No information was obtained either as to the anomeric disposition of the acetal bonds (except for the polarimetric evidence indicating the presence of a fairly high ratio of α- to β-linkages) or as to the proportions of branch points and non-reducing end-groups. Consequently, it is not yet possible to set forth a structural formula of any fundamental significance, particularly in view of the apparent heterogeneity of bond structure evidenced by the experimental data.

Acknowledgment.—We are indebted to the Corn Products Refining Co. for permitting this investigation and for the generous contribution of necessary materials and facilities.

ARGO, ILLINOIS

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, STANFORD UNIVERSITY]

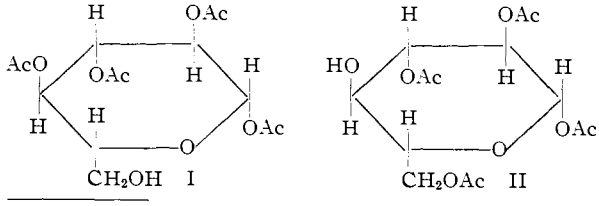
On the Structure of 1,2,3,6-Tetra-*O*-acetyl-β-D-glucose

BY WILLIAM A. BONNER

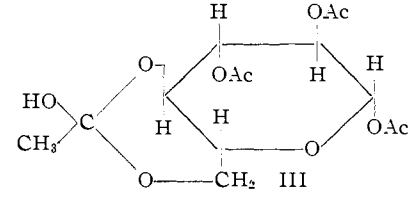
RECEIVED FEBRUARY 21, 1958

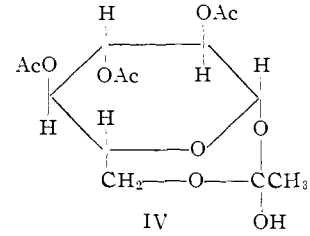
The action of very dilute alkali on 1,2,3,4-tetra-*O*-acetyl-β-D-glucose (I) leads to the formation of an isomeric tetra-*O*-acetyl-β-D-glucopyranose whose chemical behavior has been interpreted in terms of both the structures 1,2,3,6-tetra-*O*-acetyl-β-D-glucose (II) and 2,3,4-tri-*O*-acetyl-β-D-glucose 1,6-(orthoacetate) (IV). A distinction between these possibilities, favoring structure II, can be made on the basis of labeled-acetyl exchange experiments on the penta-*O*-acetyl-β-D-glucopyranose obtainable from II, and on the basis of infrared carbonyl absorption intensities. Both I and II were acetylated at −5° with radioactive acetic anhydride, affording essentially optically pure samples of monoacetyl labeled penta-*O*-acetyl-β-D-glucopyranose. When these pentaacetates were placed in a 1:1 mixture of acetic anhydride and acetic acid, containing sulfuric acid catalyst, they underwent anomerization but *failed* to exchange labeled acetyl, indicating the absence of labeled acetyl at the anomeric center in each case. The infrared carbonyl absorption intensities of both I and II established the presence of four normal acetyl groups in each molecule. These data are in accord with II and eliminate IV as the structure of the alkali engendered isomerization product of I.

In 1926, Helferich and Klein first observed[1] polarimetrically the sensitivity of 1,2,3,4-tetra-*O*-acetyl-β-D-glucose (I) to traces of alkali, and a new isomeric tetra-*O*-acetyl-β-D-glucopyranose was isolable from such an alkali-catalyzed isomerization. The latter substance has more recently been obtained both by Lewis-acid catalyzed isomerizations[2] of I, as well as by hydrolysis, followed by partial acetylation, of 1,2,3-tri-*O*-acetyl-4,6-benzylidene-β-D-glucose.[3] The isomerized acetate, although then similar in melting point to the known 2,3,4,6-tetra-*O*-acetyl-β-D-glucose, showed a mixed melting point depression with the latter,[1,6] and therefore did not have its free hydroxyl group at C1. Also, the isomerized tetraacetate could be tosylated to give a product which, after cautious saponification, yielded a mono-*O*-*p*-toluenesulfonate different from the known 3-*O*-*p*-toluenesulfonyl-D-glucose of Freudenberg and Ivers,[4] an observation which was interpreted as eliminating the possibility of a free hydroxyl at C3 in the isomerized acetate. Of the remaining structural possibilities, *i.e.*, free hydroxyl at C2 or C4, Helferich and Klein suggested the C4 alternative II as the most likely structure, although the rearranged acetate underwent some reaction with phenylhydrazine.[1] Both I and II readily yielded penta-*O*-acetyl-β-D-glucopyranose on acetylation with acetic anhydride and pyridine, thus establishing their ring size and anomeric similarity. On methylation of II with methyl iodide and silver oxide the known methyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucoside resulted in low yield,[1] a reaction clearly involving additional acetyl migration.



On the basis of the observation that both I and II as well as 2,3,4,6-tetra-*O*-acetyl-β-D-glucose all gave methyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucoside on methylation, and of the assumption that the proposed ortho-acid intermediate[5] III involved in a C6–C4 acetyl migration was unlikely because of the *trans* disposition of the groups at C4 and C5, Haworth, Hirst and Teece later cast doubt[6] on the correctness of Helferich's formulation II for the rearranged tetraacetate. Their methylation data, as well as the properties of other known tetra-*O*-acetyl-D-glucoses led them to suggest the stable





(1) B. Helferich and W. Klein, *Ann.*, **450**, 219 (1926); **455**, 173 (1927).

(2) H. Bredereck and G. Höschele, *Ber.*, **86**, 1286 (1953).

(3) A. L. Raymond, *J. Biol. Chem.*, **113**, 375 (1936).

(4) K. Freudenberg and O. Ivers, *Ber.*, **55**, 937 (1922).

(5) E. Fischer, *ibid.*, **53**, 1624 (1920).

(6) W. N. Haworth, E. L. Hirst and Ethel G. Teece, *J. Chem. Soc.*, 1405 (1930).

ortho-acid structure IV as that of the rearranged acetate, a structure arising from I by interactions between C1 and C6. Shortly thereafter Helferich and Müller offered[7] a rebuttal to the suggestions of Haworth and co-workers, arguing theoretically that a strainless *trans*-orthoacid intermediate (III) involving C6 and C4 was indeed possible, and demonstrating experimentally that methyl 2,3,4-tri-*O*-acetyl-β-D-glucoside undergoes an alkali-catalyzed isomerization into methyl 2,3,6-tri-*O*-acetyl-β-D-glucoside analogous to that originally observed for I. The evidence for the latter conclusion was the conversion *via* several steps of both alkali-isomerized products into the same methyl 2,3,6-tri-*O*-acetyl-4-*O*-*p*-toluenesulfonyl-β-D-glucoside. It was therefore pointed out that since the acetyl migration in the methyl glucoside series could not involve C1–C6 interactions, Haworth's formulation IV was in all probability incorrect. While the balance of chemical evidence appears to favor Helferich's formula II for the structure of the isomerized product from I, no further experimental evidence has appeared on this question since 1930, and the choice between structures II and IV is still an open one.[8–10]

We recently have employed[11] two newer techniques, namely, radioactive acetyl exchange under anomerizing conditions and infrared carbonyl absorption intensity, in the elucidation of the structures of three isomeric tetra-*O*-acetyl-D-mannopyranoses. The application of these same techniques to the structural problem involved in the choice between II and IV is the subject of the present paper.

1,2,3,4-Tetra-*O*-acetyl-β-D-glucose (I) was isomerized in 10^{-3} *N* aqueous alkali after the procedure of Helferich and Klein.[1] Both I and the rearranged tetraacetate from it were acetylated using radioactive acetic anhydride in pyridine at −5°. An essentially quantitative yield of almost optically pure monoacetyl-labeled penta-*O*-acetyl-β-D-glucopyranose resulted in each case. Each pentaacetate sample was dissolved in a 1:1 mixture of acetic anhydride and acetic acid 1.0 *M* in sulfuric acid. Under these conditions anomerization is complete in about an hour. After five hours each solution was thrown into water and the penta-*O*-acetyl-α-D-glucopyranose product was isolated, purified and assayed for radioactivity. In each case the α-pentaacetate product had a radioactivity level equal within experimental error to that of its β-pentaacetate precursor, *i.e.*, no labeled acetyl exchange was noted under anomerizing conditions. It previously has been abundantly demonstrated[11–14] that under anomerizing conditions acyl exchange occurs specifically at the anomeric center and at no other acyl group in the acylated aldose.

The failure to detect radioactive acetyl exchange in the pentaacetates obtained from I and its rearranged tetraacetate thus establishes that these pentaacetates bore no label at C1 and that, barring unlikely[11] and *complete* acetyl migrations *during* acetylation, the hydroxyl groups at C1 in both tetraacetate precursors already were acetylated. This result is, of course, to be expected with the pentaacetate obtained from I, and serves only to confirm the validity of the method. Such a result also would be expected with the pentaacetate arising from the rearranged tetraacetate in question, providing the latter possessed structure II. In the event that IV was its correct structure, as suggested[6] by Haworth and co-workers, one would expect some sort of distribution of labeled acetyl between C1 and C6 during acetylation, and the resulting pentaacetate should have exchanged labeled acetyl under anomerizing conditions to the extent that this distribution permitted acetyl introduction at C1. The only way in which the compound IV could have produced the observed results would be that it rearrange *completely* to I or to some intermediate equivalent to I under the acetylating conditions. This possibility is eliminated and IV is excluded as a structural possibility for the rearranged tetraacetate by the following infrared spectroscopic evidence.

Integrated infrared absorption intensities of the carbonyl stretching vibration have been employed[15] in the steroid series to determine the number of carbonyl groups in steroid ketones and acetates. We have employed[11] this same technique to determine the number of acetyl groups in partially acetylated mannose derivatives, in situations where the molecular extinction coefficient[16] for the carbonyl absorption band gave similar information. Since the integrated absorption intensity of a band is a better criterion of band intensity than is molecular extinction coefficient, as it takes cognizance of band width as well as band height,[15] we have employed this criterion in the present study.

In Table I, nos. 1 and 2 have five, no. 3 four, and no. 5 three acetyl groups per molecule. It is seen

TABLE I

INTEGRATED ABSORPTION INTENSITIES OF THE 5.72 μ CARBONYL BAND IN SEVERAL ACETYLATED D-GLUCOSE DERIVATIVES

Compound[b]	Integrated absorption intensity (I.A.I.)[a]	Ratio of I.A.I. to I.A.I. of compound 5	Theoretical I.A.I. ratio
1	0.223	1.62	1.67
2	.228	1.65	1.67
3	.179	1.30	1.33
4	.187	1.35	1.33
5	.138	1.00	1.00

[a] Arbitrary units, *cf.* Experimental. [b] 1, penta-*O*-acetyl-β-D-glucopyranose; 2, penta-*O*-acetyl-α-D-glucopyranose; 3, 1,2,3,4-tetra-*O*-acetyl-β-D-glucose; 4, rearranged tetraacetate, II or IV; 5, 3,4,6-tri-*O*-acetyl-β-D-mannose 1,2-(methyl orthoacetate).

that the theoretical ratios of the integrated absorption intensities, namely, $^5/_3$, $^5/_3$, $^4/_3$ and $^3/_3$, respectively (column 4), are in fact very closely encoun-

(7) B. Helferich and A. Müller, *Ber.*, **63**, 2142 (1930).

(8) E. Pacsu, *Advances in Carbohydrate Chem.*, **1**, 108 (1945).

(9) W. W. Pigman and R. M. Goepp, Jr., "Chemistry of the Carbohydrates," Academic Press, Inc., New York, N. Y., 1948, p. 159.

(10) M. L. Wolfrom and A. Thompson in W. W. Pigman, "The Carbohydrates," Academic Press, Inc., New York, N. Y., 1957, p. 195.

(11) W. A. Bonner, THIS JOURNAL, **80**, 2598 (1958).

(12) W. A. Bonner, *ibid.*, **73**, 2659 (1951).

(13) R. U. Lemieux and Carol Brice, *Can. J. Chem.*, **30**, 295 (1952).

(14) R. U. Lemieux, Carol Brice and G. Huber, *ibid.*, **33**, 134 (1955).

(15) R. N. Jones, D. A. Ramsay, D. S. Keir and K. Dobriner, THIS JOURNAL, **74**, 80 (1952).

(16) R. K. Ness and H. G. Fletcher, Jr., *ibid.*, **78**, 4710 (1956).

tered (column 3) in these compounds. In connection with no. 4, whose structure is in question, it is also seen in Table I that an absorption intensity ratio close to $^4/_3$ obtains. This supports our above conclusion that the rearranged tetraacetate has four acetyl groups and the normal structure II rather than three acetyl groups and the ortho-acid structure IV.

That the rearranged tetraacetate of Helferich and Klein has its free hydroxyl at C4 and not at some other D-glucose carbon is seen by examination of the physical properties of the other known tetra-*O*-acetyl-D-glucopyranoses, summarized in Table II. Examination of the literature indicates that the structures of the isomers listed in Table II appear to be based on quite firm and acceptable evidence, and there is no compelling reason to doubt the correctness of any of them. Since the tetraacetate in question belongs to the β-series, and since Table II indicates that all other possible tetraacetates in the β-series are known, structure II is the only plausible one for Helferich and Klein's compound.

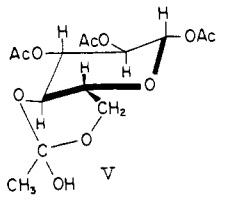
TABLE II

PHYSICAL PROPERTIES OF THE KNOWN ISOMERS OF TETRA-*O*-ACETYL-D-GLUCOPYRANOSE

Isomer with acetyl groups at carbons	Anomeric series	M.p., °C.	Specific rotation, $[\alpha]^t_D$ in $CHCl_3$	t, °C.	c, g./100 ml.	Reference
2,3,4,6	α	112.5–113	+138.9°	20	0.9	*a,b,c*
2,3,4,6	β	137.5–138	+ 14.8	18	4.1	*a,d,e*
1,2,3,4	α	102–103	+119	26	1.5	*f*
1,2,3,4	β	128–129	+ 12.1	20	6.5	*g*
1,3,4,6	α	97–98	+145	22–26	0.8–1.0	*h*
1,3,4,6	β	137–138	+ 28	..	1.3	*h,i,j*
1,2,3,6 (II)	β	134	− 33.0	21	8.2	*g*
1,2,4,6	β	127	− 13.5	20	1.8	*k*

[a] A. Georg, *Helv. Chim. Acta*, **15**, 924 (1932). [b] H. H. Schlubach and Irene Wolf, *Ber.*, **62**, 1507 (1929). [c] G. Zemplén, L. Mester and E. Eckhart, *Acta Chim. Acad. Sci. Hung.*, **4**, 73 (1954); *C.A.*, **49**, 12305 (1955). [d] C. M. McCloskey and G. H. Coleman, *Org. Syntheses*, **25**, 53 (1945). [e] G. P. Ellis and J. Honeyman, *J. Chem. Soc.*, 2053 (1952). [f] H. A. Lardy, THIS JOURNAL, **69**, 518 (1947). [g] References 1 and 2. [h] R. U. Lemieux and G. Huber, *Can. J. Chem.*, **31**, 1040 (1953). [i] E. Hardegger and J. de Pascual, *Helv. Chim. Acta*, **31**, 281 (1948). [j] A. M. Gakhokidze, *J. Gen. Chem.* (*U.S.S.R.*), **11**, 117 (1941); *C.A.*, **35**, 5467 (1941). [k] K. Freundenberg and E. Plankenhorn, *Ann.*, **536**, 257 (1938).

The following observations are pertinent regarding the feasibility of the C4–C6 ortho-acid intermediate III in the I → II isomerization, originally postulated by Helferich and later criticized by Haworth and co-workers. Examination of Fisher–Hirschfelder models discloses that a 6-membered bridge involving C4 and C6 can very readily be constructed provided that the acetoxy substituent at C4 and the acetoxymethylene at C5 are equatorially oriented. Such a situation prevails, for example, in the "C1" chair conformation[17] (V), as well as in the presumably less probable[18] boat conformations "B1" and "2B."[17] The criticisms of Haworth, Hirst and Teece thus appear to have no geometric justification.



V

Experimental

1,2,3,4-Tetra-*O*-acetyl-β-D-glucose (I) was prepared from 6-*O*-trityl-1,2,3,4-tetra-*O*-acetyl-β-D-glucose,[19] m.p. 166–167°, by the procedure of Helferich and Klein.[1] Forty-six grams of the trityl derivative yielded 23.3 g. (83%) of sirupy product. Crystallized from 30 ml. of ether, this afforded 9.1 g. of crude I, m.p. 124°. Twelve grams of crude product was recrystallized from 5 ml. of chloroform diluted with 30 ml. of ether and chilled, yielding 9.6 g. of I having m.p. 126–127°, $[\alpha]^{25}D$ +9.4° (*c* 3.3, $CHCl_3$), in reasonable agreement with the literature values (Table II).

1,2,3,6-Tetra-*O*-acetyl-β-D-glucose (II).—Compound I (6.6 g.) was isomerized in 660 ml. of 10^{-3} *N* sodium hydroxide solution after the method of Helferich and Klein.[1] After chloroform extraction and solvent removal the crude, sirupy product, 6.78 g., was dissolved in 11 ml. of pyridine and the solution was chilled to −5°. The crystalline product, containing pyridine of solvation, was placed *in vacuo* over P_2O_5 to remove the bulk of the pyridine, then placed in an evacuated drying pistol over sulfuric acid at 70°. The drying was interrupted once for pulverizing, then continued for 60 hours until the crude sample was at constant weight, 1.57 g., m.p. 118–124°, $[\alpha]^{20}D$ −23.8° (*c* 0.7, $CHCl_3$). The crude product was recrystallized twice from a mixture of 2 ml. of hot chloroform and 6 ml. of anhydrous ether, yielding 1.15 g. of a sample having m.p. 130.5–131°, $[\alpha]^{25}D$ −33.8° (*c* 1.6, $CHCl_3$). Helferich and Klein report[1] m.p. 134°, $[\alpha]^{21}D$ −33.0° ($CHCl_3$).

Acetylation of I with Radioactive Acetic Anhydride.—One-half gram of the above I was dissolved in 6 ml. of a prechilled (−5°) 1:1 mixture of pyridine and carbonyl-labeled acetic anhydride. After three days at −5° the mixture was thrown into water, allowed to stand 10 minutes and extracted twice with chloroform. The extract was washed successively with 20% hydrochloric acid, water and sodium bicarbonate solution, then dried (Na_2SO_4), filtered and freed of solvent. The vacuum-dried (P_2O_5) residue weighed 0.57 g. (102%) and had m.p. 130–131°, $[\alpha]^{25}D$ +5.1° (*c* 0.6, $CHCl_3$). For radioactivity assay and exchange experiment purposes this was recrystallized from a mixture of 2-propanol (2.5 ml.) and water (1.0 ml.), yielding 0.48 g. of monoacetyl-labeled penta-*O*-acetyl-β-D-glucopyranose having m.p. 130.5–131.5° and a radioactivity level[20,21] of 0.416 mc./mole.

Acetylation of II with Radioactive Acetic Anhydride.—The above tetraacetate II (0.50 g.) was acetylated in an identical manner using carbonyl-labeled acetic anhydride. The crude penta-*O*-acetyl-β-D-glucopyranose product, 0.57 g. (102%), had m.p. 130.5–132°, $[\alpha]^{25}D$ +5.3° (*c* 0.8, $CHCl_3$). Similar recrystallization afforded a pure sample, m.p. 130.5–131.5°, having a radioactivity level of 0.433 mc./mole.

Acetyl Exchange Experiments.—Each of the above samples of monoacetyl-labeled penta-*O*-acetyl-β-D-glucopyranose (0.20 g.) was dissolved in 5 ml. of a 1:1 mixture of acetic acid and acetic anhydride which was 1.0 *M* in sulfuric acid. The solutions were allowed to stand for 5 hours at room temperature, then thrown into water. After 10 minutes the products were extracted into chloroform, and the extracts were washed with sodium bicarbonate, dried (Na_2SO_4), filtered and freed of solvent. The crude, sirupy penta-*O*-acetyl-α-D-glucopyranose products were crystallized twice from mixtures of 2-propanol (1.2 ml.) and water (1 ml.). The α-pentaacetate (0.07 g.) deriving from I had m.p. 111–112°, $[\alpha]^{25}D$ +100° (*c* 0.7, $CHCl_3$) and a radioactivity level of 0.416 mc./mole. The α-pentaacetate (0.09 g.) deriving from II had m.p. 111–112°, $[\alpha]^{25}D$ +102.8° (*c* 0.8, $CHCl_3$), and a radioactivity level of 0.430 mc./mole.

(17) R. E. Reeves, *Advances in Carbohydrate Chem.*, **6**, 123 (1951).

(18) W. Klyne, "Progress in Stereochemistry," Butterworths Scientific Publications, London, 1954, pp. 36 ff.

(19) D. D. Reynolds and W. L. Evans, THIS JOURNAL, **60**, 2559 (1938).

(20) O. K. Neville, *ibid.*, **70**, 3501 (1948).

(21) V. A. Raaen and G. A. Ropp, *Anal. Chem.*, **25**, 174 (1953).

Infrared Absorption Studies.—Chloroform solutions of each of the substances listed in Table I were made up at a concentration of 0.025 *M*. These solutions were in turn placed in a 0.105-mm. sodium chloride cell, and the infrared spectrum of each was scanned in the region 5.0–6.2 μ, using a Perkin–Elmer model 21 double-beam infrared spectrometer. Chloroform solvent was used in a 0.107-mm. cell in the I_0 beam, and a slit-width of 57 μ was employed. The integrated absorption intensity under the region 5.72 μ carbonyl band for each sample was calculated by relationship 1

$$A = k \log (T_0/T)\nu_{max} \times \Delta\nu^{a}1/2 \qquad (1)$$

where T_0 represents the transmittance of the chloroform blank and T that of the sample, and where $\Delta\nu^{a}1/2$ is the apparent half-band width. Equation 1 represents a simplification of the "Method of Direct Integration" of Jones and co-workers.[15] The constant k in (1) cancels when taking the pertinent ratios in Table I, all instrumental and other factors being constant in the successive determinations, and was therefore not evaluated. Thus the "Integrated Absorption Intensity" column in Table I is given in arbitrarily dimensionless numbers which are significant only when converted to the ratios in Table I. It is interesting to note that when the apparent molecular extinction coefficients of the five carbonyl absorption intensities in question were calculated in the usual way, the theoretical ratios of 5/3 and 4/3 for nos. 1, 2 and 3, 4, respectively, in Table I were only very poorly approximated, thus emphasizing the validity of Jones and co-workers' contention[15] of the superiority of integrated absorption intensities over molecular extinction coefficients for such empirical comparisons.

STANFORD, CALIFORNIA

[CONTRIBUTION FROM THE LABORATORY OF CHEMICAL PHARMACOLOGY, NATIONAL CANCER INSTITUTE, NATIONAL INSTITUTES OF HEALTH]

Synthetic Polysaccharides. III. Polyglucose Sulfates[1]

BY JOHN W. WOOD AND PETER T. MORA

RECEIVED FEBRUARY 24, 1958

From synthetic polyglucoses of different molecular weight and degree of branching, polyglucose sulfates were prepared with different degrees of sulfation, preparatory to correlating certain biological activities (such as anticoagulant activity) with macromolecular properties.

The acid-catalyzed polycondensation of D-glucose in vacuum,[2] and the influence of polymerization conditions and of fractionation on the molecular weight, branching and certain other molecular properties of the polyglucoses obtained[3] were described in the previous communications in this series. We now report the preparation of polyglucose sulfates differing in molecular weight, branching and degree of sulfation.

Sulfuric acid esters of certain polymers, especially polysaccharides, are known to have blood anticoagulant activity similar to that of heparin[4] (for example, sulfuric acid esters of polyvinyl alcohol,[5] cellulose,[6] xylan,[7] chitin,[6,7] chondroitin sulfuric acid[6,7] and dextran).[8] Most of these products also exhibited toxicity, ascribed chiefly to precipitation of fibrinogen and agglutination of platelets. It appears from the literature that the common molecular features associating with these activities are macromolecular structure (preferably that of a polysaccharide) and strong electronegative charges (such as are imparted by the sulfuric acid ester groups). In the case of dextran sulfate, the influence of molecular weight and degree of substitution on these biological activities has been studied[9,10]; a relatively low molecular weight product, with two to three sulfate groups per anhydro-glucose unit, was developed in England for clinical use as an anticoagulant.

The sulfuric acid esters prepared from synthetic polyglucoses also were observed[11,12] to have anticoagulant activity similar to heparin; this activity can be reversed by protamine.[11] Moreover, it was observed recently that these preparations possess several biological activities which may be useful in the study of some aspects of blood coagulation, and lipemia clearing.[13] Sodium polyglucose sulfates, and the free acids obtained from them after eliminating the sodium by ion exchange treatment, interact with basic proteins and enzymes, often producing insoluble precipitates.[14] The synthetic polysaccharides offer a suitable model system for correlation of these biological activities with systematic changes in the molecular features, including the degree of branching.

We selected two pairs of polyglucose preparations, obtained by two different polymerization methods[2] which result in certain differences in the degree of branching,[15] and in molecular weight (see Table I). Each pair consisted of a lower and a higher molecular weight sample (preparations A, G and E, F, respectively), with the higher molecular weight sample having about twice as high a molecular weight as the other sample prepared by the same polymerization method. The molecular weights ranged from 9,300 to 28,400. From each of these polyglucoses we prepared a sulfuric acid ester by the chlorosulfonic acid–pyridine method, introducing 2.6 to 3 acid sulfate groups per an-

(1) Presented in part before the Polymer Division of the American Chemical Society at the 132nd National Meeting in New York, N. Y., September 8, 1957.

(2) P. T. Mora and J. W. Wood, THIS JOURNAL, **80**, 685 (1958).

(3) P. T. Mora, J. W. Wood, P. Maury and B. G. Young, *ibid.*, **80**, 693 (1958).

(4) For mechanism of heparin activity *cf.*, for example, A. S. Douglas, *J. Clin. Invest.*, **35**, 533 (1956).

(5) E. Chargaff, F. W. Bancroft and M. Stanley-Brown, *J. Biol. Chem.*, **115**, 156 (1936); P. Karrer, E. Usteri and B. Camerino, *Helv. Chim. Acta*, **27**, 1422 (1944).

(6) P. Karrer, H. Koenig and E. Usteri, *ibid.*, **26**, 1296 (1943).

(7) K. H. Meyer, R. P. Pirue and M. E. Odier, *ibid.*, **35**, 574 (1952).

(8) A. Grönwall, B. Ingelman and H. Mosiman, *Upsala Läkareförens. Förh.*, **50**, 397 (1945).

(9) C. R. Ricketts and K. W. Walton, *Chemistry & Industry*, 869 (1952).

(10) C. R. Ricketts and K. W. Walton, *Brit. J. Pharmacol.*, **8**, 476 (1953).

(11) P. T. Mora, unpublished results with collaborators at the Experimental Station and Stine Laboratory, du Pont Co., Wilmington, Del., 1953.

(12) E. London, R. S. Theobald and G. D. Twigg, *Chemistry & Industry*, 1060 (1955).

(13) Personal communication from Drs. S. Farber, E. Klein and I. Djerassi, Children's Cancer Research Foundation, Boston, Mass.

(14) P. T. Mora and B. G. Young, *Nature*, in press.

(15) See reference 3 for discussion of differences in branching as indicated by periodate titrations.