[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, STATE UNIVERSITY OF IOWA]

The Separation and Identification of the Products of Hydrolysis and Alcoholysis of Methylated Disaccharides

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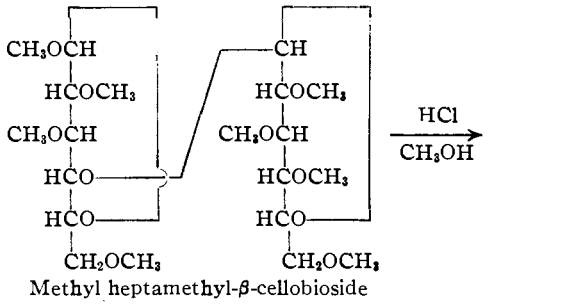
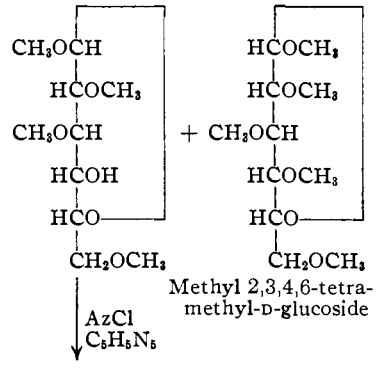
Structures of disaccharides have frequently been determined by hydrolysis of the completely methylated compounds and separation of the hydrolytic products by partition between suitable solvents. In the case of certain 6-linked disaccharides the 2,3,4-trimethyl-D-glucose sirup has been identified by conversion to the methyl β-D-glucoside. The yields of crystalline product are usually low.

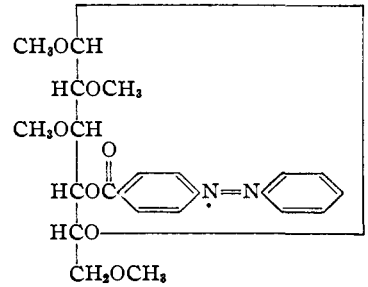
In the present work it has been shown that the point of linkage between the units of a disaccharide can be determined by the preparation and separation of the azoyl (*p*-phenylazobenzoyl) derivatives of the products obtained by hydrolysis or methyl alcoholysis of fully methylated disaccharides. Two methods based on this procedure have been developed.



Methyl heptamethyl-β-cellobioside



Methyl 2,3,4,6-tetramethyl-D-glucoside



Methyl 4-azoyl-2,3,6-trimethyl-D-glucoside

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Method I.—The first method is based upon methyl alcoholysis followed by azoylation as illustrated in the appended equations.

The methyl monoazoyltrimethylglycoside is separated from the methyl tetramethylglycoside by difference in water solubility, and identified by comparison with synthetic products. Quantitative isolation of the methyl tetramethylglycoside was not carried out in method A.

Method II.—The second method involves aqueous hydrolysis and azoylation as illustrated.

Separation of the tetramethylglycosyl azoate from the azoyltrimethylglycosyl azoate is accomplished by chromatographic adsorption on silicic acid. Separations of mixtures of this type have been reported[2] in which the pure α- or β-modifications were used. Since α- and β-mixtures of each derivative are obtained by these methods, separations were first tried with known synthetic azoates prepared under standardized equilibrium conditions. Separation of 1,2,3,4-tetramethyl-D-glucosyl azoate from 4-azoyl-2,3,6-trimethyl-D-glucosyl azoate occurred readily. A mixture of 4-azoyl-2,3,6-trimethyl-D-glucosyl azoate and 6-azoyl-2,3,4-trimethyl-D-glucosyl azoate required a longer development period before separation occurred.

Very good yields of azoates are obtained by both methods and the large azoyl group increases the molecular weight of the products to such an extent that only a small amount of methylated disaccharide is necessary.

Synthetic azoates were prepared corresponding to the products which would result from hydrolysis or methyl alcoholysis of four types of interglucose linkage. These azoates were prepared under standardized conditions producing an equilibrium mixture of α- and β-modifications which could be identified by specific rotation[3] and analysis for per cent. azoyl.[4] There was fortunately considerable difference in the specific rotations of the compounds involved in each method. These values and the results of analysis for per cent. azoyl are given in Table I.

Both methods were tested on five fully methylated disaccharides. The specific rotations of the separated products were in reasonable agreement with the values of synthetic derivatives. Results of method I applied to the five methylated disaccharides are given in Table II.

(2) Mertzweiller, Carney and Farley, THIS JOURNAL, **65**, 2367 (1943); Myrback and Tamm, *Svensk. Kem. Tid.*, **53**, 441-447 (1941).

(3) The specific rotations of all azoates were taken in U. S. P. chloroform at 25° (*c* = 0.5 approx.). The light source was a mercury-cadmium light with a Wratten F filter.

(4) Coleman and McCloskey, THIS JOURNAL, **65**, 1588 (1943).

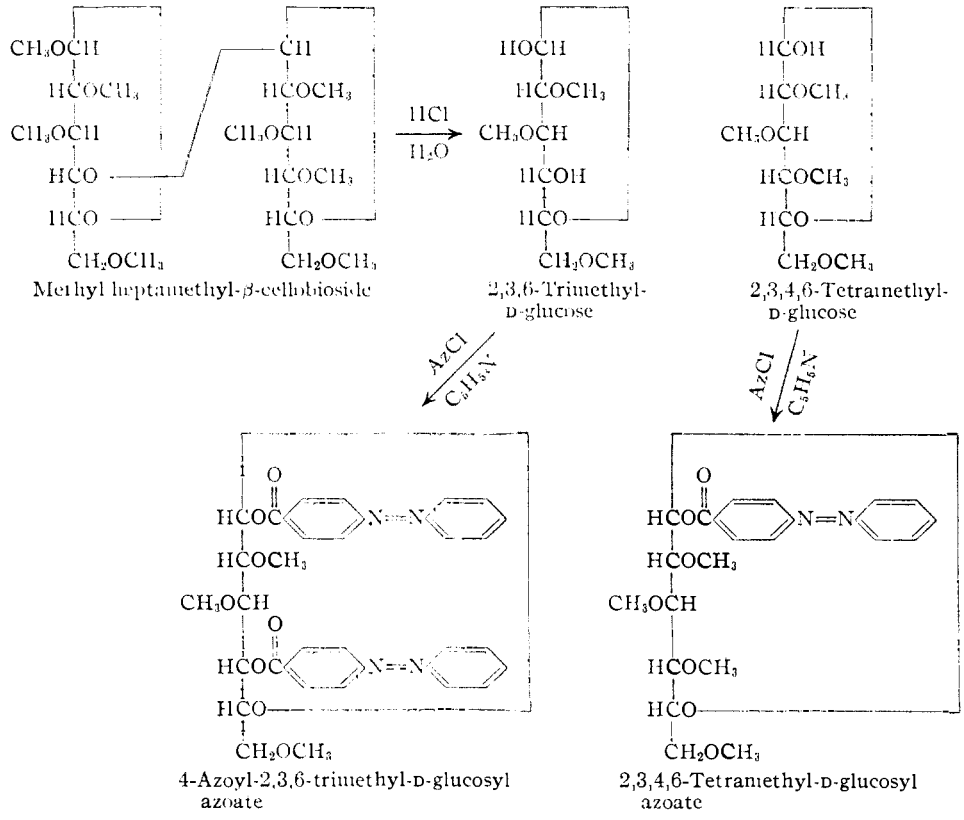


TABLE I

SYNTHETIC AZOATES

	$[\alpha]^{25}_{5438}$	Per cent. azoyl Found	Per cent. azoyl Calcd.
Methyl 2-azoyl-3,4,6-trimethyl-D-glucoside	110° 116°	48.2	47.15
Methyl 3-azoyl-2,4,6-trimethyl-D-glucoside	32 28	47.7	47.15
Methyl 4-azoyl-2,3,6-trimethyl-D-glucosiule	−6 −2	48.5	47.15
Methyl 6-azoyl-2,3,4-trimethyl-D-glucoside	51 50	47.8	47.15
2,3,4,6-Tetramethyl-D-glucosyl azoate	35 32 32	46.8	47.15
2,3,4,6-Tetramethyl-D-galactosyl azoate	63	46.4	47.15
2-Azoyl-3,4,6-trimethyl-D-glucosyl azoate	80	65.2	65.53
3-Azoyl-2,4,6-trimethyl-D-glucosyl azoate	98 107 95	64.9	65.53
4-Azoyl-2,3,6-trimethyl-D-glucosyl azoate	−1 1 −5	65.7	65.53
6-Azoyl-2,3,4-trimethyl-D-glucosyl azoate	−38 −29 −36	65.2	65.53

[a] Two or more specific rotations listed for one compound represent rotations of equilibrium mixtures obtained in separate experiments.

In method B the upper band formed by chromatographic separation of the azoates was always found to be the monoazoate. The rotation of this band indicated that there was a little contamination from the lower diazoate band. With cellobiose there was incomplete separation on the first column. The upper band was therefore separated on another column. With methyl heptamethyl-β-lactoside and methyl heptamethyl-maltoside a peculiarity was observed. By the chromatographic separation of the azoate mixture a band was obtained which was less strongly adsorbed than either the monoazoates or diazoates. After separation of this band which passed down the column more rapidly, the upper band which consisted of the monoazoates and diazoates was separated on another column. Values corresponding to the synthetic products were obtained. The identity of the band which first separated has not been determined. It constituted about 25% of the original azoate mixtures and had a specific rotation of about −40°. Table III shows the results obtained by method B applied to methylated disaccharides. Comparable values for corresponding synthetic products are also given.

When azoyl chloride dissolved in pyridine is

TABLE II

EQUILIBRIUM ROTATIONS OF AZOATES FORMED AFTER METHYL ALCOHOLYSIS OF METHYLATED DISACCHARIDES

	Azoate $[\alpha]^{25}_{5438}$	Synthetic product $[\alpha]^{25}_{5438}$
Methyl heptamethyl-β-cellobioside	−4° −3[a]	−6°
Methyl heptamethyl-β-lactoside	−8 −4	−6
Methyl heptamethylmaltoside	−6	−6
Methyl heptamethyl-β-gentiobioside	53	52
Methyl heptamethyl-β-melibioside	49 46	52

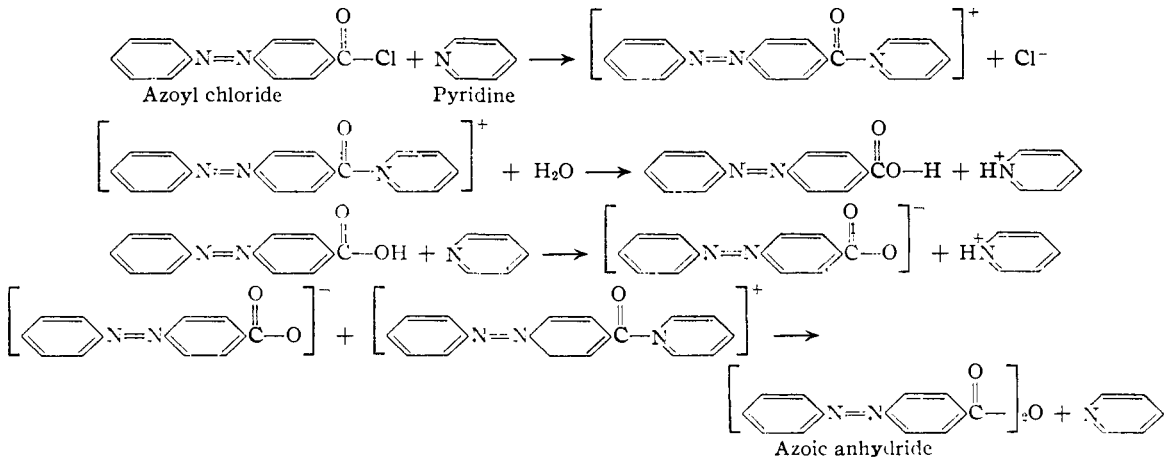
[a] Two specific rotations for one compound represent rotations of equilibrium mixtures obtained in duplicate experiments.

TABLE III

CHROMATOGRAPHIC SEPARATIONS OF AZOYLATED HYDROLYZATES (METHOD II)

	Weight, g.	$[\alpha]^{25}_{5438}$	Synthetic product $[\alpha]^{25}_{5438}$
1. Methyl heptamethyl-β-gentiobioside			
Upper band	0.1735	22	36
Lower band	0.2523	−31	−38
2. Methyl heptamethyl-β-melibioside			
Upper band	0.1349	42	63
Lower band	0.1950	−41	−38
3. Methyl heptamethyl-β-cellobioside			
Upper band	0.2587	18	36
Lower band	0.1076	− 3	− 1
Upper band separated on another column			
Upper band	0.1718	28	36
Lower band	0.0844	3	− 1
4. Methyl heptamethyl-β-lactoside			
Upper band	0.1812	19	63
Lower band	0.1031	−38	− 1
Upper band separated on another column			
Upper band	0.0475	60	63
Lower band	0.0789	− 2	− 1
5. Methyl heptamethylmaltoside			
Upper band	0.3284	22	36
Lower band	0.1310	−40	− 1
Upper band separated on another column			
Upper band	0.1215	34	36
Lower band	0.1936	7	− 1

added to a large excess of water azoic anhydride is formed in relatively high yield.[4] If slightly more than the theoretical amount of water required for hydrolysis of the anhydride is added to the pyridine solution of azoyl chloride and the mixture allowed to stand for fifteen minutes, only a small amount of anhydride is obtained. A postulated mechanism for the formation of azoic anhydride is given in the following equations



If only a limited amount of water is added the anhydride which forms remains in solution and is soon hydrolyzed. When the pyridine solution is poured into a large excess of water the anhydride is formed and is immediately precipitated due to its insolubility in water.

The small amount of azoic anhydride present in the crude synthetic azoates was removed by chromatographic adsorption on silicic acid. The anhydride passed down the column quite rapidly.

The synthetic azoates corresponding to the products formed by method I were separated by chromatographic adsorption on silicic acid into fractions having markedly different specific rotations, presumbaly the α- and β-forms. The specific rotations of these fractions and their relative weights are given in Table IV. In order to purify the fractions further, each was recrystallized twice from ligroin. The final melting points, specific rotations, crystal form, and color are given in the last columns of Table IV. In certain cases it was necessary to prepare additional material for this recrystallization. It should be noted that this series represents crystalline derivatives of all eight methyl trimethyl-D-glucopyranosides. The two samples of methyl 6-azoyl-2,3,4-trimethyl-D-glucoside obtained by the application of method I to methyl heptamethyl-β-gentiobioside and methyl heptamethyl-β-melibioside were each separated chromatographically on silicic acid. The fractions obtained in each case corresponded closely in specific rotation to those obtained from the synthetic methyl 6-azoyl-2,3,4-triethyl-D-glucoside. The sample of methyl 4-azoyl-2,3,6-trimethyl-D-glucoside obtained by the application of method I to methyl heptamethyl-β-cellobioside was separated chromatographically into the α and β modifications. These also corresponded closely in specific rotation to the fractions obtained from the synthetic methyl 4-azoyl-2,3,6-trimethyl-D-glucoside. The products thus obtained from the three disaccharides were recrystallized from ligroin and found to be identical with the corresponding recrystallized synthetic products.

TABLE IV

CHROMATOGRAPHIC SEPARATIONS OF SYNTHETIC AZOATES INTO α- AND β-MODIFICATIONS

	Weight, g.	$[\alpha]^{25}_{6438}$	Recrystallized product: $[\alpha]^{25}_{6438}$	M. p., °C.	Crystal form	Color
Methyl 2-azoyl-3,4,6-trimethyl-D-glucoside						
Upper band (β)	0.2496	43°	67°	113.5–114	Large plates	Pink
Lower band (α)	0.4330	138	153	90.8–91.4	Thick irregular masses	Deep red
Methyl 3-azoyl-2,4,6-trimethyl-D-glucoside						
Upper band (α)	0.1978	51	63	82.7–83.2	Flat needles, clusters	Red orange
Lower band (β)	0.0995	−4	−13	110–110.5	Plates	Orange
Methyl 4-azoyl-2,3,6-trimethyl-D-glucoside						
Upper band (α)	0.9132	27	25	89.6–90	Long slender needles	Lustrous red
Lower band (β)	0.4183	−63	−68	92.8–93.6[a]	Microscopic	Light pink
Methyl 6-azoyl-2,3,4-trimethyl-D-glucoside						
Upper band (α)	0.2143	75	99	80.2–80.7	Small plates	Light pink
Lower band (β)	0.0831	12	−1	120.2–120.7[a]	Needles	Light pink

[a] Freudenberg and Plankenhorn, *Ber.*, **73**, 630 (1940), give 95–96° as the melting point of methyl 4-azoyl-2,3,6-trimethyl-β-D-glucoside and 122° as the melting point of methyl 6-azoyl-2,3,4-trimethyl-β-D-glucoside.

Recrystallization of α and β equilibrium mixtures of these azoates did not prove to be satisfactory alone for the separation of the α and β forms. However, after the chromatographic separations the fractions thus obtained could be purified readily by recrystallization.

In Tables IV and V the α- or β-configuration was assigned to the purified products on the basis of the specific rotation. If the rotation of the compound was above that of the equilibrium mixture the compound was designated as α-, if below, β-.

The synthetic azoates (equilibrium mixtures) which correspond to the products formed by method II were recrystallized to constant melting point. The melting points and rotation of these compounds are given in Table V.

TABLE V

RECRYSTALLIZATION OF AZOATE EQUILIBRIUM MIXTURES TO PRODUCTS OF CONSTANT MELTING POINT

Azoate	M. p., °C.	$[\alpha]^{25}_{6438}$
2-Azoyl-3,4,6-trimethyl-α-D-glucosyl azoate[a]	162.5–163.5	+142
3-Azoyl-2,4,6-trimethyl-β-D-glucosyl azoate[a]	132.5–133.5	−51
4-Azoyl-2,3,6-trimethyl-α-D-glucosyl azoate[a]	154–155.5	+4
6-Azoyl-2,3,4-trimethyl-α-D-glucosyl azoate[a]	164.5–165.5	+25
2,3,4,6-Tetramethyl-β-D-glucosyl azoate[a]	125–126	−36
2,3,4,6-Tetramethyl-β-D-galactosyl azoate[b]	153–154	−28

[a] Recrystallized from a 1:25 chloroform ligroin solution. [b] Recrystallized from ligroin containing a few drops of chloroform.

Experimental

Hydrolysis and Methyl Alcoholysis.—In order to determine the rates of hydrolysis and methyl alcoholysis, preliminary experiments were carried out and followed polarimetrically. Under the conditions used, aqueous hydrolysis of the completely methylated disaccharide was complete in less than three hours. Methyl alcoholysis at 85° was found to be complete in twelve hours.

Method I

Methyl Alcoholysis.—Two grams of methylated sugar dissolved in 125 ml. of 3% hydrogen chloride–methanol solution was placed in a tightly stoppered pressure bottle. The reaction mixture was kept at 85° for twelve hours, then cooled and neutralized with excess silver carbonate. The solid material was filtered from the mixture and the filtrate evaporated to dryness under reduced pressure. In order to remove the last traces of methanol, toluene or ligroin was added, mixed thoroughly with the residue and evaporated.

Azoylation[5] and Separation.—The resulting sirup was dissolved in 75 ml. of dry pyridine and 3.0 g. of azoyl chloride added. The reaction mixture was allowed to stand at about 30° for twenty-four hours with occasional shaking. Two milliliters of water was added to the azoylation mixture. After about fifteen minutes the mixture became homogeneous and was treated with an excess of powdered sodium bicarbonate. The solids were filtered from the mixture and washed with acetone. The combined filtrate and washings were evaporated to dryness under reduced pressure. Approximately 100 ml. of acetone was added and the solids broken up. The mixture was warmed and the solvent allowed to evaporate until the volume was 10–15 ml. The residue was then poured into 250 ml. of water with vigorous stirring. The precipitate of azoyl derivative and azoic acid was filtered from the mixture and dried in air. The dry precipitate was triturated with 50–75 ml. of chloroform and the mixture filtered. In order to remove the azoic acid the filtrate was passed through about 25 g. of 200-mesh alumina contained in a small glass crucible with a fritted disk. The alumina was washed with chloroform until the filtrate became colorless. The chloroform was evaporated in an oven at 55° and the residue placed in a vacuum oven at 60° and 3 mm. A typical yield was 1.66 g. (85% of the theoretical). Table II gives the specific rotations of the monoazoates obtained from five completely methylated disaccharides. For three of the disaccharides the specific rotations of equilibrium mixtures obtained from duplicate experiments are listed. For comparison, the specific rotations of corresponding synthetic derivatives are also listed.

Chromatographic separation of the α and β forms of methyl monoazoyltrimethyl-D-glucosides obtained by method I was carried out on silicic acid using benzene containing 0.2% alcohol by volume as the developing solvent. The general procedure of chromatographic separation used is described under method II. The time required for development of the chromatogram in the separation of the α and β forms was from twenty-four to forty-eight hours depending on the amount of material used. Results of these separations are listed in Table IV.

Method II

Hydrolysis.—Five-tenths of a gram of completely methylated disaccharide was added to 50 ml. of 5% hydrogen chloride in water and the mixture was refluxed for

[5] The azoylation conditions are modified from those of Freudenberg and Plankenhorn, *Ber.*, **73**, 621 (1940).

three hours in an oil-bath. At the end of this time the solution was cooled in an ice-bath and neutralized with an excess of silver carbonate. The salts were removed by filtration and washed with a small amount of water. The combined filtrate and washings were treated with hydrogen sulfide to remove ionic silver. The colloidal solution was filtered through a charcoal mat and the mat washed with about 10 ml. of water. The combined filtrate and washings were concentrated at reduced pressure, not allowing the temperature to exceed 50°. Toluene was added and evaporated and the procedure repeated until most of the moisture had been removed. The sirup was placed in a vacuum oven at 50° and 1 mm. overnight.

Azoylation.—The thick sirup was dissolved in 10 ml. of pyridine which had been dried over calcium oxide and the solution transferred to a 25-ml. Erlenmeyer flask. A crystal of pyridine hydrochloride was added and the solution placed in the refrigerator at 0° for ten hours. At the end of this time the flask was immersed in an ice-bath and 1.65 g. of azoyl chloride added. The reactants were well mixed while cooled by the ice-bath and then placed in the refrigerator at 0°. After five days at 0° with intermittent agitation the flask was removed from the refrigerator and kept at 40° in a constant temperature bath for one day to complete the reaction. About 0.5 ml. of water was added to the flask and the mixture allowed to stand for fifteen minutes or longer at room temperature. At the end of this time the pyridine was removed under reduced pressure and the residue triturated with about 50 ml. of water. The solids were separated by filtration and dried in air. The dry solids were triturated with 50 to 75 ml. of chloroform and the mixture filtered by suction. This removed most of the azoic acid. The remainder of the acid in the filtrate was efficiently removed by passing the solution through about 25 g. of 200-mesh alumina contained in a small glass crucible with a fritted disk. The alumina was washed with chloroform until the washings were colorless. The combined filtrate and washings were allowed to evaporate in a current of air and the residue dried in a vacuum desiccator over concentrated sulfuric acid for at least a day. A typical yield of azoates was about 1.1 g. (92% of the theoretical).

Chromatographic Separation.—Three to five-tenths of a gram of the mixture of mono- and diazoates was dissolved in 10 ml. of chloroform and poured carefully onto a silicic acid column which had been previously prepared. The glass column was 33 mm. in diameter and 600 mm. long. It was fitted with a perforated porcelain plate at the bottom to support the silicic acid. The plate was covered with a layer of fine glass wool.

In preparing the column, a slurry of approximately 200 g. of Merck reagent grade silicic acid in 500 ml. of benzene was introduced and gas pressure applied to pack the column and remove excess solvent. The chromatogram was developed by the slow addition of benzene containing 0.1% absolute alcohol by volume. The gas pressure maintained on the surface of the liquid in the column was 20 to 30 cm. of mercury above atmospheric pressure. When the chromatogram had been properly developed, the excess solvent was removed from the column and the silicic acid column forced from the glass tube.

After mechanical separations of the bands, the azoates were eluted with chloroform containing 10–20% absolute alcohol. The chloroform solution of azoate was filtered and the filtrate evaporated to dryness in dry air or under reduced pressure. The azoate was taken up in chloroform and filtered through an asbestos pad supported by a fine fritted disk. The filtrate was allowed to evaporate to dryness in a wide weighing bottle in air and finally in a vacuum oven at 50° and 3 mm.

The results of separation of the azoates by chromatographic adsorption on silicic acid are given in Table III.

Methyl 2-Azoyl-3,4,6-trimethyl-D-glucoside.—One gram of crystalline methyl 3,4,6-trimethyl-β-D-glucoside was subjected to alcoholysis and azoylation according to the procedure described in method A. The yield of methyl 2-azoyl-3,4,6-trimethyl-D-glucoside was 1.0 g. (53% of the theoretical).

Anal. Calcd. for $C_6H_7O(OCH_3)_4(C_{13}H_9O_2N_2)$: azoyl 47.15. Found: azoyl, 48.2.

Methyl 3-Azoyl-2,4,6-trimethyl-D-glucoside.—Two grams of crystalline 2,4,6-trimethyl-D-glucose was treated according to procedure A, yield 3.8 g. (95% of the theoretical).

Anal. Calcd.: azoyl, 47.15. Found: azoyl, 47.7.

Methyl 4-Azoyl-2,3,6-trimethyl-D-glucoside.—One gram of crystalline 2,3,6-trimethyl-D-glucose was treated according to procedure A; yield 1.48 g. (74% of the theoretical).

Anal. Calcd.: azoyl, 47.15. Found: azoyl, 48.4.

Methyl 6-Azoyl-2,3,4-trimethyl-D-glucoside.—Two and nine-tenths grams of crystalline 2,3,4-trimethyl-1,6-anhydro-D-glucose was treated according to procedure A except that the methyl alcoholysis period was extended to thirty hours instead of twelve; yield 4.74 g. (75% of the theoretical).

Anal. Calcd.: azoyl, 47.15. Found: azoyl, 47.8.

2,3,4,6-Tetramethyl-D-glucosyl Azoate.—Five grams of crystalline 2,3,4,6-tetramethyl-D-glucose was azoylated according to procedure B; yield 9.4 g. (nearly theoretical).

Anal. Calcd.: azoyl, 47.15. Found: azoyl, 46.8.

2,3,4,6-Tetramethyl-D-galactosyl Azoate.—Three grams of crystalline 2,3,4,6-tetramethyl-D-galactose[6] was azoylated according to the conditions given in procedure B; yield 5.5 g. (97% of the theoretical).

Anal. Calcd.: azoyl, 47.15. Found: azoyl, 46.4.

2-Azoyl-3,4,6-trimethyl-D-glucosyl Azoate.—One and eighty-three hundredths grams of 3,4,6-trimethyl-D-glucose was azoylated according to the conditions given in procedure B; yield 5 g. (95% of the theoretical).

Anal. Calcd. for $C_6H_7O(OCH_3)_3(C_{13}H_9O_2N_2)_2$: azoyl, 65.5. Found: azoyl, 65.2.

3-Azoyl-2,4,6-trimethyl-D-glucosyl Azoate.—Five grams of crystalline 2,4,6-trimethyl-D-glucose was azoylated according to the conditions given in procedure B; yield 13.6 g. (95% of the theoretical).

Anal. Calcd.: azoyl, 65.5. Found: azoyl, 64.9.

4-Azoyl-2,3,6-trimethyl-D-glucosyl Azoate.—Five grams of crystalline 2,3,6-trimethyl-D-glucose was azoylated according to the conditions given in procedure B; yield 12.6 g. (88% of the theoretical).

Anal. Calcd.: azoyl, 65.5. Found: azoyl, 65.7.

6-Azoyl-2,3,4-trimethyl-D-glucosyl Azoate.—Five grams of 2,3,4-trimethyl-D-glucose ($[\alpha]^{25}D$ 79°) was azoylated by the conditions given in procedure B; yield 13.25 g. (92% of the theoretical).

Anal. Calcd.: azoyl, 65.5. Found: azoyl, 65.2.

Chromatographic Separation of Synthetic Mixtures.—A mixture of 0.16 g. of 2,3,4,6-tetramethyl-D-glucosyl azoate and 0.23 g. of 4-azoyl-2,3,6-trimethyl-D-glucosyl azoate was placed on a silicic acid column and the chromatogram developed with benzene containing 0.1 volume per cent. of absolute alcohol. Two bands separated readily. Their specific rotations and the values of the corresponding synthetic derivatives are listed.

	Weight, g.	$[\alpha]^{25}_{6438}$	Synthetic product, $[\alpha]^{25}_{6438}$
Upper band	0.1414	23	36
Lower band	0.2088	−8	−1

A mixture of 0.1333 g. of 4-azoyl-2,3,6-trimethyl-D-glucosyl azoate and 0.1064 g. of 6-azoyl-2,3,4-trimethyl-D-glucosyl azoate was placed on a silicic acid column and the chromatogram developed in the usual manner. Two days were required for complete separation of the bands.

	Weight, g.	$[\alpha]^{25}_{6438}$	Synthetic product $[\alpha]^{25}_{6438}$
Upper band	0.1719	1	− 1
Lower band	0.0465	−45	−38

(6) This compound was prepared by Stanley S. Brandt in this Laboratory.

Methylation of Disaccharides.—The disaccharide octaacetate was converted to the α-glycosyl chloride with titanium tetrachloride.[7] By treatment with silver carbonate and methanol the glycosyl chloride was converted to the methyl heptaacetyl-β-glycoside. The heptaacetyl compound was methylated in acetone solution with dimethyl sulfate and 50% sodium hydroxide solution using a relatively large excess of these reagents. The methylation was completed by two treatments with sodium and methyl iodide according to the procedure of Pacsu and Trister.[8] By this method, methyl heptamethyl-β-lactoside, m. p. 84.5–85.2°, methyl heptamethyl-β-cellobioside, m. p. 86–87.5°, methyl heptamethyl-β-melibioside, m. p. 105–106°, methyl heptamethyl-β-gentiobioside, m. p. 105–106° and methyl heptamethylmaltoside, b. p. 143° (0.05 mm.), $n^{25}D$ 1.4620, were prepared. The final yields based on disaccharide octaacetate were in all cases 40–60% of the theoretical.

Acknowledgment.—The authors wish to express their appreciation to the Corn Products Refining Company for financial assitance, to G. E. Hilbert of the U. S. Northern Regional Research Laboratory for a generous sample of levoglucosan, and to B. Clifford Hendricks of the University of Nebraska for seed crystals of tetramethylgalactose.

(7) Pacsu, *Ber.*, **61**, 1508 (1928).

(8) Pacsu and Trister, THIS JOURNAL, **61**, 2412 (1939).

Summary

1. A new method for the separation of the hydrolysis products of completely methylated disaccharides has been developed. This involves the introduction of azoyl (*p*-phenylazobenzoyl) groups into the positions opened by hydrolysis.

2. A similar method has been developed based on methyl alcoholysis of methylated disaccharides followed by azoylation of one of the products.

3. Both methods have been applied to five completely methylated disaccharides.

4. Crystalline azoyl derivatives of the eight methyl trimethyl-D-glucopyranosides have been obtained by chromatographic separation of the α and β mixtures.

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[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Vinyl Alcohols. XV.[1] Trisubstituted Vinyl Alcohols

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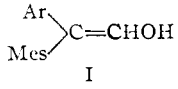
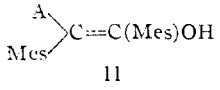
The vinyl alcohols dealt with in this series of papers, unique in that they contain only hydrocarbon substituents,[4] fall into two separate categories which may be designated as aldehyde enols and ketone enols. The stable aldehyde enols which have been made so far are 2,2-diarylvinyl alcohols in which one or both of the radicals is mesityl or isoduryl. They may be represented by formula I.



I



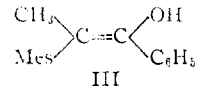
II

The ketone enols differ widely in the tendency to ketonize,[5] their stability depending on the nature of the three substituents. Those which are stable have a mesityl or a similar radical[6] in the *beta* as well as the *alpha* position and may be represented by formula II. Moreover, from a consideration of known examples, it appears that A may be any hydrocarbon residue but not hydrogen.[7]

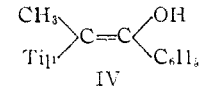
The purpose of the present work was to discover the structural elements which are necessary and sufficient to stabilize this type of enol. Eight new trisubstituted vinyl alcohols have been examined in which the structure has been varied systematically. They fall into two classes which may be designated as disubstituted acetophenones and disubstituted acetones.

Enols of Disubstituted Acetophenones

The acetophenone enols are represented by formulas III to VII.



III



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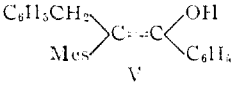

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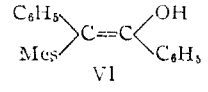
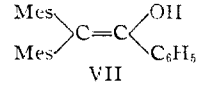
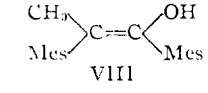


VI



VII



VIII

The first of these, 2-mesityl-1-phenyl-1-propen-1-ol (III), differs structurally from the known

(1) For the preceding communication in this series see Fuson, Byers, Rowland, Southwick and Sperati, THIS JOURNAL, **66**, 1873 (1944).

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(4) The enol form of 9-formylfluorene is stable [Wislicenus and Waldmüller, *Ber.*, **42**, 785 (1909). Wislicenus and Russ, *ibid.*, **43**, 2719 (1910)] and, if the aldehyde is classed as a diarylacetaldehyde would constitute an exception to this statement.

(5) Up to this time the relative tendencies of vinyl alcohols to ketonize have not been measured accurately. Enols which can be isolated and characterized are said to be "stable."

(6) Other radicals which have been found to resemble mesityl in their stabilizing influence are duryl, isoduryl and 3-bromomesityl.

(7) Enols are known in which A is methyl or phenyl. It is interesting to note that when A is hydroxyl the vinyl alcohol is a stable enediol. Although not a hydrocarbon residue, the radical $MesCOCH_2$— in the stable enol, 1,2,4-trimesityl-1-buten-4-on-1-ol, of Lutz and Kibler (THIS JOURNAL, **62**, 365 (1940)) should be mentioned in this connection.