159. *Degradation of Methylated Inulin to Hexamethyl Difructosan.*

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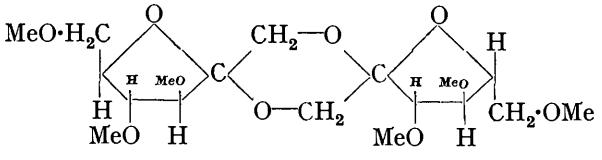
It is now well established (Haworth, Hirst, and Percival, J., 1932, 2384) that fully methylated inulin has a strong negative rotation ($[\alpha]_D$ — 54°) in chloroform solution. Earlier workers (Irvine and Steele, J., 1920, **117**, 1474) have, however, reported that preparations of methylated inulin may be obtained having positive rotations. Such preparations were made by the use of silver oxide and methyl iodide as methylating agents in the final stages of the work. We have recently encountered an instance in which methylation by this process has altered the rotation of a polysaccharide derivative (Haworth, Hirst, and Waine, J., 1935, 1299) and as the change on this occasion appeared to be connected with disaggregation of the complex unit of the polysaccharide, we wished to gain further insight into the action of silver oxide and methyl iodide on partly methylated polysaccharides. We therefore undertook a detailed examination of the reaction between dimethyl inulin and the Purdie reagents.

It was found that dimethyl inulin ($[\alpha]_D$ — 40°) could be produced either by the method of Irvine, Steele, and Shannon (J., 1922, **121**, 1060) or from inulin acetate by use of an appropriate modification of Haworth and Streight's method (*Helv. Chim. Acta*, 1932, **15**, 609). Further methylation of this substance by silver oxide and methyl iodide under specially drastic conditions invariably gave samples of methylated inulin with strong negative rotations and, beyond a slight change in viscosity the meaning of which in this series is in any case uncertain, no evidence of molecular degradation was observed. Since these experiments had given no indication of the formation of dextrorotatory substances, we proceeded to investigate the possibility of degrading the lævorotatory, fully methylated inulin. We found that boiling the substance for prolonged periods with Purdie's reagents, either in the presence or in the absence of water, had no effect and unchanged methylated inulin was recovered from the reaction mixture.

We succeeded, however, in obtaining a syrup soluble in ether and showing a strong positive rotation ($[\alpha]_D$ + 59°), as the result of heating methylated inulin with methyl iodide containing a little hydrogen iodide. This had properties identical with those given by Irvine, Steele, and Shannon for the dextrorotatory methylated inulin described by them and the analytical figures were those required by a trimethyl inulin. Nevertheless this substance was not a polysaccharide, but had the boiling point and molecular weight of a disaccharide and was, in fact, a hexamethyl difructofuranose 1 : 2-anhydride. We conclude, therefore, that dextrorotatory methylated inulin consisted mainly of this product of depolymerisation.

The reaction is exactly comparable with the similar one in which inulin acetate is depolymerised in chloroform solution by anhydrous nitric acid with formation of hexaacetyl difructofuranose 1 : 2-anhydride in good yield (Irvine and Stevenson, *J. Amer. Chem. Soc.*, 1929, **51**, 2197; Bodycote, Haworth, and Woolvin, J., 1932, 2389). In the present experiments the rotation of different samples of hexamethyl difructose anhydride varied somewhat, and since three such 1 : 2-anhydrides of fructofur-



anose are stereochemically possible (αα, αβ, and ββ with respect to the glycosidic groups of the fructofuranose units) it would appear that the mode of depolymerisation now under consideration results in the formation of more than one of these possible stereoisomerides.

Similar depolymerisation took place when dimethyl inulin ($[\alpha]_D$ — 40°) was heated with methyl iodide containing hydrogen iodide, and the product after methylation was the same as that obtained directly from trimethyl inulin. The structure of the hexamethyl difructose anhydride follows from the observation that it gives on hydrolysis 3 : 4 : 6-trimethyl fructofuranose and from the evidence previously reported (Haworth and Streight, *loc. cit.*).

Experimental.

Partial Methylation of Inulin.—(a) *Simultaneous de-acetylation and methylation of inulin acetate.* Inulin acetate prepared by Haworth and Streight's method (*Helv. Chim. Acta*, **1932**, **15**, 609) had $[\alpha]_D^{20°}$ — 33° in chloroform (*c*, 1·4), $\eta_{sp.}^{20°}$ in *m*-cresol 0·075 (0·05 g. in 5 c.c.), corresponding to an apparent chain length of 8 fructose units (by the chemical end-group method, 30 units). This acetate (12 g.) was methylated in acetone solution at 35° by the gradual addition of methyl sulphate (50 c.c.) and 30% aqueous sodium hydroxide (140 c.c.) in the usual way. The product, which was insoluble in boiling water, was isolated in the usual manner and obtained by evaporation of its solution in chloroform as a colourless granular solid, $[\alpha]_D^{20°}$ — 40° in chloroform (*c*, 1·0) (Found : OMe, 33·0. Calc. for dimethyl inulin, 32·7%). This material (2 g.) was dissolved in methyl iodide (10 g.) containing just sufficient methyl alcohol to effect solution and then boiled for 8 hours with silver oxide (5 g.). After one treatment the methoxy-content had risen to 38·4% and after a second treatment to 42·9%. The product was a white powder insoluble in ether, $[\alpha]_D^{20°}$ — 50° in chloroform (*c*, 1·0). In this series of experiments no degradation had taken place, but occasionally the product after treatment with Purdie's reagents showed slight acidity and reduced Fehling's solution. This was due to complications arising out of the action of the Purdie reagents on sodium methyl sulphate which contaminated the partly methylated inulin and was never observed when ash-free inulin was used.

(b) *Direct methylation.* Dimethyl inulin, prepared in accordance with the directions of Irvine, Steele, and Shannon (*loc. cit.*), was a crisp white powder, soluble in cold water and chloroform, insoluble in ether. $[\alpha]_{5780}^{20°}$ — 41° in chloroform (*c*, 1·6), $\eta_{sp.}^{20°}$ 0·084 in *m*-cresol (0·05 g. in 5 c.c.), corresponding to an apparent chain length of 8—9 fructose units (Found : OMe, 27·8%). This material was drastically methylated (50 hours' boiling) three times in succession by silver oxide and methyl iodide in the presence of methyl alcohol, the progress of the methylation being shown in the accompanying table.

Substance.	$[\alpha]_D^{20°}$ in chloroform.	$\eta_{sp.}^{20°}$ in *m*-cresol (*c*, 1·0).	OMe, %.
Product after first treatment	— 39°	0·066	31·5
,, ,, second ,, ...	— 40	0·05	35·0
,, ,, third ,, ...	— 43	0·033	38·0

The product after the third treatment was insoluble in boiling ether. Its rotation was only slightly lower than that of the best specimens of methylated inulin of the same methoxyl content and it was obvious that little degradation had been effected. The principal change was in the value of $\eta_{sp.}$. This may indicate some shortening of the chain length, but in view of the insolubility of the product in ether this cannot have been very marked. In this series the viscosity values can be used only for purposes of comparison, since the relationship between viscosity and chain length is highly abnormal.

Degradation of Fully Methylated Inulin. Preparation of Hexamethyl Difructosan.—Since no success had followed the attempts to obtain the supposed dextrorotatory form of methylated inulin by direct methylation of the " dimethyl " derivative, it was decided to investigate its preparation from undegraded fully methylated inulin. Supplies of the last material {$[\alpha]_D^{20°}$ — 55° in chloroform (*c*, 1·03); $\eta_{sp.}^{20°}$ 0·092 in *m*-cresol (*c*, 1·0) (corresponding with an apparent chain length of 9 fructose units); chain length by the chemical end-group method, 30; OMe, 45·4%} were obtained by Haworth, Hirst, and Percival's method (J., **1932**, 2384). Degradation of the methylated inulin was attempted in the following ways.

(a) *By boiling with Purdie's reagents in the absence of water.* Methylated inulin (4 g.) was boiled for 16 hours with methyl iodide (20 g., containing a little dry methyl alcohol) and silver oxide (10 g.). The product was extracted with chloroform and on evaporation of the solvent

was obtained as a pale yellow glass, $[\alpha]_D^{20°}$ — 52° in chloroform (*c*, 1·5); $\eta_{sp.}^{20°}$ 0·072 in *m*-cresol (*c*, 1·0). No appreciable degradation took place under these conditions.

(b) *By boiling with Purdie's reagents in the presence of water.* The above experiment was repeated with the addition of 1 c.c. of water to the reaction mixture. The product was a white solid, $[\alpha]_D^{20°}$ — 53°, identical with the material obtained in experiment (a).

(c) *By boiling with methyl iodide containing hydrogen iodide. Preparation of hexamethyl difructosan.* Methylated inulin (10 g.) was boiled for 25 minutes with methyl iodide (50 g. containing a little methyl alcohol) to which hydriodic acid (0·4 c.c.; *d* 1·7) had been added (the methylated inulin dissolved completely in 15 minutes). Silver oxide was then added, and the boiling continued for a short time. The product ($n_D^{19°}$ 1·4680) was isolated in the usual way and distilled, giving: (I) a colourless mobile syrup (2 g.), b. p. 100—140°/0·17 mm., $n_D^{19°}$ 1·4560, $[\alpha]_D^{20°}$ + 30° in chloroform. This material was slightly acid to litmus and reduced Fehling's solution; (II) *hexamethyl difructosan* as a neutral, non-reducing, pale yellow, highly viscid syrup (7·5 g.), b. p. 180°/0·1 mm., $n_D^{18°}$ 1·4702, $[\alpha]_D^{20°}$ + 59·3° in chloroform (*c*, 2·3), *M* 393, 386 (ebullioscopic in benzene). Refractionation through a Widmer column gave only fractions with the same b. p.'s and refractive indices (Found: C, 53·0; H, 8·0; OMe, 45·2. $C_{18}H_{32}O_{10}$ requires C, 52·9; H, 7·8; OMe, 45·6%; *M*, 408). A similar neutral non-reducing viscid product was obtained when the above procedure was applied to " dimethyl inulin." A typical sample of hexamethyl difructosan from dimethyl inulin had b. p. 180°/0·1 mm., $n_D^{16°}$ 1·4730, and $[\alpha]_D^{20°}$ + 38° in chloroform (*c*, 2·3). In different preparations using " dimethyl inulin " as starting material the rotation of the hexamethyl difructosan varied somewhat. Fractions (I) and (II) had properties identical with those of fractions obtained by Irvine, Steele, and Shannon during their work on the methylation of inulin.

Hydrolysis of Hexamethyl Difructosan.—Hexamethyl difructosan (2·85 g.) was hydrolysed by 0·2*N*-sulphuric acid (250 c.c.) at 95°. The reaction was followed polarimetrically: $[\alpha]_D^{20°}$ + 73° (initial value); + 72° (6 minutes); + 66° (63 minutes); + 62° (96 minutes); + 59° (136 minutes); + 56° (178 minutes); + 47·5° (255 minutes); + 42° (326 minutes); + 38·6° (constant value after 600 minutes). The end value corresponds to a value $[\alpha]_D$ + 35·5° for the trimethyl fructose formed during the hydrolysis. That this value is slightly low is accounted for by the observation that furfural derivatives are produced in small quantity during the hydrolysis. From the above figures the value of *k* for the hydrolysis was found to be approximately 0·0035 (minutes and natural logarithms). Jackson and MacDonald (*J. Bur. Standards*, 1931, **6**, 709) report *k* = 0·0083 for the hydrolysis of the difructosan, m. p. 164°. The solution was neutralised with barium carbonate and filtered (charcoal). It was then evaporated to dryness in the presence of a trace of barium carbonate. The product (3 : 4 : 6-trimethyl fructofuranose) was extracted with a warm mixture of alcohol and ether and on removal of the solvent was obtained as a colourless syrup, $n_D^{19°}$ 1·4685, $[\alpha]_D^{20°}$ + 25° in chloroform (*c*, 1·57) (Found: OMe, 41·4. Calc. for $C_9H_{18}O_6$: OMe, 41·9%). Its physical properties are identical with those of 3 : 4 : 6-trimethyl fructofuranose and with phenylhydrazine it gave in 75% yield 3 : 4 : 6-trimethyl glucosazone hydrate, m. p. 80—81°, alone or when mixed with an authentic sample (Found: C, 60·4; H, 7·2; N, 14·0; OMe, 21·8. Calc. for $C_{21}H_{28}O_4N_4$: C, 60·3; H, 7·2; N, 13·4; OMe, 22·2%).

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