

amount of ionic character found for the Pb-I bond is consistent with the more positive character of iodine. These lower limits for the amounts of ionic character in the bonds are not far from the value 35% calculated by the same method for the amount of ionic character of the bond in the sodium iodide molecule and from the value 44% for the bond in the potassium iodide molecule. It is evident that the metal-halogen bonds in these tetrahedral molecules increase in ionic character with increasing size and electro-positive character of the central metallic atom until they are comparable in character to the bonds in typical salt molecules.

Summary

The dipole moments of triphenyllead or hexa-

phenyldiplumbane, trimethyl and triethyllead chloride, diethyllead dichloride, triethyllead bromide, and triphenyllead chloride, bromide, and iodide have been measured in benzene solution. The zero moment found for triphenyllead is the result of its existence in benzene solution as the symmetrical dimer, hexaphenyldiplumbane. The large moments found for the other molecules are used to calculate lower limits for the values of the lead-halogen bond moments, which, in turn, are used to calculate lower limits for the amounts of ionic character in the bonds. The bonds are thus found to have more than 25 to 34% ionic character, which is comparable to that found in the bonds of typical salt molecules.

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

d-Glucose S-Ethyl O-Methyl Monothioacetal

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A procedure¹ was developed recently in this Laboratory for transforming *d*-galactose diethyl thioacetal (mercaptal) (IV) into monothioacetals (VII) by exchanging one thioethoxy group in the mercaptal with halogen (V) and replacing the halogen with an alkoxy group. We were interested in the extension of this series of reactions to other sugars and especially to *d*-glucose. A monothioacetal of glucose could not be obtained by this procedure since the intermediate 1-chloro-1-thioethoxy derivative (V) neither crystallized nor was obtained as a sirup of sufficient purity to yield a crystalline alcohol reaction product. The 1-chloro-1-thioethoxy derivative of *d*-gluco-*d*-gulo-heptose² (*d*- α -glucoheptose) was obtained in crystalline form in the present work as was also the corresponding 1-bromo derivative of *d*-galactose.

As another method³ developed in this Laboratory led to the synthesis of stable derivatives of the labile hemiacetals of *aldehydo-d*-glucose pentaacetate (I), it was deemed advisable to attempt the synthesis of a glucose ethyl monothioacetal

hexaacetate (III) by an analogous procedure. Since the tendency of *aldehydo-d*-galactose pentaacetate (I) to form stable hemiacetals⁴ had been well demonstrated and since the intermediate 1-chloro-1-thioethoxy derivative (V) and several monothioacetals of galactose had been prepared previously,¹ it appeared advisable to attempt this series of reactions in the galactose structure first for exploratory purposes.

We found that *aldehydo-d*-galactose pentaacetate (I) reacted with ethyl mercaptan to form a stable monothiohemiacetal (II) which differed from its previously reported oxygen analog^{4a} in that it exhibited no mutarotation in chloroform. The *aldehydo-d*-galactose monothiohemiacetal pentaacetate (II) reacted with acetic anhydride, in the presence of dry pyridine and at low temperature, to produce 1-thioethoxy-*aldehydo-d*-galactose hexaacetate (III). This substance also was obtainable as a by-product from the action of acetyl bromide on galactose diethyl mercaptal pentaacetate and this gave an alternative method of preparation which avoided the use of ethyl mercaptan as a solvent. Halogen replacement of the 1-acetate in III was obtained by

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

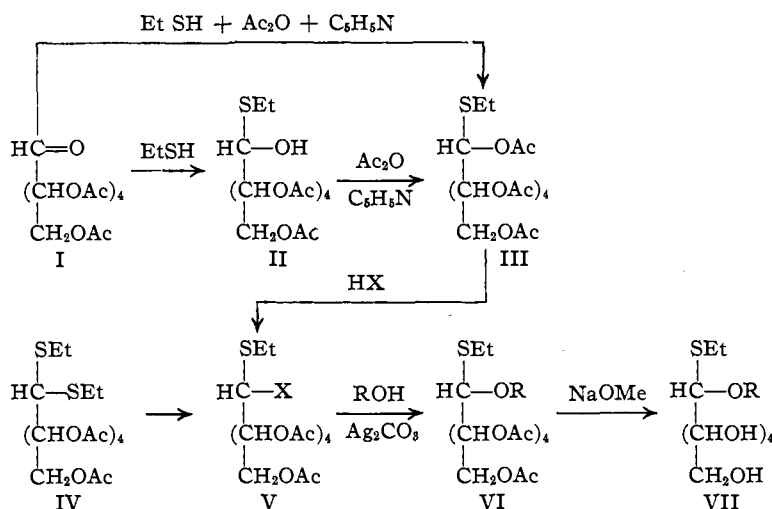
(2) Nomenclature of C. S. Hudson, *ibid.*, **60**, 1537 (1938).

(3) M. L. Wolfrom, M. Konigsberg and F. B. Moody, *ibid.*, **62**, 2343 (1940).

(4) (a) M. L. Wolfrom, *ibid.*, **52**, 2464 (1930); (b) M. L. Wolfrom and W. M. Morgan, *ibid.*, **54**, 3390 (1932).

a procedure previously employed by Montgomery, Hann and Hudson⁵ in the arabinose series. The 1-chloro-1-thioethoxy-*aldehydo-d*-galactose pentaacetate (V) formed was identical with the one previously obtained¹ by the direct reaction of a mixture of acetyl and phosphoryl chlorides upon *d*-galactose diethyl mercaptal pentaacetate. No evidence was obtained for the presence of more than one form of these derivatives in any of our reactions herein reported for galactose, although such a result is a possibility on stereochemical grounds.

Application to the glucose structure of the above series of reactions established for the galactose monothiohemiacetal (II) led to the successful synthesis of a monothioacetal of *d*-glucose, although neither the glucose monothiohemiacetal pentaacetate (II) nor the 1-chloro derivative (V) was isolated. Since a new asymmetric carbon atom was created in transforming *aldehydo-d*-glucose pentaacetate (I) into 1-thioethoxy-hexaacetate (III), two forms of the latter were possible. Both forms were obtained crystalline: one in sufficient quantity to permit the synthesis of the compound VI, which on deacetylation yielded the desired *d*-glucose S-ethyl O-methyl monothioacetal (VII) in beautifully crystalline condition.



Work is in progress in this Laboratory on the extension of these reactions to other sugar structures and on the study of the behavior of the monothioacetals under ring closure conditions.

(5) Edna M. Montgomery, R. M. Hann and C. S. Hudson, *THIS JOURNAL*, **59**, 1124 (1937).

Experimental

1-Bromo-1-thioethoxy-*aldehydo-d*-galactose Pentaacetate (V).—*d*-Galactose diethyl mercaptal pentaacetate^{4a} (32 g.) was dissolved in 20 cc. of acetyl bromide and the solution heated rapidly to boiling. Heating under reflux was continued until a pink coloration developed (five minutes). The flask was then stoppered, quickly immersed in an ice-bath and the whole placed in an icebox. Crystallization in rosetts of small needles began in a few hours and after standing overnight at icebox temperature the crystals were removed by filtration and washed thoroughly by shaking with petroleum ether. This crude material was recrystallized rapidly from dry benzene by the addition of petroleum ether; yield 12–15 g., m. p. 95–100°. The material at this stage of purity still decomposed rapidly and evolved ethyl mercaptan. After four more recrystallizations from five parts of dry benzene by the addition of two parts of petroleum ether, pure material was obtained; yield 6 g., m. p. 101°, spec. rot. (extrapolated) -13.4° (23° , c 3, abs. CHCl_3).⁶ Due to the instability of the compound, the constants recorded are probably not the maximum.

In absolute chloroform the rotation changed rapidly in the *dextro* direction. In one experiment the specific rotation was $+6^\circ$ after two hours. The solution darkened rapidly and an odor of ethyl mercaptan was distinctly noticeable.

The substance was readily soluble in the common organic solvents but was practically insoluble in petroleum ether and water. It reduced Fehling solution and evolved ethyl mercaptan on boiling with dilute alkali or acid. The substance was less stable than the analogous chloro derivative previously reported¹ but could be kept in a vacuum desiccator over soda lime for a considerable period of time. An investigation of the mother liquors yielded no other definite substance. The reaction of the bromo compound with absolute ethanol and silver carbonate yielded the previously reported galactose diethyl mercaptal pentaacetate¹ (identification by m. p. and mixed m. p.).

Anal. Calcd. for $\text{C}_8\text{H}_{12}\text{O}_5(\text{CH}_3\text{CO})_5\text{SBr}$: Br, 15.51; saponification value (six equivalents), 11.6 cc. 0.1 N NaOH per 100 mg. Found: Br, 14.75; saponification value, 11.7 cc.

1-Thioethoxy-*aldehydo-d*-galactose hexaacetate also was formed in this reaction and its isolation from this source is described below.

***aldehydo-d*-Galactose Ethyl Monothiohemiacetal Pentaacetate (II).**—*aldehydo-d*-Galactose pentaacetate^{4a} (I, 10 g.) was dissolved in 200 cc. of ethyl mercaptan at its boiling point. Crystallization (prisms) began immediately and, after cooling in an ice-bath, the crystals were removed by filtration and washed with ethyl mercaptan; yield 9 g., m. p. 137–139°.

(6) All specific rotations are recorded to the D-line of sodium light; 23° is the temperature; c is the concentration in g. per 100 cc.; absolute (abs.) CHCl_3 refers to the alcohol-free solvent.

spec. rot. -1.5° (24° , c 5, abs. CHCl_3). Recrystallization from ethyl mercaptan did not alter these constants. In absolute chloroform the rotation remained constant over a period of twenty-four hours.

The substance was very soluble in chloroform and acetone, slightly so in cold ether and insoluble in cold water and petroleum ether. It reduced Fehling solution with evolution of ethyl mercaptan. After repeated recrystallization from absolute ethanol it became sulfur free, exchanging the ethyl mercaptan for ethyl alcohol.

Anal. Calcd. for $\text{C}_8\text{H}_{13}\text{O}_6(\text{COCH}_3)_5\text{S}$: S, 7.08. Found: S, 6.6.

1-Thioethoxy-aldehyde-d-galactose Hexaacetate (III).—II (2.5 g.) was dissolved in 25 cc. of dry pyridine previously cooled to 0° . To this solution was added 50 cc. of acetic anhydride cooled to the same temperature. The whole was kept in an ice-bath for one hour, at icebox temperature for twelve hours and finally at room temperature for twelve hours. Crystallization occurred when the solution was poured into 250 cc. of ice and water; yield 2.4 g., m. p. $86-90^{\circ}$, spec. rot. $+31.2^{\circ}$ (abs. CHCl_3). Extraction of the mother liquors with chloroform yielded a negligible amount of sirup which was not amenable to crystallization. Pure material was obtained on recrystallization from five parts of hot methanol; m. p. $94-95.5^{\circ}$, spec. rot. $+38^{\circ}$ (22° , c 2.9, abs. CHCl_3).

The substance crystallized in beautiful diamond-shaped plates and was readily soluble in chloroform, acetone and warm methanol but was practically insoluble in water and petroleum ether. It reduced Fehling solution readily upon the addition of a small amount of alcohol and evolved ethyl mercaptan upon boiling with dilute hydrochloric acid.

Anal. Calcd. for $\text{C}_8\text{H}_{12}\text{O}_6(\text{COCH}_3)_5\text{S}$: C, 48.57; H, 6.12; S, 6.48; CH_3CO , 12.13 cc. 0.1 *N* NaOH per 100 mg. Found: C, 48.42; H, 6.05; S, 6.41; CH_3CO , 12.11 cc.

This substance also was obtained as a by-product from the action of acetyl bromide on galactose diethyl mercaptal pentaacetate and this gave an alternative method for its preparation which avoided the use of ethyl mercaptan as a solvent. The once-recrystallized (benzene-petroleum ether) reaction product obtained by the action of acetyl bromide on galactose diethyl mercaptal pentaacetate (32 g.), as described above for the synthesis of 1-bromo-1-thioethoxy-aldehyde-d-galactose pentaacetate, was suspended in dry benzene and dry diethylamine (15 cc.) added. The mixture was heated on a water-bath in a glass-stoppered flask at 50° until solution began, whereupon the mixture was removed from the source of heat and cooled until the vigorous reaction subsided. The dark-colored reaction mixture stood at room temperature for twenty-four hours. The precipitated diethylamine hydrobromide was removed by filtration and washed with ether. The filtrate was washed with dilute sulfuric acid (5%) and with water. Solvent removal from the dried (decolorizing charcoal) solution left a yellow sirup which was crystallized from methanol; yield 8.5-10 g., m. p. $92-94^{\circ}$, spec. rot. $+37.9^{\circ}$ (abs. CHCl_3). Pure material was obtained on two recrystallizations from methanol (5 parts); yield 8 g., m. p. $94-95.5^{\circ}$ (mixed m. p. with product described above, unchanged), spec. rot. $+38.4^{\circ}$ in abs. CHCl_3 .

Conversion of 1-Thioethoxy-aldehyde-d-galactose Hexaacetate (III) into 1-Chloro-1-thioethoxy-aldehyde-d-galac-

tose Pentaacetate.—1-Thioethoxy-aldehyde-d-galactose hexaacetate (2.3 g.) was dissolved by vigorous shaking in 40 cc. of dry ether which contained approximately 8% by weight of dry hydrogen chloride. The solution was kept at room temperature for fifteen minutes and was then placed in an icebox for twenty-four hours. The crystalline material was removed by filtration and washed well with a mixture of ether and petroleum ether (1:1); yield 1 g., m. p. $95-98^{\circ}$. Pure material was obtained on recrystallization from 8 parts of a mixture of benzene and petroleum ether (1:1); yield 0.75 g., m. p. $111-113^{\circ}$ (mixed m. p. with an authentic sample of 1-chloro-1-thioethoxy-aldehyde-d-galactose pentaacetate¹ unchanged).

1-Chloro-1-thioethoxy-aldehyde-d-gluco-d-guloheptose² Hexaacetate.—*d*-Gluco-*d*-guloheptose (*d*- α -glucoheptose) diethyl mercaptal hexaacetate³ (5 g.) was dissolved by refluxing with 3 cc. of acetyl chloride (to which one drop of water per 10 cc. had been added), 2 cc. of phosphorus oxychloride was added and the solution refluxed for four minutes, in which time the solution became brown in color. Crystallization ensued on standing at 0° for two days. The crystalline material was removed by filtration and washed with cold anhydrous ether-petroleum ether (1:1); yield 3.2 g., m. p. $115-120^{\circ}$. Pure material was obtained on one recrystallization effected from five parts of absolute chloroform by the addition of ten parts of anhydrous ether-petroleum ether (1:1); m. p. $138-139^{\circ}$; spec. rot. (extrapolated) $+36.7^{\circ}$ (25° , c 4, abs. CHCl_3). The rotation in chloroform changed slowly in the *levo* direction (spec. rot. -7° after twenty hours) and an odor of ethyl mercaptan was evolved. The substance was soluble in the common organic solvents except petroleum ether and reduced hot Fehling solution.

Anal. Calcd. for $\text{C}_9\text{H}_{15}\text{O}_6(\text{CH}_3\text{CO})_5\text{SCl}$: Cl, 6.53; S, 5.90; CH_3CO (seven equivalents), 12.9 cc. 0.1 *N* NaOH per 100 mg. Found: Cl, 6.69; S, 6.00; CH_3CO , 12.9 cc.

α -1-Thioethoxy-aldehyde-d-glucose Hexaacetate (III).—*aldehyde-d*-Glucose pentaacetate⁴ (20 g.) was suspended in a mixture of ethyl mercaptan (20 cc.) and dry pyridine (40 cc.). The solution was cooled in a solid carbon dioxide-acetone bath and a mixture of acetic anhydride (150 cc.) and pyridine (40 cc.), cooled to the same temperature, was added. The reaction mixture was kept in the bath for six hours with occasional shaking to complete solution and was then placed in an ice-salt bath for twelve hours, after which the solution was poured into two liters of ice and water. The resultant mixture was extracted with chloroform and the extract washed consecutively with sulfuric acid (5%), water, cold saturated sodium bicarbonate and finally with water. The sirup obtained on solvent removal from the dried (decolorizing charcoal) extract was crystallized from absolute ethanol; yield 13-15 g., m. p. $101-102^{\circ}$. Pure material was obtained on two further crystallizations from absolute ethanol; yield 8-9 g., m. p. $103-104^{\circ}$, spec. rot. $+12.5^{\circ}$ (27° , c 3.24, abs. CHCl_3).

The substance was readily soluble in chloroform, acetone and warm ethanol but was practically insoluble in water and petroleum ether. It reduced hot Fehling solution and evolved ethyl mercaptan on treatment with dilute acid or alkali.

(7) Experimental work by Mr. F. B. Moody.

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

Anal. Calcd. for $C_8H_{12}O_6(CH_3CO)_6S$: S, 6.48; CH_3CO , 12.13 cc. 0.1 *N* NaOH per 100 mg. Found: S, 6.44; CH_3CO , 12.12 cc.

Investigation of the alcoholic mother liquors yielded no other form of the compound but considerable *aldehydo-d*-glucose heptaacetate⁹ (4.3 g., m. p. 116–118°) was found therein.

***β*-1-Thioethoxy-aldehydo-d-glucose Hexaacetate (III).**—*aldehydo-d*-Glucose pentaacetate⁸ (2 g.) was dissolved in ethyl mercaptan (100 cc.). An equal volume of petroleum ether was added and the whole cooled to the temperature of a solid carbon dioxide-acetone bath, whereupon a solid product separated; yield 1.3 g. This material was suspended in a mixture of dry pyridine (5 cc.) and ethyl mercaptan (5 cc.) and the whole cooled in a solid carbon dioxide-acetone bath. Twenty-five cc. of an acetic anhydride-pyridine mixture (2:1) cooled to the same temperature, was added and the reaction mixture kept in the bath for two and one-half hours. The solution then stood at 15° overnight and finally at room temperature for two hours, after which it was poured into ice and water (400 cc.). The mixture was extracted with chloroform and the extract washed successively with sulfuric acid (5%), water, aqueous sodium bicarbonate and finally with water. The semicrystalline mass obtained on solvent removal from the dried extract was crystallized from absolute ethanol; yield 0.4 g. The melting point (103–104°), rotation (+12.6°, abs. $CHCl_3$) and mixed melting point identified it as the above-described α -form.

The mother liquors were concentrated and allowed to crystallize, yielding beautiful rod-shaped crystals; yield 0.2 g., m. p. 85–87°. Pure material was obtained on two further crystallizations from absolute ethanol; yield 0.15 g., m. p. 85–87°, spec. rot. -1.8° (23°, *c* 2.85, abs. $CHCl_3$).

The compound possessed solubilities similar to those of the α -form.

Anal. Calcd. for $C_8H_{12}O_6(CH_3CO)_6S$: C, 48.57; H, 6.12; S, 6.48; CH_3CO , 12.13 cc. 0.1 *N* NaOH per 100 mg. Found: C, 48.41; H, 5.93; S, 6.46; CH_3CO , 12.25 cc.

***d*-Glucose S-Ethyl O-Methyl Monothioacetal Pentaacetate (VI).**—A chloroform (20 cc.) solution of α -1-thioethoxy-*aldehydo-d*-glucose hexaacetate (2 g.) was cooled to 0° and aluminum chloride (2 g.) added with gentle agitation. A light granular addition product separated. The solution was kept at 5° for thirty minutes, washed with cold water and dried immediately over Drierite (anhydrous calcium sulfate). The dried chloroform solution, diluted with an equal volume of dry methanol, was added dropwise with vigorous mechanical stirring over a period of thirty minutes to a mixture of silver carbonate (5 g.), freshly dried, powdered Drierite (20 g.) and dry methanol (25 cc.) in a three-necked flask, equipped with a mercury sealed mechanical stirrer and a drying tube. The mixture was stirred for eighteen hours at room temperature. The inorganic salts were then removed by filtration through a bed of Super-Cel (Johns-Manville) and the clear, colorless filtrate was concentrated under reduced pressure to a sirup. The colorless sirup was dissolved in a minimum of methanol and made just opalescent with water. The product crystallized on standing at ice-

box temperature; yield 0.65 g., m. p. 64–66°. Pure material was obtained after four recrystallizations from the methanol-water mixture; yield 0.56 g., m. p. 69–71°, spec. rot. $+27.1^\circ$ (27°, *c* 4.3, abs. $CHCl_3$).

The substance crystallized in plates and was readily soluble in chloroform, ether, acetone and warm methanol, but was practically insoluble in water and petroleum ether. It showed no reduction toward hot Fehling solution and evolved ethyl mercaptan on heating with dilute hydrochloric acid, the hydrolyzate being reducing.

Anal. Calcd. for $C_9H_{16}O_6(CH_3CO)_5S$: C, 48.91; H, 6.49; S, 6.87; CH_3CO , 10.7 cc. 0.1 *N* NaOH per 100 mg. Found: C, 49.20; H, 6.24; S (micro), 6.47; CH_3CO , 10.6 cc.

***d*-Glucose S-Ethyl O-Methyl Monothioacetal (VII).**—*d*-Glucose S-ethyl O-methyl monothioacetal pentaacetate (VI, 0.3 g.) was dissolved in anhydrous methanol (1 cc.), 0.1 cc. of 0.2 *N* sodium methylate was added and the solution allowed to stand at room temperature for fifteen minutes. Crystallization occurred on cooling to 0°. An equal volume of cold dry ether was added and the crystals were removed by filtration; yield 0.13 g., m. p. 115–118°. Pure material was obtained after two more recrystallizations from absolute methanol by the addition of dry ether; yield 0.10 g., m. p. 116–18°, spec. rot. $+47.8^\circ$ (23°, *c* 2.5, H_2O).

The substance crystallized in beautiful needles. It showed no reduction toward hot Fehling solution but on acid hydrolysis ethyl mercaptan was liberated and the hydrolyzate was reducing. The material was soluble in water, warm methanol and was practically insoluble in ether, acetone and chloroform.

Anal. Calcd. for $C_9H_{20}O_6S$: C, 42.13; H, 7.87; S, 12.51. Found: C, 42.40; H, 7.85; S (micro), 12.03.

We are indebted to Mr. John Walker (W. P. A. Project 18695) for assistance rendered in the analytical determinations. We also acknowledge the assistance of Mr. Irving Auerbach (N. Y. A. Project O. S. U. 170) and of Mr. Walter Anderson.

Summary

1. 1 - Bromo - 1 - thioethoxy - *aldehydo* - *d*-galactose pentaacetate (V) was synthesized by the action of acetyl bromide upon *d*-galactose diethyl mercaptal pentaacetate (IV). V on reaction with ethanol and silver carbonate yielded the previously reported form of *d*-galactose diethyl monothioacetal pentaacetate (VI).

2. 1 - Chloro - 1 - thioethoxy - *aldehydo* - *d*-gluco-*d*-gulo-heptose hexaacetate was synthesized by the action of acetyl chloride and phosphorus oxychloride upon *d*-gluco-*d*-gulo-heptose diethyl mercaptal hexaacetate.

3. *aldehydo-d*-Galactose ethyl monothioacetal pentaacetate (II) was synthesized. II on acetylation yielded 1-thioethoxy-*aldehydo-d*-galactose hexaacetate (III), which was converted into the previously reported form of 1-chloro-1-thio-

(9) M. L. Wolfrom, *THIS JOURNAL*, 87, 2498 (1938).

