoring the chair form structures over the boat forms.[4] The hexosans offered a possibility of testing these arguments experimentally. The results indicate that for each of the ten D-hexosans examined it is indeed the chair form, 1C, which is adopted by the molecule in solution.

Discussion and Results

In a preceding article of this series[5] a theory has been presented which states that cuprammonium reacts with two hydroxyl groups to form a complex only when the two groups are located at or near a particular distance from each other. For hydroxyl groups on adjacent carbon atoms the complex-forming distance is realized when the groups are oriented at the true *cis*-position (0° angle) or at a 60° angle from each other. No complexes are formed at the 120 and 180° angles. When two hydroxyl groups on adjacent carbon atoms are oriented at the 60° angle it has been found to hold that when the angle, as previously defined,[5] is negative, cuprammonium produces a strongly levorotatory shift in optical rotation, and when the angle is positive, the shift is strongly dextrorotatory.

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(1) One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, U. S. Department of Agriculture. Article not copyrighted.

(2) Reeves, THIS JOURNAL, **71**, 215 (1949).

(3) Reeves, *ibid.*, **71**, 1737 (1949).

(4) Hassel and Ottar, *Acta Chemica Scandinavica*, **1**, 929 (1947).

(5) Reeves, THIS JOURNAL, **71**, 212 (1949).

D-Glucosan<1,5>β<1,6> (levoglucosan) has been shown by a conductometric technique to form a complex with cuprammonium,[6] but the complex does not exhibit a large shift in optical rotation such as often accompanies complex formation of the glycosides. It has been found that 3-methyl-D-glucosan<1,5>β<1,6> behaves in exactly the same manner in cuprammonium solution. In this case only the hydroxyl groups on carbon atoms 2 and 4 are free. Therefore levoglucosan and 3-methyllevoglucosan react at position 2 and 4 yielding a different kind of complex from that occurring in the glucosides and galactosides since hydroxyl groups not on adjacent carbon atoms are involved.

Employing the accepted interatomic distances of 1.54 Å. for the C–C bond and 1.45 Å. for the C–O bond, it is possible to calculate the distances between oxygen atoms of hydroxyl groups on adjacent carbon atoms corresponding to the various projected angles the carbon oxygen bonds make with respect to each other. Some of the angles and distances are as follows: 0°, 2.51 Å.; 60°, 2.86 Å.; 120°, 3.45 Å.; 180°, 3.71 Å. Thus distances of approximately 2.5 to 2.9 Å. are definitely complex-forming, while distances of 3.45 Å., and greater, are not complex-forming. The distance between the oxygen atoms on the second and fourth carbon atoms of levoglucosan is very different in the 1C and 3B conformations. Although the exact values depend upon knowledge we do not now possess regarding the exact shape of the pyranose ring it is apparent that for the 1C form the O_2–O_4 distance may be less than 3 Å., while for the 3B form the distance is probably greater than 5 Å. Therefore 3-methyllevoglucosan and, by analogy, levoglucosan, are believed to exist in solution in the 1C conformation.

D-Galactosan<1,5>β<1,6> has already been shown to exist in the 1C conformation.[3] It is now found that 2-methyl-D-galactosan<1,5>β<1,6> also exists in this conformation. In these instances the 1C form was apparent because it would produce the strongly dextrorotatory complex observed, while the 3B form, if it existed, would give a levorotatory complex. Four other anhydrides of the <1,5>β<1,6> type, D-mannosan, 4-methyl-D-mannosan, 4-benzyl-D-mannosan and D-altrosan also reveal their 1C conformation by the direction of rotation of their cuprammonium complexes. In each of these instances the 3B form would have resulted in complexes having the opposite direction of rotation from that observed.

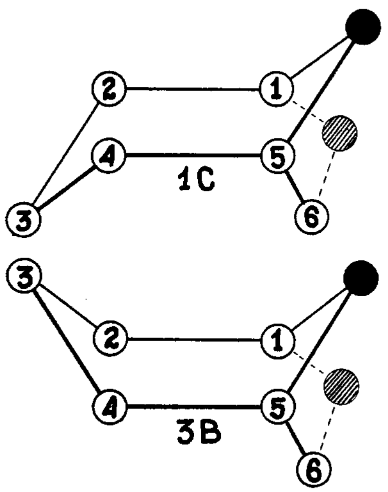

Fig. 1.—The two ring conformations capable of forming <1,5>β<1,6> anhydrides in the D-aldohexose series.

D-Idosan<1,5>β<1,6> and 3-methyl-D-idosan<1,5>β<1,6> have the opposite configuration of carbon atoms 2, 3 and 4 from the D-glucosans. As a result 3-methyl-D-idosan in the 1C form would not be expected to react with cuprammonium, nor was any reaction observed. Had it existed in the 3B form reaction should have occurred exactly as in the case of 3-methyllevoglucosan in the 1C conformation. D-Idosan is an exceedingly poor complex-former, but it appears to form compensating complexes of intermediate rotational shift. This behavior is in agreement with the expectations for ring conformation 1C.

The specific rotations in water and cuprammonium solution and the conductometric behavior in cuprammonium solution for the ten D-hexosans are given in Table I. These data show all the substances except 3-methyl-D-idosan to be complex-formers. In Table II are listed the rotational shifts for the hexosans, and the behavior antici-

TABLE I

THE PROPERTIES OF SOME D-HEXOSE<1,5>β<1,6> ANHYDRIDES IN WATER AND IN CUPRAMMONIUM SOLUTION

Substance	Specific rotation,[a] deg., (g./100 ml.) Water D line	Water 436 mμ	Cupra B[b] 436 mμ	ΔSp. res.[c] ohm, cm.
D-Glucosan	− 65 (0.56)	−127 (0.56)	− 144 (0.62)	53
3-Methyl-D-glucosan	− 58 (1.25)	−117 (1.25)	− 143 (0.97)	69
D-Galactosan	− 22 (0.83)	− 47 (1.37)	+ 620 (0.76)	193
2-Methyl-D-galactosan	− 35 (0.97)	− 70 (0.97)	+ 475 (1.92)	199
D-Mannosan	−125 (1.13)	−241 (1.13)	−1115 (1.16)	234
4-Methyl-D-mannosan	−117[d] (0.8)	−217[d] (0.8)	− 940[d] (0.61)	234
4-Benzyl-D-mannosan	− 83 (1.1)	−160 (1.1)	− 700 (0.74)	...
D-Altrosan	−210 (0.69)	−410 (0.69)	+ 462 (0.65)	135
D-Idosan	− 91 (0.74)	−175 (0.74)	− 576 (0.43)	18[e]
3-Methyl-D-idosan	− 84 (0.99)	−164 (0.99)	− 178 (0.6)	8

[a] Except in the 4-methyl-D-mannosan all rotation measurements were made at 25°. [b] Cupra B is a standard cuprammonium solution containing 15 g. of copper, 240 g. of ammonia, and 1 g. of glycerol per liter. [c] The increase in specific resistance at 25° of 0.010 molar hexosan in Cupra A—a standard cuprammonium solution containing 0.010 mole of copper, 3 moles of ammonia, and 10 ml. of ethanol per liter. [d] These measurements were made at 30°. [e] The reason for this exceptionally low increase in specific resistance is not clear; however, the rotational shift shows the substance to be in the complex-forming group.

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(6) Reeves and Jung, *ibid.*, **71**, 209 (1949).

TABLE II

COMPARISON OF OBSERVED BEHAVIOR IN CUPRAMMONIUM OF SOME D-HEXOSE<1,5>β<1,6> ANHYDRIDES, WITH THE BEHAVIOR PREDICTED FOR TWO DIFFERENT RING FORMS

Substance	Observed behavior Rotational shift,[a] degrees	 Complex formation	Anticipated behavior for ring conformation 1C	 3B
D-Glucosan	− 28	Yes	Low shift complex	Compensating[b] complexes
3-Methyl-D-glucosan	− 46	Yes	Low shift complex	No complex
D-Galactosan	+1081	Yes	Dextro shift	Levo shift
2-Methyl-D-galactosan	+ 959	Yes	Dextro shift	Levo shift
D-Mannosan	−1416	Yes	Levo shift	Dextro shift
4-Methyl-D-mannosan	−1272	Yes	Levo shift	Dextro shift
4-Benzyl-D-mannosan	−1360	Yes	Levo shift	Dextro shift
D-Altrosan	+1413	Yes	Dextro shift	Levo shift
D-Idosan	− 635	Yes	Compensating[b] complexes	Low shift complex
3-Methyl-D-idosan	− 25	No	No complex	Low shift complex

[a] Rotational shift equals ($[\alpha]_{436}$ cupra B − $[\alpha]_{436}$ water) × mol. wt./100. [b] Compensating complexes usually have rotational shifts of ± 200 to ± 650°.

pated for each substance oriented in each of the two possible ring conformations 1C and 3B. It will be noted that the experimental data are in agreement with the 1C form for each substance.

Experimental

Optical rotations were measured with the sodium D line or the mercury blue line (436 mμ), as indicated.

Rotations in Cupra B—a standard cuprammonium solution containing 15 g. of copper, 240 g. of ammonia and 1 g. of glycerol per liter—were measured in 0.5-dm. tubes.

Resistance measurements were observed in Cupra A—a standard dilute cuprammonium solution containing 0.01 mole of copper, 3.0 moles of ammonia and 10 ml. of ethanol per liter.[6] Measurements at a series of glycoside dilutions were plotted on coördinate paper and the value at 0.01 molar hexosan concentration was read from the smooth curve through the experimental points. The cell employed had a constant of 0.116 as determined against 0.1 molar potassium chloride solution.

The D-glucosan, D-galactosan, D-mannosan, D-altrosan and D-idosan were crystalline preparations with constants closely agreeing with values given in the literature.

2,4-Dibenzyl-3-methyl-D-glucosan<1,5>β<1,6> was prepared by methylating 5 g. of 2,4-dibenzyllevoglucosan[7] dissolved in 25 ml. of dry acetone and 25 ml. of methyl iodide, by stirring for eight hours under reflux with 20 g. of silver oxide and 2 g. of anhydrous calcium sulfate. The sirup which remained after filtration and removal of the solvents was then remethylated as before. The product from the second methylation was distilled in vacuum at 1 mm. at a bath temperature of 210–240°. The 2,4-dibenzyl-3-methylevoglucosan was a colorless sirup having a sp. rot. of −24° (*c* 2.5, chloroform, D line).

Anal. Calcd. for $C_{21}H_{24}O_5$ (356.4): C, 70.77; H, 6.79. Found: C, 70.27; H, 6.96.

3-Methyl-D-glucosan<1,5>β<1,6> was prepared in two different ways: (a) One gram of 2,4-dibenzyl-3-methyllevoglucosan was dissolved in 20 ml. of glacial acetic acid and stirred with 500 mg. of palladium-on-charcoal (5% palladium) in an atmosphere of hydrogen until two moles of hydrogen had been absorbed per mole of anhydride. The solution was then filtered and evaporated to dryness in vacuum. The residue was distilled at 0.5 mm. at a bath temperature of 110–120°. The distillate, weighing 460 mg., crystallized on standing overnight in a desiccator. Recrystallization from a mixture of acetone, ether and petroleum ether gave a product melting at 65–66°, sp. rot. −64.8° (*c* 5.9, acetone, D line). The specific rotations of this substance in water and cuprammonium solutions are given in Table I.

Anal. Calcd. $C_7H_{12}O_5$ (176.17): C, 47.72; H, 6.87; OCH_3, 17.62. Found: C, 48.02, 47.89; H, 6.98, 6.99; OCH_3, 17.89.

(b) One gram of phenyl 2,4,6-triacetyl-3-methyl-β-D-glucopyranoside was placed in a brass tube and boiled for nine hours with 20 ml. of 2.5 *N* aqueous potassium hydroxide solution.[8] The solution was then cooled, neutralized with dilute sulfuric acid and an excess of bromine water was added. The tribromophenol which precipitated was removed by filtration. The aqueous filtrate was evaporated to dryness *in vacuo* and the salts were extracted with acetone and hot absolute ethanol. The combined extracts were evaporated to dryness and the residue was distilled at 1 mm. and a bath temperature of 160–175°. The distillate weighed only 41 mg., but it crystallized on standing. After recrystallization from a mixture of benzene and ether the product melted at 64–65°, and had a sp. rot. of −64.5° (*c* 0.52, acetone, D line). The melting point of this preparation was not depressed when mixed with a sample of the substance prepared from 2,4-dibenzyl-3-methyllevoglucosan.

2-Methyl-D-galactosan<1,5>β<1,6> has been reported as a sirup by McCreath and Smith.[9] 3,4-Isopropylidene-D-galactosan<1,5>β<1,6>,[10] m.p. 149–50°, 3.9 g. was dissolved in acetone and methylated with a large excess of methyl iodide and silver oxide. The product was isolated and the methylation repeated. The sirupy 2-methyl-3,4-isopropylidenegalactosan gave 15.3% methoxyl on analysis (calcd. 14.3%), and it was not further purified or characterized. This substance has previously been obtained as a sirup[9] and in the form of low-melting crystals.[11] Upon refluxing 2.7 g. of the sirup in 50 ml. 0.5 *N* H_2SO_4 and 25 ml. alcohol the rotation reached a constant value of −1.00° (D-line, 1 dm.) in one and five-tenth hours. The acid was removed with barium carbonate and the product, on evaporation of the solution, was distilled in a micro distillation outfit at 110° and 1 mm. pressure. The distillate crystallized, and was recrystallized from acetone in which it was difficultly soluble. This product melted at 115–116° and weighed 1.22 g. Fractional sublimation of this product at a temperature below 110° gave six fractions, total wt. 1.13 g., all melting sharply at 116–117°. The specific rotations of this preparation are given in Table I.

Anal. Calcd. for $C_7H_{12}O_5$ (176.17): C, 47.72; H, 6.87; OCH_3, 17.62. Found: C, 47.74, 47.87; H, 6.80, 6.94; OCH_3, 17.98.

4-Methyl-D-mannosan<1,5>β<1,6> was prepared by dissolving 1.36 g. of 2,3-isopropylidene-4-methyl-D-mannosan<1,5>β<1,6>[12] in 25 ml. of 0.1 *N* sulfuric acid and allowing the solution to stand at room temperature for twenty-four hours. The product was isolated as described for 2-methylgalactosan. It was a colorless sirup. The specific rotations of this preparation are given in Table I.

Anal. Calcd. for $C_7H_{12}O_5$ (176.17): C, 47.72; H, 6.87; OCH_3, 17.62. Found: C, 47.85, 47.63; H, 6.87, 7.04; OCH_3, 17.94.

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[7] Zemplén, Csűrös and Angyal, *Ber.*, **70**, 1848 (1937).

[8] This reaction has been reported by McCloskey and Coleman, *J. Org. Chem.*, **10**, 184 (1945), however the 3-methyllevoglucosan was not isolated nor characterized. These workers deacetylated and then eliminated the phenyl group in two separate steps.

[9] McCreath and Smith, *J. Chem. Soc.*, 387 (1939).

[10] Hann and Hudson, THIS JOURNAL, **64**, 2435 (1942).

[11] James, Smith, Stacey and Wiggins, *J. Chem. Soc.*, 625 (1946).

[12] Knauff, Hann and Hudson, THIS JOURNAL, **63**, 1447 (1941).

4-Benzyl-D-mannosan<1,5>β<1,6> was obtained by partial hydrolysis of the 2,3-isopropylidene-4-benzyl-D-mannosan of Haskins, Hann and Hudson.[13] Two and four-tenths grams of the isopropylidene derivative was dissolved in 25 ml. of acetone and 2 ml. of 5 *N* sulfuric acid was added. The solution was warmed to 40° while water was gradually added to make a total volume of 50 ml. The solution was kept at this temperature for five hours and the rotation became constant at −1.57° (0.5-dm. tube). On evaporation of the acetone from this solution 1.49 g. of unchanged starting material was recovered. Repeated extraction of the remaining aqueous solution with chloroform yielded 525 mg. of 4-benzyl-mannosan which crystallized on evaporation of the chloroform. On recrystallization from a mixture of chloroform and petroleum ether the product melted at 122–123°, $[\alpha]^{25}_{D}$ −76° (*c* 1.08, chloroform). The substance did not reduce hot Fehling solution. The optical rotations in water and in cuprammonium are given in Table I.

Anal. Calcd. for $C_{13}H_{16}O_5$ (252.26): C, 61.89; H, 6.39. Found: C, 62.14, 62.08; H, 6.58, 6.54.

Methyl 3-methyl-β-D-idopyranoside was prepared by stirring 1.5 g. of methyl 3-methyl-4,6-benzylidene-β-D-idoside,[14] m.p. 102°, in an atmosphere of hydrogen with 1 g. of palladium on charcoal (5% Pd) until 300 ml. of hydrogen had been absorbed. The solution was filtered and evaporated to dryness in vacuum. Fractional distillation of the residue at 0.2 mm. at bath temperatures from 110–130° gave four sirupy fractions all having sp. rot. of −65° ± 3° (acetone, D line). The total distillate weighed 807 mg. The specific rotations of this product in water and in cuprammonium are as follow: −51° (*c* 0.7, water, D line), −94° (*c* 0.7, water, 436 mμ), −88° (*c* 0.5, Cupra B, 436 mμ). In spite of the low rotational shift in cuprammonium solution the substance gave definite evidence of complex formation by the conductometric technique. The increase in sp. resistance of an 0.01 molar solution of the idoside in Cupra A amounted to 88 ohm/cm. Wiggins[15] has also reported the preparation of methyl 3-methyl-β-D-idoside as a sirup. He removed the benzylidene group by acid hydrolysis and found sp. rot. −53.6° (D line) for the solution in water containing oxalic acid.

Anal. Calcd. for $C_8H_{16}O_6$ (208.21): C, 46.15; H, 7.75; OCH_3, 29.83. Found: C, 46.36, 46.04; H, 7.50, 7.55; OCH_3, 29.4.

3-Methyl-D-idosan<1,5>β<1,6> was prepared in a manner analogous to the preparation of D-idosan by Sorkin and Reichstein.[14] Methyl 3-methyl-β-D-idoside, 589 mg., was boiled for six hours under reflux with 25 ml. of *N* sulfuric acid. The levorotation increased from an initial value of −1.11 to −1.38° (1-dm. tube) in about three hours and remained approximately constant thereafter.[16] The acid was removed with barium carbonate and the filtered solution was evaporated to dryness in vacuum. Distillation of the residue at 0.01 mm. at bath temperature of 90–110° gave 273 mg. of crystalline distillate melting at 103°. After recrystallization from a mixture of acetone and ether the product melted at 104–6°, and had a sp. rot. of −107° (*c* 0.99, acetone, D line). The sp. rots. of this product in water and cuprammonium solutions are given in Table I.

Anal. Calcd. for $C_7H_{12}O_5$ (176.17): C, 47.72; H, 6.87; OCH_3, 17.62. Found: C, 47.69, 47.92; H, 6.99, 6.98; OCH_3, 18.4.

All of the new substances described above failed to reduce hot Fehling solution.

Acknowledgments.—Some of the substances used in this work were supplied by Drs. C. S. Hudson, N. K. Richtmyer, and R. M. Hann. The micro carbon and hydrogen analyses were performed by Mr. L. E. Brown and the methoxyl analyses, by Mr. L. W. Mazzeno, Jr. The helpful advice of Dr. R. J. Dimler during the course of this work is gratefully acknowledged.

Summary

It is observed that only two of the eight Sachse strainless pyranose ring conformations meet the steric requirements of the hexose<1,5>β<1,6> anhydrides (the levoglucosan type of anhydrides). Furthermore, only one of these two conformations would result in the behavior observed for five D-hexosans, four monomethyl-D-hexosans, and one monobenzyl-D-hexosan. Therefore a definite assignment of conformation can be made for the pyranose ring in this group of substances. The ring must exist in the chair form 1C, the one in which the ring oxygen atom and carbon atom 6 project on opposite sides of the plane of carbon atoms 1,2,4,5.

Methyl 3-methyl-β-D-idoside, 2,4-dibenzyl-3-methyl-D-glucosan<1,5>β<1,6>, and 4-methyl-D-mannosan<1,5>β<1,6> were prepared in the form of sirups and were characterized by means of optical rotations.

3-Methyl-D-glucosan<1,5>β<1,6>, 2-methyl-D-galactosan<1,5>β<1,6>, 4-benzyl-D-mannosan<1,5>β<1,6>, and 3-methyl-D-idosan<1,5>β<1,6> were prepared in crystalline form.

NEW ORLEANS, LOUISIANA RECEIVED JANUARY 10, 1949

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[13] Haskins, Hann and Hudson, THIS JOURNAL, **70**, 1290 (1948).

[14] Sorkin and Reichstein, *Helv. Chim. Acta*, **28**, 1 (1945).

[15] L. F. Wiggins, *J. Chem. Soc.*, 522 (1944).

[16] This hydrolysis was performed by Wiggins (see ref. 15) at 95°. He noted a similar increase in levorotation, but failed to attribute the unusual behavior to the formation of 3-methylidosan.