acetone–methanol melted at 89°, and gave no depression with the above described α-stigmastenyl benzoate; $[\alpha]_D$ +11° (23.6 mg., 2 cc. of chloroform, l = 1 dm., $\alpha^{23}D$ +0.13°).

Anal. Calcd. for $C_{36}H_{54}O_2$, C.: C, 83.34; H, 10.49. Found: C, 83.01; H, 10.55.

α-Stigmastenol.—A sample (0.3 g.) of the first described benzoate was boiled with 30 cc. of a 5% solution of potassium hydroxide in alcohol for two hours. Water was then added in the sterol extracted with ether. It crystallized from methanol in big leaflets, containing solvent of crystallization. After drying in a vacuum at 80° it melted at 115°. Mixed with an authentic sample of α-spinastenol (m. p. 114°) there was no depression of the melting point; $[\alpha]^{23}D$ +24° (24.2 mg., 2 cc. of chloroform, l = 1 dm., $\alpha^{23}D$ +0.29°) in good agreement with the rotation reported for α-spinastenol ($[\alpha]_D$ +26).

Anal. Calcd. for $C_{29}H_{50}O$: C, 83.98; H, 12.16; Found: C, 84.05; H, 12.12.

α-Stigmastenyl Acetate.—Two-tenths gram of the α-stigmastenol just described was heated on the steam-bath with 10 cc. of acetic anhydride. On cooling the acetate came out in the form of big leaflets. It was recrystallized from benzene–alcohol: m. p. 118°, $[\alpha]^{23}D$ +16° (18.9 mg., 2 cc. of chloroform, l = 1 dm., $\alpha^{23}D$ +0.15°); no depression with α-spinastenyl acetate (m. p. 117°, $[\alpha]_D$ +15°).

Anal. Calcd. for $C_{31}H_{52}O_2$: C, 81.58; H, 11.48. Found: C, 82.02; H, 11.63.

Summary

Ozonization of α-spinasterol yields ethylisopropylacetaldehyde.

α-Spinastenol is identical with α-stigmastenol, the hydrogenation product of 7-dehydrostigmasterol.

In view of these experimental findings a structure formula, that of $\Delta^{8:14,22:23}$-stigmastadienol-3, is proposed for α-spinasterol.

NEW BRUNSWICK, N. J. RECEIVED JULY 5, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

Derivatives of the Aldehydrol Form of Sugars. III.[1] Carbon One Asymmetry

BY M. L. WOLFROM, M. KONIGSBERG AND F. B. MOODY

In continuation of our studies on derivatives of the aldehydrol form of sugar acetates, we wish to report on a number of such substances obtained in this Laboratory. Most of these compounds are new and those that are not have been prepared by methods that are novel or by methods that have not been applied previously to the derivatives in question.

The *aldehydo*-form of *d*-mannose pentaacetate has been reported[2] in the form of its crystalline ethyl hemiacetal (I).[3] The corresponding methyl hemiacetal was desired for further synthetic work and was obtainable readily in crystalline form. It was convertible on further acetylation into the *aldehydo-d*-mannose heptaacetate (II) recorded by Pirie.[4] These two hemiacetals of *aldehydo-d*-mannose pentaacetate showed a simple downward mutarotation in absolute chloroform and thus correspond to the α-isomer of the two isomeric ethyl hemiacetals of methyl *aldehydo-d*-galacturonate tetraacetate reported by Dimler and Link.[5] These authors have adopted the α and β prefixes for the two isomeric forms of these acyclic derivatives in which the isomerism is concerned only with the asymmetry of the aldehyde carbon atom. This designation is based on the usage proposed by Hudson,[6] in which that derivative in the cyclic *d*-series having the more positive rotation is assigned the prefix α. This nomenclature need lead to no confusion with the usual α,β cyclic sugar nomenclature, if the prefix *aldehydo* be included in the name. It will be adopted in the present communication.

Mild acetylation of this stable methyl hemiacetal of *aldehydo-d*-mannose pentaacetate produced one form of the 1-methoxy-*aldehydo-d*-mannose hexaacetate (III). The second form of this derivative was obtained by application of the interconversion conditions described by Hudson and co-workers[7] for the corresponding acyclic isomers of *d*-arabinose, obtained by them by the acetolysis of β-methyl-*d*-arabinoside.

Mild acetylation of the stable methyl hemi-

(1) Previous publications in this series: (a) M. L. Wolfrom, THIS JOURNAL, **57**, 2498 (1935); (b) M. L. Wolfrom and M. Konigsberg, *ibid.*, **60**, 288 (1938).

(2) M. L. Wolfrom and M. Konigsberg, *ibid.*, **61**, 574 (1939).

(3) The Roman numerals refer to the general type structures of these acyclic sugar derivatives as represented in Fig. 1.

(4) N. W. Pirie, *Biochem. J.*, **30**, 374 (1936).

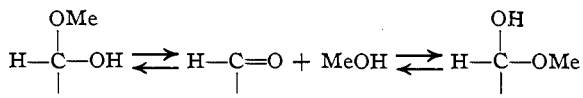
(5) R. J. Dimler and K. P. Link, THIS JOURNAL, **62**, 1216 (1940).

(6) C. S. Hudson, *ibid.*, **31**, 66 (1909).

(7) Edna M. Montgomery, R. M. Hann and C. S. Hudson, *ibid.*, **59**, 1124 (1937).

acetal of *aldehydo-d*-galactose pentaacetate[8] produced the two isomeric forms of 1-methoxy-*aldehydo-d*-galactose hexaacetate together with some *aldehydo-d*-galactose heptaacetate. We also record now the second form of the corresponding ethoxy derivative of *d*-galactose, one form of which has been reported previously.[1b]

The acyclic acetates of *d*-mannose, *d*-galactose and *l*-fucose form crystalline hemiacetals but this property is not shared by all of the acyclic sugar acetates, such as those of glucose and arabinose. We have found, however, that mild acetylation of a concentrated methanol solution of the *aldehydo*-acetates of the latter two sugars will yield the two forms of the 1-methoxy derivative (III) together with some of the 1,1-diacetate (II). This would indicate that the methanol solution of these *aldehydo*-acetates contains an equilibrium mixture of the two isomeric hemiacetals and the free carbonyl form.



The above acetylation reaction was first applied in the arabinose structure, since the two isomeric forms of the 1-methoxy derivative were already known in the *d*-arabinose series.[7] As our supply of arabinose was of the *l*-variety, our products were the enantiomorphs of those reported by Hudson and co-workers for *d*-arabinose. The constants obtained by us were in complete agreement with those obtained by the above workers. Having established the applicability of the reaction for arabinose, it was then extended successfully to *d*-glucose.

Table I gives a tabulation of those acyclic sugar derivatives that are known in the two forms predictable on stereochemical grounds and which differ in the asymmetry of the aldehyde carbon atom. It is to be noted that the isomeric 1-alkoxy-1-acetate (III) derivatives show very small rotation differences, whereas the one known isomeric pair of hemiacetals shows quite a large rotation difference.

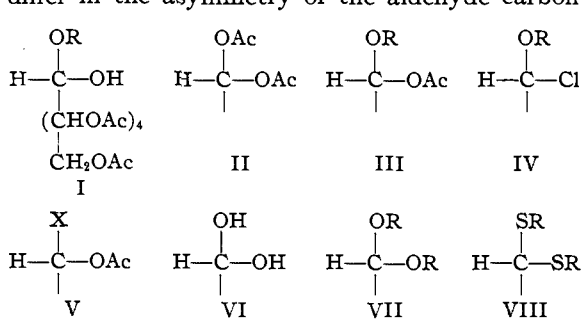


FIG. 1.—TYPE STRUCTURES

Halogen replacement of the 1-acetate in the 1-methoxy (and ethoxy) *aldehydo-d*-galactose hexaacetate by the general methods used by Hudson and co-workers[7] in the arabinose structure leads to the 1-chloro-1-methoxy (and ethoxy[1b]) *aldehydo-d*-galactose pentaacetate (IV) previously reported from this Laboratory. The corresponding 1-chloro-1-methoxy-*aldehydo-d*-mannose pentaacetate also was obtained. The halogen in these derivatives is replaceable by hydroxyl or alkoxyl with extreme ease and evidence is now presented that the mutarotation observed previously[1b] for this structure in supposedly anhydrous media is due to reaction with traces of moisture, leading to the formation of the *aldehydo-d*-galactose pentaacetate which now has been isolated from these solutions in the form of its crystalline ethyl hemiacetal.

To the list of acetyl halide carbonyl addition compounds of the *aldehydo*-sugar acetates (V) now known,[1] we add the crystalline acetyl bromide compounds of *aldehydo-d*-mannose pentaacetate and *aldehydo-l*-rhamnose tetraacetate. The halogen in this type of derivative is not as reactive as in the corresponding 1-alkoxy structure. Treatment of the previously known 1-bromo-*aldehydo-d*-galactose hexaacetate[1a] with ethanol and silver carbonate led to the isolation of the ethyl hemiacetal of *aldehydo-d*-galactose pentaacetate, thus indicating that the acetyl bromide had been replaced by ethanol on the carbonyl group under these experimental conditions. Although Hudson and co-workers[7] isolated two forms of 1-chloro-1-methoxy-*aldehydo-d*-arabinose tetraacetate, this isomerism has not been demonstrated for the 1-halogeno-1-acetate *aldehydo*-sugar structures. Further work will undoubtedly lead to the establishment of this predictable isomerism.

The aldehydrol (VI) of *aldehydo-d*-mannose pentaacetate has been obtained as a substance crystallizing with one mole of acetone of crystallization. This rather peculiar compound was studied in some detail. We can now report that the aldehydrol forms of *aldehydo-d*-galactose pentaacetate and of *aldehydo-d*-mannose pentaacetate exhibit no mutarotation in aqueous solution, which fact is predictable on stereochemical

(8) M. L. Wolfrom and W. M. Morgan, THIS JOURNAL, **54**, 3390 (1932).

TABLE I

α,β ISOMERS OF *aldehydo*-SUGAR ACETATES

Substance	M. p., °C.	Spec. rot. ($CHCl_3$)	
α-1-Chloro-1-methoxy-*aldehydo-d*-arabinose tetraacetate	73	+52.5°	Montgomery,
β-1-Chloro-1-methoxy-*aldehydo-d*-arabinose tetraacetate	71	+29	Hann,
α-1-Methoxy-*aldehydo-d*-arabinose pentaacetate	68	+35	and
β-1-Methoxy-*aldehydo-d*-arabinose pentaacetate	76	+27	Hudson[7]
α-1-Methoxy-*aldehydo-l*-arabinose pentaacetate	67	−34	This work
β-1-Methoxy-*aldehydo-l*-arabinose pentaacetate	76	−27	This work
α-1-Methoxy-*aldehydo-d*-glucose hexaacetate	103	+ 4	This work
β-1-Methoxy-*aldehydo-d*-glucose hexaacetate	61	− 3	This work
α-1-Methoxy-*aldehydo-d*-mannose hexaacetate	84	+23	This work
β-1-Methoxy-*aldehydo-d*-mannose hexaacetate	96	+11	This work
α-1-Methoxy-*aldehydo-d*-galactose hexaacetate	101	+ 4	This work
β-1-Methoxy-*aldehydo-d*-galactose hexaacetate	123	+ 2	This work
α-1-Ethoxy-*aldehydo-d*-galactose hexaacetate	84	+ 9	This work
β-1-Ethoxy-*aldehydo-d*-galactose hexaacetate	97	+ 3	Wolfrom and Konigsberg[1b]
Methyl *aldehydo-d*-galacturonate α-ethyl hemiacetal 2,3,4,5-tetraacetate	105	+41	Dimler and Link[5]
Methyl *aldehydo-d*-galacturonate β-ethyl hemiacetal 2,3,4,5-tetraacetate	127	− 7	Dimler and Link[5]

grounds and on the basis of the structures assigned to these derivatives. These substances show a mutarotation in absolute chloroform due to dissociation of the water from the carbonyl group.

As a further contribution to the study of the acyclic sugar derivatives, we wish to include the synthesis from the mercaptal of the dimethyl acetal (and its tetraacetate) of *l*-arabinose (VII), enantiomorphic to the substance synthesized by Hudson and co-workers[7] by another method. We have obtained further the diethyl acetal (and its tetraacetate) of *l*-arabinose. We also wish to record the crystalline hexaacetate of the diethyl thioacetal (VIII) of *d*-α-glucoheptose (*d*-gluco-*d*-gulo-heptose[9]).

Experimental

WITH F. B. MOODY

aldehydo-d-**Mannose Pentaacetate Aldehydrol (with One Mole of Acetone of Crystallization).**—*d*-Mannose diethyl mercaptal pentaacetate[4] (50 g.) was demercaptalated as described by Wolfrom and Konigsberg.[2] The dried chloroform (alcohol-free) extract so obtained was concentrated under reduced pressure to a sirup and this was dissolved in acetone and then ligroin was added just to incipient opalescence. Crystallization at this point was effected only by the addition of a few cc. of water; yield 32.6 g. Pure material was obtained on several further crystallizations effected in the same manner; m. p. 68–70°; spec. rot. +24° (extrapolated) ⟶ +9° (22°; *c*, 2.6; abs. $CHCl_3$[10]); spec. rot. +26° (23°; *c*, 5.5; H_2O; no mutarotation). *aldehydo-d*-galactose pentaacetate aldehydrol also exhibited a stable rotation in water solution; spec. rot. +4° (20°; *c*, 1.0; H_2O; no mutarotation).

The substance was very soluble in cold water and slightly so in ether and toluene. It was practically insoluble in ligroin and was soluble in the other common organic solvents. The compound was unstable and at room temperature the pure material slowly softened. At 40° the crystalline material changed to a sirup in about an hour with loss of acetone and acetic acid. It was handled conveniently by working in a 0° cold room.

An absolute chloroform solution of the substance of a 5.8 (g. per 100 cc. soln.) concentration became opaque in twenty minutes at 23° due to separation of water. The presence of acetone in the crystals, dried in the air below room temperature, was determined by passing a stream of dry air over the crystals maintained at the temperature of boiling chloroform and absorbing the vapors in an alkaline, dilute methanol solution of benzaldehyde. The yellow crystals that formed were identified as dibenzalacetone; m. p. 110–111°; mixed m. p. unchanged.[11] As the substance was unstable and difficult to dry, the analyses obtained were only approximate.

Anal. Calcd. for $C_6H_7O_6(CH_3CO)_5H_2O\cdot CH_3COCH_3$: C, 48.9; H, 6.5; CH_3CO, 10.7 cc. 0.1 *N* NaOH per 100 mg. Found: C, 48.5; H, 6.2; CH_3CO, 10.9 cc.

The substance yielded a semicarbazone that was shown by melting point and mixed melting point to be identical with that described by Wolfrom and Georges.[12] It was also convertible into the *aldehydo-d*-mannose methyl hemiacetal described below on acetone removal and recrystallization from methanol.

aldehydo-d-**Mannose Pentaacetate Methyl Hemiacetal.**—This substance was synthesized from *d*-mannose diethyl mercaptal pentaacetate (50 g.) according to the procedure described[2] for the corresponding ethyl hemiacetal except that alcohol-free chloroform was employed and methanol was substituted for ethanol; yield 25 g. of m. p. 98–101°.

(9) Nomenclature of C. S. Hudson, THIS JOURNAL, **60**, 1537 (1938).

(10) All rotations are recorded to the D line of sodium light; 22° is the temperature; *c* is the concentration in g. per 100 cc. soln.; abs. $CHCl_3$ refers to the pure alcohol-free solvent.

(11) D. Vorländer and K. Hobohm, *Ber.*, **29**, 1840 (1896).

(12) M. L. Wolfrom and L. W. Georges, THIS JOURNAL, **58**, 1781 (1936); *cf.* ref. 2.

Pure material was obtained on methanol recrystallization; m. p. 102–104°; spec. rot. +27.5° (extrapolated) ⟶ +17° (23°; *c*, 5; abs. $CHCl_3$).

The substance reduced Fehling solution and gave a positive Schiff aldehyde test. Its solubilities were similar to those of the corresponding ethyl hemiacetal.[2]

Anal. Calcd. for $C_6H_7O_6(CH_3CO)_5CH_3OH$: C, 48.32; H, 6.21; OCH_3, 7.34; CH_3CO, 11.9 cc. of 0.1 *N* NaOH per 100 mg. Found: C, 48.13; H, 6.07; OCH_3, 7.47; CH_3CO, 11.9 cc.

The substance yielded *aldehydo-d*-mannose heptaacetate[4] (m. p. 120–121°, mixed m. p. unchanged; CH_3CO, 14.2 cc. 0.1 *N* NaOH per 100 mg.; calcd., 14.2 cc.) on acetylation with fifteen parts of an acetic acid (20 vol.), acetic anhydride (30 vol.), sulfuric acid (1 vol.) mixture.

1-Bromo-*aldehydo-d*-mannose Hexaacetate.—The acetone compound of *aldehydo-d*-mannose pentaacetate aldehydrol (15 g.) was held under reduced pressure at 75° until the melt ceased bubbling. The resultant sirup was treated with acetyl bromide (35 cc.) for one hour at room temperature and the separated semi-solid mass obtained on pouring the reaction mixture into ice and water was removed with ether (alcohol-free) and obtained crystalline on concentration of the dried extract; yield 6.8 g. (2 crops), m. p. 110–114°. Pure material was obtained on further crystallization from ether (alcohol-free); m. p. 115–116°; spec. rot. +92° (22°; *c*, 5.5; abs. $CHCl_3$).

Anal. Calcd. for $C_6H_7O_6(CH_3CO)_6Br$: Br, 15.58; saponification value (7 equivalents), 13.6 cc. 0.1 *N* NaOH per 100 mg. Found: Br, 15.27; saponification value, 13.5 cc.

1-Bromo-*aldehydo-l*-rhamnose Pentaacetate.—*l*-Rhamnose diethyl mercaptal tetraacetate[4] (50 g.) was demercaptalated according to the procedure described for the corresponding mannose compound[2] and the resultant sirup obtained on chloroform removal was treated for two hours at room temperature with acetyl bromide (130 cc.) and the product isolated and purified as described previously for 1-bromo-*aldehydo-d*-mannose hexaacetate; yield 11.1 g., m. p. 112–113°, spec. rot. −103° (25°; *c*, 5; abs. $CHCl_3$).

The crystalline substance was soluble in the common solvents except petroleum ether and water.

Anal. Calcd. for $C_6H_8O_5(CH_3CO)_5Br$: C, 42.21; H, 5.09; Br, 17.6; saponification value (6 equivalents), 13.2 cc. of 0.1 *N* NaOH per 100 mg. Found: C, 42.42; H, 5.11; Br, 17.75; saponification value, 13.2 cc.

Hydrolysis of the bromine in this substance according to the procedure described below for the corresponding galactose compound led to a halogen-free sirup which was not amenable to crystallization.

α-1-Methoxy-*aldehydo-d*-mannose Hexaacetate.—*aldehydo-d*-Mannose pentaacetate (24 g.) was acetylated for nine hours at 0° with dry pyridine (300 cc.) and acetic anhydride (600 cc.). The resultant sirup obtained on pouring the acetylation mixture into a large excess of ice and water was taken up in chloroform and the extract washed successively with 5% sulfuric acid, 5% sodium bicarbonate and water. The sirup obtained on solvent removal from the washed and dried chloroform extract, slowly crystallized on standing and was recrystallized from 50% methanol; yield 17.9 g. (2 crops), m. p. 82°. Pure material was obtained on further recrystallization from 50% methanol; m. p. 84–85°, spec. rot. +23° (28°; *c*, 10; abs. $CHCl_3$).

The substance was soluble in the common organic solvents except petroleum ether. It was practically insoluble in water. It reduced boiling Fehling solution and gave a negative Schiff aldehyde test.

Anal. Calcd. for $C_6H_7O_6(CH_3CO)_6OCH_3$: C, 49.14; H, 6.08; OCH_3, 6.68; CH_3CO, 12.9 cc. of 0.1 *N* NaOH per 100 mg. Found: C, 49.09; H, 6.30; OCH_3, 6.74; CH_3CO, 12.8 cc.

β-1-Methoxy-*aldehydo-d*-mannose Hexaacetate.—α-1-Methoxy-*aldehydo-d*-mannose hexaacetate (10 g.) was transformed into the corresponding β-isomer according to the general procedure of Montgomery, Hann and Hudson,[7] employing 125 cc. of the interconverting mixture (30 cc. 99.5% acetic acid, 70 cc. acetic anhydride, 8 g. freshly fused zinc chloride). An equilibrium specific rotation of +19° was attained in ten minutes at room temperature. The specific rotation of the starting material in the same mixture but with the omission of the zinc chloride was +29° and this value was unchanged over an observation period of two hours. After the solution containing the zinc chloride had attained equilibrium it was poured into 1 liter of ice and water, extracted with chloroform and the sirup resulting on chloroform removal of the washed and dried extract was obtained crystalline from methanol by the addition of an equal volume of water; 4.4 g., m. p. 72–75°. Pure material was obtained on several recrystallizations from 50% methanol; 1.8 g., m. p. 95.5–96°, mixed m. p. with the α-isomer (m. p. 84–85°) 67–70°, spec. rot. +11° (31°; *c*, 10; abs. $CHCl_3$).

The substance exhibited similar properties and solubilities to those of the α-isomer but was less soluble in 50% methanol.

Anal. Calcd. for $C_6H_7O_6(CH_3CO)_6OCH_3$: C, 49.14; H, 6.08; OCH_3, 6.68; CH_3CO, 12.9 cc. of 0.1 *N* NaOH per 100 mg. Found: C, 49.39; H, 6.04; OCH_3, 6.72; CH_3CO, 13.0 cc.

On working up the first mother liquor material from 50% methanol followed by ether–ligroin, the α-isomer (0.6 g.) was found. This was identified by melting point (84–85°) and mixed melting point; spec. rot. +23° (abs. $CHCl_3$).

1-Chloro-1-methoxy-*aldehydo-d*-mannose Pentaacetate.—This substance was prepared according to the general procedure of Hudson and co-workers.[7] α-1-Methoxy-*aldehydo-d*-mannose hexaacetate (5 g., m. p. 84–85°) was dissolved in 50 cc. of absolute chloroform and treated for thirty minutes at 0° with 5 g. of anhydrous aluminum chloride. The chloroform solution was then washed with cold water, dried and the solvent removed (35°) under reduced pressure. The resultant sirup was dissolved in 20 cc. of anhydrous ether and immediate crystallization was effected by the addition of two volumes of low boiling petroleum ether (previously dried over sodium); yield 2.5 g., m. p. 109–111°. Since the material was quite unstable, especially when impure, it was obtained in pure form by refluxing (followed by cooling) with several portions of anhydrous ether; m. p. 116–118°, spec. rot. +71°, slowly decreasing (+25° after twenty hours) (28°; *c*, 4; abs. $CHCl_3$).

Anal. Calcd. for $C_7H_{10}O_6Cl(CH_3CO)_5$: Cl, 8.04; saponification value (6 equivalents), 13.6 cc. 0.1 *N* NaOH per 100 mg. Found: Cl, 7.96; saponification value, 13.6 cc.

α and β Forms of 1-Methoxy-*aldehydo*-*d*-glucose Hexaacetate.—*aldehydo*-*d*-Glucose pentaacetate[13] (20 g.) was acetylated in methanol under the same conditions as described below for the corresponding *l*-arabinose compound. On working up the product from ether–ligroin three substances were isolated: *aldehydo*-*d*-glucose heptaacetate,[13a] m. p. 117–119°, mixed m. p. unchanged, spec. rot. +8.1° (24°; *c*, 5; $CHCl_3$); α-methoxy-*aldehydo*-*d*-glucose hexaacetate, m. p. 103–104°, spec. rot. +3.8° (24°; *c*, 5; $CHCl_3$), crystallizing in lustrous plates; β-1-methoxy-*aldehydo*-*d*-glucose hexaacetate, m. p. 61–62°, spec. rot. −3° (25°; *c*, 4; abs. $CHCl_3$), crystallizing in needles.

Anal. Calcd. for $C_6H_7O_6(CH_3CO)_6OCH_3$: C, 49.14; H, 6.08; OCH_3, 6.68; CH_3CO, 12.9 cc. 0.1 *N* NaOH per 100 mg. Found for α-isomer: C, 49.01; H, 6.13; CH_3CO, 12.9 cc. Found for β-isomer: OCH_3, 6.64; CH_3CO, 12.9 cc.

WITH M. KONIGSBERG

α and β Forms of 1-Methoxy-*aldehydo*-*d*-galactose Hexaacetate.—*aldehydo*-*d*-Galactose pentaacetate methyl hemiacetal[8] (20 g.) was acetylated under the same conditions as previously described for the corresponding mannose compound. The reaction was worked up in the same manner and the crude product obtained was recrystallized from methanol; yield 12.3 g., m. p. 120–123°. A second crop of material was obtained from the mother liquors; 5.7 g., m. p. 95–102°. The first crop was recrystallized from methanol; yield 9 g., m. p. 123–124°, spec. rot. +2.1° (22°; *c*, 5; $CHCl_3$). These constants did not change on further recrystallization from methanol or ether. This material formed massive, rectangular crystals and exhibited solubilities similar to the corresponding mannose derivative.

Anal. Calcd. for $C_6H_7O_6(CH_3CO)_6(OCH_3)$: OCH_3, 6.68; CH_3CO, 12.9 cc. 0.1 *N* NaOH per 100 mg. Found: OCH_3, 6.64; CH_3CO, 12.9 cc.

The mother liquors from the recrystallization of the first material were combined with the lower melting crystals and recrystallized several times from methanol; yield 3.7 g., m. p. 105–106°, spec. rot. +3.9° (23°; *c*, 5; $CHCl_3$). This fraction showed no depression in melting point with an authentic specimen of *aldehydo*-*d*-galactose heptaacetate[14] (m. p. 106°; spec. rot. +4.0°, $CHCl_3$; CH_3CO, 14.1 cc. 0.1 *N* NaOH per 100 mg., calcd., 14.1 cc.). The combined mother liquors yielded 3.2 g. of a third product, which upon several recrystallizations from methanol by the addition of ligroin had these physical constants: m. p. 101°, mixed m. p. with first form (m. p. 123–124°) 95–106°, mixed m. p. with *aldehydo*-*d*-galactose heptaacetate (m. p. 106°) 93–96°, spec. rot. +3.5° (23°; *c*, 5; $CHCl_3$).

Anal. Calcd. for $C_6H_7O_6(CH_3CO)_6(OCH_3)$: OCH_3, 6.68; CH_3CO, 12.9 cc. 0.1 *N* NaOH per 100 mg. Found: OCH_3, 6.50; CH_3CO, 12.9 cc.

The proportions of these three compounds varied widely with different preparations but in all runs the acetylated hemiacetals predominated.

α-1-Ethoxy-*aldehydo*-*d*-galactose Hexaacetate.—This substance was isolated from the dilute alcoholic mother liquors of the *aldehydo*-1-ethoxy-*d*-galactose hexaacetate previously reported[1b] and was purified by recrystallization from dilute alcohol and ether: m. p. 84–85°, spec. rot. +9.3° (23°; *c*, 5; $CHCl_3$). It crystallized as lustrous flakes whereas its isomer crystallized as fine needles. The solubilities of the two compounds were very similar. The constants found[1b] on the previously reported form were: m. p. 97°, spec. rot. +3.4° ($CHCl_3$).

Anal. Calcd. for $C_6H_7O_6(CH_3CO)_6(OC_2H_5)$: OC_2H_5, 9.42; CH_3CO, 12.6 cc. 0.1 *N* NaOH per 100 mg. Found: OC_2H_5, 9.27; CH_3CO, 12.6 cc.

α and β Forms of 1-Methoxy-*aldehydo*-*l*-arabinose Pentaacetate.—*aldehydo*-*l*-Arabinose tetraacetate[15] (15 g.) was dissolved in methanol (15 cc.) and cooled in an acetone–solid carbon dioxide-bath. To this was added slowly a solution of anhydrous pyridine (60 cc.) and acetic anhydride (120 cc.), previously cooled to the same temperature. The mixture was maintained at the temperature of this cooling bath for four hours and was then packed in an ice–salt mixture and placed in an ice-box overnight. The solution was then poured into 1.5 liters of ice and water and extracted with chloroform. The extract was washed successively with cold 5% sulfuric acid, cold sodium bicarbonate solution and water. The sirup obtained on solvent removal from the dried (decolorizing charcoal) chloroform extract was dissolved in ether (alcohol-free) and crystallized by the addition of ligroin.

There was always formed a mixture of three products, various runs giving different proportions. They were successfully fractionated from ether–ligroin, the form present in the greater amount separating first. Final purifications were effected from the same solvent mixture, except in the case of the *aldehydo*-*l*-arabinose hexaacetate, where methanol–water was found to be advantageous. Two of these products were the enantiomorphs of the two isomeric forms of 1-methoxy-*aldehydo*-*d*-arabinose pentaacetate described by Hudson and co-workers[7] and the third product was *aldehydo*-*l*-arabinose hexaacetate.[1a] For the typical experiment cited there was obtained: *aldehydo*-*l*-arabinose hexaacetate, 2.5 g., m. p. 88–89°, mixed m. p. unchanged, spec. rot. −27° (23°; *c*, 4; $CHCl_3$); α-1-methoxy-*aldehydo*-*l*-arabinose pentaacetate, 3.3 g., m. p. 67–68°, mixed m. p. with *aldehydo*-*l*-arabinose hexaacetate 62–64°, spec. rot. −34° (20°; *c*, 4; $CHCl_3$); β-1-methoxy-*aldehydo*-*l*-arabinose pentaacetate, 5.5 g., m. p. 76–77°, mixed m. p. with *aldehydo*-*l*-arabinose hexaacetate 69–83°, mixed m. p. with α-isomer, 53–70°, spec. rot. −27° (23°; *c*, 5; $CHCl_3$). These constants are in excellent agreement with those cited by Hudson and co-workers for the corresponding enantiomorphic compounds (m. p. 68–70°, spec. rot. +35° in $CHCl_3$; m. p. 76°, spec. rot. +27° in $CHCl_3$).

Anal. Calcd. for $C_5H_6O_5(CH_3CO)_5(OCH_3)$: C, 49.0; H, 6.2; CH_3CO, 12.7 cc. 0.1 *N* NaOH per 100 mg. Found for α-isomer: C, 48.7; H, 6.0; CH_3CO, 12.8 cc. Found for β-isomer: C, 48.8; H, 6.1; CH_3CO, 12.8 cc.

Preparation of 1-Chloro-1-methoxy-*aldehydo*-*d*-galactose Pentaacetate.—1-Methoxy-*aldehydo*-*d*-galactose hexaace-

(13) M. L. Wolfrom, THIS JOURNAL, **51**, 2188 (1929).

(14) F. Micheel, H. Ruhkopf and F. Suckfüll, *Ber.*, **68**, 1523 (1935).

(15) M. L. Wolfrom and Mildred R. Newlin, THIS JOURNAL, **52**, 3619 (1930).

tate (m. p. 123–124°; 5 g.) was dissolved in 400 cc. of dry ether (containing 2–3 g. of dry hydrogen chloride per 100 cc.) and the solution was kept at ice-box temperature overnight, whereupon the crystalline reaction product that had separated was removed by filtration and washed with dry ether; yield 3.5 g., m. p. 151–153°. Pure material was obtained on recrystallization from a mixture of dry benzene (4 parts) and ligroin (1 part); yield 2.6 g., m. p. 155–156°; spec. rot. −38° ⟶ +15° (25°; *c*, 5; abs. $CHCl_3$; 24 hours), spec. rot. −53° ⟶ −42.5° (26°; *c*, 5; C_6H_6; 10 hours).

The product was identical (mixed m. p. unchanged) with that described by Wolfrom and Weisblat[16] as synthesized by the action of acetyl chloride upon *d*-galactose dimethyl acetal pentaacetate. The same chloro compound was isolated when the lower melting isomer (m. p. 101°) was treated in similar fashion.

***aldehydo-d*-Galactose Pentaacetate from 1-Chloro-1-ethoxy-*aldehydo-d*-galactose Pentaacetate.**—When 1-chloro-1-ethoxy-*aldehydo-d*-galactose pentaacetate[1b] (2 g.) was dissolved in dry benzene containing silver carbonate and a desiccant and the mixture shaken, the benzene became free of halogen in approximately eight hours. The silver salts were removed by filtration and the partially crystalline mass obtained on solvent removal was recrystallized from ethanol and identified as *aldehydo-d*-galactose pentaacetate ethyl hemiacetal[17] (1.2 g., m. p. 133–134°, mixed m. p. unchanged) which on crystallization from water yielded the aldehydrol[17] (m. p. 123–125°; mixed m. p. unchanged).

In spite of various precautions used in attempts to exclude traces of atmospheric moisture, the same results were always obtained. The same product was obtained by replacing the benzene with absolute chloroform or anhydrous ether.

Treatment of the chloro compound in dry pyridine solution with silver fluoride resulted in the formation of *aldehydo-d*-galactose pentaacetate, identified as its ethyl hemiacetal. The same product was identified as the reaction product between the chloro compound and silver mercaptide in benzene solution containing Drierite (anhydrous calcium sulfate).

***l*-Arabinose Dimethyl Acetal Tetraacetate.**—*l*-Arabinose diethyl mercaptal tetraacetate[15] (50 g.) was dissolved in 500 cc. of absolute methanol and 60 g. of finely powdered cadmium carbonate was added. A solution of 165 g. of mercuric chloride in 400 cc. of absolute methanol was then added and the mixture refluxed for ten hours with vigorous mechanical stirring. The cooled mixture was filtered and the residue washed with methanol. The filtrate was concentrated to 100 cc. and then poured into 300 cc. of chloroform. This solution was washed free of halide, dried, decolorized and concentrated to a thick sirup under reduced pressure (35–40°). The product crystallized in beautiful prisms from ether by the addition of petroleum ether; yield 25 g. (two crops), m. p. 75–78°. Pure material was obtained on two recrystallizations from the same solvents; m. p. 81°, spec. rot. −22° (20°; *c*, 5; $CHCl_3$). Hudson and co-workers[7] record for the enantiomorph synthesized by a different procedure: m. p. 80° (cor.), spec. rot. +22° ($CHCl_3$).

Anal. Calcd. for $C_5H_6O_4(CH_3CO)_4(OCH_3)_2$: C, 49.4; H, 6.6; CH_3CO, 11.0 cc. 0.1 *N* NaOH per 100 mg. Found: C, 49.1; H, 6.5; CH_3CO, 10.9 cc.

***l*-Arabinose Dimethyl Acetal.**—*l*-Arabinose dimethyl acetal tetraacetate (5 g.) was treated for five hours at ice-box temperature with 12 cc. of 0.1 *N* sodium methylate, whereupon the product was crystallized by the addition of ether; yield 2.5 g., m. p. 119–121°. Pure material was obtained from methanol by the addition of ether; m. p. 121–122°, spec. rot. +20° (22°; *c*, 5; H_2O). Hudson and co-workers[7] record for the enantiomorphic compound: m. p. 122°, spec. rot. −19° (H_2O).

Anal. Calcd. for $C_5H_{10}O_4(OCH_3)_2$: C, 42.8; H, 8.2; OCH_3, 31.6. Found: C, 42.3; H, 8.1; OCH_3, 31.5.

***l*-Arabinose Diethyl Acetal Tetraacetate.**—*l*-Arabinose diethyl mercaptal (50 g.) was demercaptalated, in ethanol, under the same conditions as previously described in the preparation of the corresponding methyl derivative. The product crystallized from a concentrated ethanol solution on standing at ice-box temperature; yield 13.6 g. (two crops), m. p. 55–59°. Pure material was obtained on one recrystallization from ethanol; m. p. 59°, spec. rot. −17.5° (23°; *c*, 5; $CHCl_3$).

The product crystallized in massive, rectangular crystals which were soluble in acetone, ether, chloroform and alcohol. It was practically insoluble in water and ligroin and reduced Fehling solution only after acid hydrolysis.

Anal. Calcd. for $C_5H_6O_4(CH_3CO)_4(OC_2H_5)_2$: C, 52.03; H, 7.19; OC_2H_5, 22.97; CH_3CO, 10.2 cc. 0.1 *N* NaOH per 100 mg. Found: C, 51.97; H, 7.22; OC_2H_5, 23.06; CH_3CO, 10.1 cc.

***l*-Arabinose Diethyl Acetal.**—*l*-Arabinose diethyl acetal tetraacetate (4 g.) was treated for several hours at ice-box temperature with 50 cc. of 0.1 *N* sodium ethylate. The sirup obtained on solvent removal under reduced pressure was redissolved in a small amount of absolute ethanol and crystallized on the addition of dry ether; yield 1.6 g., m. p. 108–109°. Pure material was obtained on recrystallization from ethanol–ether; m. p. 109°; spec. rot. +16° (22°; *c*, 5; H_2O).

The substance reduced Fehling solution only after acid hydrolysis. It was soluble in water, alcohol and hot acetone. It was practically insoluble in ether, chloroform and benzene.

Anal. Calcd. for $C_5H_{10}O_4(OC_2H_5)_2$: C, 48.2; H, 8.99; OC_2H_5, 41.18. Found: C, 48.5; H, 9.1; OC_2H_5, 41.05.

***aldehydo-d*-Galactose Pentaacetate Ethyl Hemiacetal from 1-Bromo-*aldehydo-d*-galactose Hexaacetate.**—1-Bromo-*aldehydo-d*-galactose hexaacetate[1a] (1 g.) was dissolved in absolute ethanol (50 cc.) and silver carbonate (1 g.) was added. After refluxing for one hour, the silver salts were removed by filtration and the crystalline material obtained on concentration of the filtrate was recrystallized from absolute ethanol. The product (0.5 g.) was identified as *aldehydo-d*-galactose ethyl hemiacetal[17] by melting point and mixed melting point.

***d*-Gluco-*d*-gulo-heptose[9] Diethyl Mercaptal Hexaacetate.**[18]—*d*-α-Glucoheptose diethyl mercaptal was prepared

(16) M. L. Wolfrom and D. I. Weisblat, THIS JOURNAL, **62**, 878 (1940).

(17) M. L. Wolfrom, *ibid.*, **52**, 2464 (1930).

(18) Mildred R. Newlin, Ph.D. Dissertation, The Ohio State University, 1932.

as described by E. Fischer[19] except that it was found unnecessary to heat the hydrochloric acid to effect solution of the sugar (finely powdered). The mercaptal (8 g.) was acetylated overnight with pyridine (32 cc.) and acetic anhydride (64 cc.) and crystallization of the product took place immediately on pouring into 1 liter of ice and water. Pure material was obtained on recrystallization from methanol by the addition of water; yield 13.9 g., m. p. 99–100°, spec. rot. −12° (25°; *c*, 4; U. S. P. $CHCl_3$). The substance crystallized in fine prisms and was soluble in the common solvents except water and petroleum ether.

Anal. Calcd. for $C_9H_{13}O_6S_2(CH_3CO)_6$: S, 11.3; CH_3CO, 10.6 cc. 0.1 *N* NaOH per 100 mg. Found: S, 11.2; CH_3CO, 10.6 cc.

Demercaptalation of *d*-α-glucoheptose hexaacetate yielded sirups which were not amenable to crystallization.

We acknowledge the general assistance rendered by N. Y. A. Project O. S. U. 167 and the analytical assistance given by Mr. John Walker (W. P. A. Project 18062).

Summary

1. The methyl hemiacetal and the aldehydrol (with one mole of acetone of crystallization) of *aldehydo-d*-mannose pentaacetate have been synthesized.

2. 1-Bromo-*aldehydo-d*-mannose hexaacetate and 1-bromo-*aldehydo-l*-rhamnose pentaacetate have been synthesized.

3. Two stereoisomeric forms (denoted as α and β) of the 1-methoxy-1-acetate of the *aldehydo*-acetates of *d*-glucose, *d*-mannose, *d*-galactose and *l*-arabinose have been synthesized. The synthesis of the second isomer of the corresponding 1-ethoxy derivative of *d*-galactose is reported.

4. 1-Bromo-*aldehydo-d*-galactose hexaacetate and 1-chloro-1-ethoxy-*aldehydo-d*-galactose pentaacetate have been converted to *aldehydo-d*-galactose pentaacetate ethyl hemiacetal.

5. 1-Chloro-1-methoxy-*aldehydo-d*-mannose pentaacetate has been synthesized.

6. The dimethyl and diethyl acetals (and their tetraacetates) of *l*-arabinose have been synthesized from *l*-arabinose diethyl mercaptal.

7. *d*-Gluco-*d*-gulo-heptose diethyl mercaptal hexaacetate has been synthesized.

8. All compounds reported have been obtained in pure, crystalline condition.

COLUMBUS, OHIO RECEIVED JULY 8, 1940

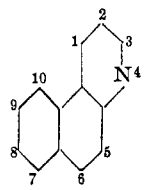
(19) E. Fischer, *Ber.*, **27**, 673 (1894).

[CONTRIBUTION FROM THE AVERY LABORATORY OF CHEMISTRY OF THE UNIVERSITY OF NEBRASKA]

Nitro and Aminobenzo[f]quinolines and Derivatives

BY W. JACK CLEM[1] AND CLIFF S. HAMILTON

At the beginning of this investigation, which had for its purpose the study of benzo[f]quinolines with substituents in the benzo-ring, the only mononitro derivative recorded was 7-nitrobenzo[f]quinoline, first prepared by Claus and Besseler[2] by the direct nitration of benzo[f]quinoline.



Benzo[f]quinoline

They also reported the corresponding amine and later Armit and Robinson[3] established its structure and thereby that of the nitro compound.

Small amounts (10 g.) of benzo[f]quinoline, prepared by a modification of the method of Knueppel,[4] were nitrated successfully at temperatures of −15° to −10° to give 7-nitrobenzo[f]quinoline, but attempts to carry out the reaction with 50-g. quantities gave mixtures containing large quantities of a dinitrobenzo[f]quinoline from which it was almost impossible to separate pure 7-nitrobenzo[f]quinoline. The dinitrobenzo[f]quinoline was shown to be identical with that obtained by Hepner[5] by reducing to the corresponding diamine and the structure was demonstrated by nitrating 7-nitrobenzo[f]quinoline to give the same compound. This established one nitro group in the 7-position and as Hepner[5] had already shown that the groups are in meta positions with respect to each other and both are in the benzo-ring, the compound must be 7,9-dinitrobenzo[f]quinoline, and the corresponding diamine is 7,9-diaminobenzo[f]quinoline.

(1) Parke, Davis and Company Fellow.

(2) Claus and Besseler, *J. prakt. Chem.*, [2] **57**, 49 (1898).

(3) Armit and Robinson, *J. Chem. Soc.*, **127**, 1604 (1925).

(4) Knueppel, *Ber.*, **29**, 703 (1896).

(5) Hepner, *Sitzber. Akad. Wiss. Wien, Math.-naturw. Klasse. Abt. IIb*, **115**, 847 (1906).