combined (49 mg.) and recrystallized several times from methanol. The pure compound, tentatively assigned structure VIII, formed rosets of elongated platelets melting at 218–219° (dec.); $[\alpha]^{21}\text{D}$ +143.5° (2.67°, 18.6 mg. in 2 cc., 2 dm.). The absorption curve showed a well-defined single maximum at 254 mμ, ε 10,400 (in ethanol).

Anal. Calcd. for $C_{29}H_{44}O_5$: C, 73.68; H, 9.38. Found: C, 73.50; H, 9.49.

The compound failed to react with 2,4-dinitrophenylhydrazine under the usual conditions.[6]

We are greatly indebted to Dr. N. H. Coy of the Vitamin Laboratory of E. R. Squibb and Sons for the spectrographic measurements. The microanalyses were carried out by Mr. J. F. Alicino of this Laboratory.

Summary

Mild oxidation of α(Δ^{8-14})-cholestenyl acetate with chromic acid results in the formation of a number of ketonic compounds. Both methylene groups in α-position to the 8,14-double bond are attacked. The double bond itself either remains unchanged, or adds oxygen in form of an epoxide group or of tertiary hydroxyl groups. The compound formed in largest amount is the 7-keto-8,14-oxide previously obtained via the corresponding 7-hydroxy compound from γ(Δ^{7-8})-cholestenyl acetate.

New Brunswick, N. J. Received March 27, 1943

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[6] The fact that compounds VI, VII and VIII which undoubtedly are ketones could not be derivatized with 2,4-dinitrophenylhydrazine must be ascribed to steric factors, that is, most probably to the presence of interfering groups in positions 8 and 14. However, it must be admitted that this explanation does not account for the failure of 3-(β)-acetoxy-Δ^{8-14}-ergostenedione-7,15 to yield a dinitrophenylhydrazone, although this compound readily reacts with hydrazine to form a pyridazine derivative.[5a]

[Contribution from the Chemical Laboratory of The Ohio State University]

The Action of Diazomethane upon Acyclic Sugar Derivatives. V.[1] Halogen Derivatives

By M. L. Wolfrom and Robert L. Brown[2]

The conversion of a diazomethyl to a chloro- or bromomethyl group with halogen hydride was established by Curtius.[3] Such conversions have been effected[4] with 1-diazo-1-desoxy-*keto*-D-fructose tetraacetate and 1-diazo-1-desoxy-*keto*-D-glucoheptulose pentaacetate. In the present work, the optical rotations of these previously reported halogen derivatives have been remeasured and new values established in several cases. 1-Diazo-1-desoxy-*keto*-D-galaheptulose pentaacetate[1] (I) has now been converted to the 1-chloro and 1-bromo derivatives in the same manner. The 1-chloro compound exhibited dimorphism. The 1-iodo derivatives in these three sugar structures were then obtained from the chloro-compounds by halogen interchange[5] with sodium iodide in acetone.[6]

Table I

Comparative Rotatory Powers of 1-Halo-*keto*-acetates

Substance	M. p., °C.	$[\alpha]^{21-28}\text{D}$ abs. $CHCl_3$	[*M*]
1-Chloro-*keto*-D-fructose tetaacetate[4]	77.5–78	+68°	+24,900
1-Bromo-*keto*-D-fructose tetraacetate	67–68	+65	+26,800
1-Iodo-*keto*-D-fructose tetraacetate	55–56	+63	+28,900
1-Chloro-*keto*-D-glucoheptulose pentaacetate	100–101	− 2.8	− 1,200
1-Bromo-*keto*-D-glucoheptulose pentaacetate	87–88	− 5.5	− 2,700
1-Iodo-*keto*-D-glucoheptulose pentaacetate	79–81[a] 89–90[a]	− 9.9	− 5,200
1-Chloro-*keto*-D-galaheptulose pentaacetate	101–102[a]	−33	−14,500
1-Bromo-*keto*-D-galaheptulose pentaacetate	124–125	−36	−17,400
1-Iodo-*keto*-D-galaheptulose pentaacetate	144–146	−45	−23,900

[a] Dimorphic.

The measured physical constants obtained for the three 1-halo-derivatives of each of these acetylated *keto*-sugar structures are tabulated in Table I. The melting points show a decrease in the sequence Cl → Br → I for the D-fructose and D-glucoheptulose (D-gluco-D-sorbo-heptose) structures but exhibit an increase for D-galaheptulose (D-gala-L-fructo-heptose). The trend of molecular rotation sequence is reversed in the D-fructose

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[1] Previous publication in this series: M. L. Wolfrom, R. L. Brown and E. F. Evans, This Journal, **65**, 1021 (1943).

[2] Du Pont Fellow, 1941-1942.

[3] (a) T. Curtius, *Ber.*, **16**, 754, 2230 (1883); (b) *J. prakt. Chem.*, [2] **38**, 396 (1888).

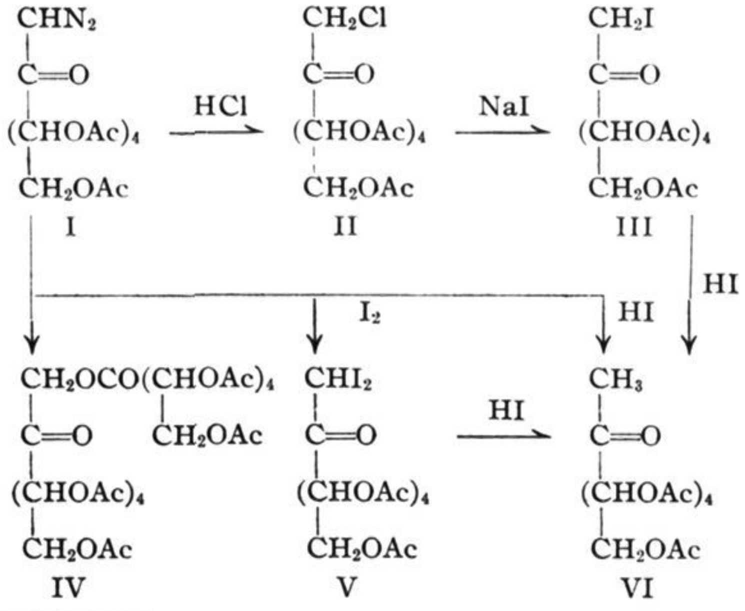
[4] M. L. Wolfrom, S. W. Waisbrot and R. L. Brown, This Journal, **64**, 1701 (1942).

[5] W. H. Perkin and B. F. Duppa, *Ann.*, **112**, 125 (1859); P. van Romburgh, *Rec. trav. chim.*, 1, 233 (1882).

[6] H. Finkelstein, *Ber.*, **43**, 1528 (1910).

series when compared to the D-gala-L-fructoheptose (D-galaheptulose) compounds, in accordance with the enantiomorphic fructose structures present. The interchange of halogen on carbon one has a relatively small effect on the rotatory power. An even smaller effect in rotation between the bromo and iodo derivatives on carbon six of an acyclic sugar structure has been reported[7] for 6-bromo-D-glucose diethyl mercaptal tetrabenzoate (spec. rot. +39° in $CHCl_3$ at 25° and D line; $[M]$ +30,000) and 6-iodo-D-glucose diethyl mercaptal tetrabenzoate (spec. rot. +39° in $CHCl_3$ at 27° and D line; $[M]$ +32,000). These effects are in contrast to the large differences in rotation observable on halogen interchange when the halogen is attached to the carbonyl carbon of aldoses in their cyclic or acyclic[8] forms. It is of interest to note the comparative rotatory powers of 1-chloro-*keto*-D-fructose tetraacetate (spec. rot. +68° in $CHCl_3$ at 22° and D line; $[M]$ +24,900) and 6-chloro-*keto*-D-fructose tetraacetate[9] (spec. rot. +45° in $CHCl_3$ at 20° and D line; $[M]$ +16,500).

Curtius[3b] has shown that the diazomethyl group reacts with organic acids to form esters. This has been applied[10] to the synthesis of *keto*-acetates through the reaction of acetic acid with the diazomethyl ketones of the acetylated sugars. In the present work we report the synthesis of the 1-(O-pentaacetyl-D-galactonate) (IV), 1-(O-pentaacetyl-D-gluconate) and 1-(O-tetraacetyl-D-arabonate) of *keto*-D-galaheptulose pentaacetate. These compounds were obtained on reaction of the diazomethyl ketone I with the corresponding fully acetylated sugar acid in benzene solution.



Curtius[11] had demonstrated that the diazomethyl group reacted readily with iodine to form a diiodomethyl group. This reaction was attempted with 1-diazo-1-desoxy-*keto*-D-galaheptulose pentaacetate (I) without success until it was noted that irradiation promoted the reaction. Prolonged irradiation produced decomposition. The 1,1-diiodo-*keto*-D-galaheptulose pentaacetate (V) so formed is a very interesting substance and should lead to the synthesis of other sugar derivatives of significance.

It was found that treatment of the diazomethyl ketone I with the proper concentration of hydriodic acid led to the reduction of carbon one to yield 1-desoxy-*keto*-D-galaheptulose pentaacetate, (VI). Similar treatment of the 1-iodo (III) and 1,1-diiodo (V) derivatives led to the production of the same compound. VI was isolated in dimorphic forms melting at 65.5–67.5° and 78–79° and showing like rotation in solution. That these forms were homogeneous dimorphs is clearly shown by the comparative X-ray diffraction powder diagrams[12] of Fig. 1 and the measurements on these tabulated in Table II. VI gave a positive iodoform test and formed an oxime.

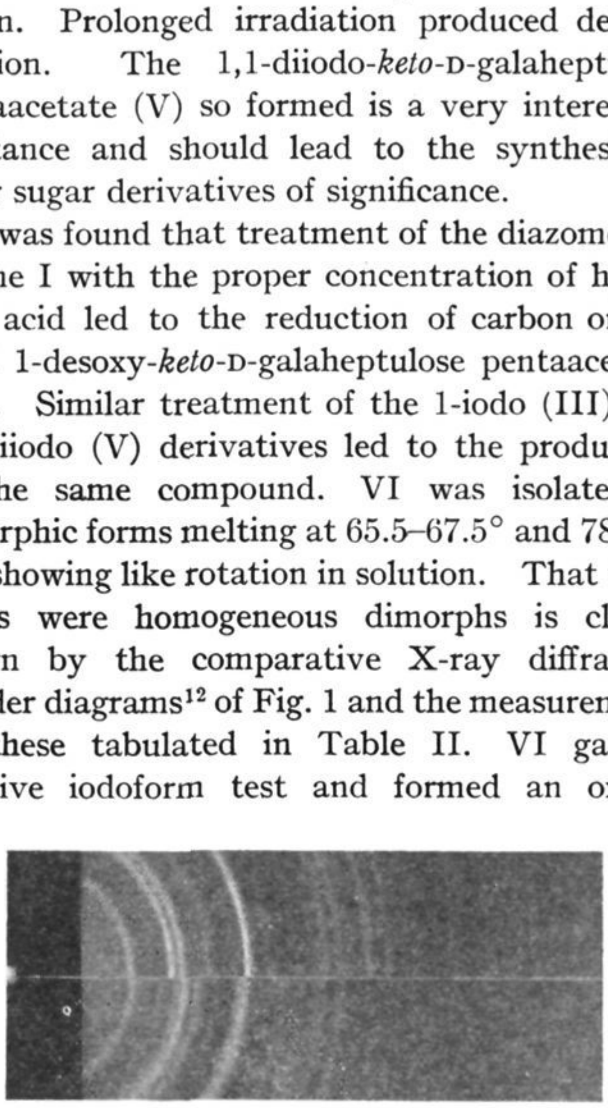


Fig. 1.—Comparative X-ray powder diagrams of the dimorphic forms (upper, m. p. 65.5–67.5°; lower, m. p. 78–79°) of 1-desoxy-*keto*-D-galaheptulose pentaacetate (*cf.* ref. 12 and Table II).

Similar hydriodic acid reduction of 1-diazo-1-desoxy-*keto*-D-fructose tetraacetate[4] led to the formation of 1-desoxy-*keto*-D-fructose tetraacetate, previously synthesized[13] by the action of diazomethane upon *aldehydo*-D-arabinose tetraacetate.

The reduction of ethyl diazoacetate to ethyl

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[7] M. L. Wolfrom and C. C. Christman, THIS JOURNAL, **57**, 713 (1935).

[8] M. L. Wolfrom and R. L. Brown, *ibid.*, **65**, 951 (1943).

[9] D. H. Brauns, *ibid.*, **42**, 1846 (1920); E. Pacsu and F. V. Rich, *ibid.*, **55**, 3018 (1933).

[10] M. L. Wolfrom, S. W. Waisbrot and R. L. Brown, *ibid.*, **64**, 2329 (1942).

[11] T. Curtius, *Ber.*, **18**, 1283 (1885).

[12] For the X-ray photographs and measurements we are indebted to Dr. F. R. Senti of the Eastern Regional Laboratory, United States Department of Agriculture, Philadelphia, Pennsylvania.

[13] M. L. Wolfrom, D. I. Weisblat, W. H. Zophy and S. W. Waisbrot, THIS JOURNAL, **63**, 201 (1941).

acetate with zinc and acetic acid has been described by Curtius.[3b] An indirect reduction of diazoacetophenone through the following reaction sequence has been noted by Wolff.[14] $C_6H_5COCHN_2 \rightarrow C_6H_5COCH{=}N{-}NH_2 \rightarrow C_6H_5COCH(NH)_2 \xrightarrow{NaOH} C_6H_5COCH_3$. In the present work we describe the direct reduction of diazoacetophenone with hydriodic acid to yield acetophenone. Since diazoacetophenone is conveniently synthesized from benzoic acid through the reaction of diazomethane with benzoyl chloride,[15] the above reduction can be formally considered, in respect to the organic acid, as a reversal of the haloform reaction.

All substances herein described were obtained in crystalline form and purified to constant rotation and melting point.

Extension of this work is in progress in this Laboratory.

Experimental

1-Chloro-*keto*-D-galaheptulose Pentaacetate (II).—1-Diazo-1-desoxy-*keto*-D-galaheptulose pentaacetate[1] (2.0 g.) was suspended in 30 cc. of acetone–dry ether (1:15) and treated with a stream of dry hydrogen chloride until cessation of nitrogen evolution (five to ten minutes). To the solution was added a small amount of decolorizing carbon and the suspension warmed a few minutes, filtered and concentrated to a volume of 20 cc., whereupon crystallization was initiated by the addition of petroleum ether (b. p. 30–60°) and cooling; yield 1.9 g., m. p. 90–102°, spec. rot. −33° (26°, *c* 2.5).[16]

Recrystallization of the above material from seven parts of ether yielded massive prisms of specific rotation −32.8° (24°, *c* 2.7) which softened at 89° and melted sharply at 101°. The addition of 25 cc. of petroleum ether to the recrystallization mother liquors, followed by cooling, resulted in the formation of rosets of flat, fan-shaped crystals of specific rotation −32.5° (28°, *c* 4.7) which melted at 89–90°, the melt, however, remaining slightly cloudy up to 102° at which temperature it became clear. Further crystallizations of these two modifications failed to alter their constants. All attempts to obtain one of the two forms completely uncontaminated with the other were fruitless, although either component could be obtained at will as the predominant component of the mixture. Thus it would appear that 1-chloro-*keto*-D-galaheptulose pentaacetate formed two dimorphic modifications (m. p. 89–90° and 101–102°) which were of such a character that they could not readily be completely separated.

The substance (in either modification) was soluble in acetone, chloroform and benzene, moderately soluble in ether and was insoluble in petroleum ether and water. The compound reduced hot Fehling solution but gave no precipitate upon boiling with alcoholic silver nitrate.

Anal. Calcd. for $C_7H_8O_6Cl(CH_3CO)_5$: C, 46.53; H, 5.28; Cl, 8.08; saponification value (6 equiv.), 13.67 cc. 0.1 *N* NaOH per 100 mg. Found: C, 46.23; H, 5.37; Cl, 8.08; saponification value, 13.62 cc.

1-Chloro-*keto*-D-glucoheptulose pentaacetate[4] was purified by ether crystallization; m. p. 100–101°, spec. rot. −2.8° (28°, *c* 5). These constants differ slightly in the rotatory value from those previously recorded[4]: m. p. 100–101°, spec. rot. −5.5° (22°, *c* 5).

1-Bromo-*keto*-D-galaheptulose Pentaacetate.—1-Diazo-1-desoxy-*keto*-D-galaheptulose pentaacetate (3.0 g.) was treated as described above for the synthesis of 1-chloro-*keto*-D-galaheptulose pentaacetate except that hydrogen bromide was substituted for the hydrogen chloride; yield 2.95 g., m. p. 122–125°. Shaking the crystals with a small amount of ether removed most of the color. Pure material was obtained after two crystallizations from acetone–ether by the addition of petroleum ether; m. p. 124–125°, spec. rot. −36° (28°, *c* 5.3).

The bromo derivative was somewhat less soluble in all solvents than the corresponding chloro compound. It reduced hot Fehling solution but gave no precipitate upon boiling with alcoholic silver nitrate.

Anal. Calcd. for $C_7H_8O_6Br(CH_3CO)_5$: C, 42.25; H, 4.79; Br, 16.53; saponification value (6 equiv.), 12.41 cc. 0.1 *N* NaOH per 100 mg. Found: C, 41.92; H, 5.05; Br, 16.64; saponification value, 12.46 cc.

1-Bromo-*keto*-D-fructose tetraacetate[4] was purified[17] by ether crystallization: m. p. 67–68°, spec. rot. +65° (21°, *c* 3); constants previously reported[4]: m. p. 68°, spec. rot. +62.5° (26°, *c* 4). **1-Bromo-*keto*-D-glucoheptulose pentaacetate**[4] was purified by ether crystallization: m. p. 87–88°, spec. rot. −5.5° (28°, *c* 5); constants previously reported[4]: m. p. 86–87°, spec. rot. −4.0° (24°, *c* 5).

1-Iodo-*keto*-D-galaheptulose Pentaacetate (III).—To a solution of 1-chloro-*keto*-D-galaheptulose pentaacetate (4.0 g., 1 mole) in 50 cc. of acetone was added a solution of sodium iodide (4.1 g., 3 moles) in 20 cc. of acetone. The solution assumed a brown color and there resulted a slow precipitation of very finely divided sodium chloride which was removed by centrifugation and washed with acetone. The residue obtained on solvent removal was dissolved in chloroform and washed successively with dilute aqueous sodium thiosulfate and water. A crystalline product was obtained on solvent removal from the dried chloroform solution; yield 4.5 g. (93%) of a very light yellow crystalline product, m. p. 139–143°, spec. rot. −42°. Washed with warm ether to remove the color, the product was recrystallized by solution in a minimum of warm acetone followed by the addition of ether to yield pure 1-iodo-*keto*-D-galaheptulose pentaacetate; m. p. 144–146°, spec. rot. −44.8° (26°, *c* 3.2).

The substance crystallized as white, hexagonal, iridescent leaflets. It was much less soluble in all solvents than the corresponding chloro and bromo analogs. In contrast to the chloro and bromo compounds the iodo-ketose gave a precipitate when boiled with alcoholic silver nitrate. It reduced warm Fehling solution readily.

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(14) L. Wolff, *Ann.*, **394**, 23 (1912).

(15) (a) F. Arndt and J. Amende, *Ber.*, **61**, 1122 (1928); (b) W. Bradley and R. Robinson, *J. Chem. Soc.*, 1310 (1928).

(16) Unless otherwise noted, all rotations were taken in absolute chloroform solution and at the D line of sodium light; 26° is the temperature, *c* is the concentration in g. subs. per 100-cc. soln.

(17) Experimental work by Mr. Evan F. Evans of this Laboratory.

Anal. Calcd. for $C_{17}H_{23}O_{11}I$: C, 38.50; H, 4.37; I, 23.93; saponification value (6 equiv.), 11.31 cc. 0.1 *N* NaOH per 100 mg. Found: C, 38.70; H, 4.48; I, 24.09; saponification value, 11.39 cc.

1-Iodo-*keto*-D-glucoheptulose Pentaacetate.—This substance was synthesized from 1-chloro-*keto*-D-glucoheptulose pentaacetate[4] (3.8 g.) according to the procedure described above for the corresponding galaheptulose derivative; yield 4.4 g., m. p. 74–79°, spec. rot. −9.2°. The substance was recrystallized from ten parts of warm ether by the addition of an equal volume of petroleum ether and cooling to yield pure 1-iodo-*keto*-D-glucoheptulose pentaacetate; m. p. 79–81°, spec. rot. −9.9° (25°, *c* 4.3).

The substance crystallized as white, elongated prisms. It was less soluble in the common solvents than the corresponding chloro and bromo derivatives but decidedly more soluble than its galaheptulose analog. In contrast to the 1-chloro- and 1-bromoglucoheptulose derivatives[4] this substance gave a precipitate when boiled with alcoholic silver nitrate. It readily reduced warm Fehling solution.

Anal. Calcd. for $C_{17}H_{23}O_{11}I$: C, 38.50; H, 4.37; I, 23.93: saponification value (6 equiv.), 11.31 cc. 0.1 *N* NaOH per 100 mg. Found: C, 38.75; H, 4.36; I, 23.75; saponification value, 11.34 cc.

1-Iodo-*keto*-D-fructose Tetraacetate.[17]—This substance was synthesized from 1-chloro-*keto*-D-fructose tetraacetate[4] (1.4 g.) according to the procedure described above for the corresponding galaheptulose derivative. The product was crystallized from alcohol by the addition of water; yield 1.5 g., m. p. 53–56°. Pure material was obtained on further crystallization performed in the same manner; m. p. 55–56°, spec. rot. +63° (21.5°, *c* 3).

The substance was soluble in acetone, chloroform and warm alcohol, moderately so in ether and was practically insoluble in petroleum ether and water. The compound formed a precipitate on heating with alcoholic silver nitrate.

Anal. Calcd. for $C_{14}H_{19}O_9I$: C, 36.69; H, 4.18; I, 27.70. Found: C, 37.00; H, 4.22; I, 27.91.

***keto*-D-Galaheptulose Pentaacetate 1-(O-Pentaacetyl-D-galactonate) (IV).**—A solution of 1-diazo-1-desoxy-*keto*-D-galaheptulose pentaacetate (2.0 g., 1 mole) and D-galactonic acid pentaacetate[18] (3.8 g., 2 moles) in 50 cc. of benzene was heated under reflux for three hours. The benzene was removed under reduced pressure and the residual sirup dissolved in 60 cc. of chloroform (the excess acid was more readily removed from a chloroform solution than from a benzene solution). The unreacted galactonic acid was washed from the solution with several portions of aqueous sodium bicarbonate and the chloroform extract was washed with water, dried and concentrated to 10 cc. Petroleum ether (b. p. 30–60°) was added slowly to opalescence whereupon the substance precipitated as a light yellow crystalline powder. Portionwise addition of petroleum ether was continued until there was no further precipitation; yield 2.4 g., m. p. 165–170°, spec. rot. +16.5°. Recrystallization was effected by solution of the crude material in 50 parts of hot ethanol (95%) followed by the addition of warm water to incipient crystallization and cooling to 0°. Three additional crystallizations from fifty parts of absolute ethanol yielded the pure ketose ester; spec. rot. +13.0° (31°, *c* 4.8), melting points taken simultaneously in soft glass and Pyrex were 165–167° and 171.5–172.5°, respectively. The melt in the soft glass capillary became discolored while that in Pyrex did not and, upon cooling, the melt in the latter crystallized whereas that in the former did not.

Anal. Calcd. for $C_{33}H_{44}O_{23}$: C, 49.01; H, 5.48; saponification value (11 equiv.), 13.60 cc. 0.1 *N* NaOH per 100 mg. Found: C, 49.18; H, 5.54; saponification value, 13.68 cc.

***keto*-D-Galaheptulose Pentaacetate 1-(O-Pentaacetyl-D-gluconate).**—1-Diazo-1-desoxy-*keto*-D-galaheptulose pentaacetate (4.0 g., 1 mole) and D-gluconic acid pentaacetate[19] (7.6 g., 2 moles) reacted in the same manner as described above for the synthesis of the corresponding 1-(O-pentaacetyl-D-galactonate) ester. The dry chloroform extract was evaporated to a thick sirup which was dissolved in 15 cc. of warm ether, whereupon crystallization was initiated. Petroleum ether was added portionwise until crystallization was complete; yield 4.8 g., m. p. 80–105°, spec. rot. +19.5°. The product was recrystallized (decolorizing carbon) four times from twelve parts of absolute ethanol to yield the pure ketose ester; m. p. 112–113°, spec. rot. +22.0° (30°, *c* 6.1). The compound was three to four times more soluble in the common solvents than the corresponding galactonate derivative.

Anal. Calcd. for $C_{33}H_{44}O_{23}$: C, 49.01; H, 5.48; saponification value (11 equiv.), 13.60 cc. 0.1 *N* NaOH per 100 mg. Found: C, 49.15; H, 5.36; saponification value, 13.70 cc.

***keto*-D-Galaheptulose Pentaacetate 1-(O-Tetraacetyl-D-arabonate).**—A solution of 1-diazo-1-desoxy-*keto*-D-galaheptulose pentaacetate (4.0 g., 1 mole) and D-arabonic acid tetraacetate[20] (6.2 g., 2 moles) in 100 cc. of benzene was heated under reflux for three hours and subsequently treated as in the preparation of the corresponding 1-(O-pentaacetyl-D-galactonate) derivative; yield 4.3 g., m. p. 128–139°, spec. rot. +28°. Four crystallizations from forty parts of absolute ethanol yielded pure material; m. p. 155.5–156.5° (Pyrex glass), 153–155° (soft glass), spec. rot. +22.5° (32°, *c* 5.9).

The substance crystallized as white, very thin, elongated rectangular leaflets. It was somewhat more soluble in the common solvents than the corresponding galactonate derivative.

Anal. Calcd. for $C_{30}H_{40}O_{21}$: C, 48.91; H, 5.47; saponification value (10 equiv.), 13.58 cc. 0.1 *N* NaOH per 100 mg. Found: C, 49.10; H, 5.53; saponification value, 13.54 cc.

1,1-Diiodo-*keto*-D-galaheptulose Pentaacetate (V).—A quantity of 2.02 g. (1 mole) of 1-diazo-1-desoxy-*keto*-D-galaheptulose pentaacetate was suspended in 15 cc. of absolute ethanol and 30 cc. (1.2 moles) of a solution of iodine (0.38 *N*) in absolute ethanol was added slowly in small portions while the mixture was irradiated at a distance of about one inch from a No. 1 photoflood bulb. The solution was rapidly decolorized until about 75% (18

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[18] C. D. Hurd and J. C. Sowden, THIS JOURNAL, **60**, 235 (1938); M. L. Wolfrom and D. I. Weisblat, *ibid.*, **61**, 576 (1939).

[19] R. T. Major and E. W. Cook, *ibid.*, **58**, 2474 (1936).

[20] G. Robbins and F. Upson, *ibid.*, **62**, 1074 (1940).

cc.) of the theoretical quantity of the iodine had been added; thereafter, there was no observable decolorization and the remainder (12 cc.) of the iodine solution was added and the mixture irradiated a further five minutes. The temperature of the mixture was maintained below the boiling point of the solvent by cooling frequently in an ice-bath. Soon after the reaction was initiated, the suspended diazo compound disappeared and leaflets of the crystalline product began to precipitate. After the final irradiation the mixture was cooled to the temperature of ice–salt and filtered. The precipitate was shaken with petroleum ether to remove iodine, then filtered and dried under reduced pressure; yield 2.7 g. (88%), m. p. 158–160°. Recrystallization was effected from a minimum of chloroform by the addition of petroleum ether; m. p. 160–163°, spec. rot. +13° (19°, *c* 2). Due to the inherent instability of the substance, these constants are provisional. All operations following the irradiation were carried out in very dim artificial light in order to minimize decomposition.

1,1-Diiodo-*keto*-D-galaheptulose pentaacetate formed colorless crystals. The substance, in chloroform, acetone or ethanol solution, decomposed rapidly with the liberation of iodine, when exposed to diffused sunlight or to artificial light. The compound reduced Fehling solution rapidly at room temperature.

Anal. Calcd. for $C_{17}H_{22}O_{11}I_2$: C, 31.11; H, 3.38; I, 38.68. Found: C, 31.90; H, 3.60; I, 37.90.

1-Desoxy-*keto*-D-galaheptulose Pentaacetate (VI).—To a chloroform (15 cc.) solution of 1-diazo-1-desoxy-*keto*-D-galaheptulose pentaacetate (2.0 g.) in a 30-cc. separatory funnel was added 4 cc. of 47% hydriodic acid. The mixture was shaken carefully. There resulted a copious evolution of nitrogen with the formation of iodine and the evolution of a considerable quantity of heat. Shaking was continued until there was no further evolution of nitrogen (one to two minutes), whereupon the mixture was diluted with water and the chloroform layer removed and washed with water, dilute aqueous sodium thiosulfate and again with water. The dried solution was concentrated to 5 cc. under a stream of dry air and crystallization was initiated when petroleum ether was added to opalescence and the solution cooled to 0°; yield 1.8 g. (three crops), m. p. 65–76°, spec. rot. −12.5° (25°, *c* 4).

Recrystallization from ether by the addition of petroleum ether resulted in the isolation of two modifications of the compound. The one form crystallized as heavy hexagonal plates and melted at 65.5-67.5°. When the melting point bath was held at 70° for one hour the melt resolidified to melt thereafter at 78–79°, the melting point of the higher-melting modification. Either modification could be obtained at will by solution of the compound in ether and boiling to remove nuclei, followed by the addition of petroleum ether to opalescence and the simultaneous nucleation with the desired dimorph. In either modification, the pure compound exhibited a specific rotation of −14° (28°, *c* 3). That these modifications were homogeneous dimorphs is clearly shown by the comparative X-ray diffraction powder diagrams[12] of Fig. 1 and the measurements on these tabulated in Table II.

1-Desoxy-*keto*-D-galaheptulose pentaacetate was soluble in all of the common solvents except petroleum ether and water. It gave a positive iodoform (m. p. 119–120°, mixed m. p. unchanged) test.[21] The compound reduced hot Fehling solution and under the conditions of the Seliwanoff[22] reaction the compound gave first a yellow color followed closely by the cherry-red color characteristic of ketoses. *aldehydo*-D-Galactose pentaacetate, when subjected to the same treatment, gave a yellow color which persisted for some time and then very slowly assumed a slightly reddish hue.

Anal. Calcd. for $C_7H_9O_6(CH_3CO)_5$: C, 50.49; H, 5.98; CH_3CO, 12.37 cc. 0.1 *N* NaOH per 100 mg. Found: C, 50.20; H, 6.02; CH_3CO, 12.41 cc.

1-Desoxy-*keto*-D-galaheptulose pentaacetate was likewise formed, in practically quantitative yield, by the hydriodic acid (47%) reduction of the 1-iodo and of the 1,1-diiodo-*keto*-D-galaheptulose pentaacetate. The reduction was performed in the manner described above and the product was isolated in the higher melting modification and identified by melting point (78–79°) and mixed melting point (unchanged).

It was noted that there was little or no evidence of reaction when 30% hydriodic acid was substituted for the 47% reagent in the reduction of the monoiodo derivative.

TABLE II

X-RAY DIFFRACTION PATTERNS[a] (FIG. 1) OF THE DIMORPHIC FORMS OF 1-DESOXY-*keto*-D-GALAHEPTULOSE PENTAACETATE

M. p. 65.5–67.5°		M. p. 78–79°	
Interplanar spacing, Å.	Relative intensity[b]	Interplanar spacing, Å.	Relative intensity[b]
9.3	S−	9.7	S−
7.0	S	7.6	W+
6.5	S	7.1	W
6.0	W−	6.7	S
5.6	M−	6.2	M+
5.04	W	4.96	S
4.76	S+	4.71	W−
4.35	W	4.48	W−
3.75	W	4.24	W
3.61	M−	4.00	W+
3.48	M−	3.85	W
3.34	W	3.70	W+
3.19	M	3.51	W+
3.03	M−	3.35	W
2.84	W−	3.17	W
2.58	W−	2.57	W−
2.40	W		
2.26	W		
2.19	W−		

[a] *Cf.* ref. 12. The powder diagrams were obtained with copper K_α radiation. The samples were in the form of pressed rods of *ca.* 0.5 mm. diameter. [b] The relative intensities of the lines on the photographs are expressed by the symbols: S = strong; M = medium; W = weak.

1-Desoxy-*keto*-D-galaheptulose Oxime Pentaacetate.—A solution of 1-desoxy-*keto*-D-galaheptulose (0.50 g., 1 mole) in absolute ethanol (10 cc.) was treated with a solution of hydroxylamine hydrochloride (0.17 g., 2 moles) and potassium acetate (0.36 g., 3 moles) in 5 cc. of ethanol

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[21] Experiment performed by Mr. Stephen M. Olin of this Laboratory.

[22] T. Seliwanoff, *Ber.*, **20**, 181 (1887).

water (1:1) and allowed to stand at room temperature for three hours. The reaction mixture was concentrated to dryness with a stream of dry air and the methanol extract of the residue was concentrated to 1 cc. Crystallization ensued upon the addition of 5 cc. of water and cooling; yield 0.37 g., m. p. 120–124°. Purification was effected on crystallization from methanol–water and acetone–petroleum ether; m. p. 125.5–126.5°, spec. rot. +28° (29°, *c* 2).

The compound crystallized in rosets of elongated plates. It was soluble in all of the common solvents except petroleum ether and water.

Anal. Calcd. for $C_7H_{10}O_6N(CH_3CO)_5$: C, 48.68; H, 6.01; N, 3.34. Found: C, 48.47; H, 6.08; N, 3.34.

Preparation of 1-Desoxy-*keto*-D-fructose Tetraacetate from 1-Diazo-1-desoxy-*keto*-D-fructose Tetraacetate.[17]—1-Diazo-1-desoxy-*keto*-D-fructose tetraacetate[4] (4.0 g.) was reduced with hydriodic acid as described above for the corresponding galaheptulose derivative and the product was isolated in the same manner; yield 2.5 g., m. p. 79–83°, spec. rot. +57° (20°, *c* 3). Pure material was obtained on further crystallization from absolute ethanol–petroleum ether and from 95% ethanol; m. p. 81–83°, spec. rot. +56° (20°, *c* 3). The substance was iodine-free and gave a positive iodoform reaction. The oxime was prepared; m. p. 112–113°, spec. rot. +9° (24°, *c* 3). The reported[13] constants for 1-desoxy-*keto*-D-fructose tetraacetate are: m. p. 77–78°, spec. rot. +55.5° (30°, *c* 3), oxime of m. p. 112–113° and spec. rot. +9° (33°, *c* 3). A mixed melting point between the substances prepared by these two methods was found to be 77–82° (oxime mixed m. p. unchanged). The melting point of the product prepared by the previous method could not be raised, indicating the presence of a difficultly removable impurity in an amount sufficient to lower the melting point slightly, but the identity of the two products is considered demonstrated.

Acetophenone from Diazoacetophenone and Hydriodic Acid.—An amount of 2.20 g. of diazoacetophenone, prepared according to the method of Bradley and Robinson,[15b] was treated with hydriodic acid as described above for the synthesis of 1-desoxy-*keto*-D-galaheptulose pentaacetate and the product was isolated on solvent removal from the final dried chloroform solution; yield 1.75 g. (theory 1.82 g.), m. p. 15–18°, b. p. (capillary) 200°, m. p. of phenylhydrazone,[23] 103–104° (mixed m. p. unchanged). These data identify the product as acetophenone, for which the generally accepted constants are: m. p. 20°, b. p. 202°, m. p. of phenylhydrazone, 105°.

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Summary

1. New rotatory values for 1-bromo-*keto*-D-fructose tetraacetate and 1-chloro-(and 1-bromo)-*keto*-D-glucoheptulose pentaacetate have been determined.

2. 1-Chloro(II)-(and 1-bromo)-*keto*-D-galaheptulose pentaacetate have been synthesized.

3. The 1-iodo derivatives of the *keto*-acetates of D-fructose, D-glucoheptulose and D-galaheptulose (III) have been synthesized.

4. 1-(O-Pentaacetyl-D-galactonate) (IV), 1-(O-pentaacetyl-D-gluconate) and 1-(O-tetraacetyl-D-arabonate) of *keto*-D-galaheptulose pentaacetate have been synthesized.

5. 1,1-Diiodo-*keto*-D-galaheptulose pentaacetate (V) has been synthesized.

6. Hydriodic acid reduction of 1-diazo-1-desoxy-*keto*-D-galaheptulose pentaacetate (I) or of 1-iodo(III)-(or 1,1-diiodo-)-*keto*-D-galaheptulose pentaacetate (V) yielded 1-desoxy-*keto*-D-galaheptulose pentaacetate (VI), further characterized by its oxime.

7. Hydriodic acid reduction of 1-diazo-1-desoxy-*keto*-D-fructose tetraacetate yielded the previously-described 1-desoxy-*keto*-D-fructose tetraacetate. This type of reduction was shown to be applicable to diazoacetophenone.

8. Dimorphic modifications of the 1-chloro-(and 1-desoxy-)-*keto*-D-galaheptulose pentaacetate are described.

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[23] H. Reisenegger, *Ber.*, **16**, 662 (1883).