to the curve for pure water. In the absence of data a determination of the vapor pressure of the saturated solution at any one temperature will enable the entire curve to be drawn with a good degree of approximation.

It may be remarked that equations (5) and (6) apply equally well to the case of non-aqueous solutions, with the same assumptions, when the corresponding heat quantities are used. We may again predict a fairly close parallelism between the log P–$1/T$ curves for pure solvent and saturated solution. For a given value of ΔH_s, we would expect the deviation in slope for a non-aqueous solution to be much greater than for an aqueous solution. The heat of vaporization of water is abnormally high, and the solubility of electrolytes (or other solutes) expressed in terms of mole fractions are lower in water than in most other liquids. Consequently, for non-aqueous solutions, $\Delta H_s/N_1$ would be larger, and at the same time ΔH smaller, than for water. On the other hand, it must be pointed out that deviations of solutions from ideality are as a rule much less in other liquids than in water, particularly in the case of organic liquids, where many approximately ideal solutions are known. Therefore, for a great many solutions of organic substances, ΔH_s will be very small or zero, and for them the slopes of the vapor pressure curves will be sensibly parallel.

Finally, the assumptions under which equation (1) was derived make it possible to apply it to the case where a liquid is the saturating phase, provided only that its composition does not change with temperature. Owing to the phenomenon of mutual solubility, this will not ordinarily be true. Nevertheless, if the change in composition is not great, we may expect an approximate parallelism between the log P–$1/T$ curves if the "solute" is non-volatile; and between the log p_1–$1/T$ curves for the instance of an appreciably volatile solute.

Summary

1. An explanation is offered for the parallelism of the log P–$1/T$ curves for some saturated aqueous solutions and pure water.

2. An equation is developed from which it is predicted that this phenomenon will be true in general for saturated solutions, both aqueous and non-aqueous.

3. It is suggested that in the absence of data, a knowledge of the vapor pressure of a saturated solution at one temperature will make it possible to obtain the entire curve to a good degree of approximation.

BLUFFTON, OHIO RECEIVED AUGUST 31, 1936

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF MERCK & CO., INC.]

The Acetyl Derivatives of Gluconic and Xylonic Acids

BY RANDOLPH T. MAJOR AND ELMER W. COOK

The only record in the literature of an acetylated sugar acid is that described by Upson and Bartz. These investigators prepared 2,3,4,6-tetraacetyl-*d*-gluconic acid monohydrate by the acetylation of δ-*d*-gluconolactone.[1] This reaction has been repeated in this Laboratory. Tetraacetyl-*d*-gluconic acid monohydrate with practically the same melting point reported by the previous workers was obtained but the optical activity found was different. Since the previous investigators did not report the solvent used for the measurement of the optical activity it seems probable that a different solvent was used in this Laboratory than the one used by Upson and Bartz. Tetraacetyl-*d*-gluconic acid monohydrate was also prepared by the oxidation of tetraacetyl-*d*-glucose.

Pentaacetyl-*d*-gluconic acid has been prepared by two different processes. The first was by the oxidation of aldehydo-*d*-glucose pentaacetate.[2] In the course of attempts to improve the methods of obtaining aldehydo-*d*-glucose pentaacetate, it was found that *d*-glucose tetraacetate gave the ring form of tetraacetyl-*d*-glucose semicarbazone with semicarbazide. This had been prepared previously by Wolfrom, Georges and Soltzberg by acetylation of *d*-glucose semicarbazone.[2b]

The second method of preparing pentaacetyl-*d*-gluconic acid was by further acetylation of

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[1] Upson and Bartz, THIS JOURNAL, **53**, 4226 (1931).

[2] (a) Wolfrom, *ibid.*, **51**, 2190 (1929); (b) Wolfrom, Georges and Soltzberg, *ibid.*, **56**, 1795 (1934).

tetraacetyl-*d*-gluconic acid. All attempts to acetylate *d*-gluconic acid directly by means of acetic anhydride with either zinc chloride or pyridine gave a gummy mixture.

Ethyl pentaacetyl-*d*-gluconate was prepared by esterification of the corresponding acid. This ester had been prepared previously by Volpert by acetylation of ethyl *d*-gluconate.[3] Pentaacetyl-*d*-gluconic phenylhydrazide was synthesized by acetylating gluconic phenylhydrazide.

The tetraacetylxylonic acids have been synthesized by the oxidation of the corresponding aldehydoxylose tetraacetates. Aldehydo-*d*-xylose tetraacetate was prepared first by Wolfrom, Newlin and Stahly.[4] A more satisfactory method of obtaining this compound, as well as its levo and racemic isomers, was found to be by acetylation of xylose triacetate semicarbazone followed by treatment with nitrous acid[2b] (p. 1794). In the acetylation of xylose semicarbazone the principal product obtained was a xylose semicarbazone tetraacetate with a ring structure.

Experimental

2,3,4,6-Tetraacetylgluconic Acid Monohydrate

Acetylation of δ-Gluconolactone.—Fused zinc chloride (20 g.) was dissolved in 250 cc. of acetic anhydride and the solution cooled to 0°. δ-Gluconolactone (50 g.) was added with stirring and the mixture kept at 0° for thirty minutes. Thereafter the mixture was allowed to come to room temperature. With occasional shaking all of the lactone soon dissolved. After standing for twenty-four hours the solution was poured into 1000 cc. of ice water. The mixture was stirred for one and one-half hours when tetraacetylgluconic acid monohydrate separated; yield 80%; m. p. 114–115°.[5]

Oxidation of Tetraacetylglucose.—Tetraacetylglucose[6] (5 g.) was dissolved in 125 cc. of hot water in a flask and the solution quickly cooled to room temperature. Potassium bicarbonate (4.4 g.) was added and allowed to dissolve; this was followed by the addition of 1.5 g. of bromine. The flask was stoppered and shaken, the stopper being removed occasionally to relieve the pressure from the carbon dioxide. As soon as the bromine had reacted, additional bromine (0.9 g.) was introduced to complete the reaction. The oxidation was complete in about forty minutes. The solution was cooled to 0° and 23 cc. of 1.93 normal hydrochloric acid was added. Upon standing tetraacetylgluconic acid monohydrate separated; yield 0.7 g. An additional quantity was recovered from the mother liquors by extraction with chloroform; m. p. 114–115°; $[\alpha]^{20}_{\mathrm{D}}$ −5° (alcohol; *c*, 2).

Anal. Calcd. for $C_{14}H_{22}O_{12}$: C, 43.96; H, 5.80. Found; C, 44.10; H, 5.97.

Pentaacetylgluconic Acid

***d*-Glucose Semicarbazone Tetraacetate.**—Glucose tetraacetate (0.5 g.) was dissolved in 5 cc. of warm water and the solution cooled quickly to room temperature. Semicarbazide hydrochloride (0.16 g. or 1 mol) and potassium acetate (0.22 g. or 1.6 mol) were added and the mixture shaken until dissolved. Soon glucose semicarbazone tetraacetate separated as an oil which on standing for two to three days crystallized. The product was recrystallized from water. Thus crystallized the hydrated compound sintered at 118–120° and melted around 163°. When dried at 110° the melting point became 171°; $[\alpha]^{20}_{\mathrm{D}}$ −53° (alcohol; *c*, 2); $[\alpha]^{20}_{\mathrm{D}}$ −6.5° (alcohol-free chloroform, *c*, 2).[7]

Anal. Calcd. for $C_{15}H_{23}O_{10}N_3$: C, 44.45; H, 5.72; N, 10.37. Found: C, 44.63; H, 5.98; N, 10.30.

Oxidation of Pentaacetylaldehydoglucose.—Pentaacetylaldehydo-*d*-glucose was oxidized with bromine by the same method previously described for the oxidation of tetraacetyl-*d*-glucose. The pentaacetylgluconic acid monohydrate obtained was recrystallized from water; m. p. 72–73°; $[\alpha]^{20}_{\mathrm{D}}$ +7.5° (alcohol-free chloroform; *c*, 2); yield 64%.

Anal. Calcd. for $C_{16}H_{24}O_{13}$: C, 45.26; H, 5.69. Found: C, 45.42; H, 5.80. An acetyl determination showed five acetyl groups.

Acetylation of Tetraacetylgluconic Acid.—Tetraacetyl-*d*-gluconic acid monohydrate (50 g.) was dissolved in 188 cc. of acetic anhydride (ice-bath) containing 18 g. of zinc chloride in solution. After standing in the ice-bath for thirty minutes the solution was allowed to come to room temperature and remain at this temperature for twenty-four hours. The solution was then poured into 1000 cc. of ice water and thoroughly stirred. Pentaacetylgluconic acid crystallized after about one hour and an additional amount was recovered from the mother liquor by extraction with chloroform. The crude product thus obtained from the acetylation melted at 93–95° but on standing the melting point changed, finally becoming as low as 55°. By recrystallizing from water the monohydrate of melting point 72–73° was obtained. A mixed melting point with a specimen obtained as described in the preceding paragraph showed no depression; yield 90%.

Anhydrous Pentaacetylgluconic Acid.—Pentaacetylgluconic acid monohydrate (50 g.) recrystallized from absolute alcohol was dissolved in 500 cc. of hot toluene. About 100 cc. of the toluene was distilled on an oil-bath. Upon cooling anhydrous pentaacetylgluconic acid separated. The product was filtered and washed successively with toluene and petroleum ether; m. p. 110–111°; $[\alpha]^{20}_{\mathrm{D}}$ +11.5° (alcohol-free chloroform; *c*, 2). Upon standing in the air for several days the anhydrous acid did not take up water of crystallization as its melting point remained unchanged.

Anal. Calcd. for $C_{16}H_{22}O_{12}$: C, 47.27; H, 5.46. Found: C, 47.30; H, 5.53.

Ethyl Pentaacetylgluconate.—Pentaacetyl-*d*-gluconic acid (10 g.) was dissolved in 30 cc. of absolute alcohol con-

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[3] Volpert, *Ber.*, **19**, 2622 (1886).

[4] Wolfrom, Newlin and Stahly, THIS JOURNAL, **53**, 4382 (1931).

[5] Upson and Bartz[1] give 114–117° as the melting point of tetraacetylgluconic acid monohydrate.

[6] Fischer, *Ber.*, **45**, 914 (1912).

[7] Wolfrom, Georges and Soltzberg[2b] give 171–172° as the melting point and $[\alpha]^{25}_{\mathrm{D}}$ −9° (chloroform, *c*, 3.8) as the optical rotation of *d*-glucose semicarbazone tetraacetate.

taining 2% hydrogen chloride and the solution warmed at 60° for four minutes. Upon cooling and stirring a solid crystallized. It was filtered and washed with a little alcohol; m. p. 103–104°; $[\alpha]^{20}\text{D}$ +20.5° (alcohol-free chloroform, *c*, 2).[8] Ethyl pentaacetylgluconate was also prepared by acetylating ethyl gluconate in the usual manner with either pyridine or fused zinc chloride. For analysis a sample fused and dried at 120° was allowed to cool and solidify *in vacuo* over sulfuric acid.

Anal. Calcd. for $C_{12}H_{26}O_{12}$: C, 49.75; H, 6.04. Found: C, 49.84; H, 6.19.

Pentaacetylgluconicphenylhydrazide.—Gluconicphenylhydrazide (10 g.) was added to 50 cc. of acetic anhydride containing 4 g. of zinc chloride (fused) in solution. The mixture was kept cold during the first thirty minutes and then was allowed to stand for twenty-four hours at room temperature. A gum formed when the acetylation mixture was poured into ice water. The mixture was extracted with chloroform and the chloroform extract washed with sodium bicarbonate in ice water and finally with water. The extract was evaporated *in vacuo*, when the gummy residue slowly started to crystallize. It was recrystallized from alcohol by the addition of ether accompanied by cooling; yield of pentaacetylgluconic phenylhydrazide, 90%; m. p. 152–154°; $[\alpha]^{20}\text{D}$ +28° (alcohol, *c*, 2).

Anal. Calcd. for $C_{22}H_{28}O_{11}N_2$: C, 53.20; H, 5.69; N, 5.64. Found: C, 53.14; H, 5.65; N, 5.65.

***d*-Xylose Semicarbazone Tetraacetate.**—Finely powdered *d*-xylose semicarbazone (26 g.) was stirred into 180 cc. of pyridine and 120 cc. of acetic anhydride at 60–70° for six hours. At the end of this time practically all the xylose semicarbazone had dissolved. After the solution had stood at room temperature for one to two days 10 g. of crystalline material separated. The acetylation mixture was poured into ice water and after standing for one hour was extracted with chloroform. The extract was washed successively with cold dilute sulfuric acid, sodium bicarbonate and ice water. After it had been dried over calcium chloride the extract was evaporated *in vacuo* and the residue crystallized from absolute alcohol. The product (3 g.) was the same as that separated from the acetylation mixture. It was recrystallized from absolute alcohol; m. p. 232–233°; $[\alpha]^{20}\text{D}$ +21° (methanol, *c*, 1). Treatment in aqueous solution with nitrous acid did not produce aldehydo-*d*-xylose tetraacetate.

Anal. Calcd. for $C_{14}H_{21}O_9N_3$: C, 44.78; H, 5.64; N, 11.20. Found: C, 45.03; H, 5.70; N, 11.37.

However, the mother liquors from the tetraacetate, m. p. 232–233°, gave a sirup which on treatment with dilute nitrous acid yielded aldehydo-*d*-xylose tetraacetate.

Aldehydo-*l*-xylose Tetraacetate.—*l*-Xylose triacetate (51 g.)[9] was added to a warm alcoholic solution containing a 10% excess of semicarbazide. After warming for fifteen to twenty minutes the solution was evaporated *in vacuo* to a gum. The gum was dissolved in 86 cc. of pyridine and treated with 57 cc. of acetic anhydride accompanied by cooling. After the solution had stood for twenty-four hours at room temperature it was poured into ice water. The mixture was allowed to stand for an hour and then extracted with chloroform. The extract was washed successively with cold dilute sulfuric acid, sodium bicarbonate and water. After it had been dried over calcium chloride the extract was evaporated *in vacuo* to a gum. The gum was refluxed for twenty minutes, in a solution of 6.5 g. of oxalic acid in 250 cc. of methanol. The gum which was obtained by evaporation *in vacuo* was dissolved in 800 cc. of water; 75 g. of sodium nitrite in 200 cc. of water was added. Accompanied by slow stirring and cooling to 15–20°, 180 cc. of 6 normal hydrochloric acid was added gradually. This was followed by portionwise addition of 60 g. of sodium nitrite and gradual addition of 120 cc. of 6 normal hydrochloric acid. Again 60 g. of sodium nitrite was added and 120 cc. of 6 normal hydrochloric acid. Finally 60 g. of sodium nitrite was added and the solution stirred vigorously with norite. The mixture was filtered and the filtrate extracted with chloroform. After the extract had been dried over calcium chloride it was evaporated *in vacuo*. Aldehydo-*l*-xylose tetraacetate soon crystallized out of the resulting gum and with the addition of dry ether was filtered. It was recrystallized from dry ether; yield 33%; m. p. 90–91°; $[\alpha]^{20}\text{D}$ +22.5° (alcohol-free chloroform, *c*, 2).[10] Aldehydo-*d*,*l*-xylose tetraacetate made by mixing equal quantities of the *d* and *l* forms melted at 85–86°.

Anal. Calcd. for $C_{18}H_{18}O_9$: C, 49.03; H, 5.70. Found: C, 49.09; H, 5.53.

Tetraacetylxylonic Acid.—Aldehydoxylose tetraacetate (18.7 g.) was dissolved in 400 cc. of warm water at 50° in a flask and the solution quickly cooled to room temperature. Bromine (10.5 g.) was added followed by 9.5 g. of calcium carbonate. The mixture was stirred occasionally and after two hours the oxidation was nearly complete. The mixture was extracted with chloroform to remove any unreacted aldehydoxylose tetraacetate. It was then made acid with 104 cc. of 1.9 normal hydrochloric acid and extracted with chloroform. The extract was dried over calcium chloride and evaporated *in vacuo* to a gum. Petroleum ether was added and upon stirring tetraacetylxylonic acid crystallized. It was recrystallized from benzene; yield 90%.

Tetraacetyl-*d*-xylonic acid melted at 86–88°; $[\alpha]^{20}\text{D}$ +5° (alcohol, *c*, 2); $[\alpha]^{20}\text{D}$ −2° (alcohol-free chloroform, *c*, 2).

Anal. Calcd. for $C_{13}H_{18}O_{10}$: C, 46.69; H, 5.43. Found: C, 46.46; H, 5.52.

Tetraacetyl-*l*-xylonic acid melted at 86–88°; $[\alpha]^{20}\text{D}$ −4.5° (alcohol, *c*, 2).

Tetraacetyl-*d*,*l*-xylonic acid melted at 134–135°; $[\alpha]^{20}\text{D}$ 0° (alcohol, *c*, 2).

Anal. Calcd. for $C_{13}H_{18}O_{10}$: C, 46.69; H, 5.43. Found: C, 46.77; H, 5.39.

A mixture of equal quantities of tetraacetyl-*d*-xylonic acid and tetraacetyl-*l*-xylonic acid crystallized out of toluene also melted at 134–135°.

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(8) Volpert[3] gave 103.5° as the melting point of ethyl pentaacetylgluconate.

(9) Prepared by the method described by Hudson and Dale, THIS JOURNAL, **40**, 999 (1918), for the preparation of *d*-xylose triacetate.

(10) Wolfrom, Newlin and Stahly[4] give 87–89° as the melting point and $[\alpha]^{26}\text{D}$ −15.9° in chloroform as the optical rotation of aldehydo-*d*-xylose tetraacetate.

Summary

1. Tetraacetyl-*d*-gluconic acid has been prepared by the oxidation of tetraacetyl-*d*-glucose with bromine.
2. Pentaacetyl-*d*-gluconic acid was obtained by the oxidation of aldehydo-*d*-glucose pentaacetate and by acetylation of tetraacetyl-*d*-gluconic acid.
3. Ethyl pentaacetyl-*d*-gluconate and pentaacetyl-*d*-gluconic phenylhydrazide were prepared.
4. The ring form of *d*-xylose semicarbazone tetraacetate was isolated.
5. Aldehydoxylose tetraacetates have been prepared by the treatment of the corresponding semicarbazones with nitrous acid.
6. Tetraacetylxylonic acids have been obtained by the oxidation of aldehydoxylose tetraacetates.

RAHWAY, N. J. RECEIVED SEPTEMBER 17, 1936

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF MERCK & CO., INC.]

Preparation and Properties of Pentaacetyl-2-keto-*d*-glucoheptonic Acid

BY RANDOLPH T. MAJOR AND ELMER W. COOK

The 2-keto-sugar acids have acquired in recent years considerable interest due to the fact that the enol forms of these acids have been shown to be vitamin C and its homologs.[1]

A new method of preparing the acetyl derivatives of these acids has become possible since the recent synthesis of the fully acetylated sugar acids.[2]

The acetyl sugar acid was converted into its acid chloride with phosphorus pentachloride; it is noteworthy that thionyl chloride was not a satisfactory agent for the purpose. The chloride was converted into the corresponding cyanide by means of silver cyanide. This was hydrolyzed in turn to the corresponding acid. This acid could be esterified readily.

The series of reactions described above has been carried through to completion starting with pentaacetyl-*d*-gluconic acid and through, except for the last step, with tetraacetyl-*d*,*l*-xylonic acid.

Attempts are being made to hydrolyze the acetyl groups and enolize the keto group of pentaacetyl-2-ketoglucoheptonic acid and its ester to give a homolog of vitamin C.

Experimental

Acetylated Sugar Acid Chloride.—The dry fully acetylated sugar acid was added with cooling to a suspension of one molecular equivalent of phosphorus pentachloride in ten times its weight of dry ether. The reaction was soon complete as shown by disappearance of the phosphorus pentachloride.

Pentaacetyl-*d*-gluconyl Chloride.—After the solution had stood at room temperature for two or three hours the ether was evaporated *in vacuo*. Dry xylene was then added. This and the phosphorus oxychloride formed in the reaction were removed by evaporation at 45 to 50° *in vacuo*. The addition of xylene followed by evaporation *in vacuo* was repeated twice. The residual gum was dissolved in dry ether. Upon evaporation in a slight vacuum beautiful white crystals separated; m. p. 68–70°; yield, 88%; $[\alpha]^{20}_{D}$ +2° (alcohol-free chloroform, *c*, 2).

Anal. Calcd. for $C_{16}H_{21}O_{11}Cl$: C, 45.22; H, 4.99; Cl, 8.35. Found: C, 45.60; H, 4.90; Cl, 8.27.

With water the acid chloride gave pentaacetyl-*d*-gluconic acid monohydrate, m. p. 72–73°.[2]

Tetraacetyl-*d*,*l*-xylonyl Chloride.—White crystals appeared soon after solution of the phosphorus pentachloride. The precipitate was recrystallized from dry ether; m. p. 90–92°; yield, 71%; $[\alpha]^{20}_{D}$ 0° (alcohol-free chloroform, *c*, 2).

Anal. Calcd. for $C_{13}H_{17}O_{9}Cl$: C, 44.26; H, 4.86; Cl, 10.08. Found: C, 44.25, 44.33; H, 4.80, 5.03; Cl, 10.18, 10.32.

Ethyl Ester of Acetylated Sugar Acids.—When a solution of an acetylated sugar acid chloride in absolute alcohol was evaporated *in vacuo* a crystalline residue was left which was washed with cold water and recrystallized from absolute alcohol.

Ethyl pentaacetyl-*d*-gluconate melted at 103–104°.[3]

Ethyl tetraacetyl-*d*,*l*-xylonate melted at 70–72°; $[\alpha]^{20}_{D}$ 0° (alcohol, *c*, 0.06).

Anal. Calcd. for $C_{15}H_{22}O_{10}$: C, 49.70; H, 6.12. Found: C, 49.53; H, 6.13.

Pentaacetyl-*d*-gluconamide.—Dry ammonia was bubbled through a solution of pentaacetyl-*d*-gluconic acid chloride in dry ether. The white precipitate which formed was washed with water to remove ammonium chloride. The pentaacetyl-*d*-gluconamide which remained melted at 183–184°.[4]

Tetraacetyl-*d*,*l*-xylonamide.—This compound was prepared in the same way as pentaacetyl-*d*-gluconamide except that it did not precipitate from the ether with the

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[1] Hirst, *Chemistry and Industry*, 221 (1933); Haworth, *ibid.*, 482 (1933).

[2] Major and Cook, THIS JOURNAL, **58**, 2474 (1936).

[3] Volpert, *Ber.*, **19**, 2622 (1886), gives 103.5° as the melting point of ethyl pentaacetyl-*d*-gluconate.

[4] Zemplén and Kiss, *Ber.*, **60**, 170 (1927), give 183.5–184° as the melting point of pentaacetyl-*d*-gluconamide.