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# Aldehydo Derivatives of *d*-[α-Galaheptose][1]

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In previous studies upon the heptose sugars derived from *d*-galactose[2,3] attention has been called to the parallelism in physical and chemical properties and in rotational behavior of certain of their *ring* derivatives with those of the hexose derivatives of similar space configurations on carbons one to five inclusive. It was pointed out that no such generalization seemed valid for the mercaptal derivatives, and in order to test this point further the study of the open chain derivatives of *d*-(α-galaheptose), which is configurationally related to *l*-mannose, was undertaken.

Application of the Wolfrom method of controlled hydrolysis, with mercuric chloride and cadmium carbonate, of sugar mercaptal acetates having the *cis* configuration on carbons two and three, previously has led only to sirupy products instead of the desired crystalline aldehydo acetates.[4] However, when *d*-(α-galaheptose) diethyl mercaptal hexaacetate was subjected to this reaction, crystalline aldehydo-*d*-(α-galaheptose) hexaacetate was obtained in high yield, and indeed this substance was sufficiently stable to permit its preparation rapidly at a higher temperature than is customary. Its isolation led to the preparation of a series of open chain derivatives which could be compared with similar compounds of the mannose series, since many aldehydo-*d*-mannose derivatives are known.

TABLE I

COMPARISON OF SPECIFIC ROTATIONS $[\alpha]^{20}$D OF COMPOUNDS IN THE *d*-MANNOSE AND *d*-α-GALAHEPTOSE SERIES

| | *d*-Mannose series | *d*-α-Galaheptose series |
|---|---|---|
| Ethyl mercaptal | − 2.8[5] | − 9.7 |
| Ethyl mercaptal acetate | +31.2[6] | + 5.6 |
| Aldehydo acetate | Not crystalline | +27.0 |
| Aldehydo oxime penta- or hexaacetate | +15[7] | +16.3 |
| Aldehydo oxime hexa- or heptaacetate | − 8.5[7] | +38.6 |
| Aldehydo hepta- or octa-acetate | + 0.4[6] | +29.8 |
| Acid nitrile penta- or hexaacetate | − 1.1[8] | +31.7 |
| Aldehydo semicarbazone penta- or hexaacetate | + 9.3[7] | +16.7 |
| Semicarbazone | −53 → −43[9] | −22 → +32.9 |
| Oxime | + 7.5 → + 3.2[10] | − 5.0 → −1.6 |

This comparison, as set forth in Table I, indicated that no regularity in either magnitude or sign of rotation is apparent among the open chain compounds of the two series of derivatives. It is thus at variance with the results obtained on comparison of the ring compounds, where an excellent agreement in both value and sign exists in similar compounds of *l*-mannose and *d*-α-galaheptose. Although no correspondence in rotation seems to exist among the open chain derivatives, a similarity in chemical reactivity has been noted in at least one important reaction, namely, the low temperature acetylation of the sugar oximes:[11] arabinose, xylose and rhamnose oximes yield only nitrile acetates; glucose oxime forms the ring oxime acetate; galactose oxime yields a mixture of ring oxime acetate, aldehydo oxime acetate and nitrile acetate; mannose oxime gives almost exclusively the aldehydo oxime acetate. Upon acetylation of α-galaheptose oxime with pyridine and acetic anhydride at room temperature, aldehydo heptaacetyl α-galaheptose oxime was obtained in high yield, thus showing that the heptose behaves like mannose in this reaction.

The oxime heptaacetate, upon heating above the melting point, readily loses acetic acid to form hexaacetyl α-galaheptonic acid nitrile, a reaction characteristic of completely acetylated open chain oximes.[8] The acetylated nitrile has a specific rotation of +31.7°, thus agreeing in sign with that expected for an acetylated nitrile having an acetoxyl group on the right of carbon 2.[12]

Direct acetylation of α-galaheptose semicarbazone yields the open chain acetate, identical

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(1) Publication authorized by the Surgeon General, U. S. Public Health Service.

(2) Hann, Merrill and Hudson, THIS JOURNAL, **57**, 2100 (1935).

(3) Hann and Hudson, *ibid.*, **59**, 548 (1937).

(4) Wolfrom and Soltzberg, *ibid.*, **58**, 1783 (1936).

(5) Pacsu and Kary, *Ber.*, **62**, 2811 (1929).

(6) Pirie, *Biochem. J.*, **30**, 374 (1936).

(7) Wolfrom and Georges, THIS JOURNAL, **58**, 1781 (1936).

(8) Wolfrom and Thompson, *ibid.*, **53**, 630 (1931).

(9) Maquenne and Goodwin, *Bull. soc. chim.*, [3] **31**, 1075 (1904).

(10) Jacobi, *Ber.*, **24**, 699 (1891).

(11) Deulofeu, Cattaneo and Mendivelzua, *J. Chem. Soc.*, 147 (1934).

(12) Deulofeu, *Nature*, **131**, 548 (1933).

in rotation and melting point with that derived from the aldehydo acetate by treatment with semicarbazide. Similar reactions applied to mannose semicarbazone have yielded analogous results.[7]

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## Experimental

**$d$-[$\alpha$-Galaheptose] Ethyl Mercaptal.**—A solution of 5 g. of $d$-$\alpha$-galaheptose monohydrate in 10 cc. of concentrated hydrochloric acid was shaken, at room temperature, with 10 cc. of technical ethyl mercaptan, when slight warming and a rapid crystallization of the mercaptal took place. After standing for one hour, 25 cc. of ice water was added and the precipitate filtered and dried; yield 6.5 g. (94%). The mercaptal crystallizes from 100 parts of hot water in colorless plates melting at 204–205° (corr.) and showing a specific rotation[13] of −9.7° in purified pyridine (*c*, 1.62: *l*, 4).

*Anal.* Calcd. for $C_{11}H_{24}O_6S_2$: S, 20.3. Found: S, 20.3.

**$d$-[$\alpha$-Galaheptose] Ethyl Mercaptal Hexaacetate.**—The solution of 9.7 g. of the galaheptose mercaptal in a mixture of 100 cc. of pyridine and 100 cc. of acetic anhydride was completed by gentle heat, and the reaction mixture, after standing at room temperature for forty-eight hours, was poured upon crushed ice. The crystalline precipitate was filtered and recrystallized from 5 parts of 95% alcohol, separating in a yield of 16.8 g. (97%).

The mercaptal acetate crystallizes in colorless needles, melting at 145–146° (corr.) and having a rotation in chloroform of +5.6° (*c*, 1.85: *l*, 4).

*Anal.* Calcd. for $C_{23}H_{36}O_{12}S_2$: S, 11.3. Found: S, 11.3.

**Aldehydo-$d$-[$\alpha$-galaheptose] Hexaacetate.**—To a solution of 10 g. of $\alpha$-galaheptose ethyl mercaptal hexaacetate and 17.6 g. of mercuric chloride in 150 cc. of acetone, 10 g. of washed cadmium carbonate was added and the resulting reaction mixture refluxed gently for two hours, 10 g. more of cadmium carbonate being added in small amounts as the reaction proceeded. The separated solid was filtered off and washed with 100 cc. of hot acetone, and the filtrate and washings concentrated *in vacuo* to a sirup. The dry sirup was extracted with four portions of 25 cc. of warm chloroform, and the chloroform extract concentrated *in vacuo* to a sirup, the last traces of chloroform being removed by successive evaporations with small amounts of acetone. Crystallization of the aldehydo acetate occurred during this procedure. The semi-solid residue was dissolved in about 300 cc. of acetone, the solution filtered through a precoated filter, and the filtrate concentrated to 50 cc. by an air current, when the aldehydo acetate readily separated in a yield of 6.5 g. The filtrate, upon treatment with 40 cc. of water, yielded an additional 1.2 g.; total yield 7.7 g. (95%).

Aldehydo-$\alpha$-galaheptose hexaacetate separates from its solution in 25 parts of boiling acetone in microcrystalline pearly plates, which melt at 173–174° (corr.) and have a specific rotation in absolute chloroform of +27.0° (*c*, 1.43: *l*, 4).

*Anal.* Calcd. for $C_{19}H_{26}O_{13}$: C, 49.32; H, 5.67; $COCH_3$, 55.85. Found: C, 49.13; H, 5.88; $COCH_3$, 56.01.

**$d$-[$\alpha$-Galaheptose] Oxime.**—A mixture of 30 g. of $\alpha$-galaheptose monohydrate, 42.3 g. of fused potassium acetate and 19.8 g. of hydroxylamine hydrochloride was dissolved in 45 cc. of water and maintained at 60° for ten minutes, then cooled in an ice-bath, crystallization of the oxime taking place after two hours; yield 31.6 g. (98%). The substance is quite soluble in water, but may be recrystallized in a yield of 60% by solution in 2 parts of water at 75°, and subsequent standing for twenty-four hours in an ice chest.

$d$-$\alpha$-Galaheptose oxime crystallizes in colorless prisms melting at 179° with decomposition. Its aqueous solutions show mutarotation, changing slowly from an initial value of −5.0° to an equilibrium value of −1.6° in twenty-four hours (*c*, 2.23: *l*, 4).

*Anal.* Calcd. for $C_7H_{15}O_7N$: C, 37.31; H, 6.72; N 6.22. Found: C, 37.45; H, 6.82; N, 6.08.

**Aldehydo-$d$-[$\alpha$-galaheptose] Oxime Hexaacetate.**—A solution of hydroxylamine was prepared by refluxing 1 g. of pulverized hydroxylamine hydrochloride and 2.2 g. of fused potassium acetate in 25 cc. of absolute alcohol. The separated potassium chloride was filtered off, and 2.5 g. of aldehydo-$\alpha$-galaheptose hexaacetate dissolved in the filtrate by gentle heat. The solution was concentrated to dryness by an air current, the crystalline residue was taken up in 25 cc. of water, and the solid filtered and dried; yield 2.4 g. (92%). The compound is relatively unstable but may be recrystallized by solution in 5 parts of warm 95% alcohol and addition of 10 parts of water.

Aldehydo-$\alpha$-galaheptose oxime hexaacetate crystallizes in colorless needles, melting at 130° (corr.) and having a specific rotation of +16.3° (*c*, 0.84: *l*, 4) in absolute chloroform.

*Anal.* Calcd. for $C_{19}H_{27}O_{13}N$: C, 47.78; H, 5.70; $COCH_3$, 54.09. Found: C, 47.62; H, 5.90; $COCH_3$, 54.27.

**Aldehydo-$d$-[$\alpha$-galaheptose] Oxime Heptaacetate.**—(1) A suspension of 5 g. of $\alpha$-galaheptose oxime in a mixture of 50 cc. of pyridine and 50 cc. of acetic anhydride was allowed to stand overnight at room temperature and then agitated for two hours on a shaking machine, when solution was complete. The oxime acetate crystallized readily upon addition of ice. The crystalline material had a rotation of +37.5° and was obtained in a yield of 9.5 g. (83%). (2) A solution of 2.2 g. of $\alpha$-galaheptose oxime hexaacetate in 10 cc. of pyridine was cooled in ice and salt and 10 cc. of acetate anhydride added dropwise with constant stirring. After one hour 50 g. of finely chopped ice was added, when the heptaacetate separated in a yield of 1.9 g. (79%).

Aldehydo-$d$-[$\alpha$-galaheptose] oxime heptaacetate crystallizes from 10 parts of 35% ethyl alcohol in long needles melting at 125–126° (corr.) and when recrystallized to constant properties gives a specific rotation of +38.6° in chloroform (*c*, 1.24: *l*, 4).

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(13) All rotations are constant specific rotations at 20° for sodium light, *c* is concentration in grams in 100 cc. of solution, and *l* is the tube length in decimeters.

*Anal.* Calcd. for $C_{21}H_{29}O_{14}N$: C, 48.53; H, 5.63; $COCH_3$, 58.00; N, 2.70. Found: C, 48.66; H, 5.50; $COCH_3$, 57.88; N, 2.73.

***d*-[α-Galaheptonic] Nitrile Hexaacetate.**—(1) One gram of α-galaheptose oxime heptaacetate was melted and heated gradually to 170° in an oil-bath, the melt solidifying as the temperature increased, and acetic acid was liberated. The solid was dissolved in 50 cc. of 95% alcohol and upon cooling crystallization ensued; yield 0.7 g. (80%) of material melting at 193–194° (corr.). (2) A suspension of one gram of α-galaheptose oxime and 1 g. of fused sodium acetate in 5 cc. of acetic anhydride was heated gently to solution of the oxime when a vigorous reaction occurred and the mixture became very dark. After refluxing for six minutes, the mixture was poured into crushed ice, giving a dark brown crystalline powder; yield 2.0 g. Upon recrystallization 1.1 g. (54%) of nitrile hexaacetate was obtained. (3) Acetylation of 1 g. of the oxime heptaacetate by sodium acetate and acetic anhydride yielded 0.9 g. (quantitative) of the acetylated nitrile. *d*-α-Galaheptonic acid nitrile hexaacetate crystallizes from 100 parts of 95% alcohol in plates melting at 194° (corr.) and exhibiting a specific rotation of +31.7° in chloroform (*c*, 1.23: *l*, 4).

*Anal.* Calcd. for $C_{19}H_{25}O_{12}N$: C, 49.65; H, 5.49. Found: C, 49.80; H, 5.60.

***d*-[α-Galaheptose] Semicarbazone.**—A solution of semicarbazide prepared by refluxing 5.8 g. of semicarbazide hydrochloride and 5.2 g. of finely powdered fused potassium acetate in 35 cc. of absolute alcohol was filtered to remove the separated potassium chloride, and added to a solution of 10 g. of α-galaheptose monohydrate in 15 cc. of water. A small portion of the solution was removed and crystallized after about three days. Upon seeding the main portion crystallization progressed and a first yield of 8.7 g. was obtained directly, a second crop of 1.4 g. (total yield 80%) being obtained from the mother liquors.

*d*-α-Galaheptose semicarbazone crystallizes from solution in one part of water by addition of two parts of 95% alcohol in colorless needles which melt at 136–137° (corr.). Aqueous solutions of the substance show mutarotation changing from −22 to +32.9° in twenty-four hours (*c*, 0.83; *l*, 4).

*Anal.* Calcd. for $C_8H_{17}O_7N_3$: C, 35.93; H, 6.41. Found: C, 35.72; H, 6.49.

**Aldehydo-*d*-[α-galaheptose] Semicarbazone Hexaacetate.**—(1) A suspension of 5 g. of finely powdered semicarbazone in a mixture of 30 cc. of pyridine and 15 cc. of acetic anhydride was dissolved by vigorous shaking for two hours and the solution poured upon 500 g. of crushed ice. Complete solution, followed by slow crystallization of 4.5 g. (46%) of crystalline material, took place. Upon recrystallization from 10 parts of boiling water a yield of 2.3 g. of crystalline acetate, melting at 180° and unchanged in melting point upon admixture with the semicarbazone acetate, obtained from aldehydo-α-galaheptose hexaacetate, was obtained. (2) A solution of 1.6 g. of aldehydo-α-galaheptose hexaacetate, 0.4 g. of semicarbazide hydrochloride and 0.5 g. of fused potassium acetate in 13 cc. of 70% ethyl alcohol was refluxed gently for ten minutes, the alcohol was driven off by air blast and 25 cc. of water was added to the sirupy residue; crystallization of 1.1 g. (61%) of the semicarbazone acetate occurred readily.

Aldehydo-α-galaheptose semicarbazone hexaacetate crystallizes from 25 parts of water in clusters of shining small well-formed plates which melt at 180° (corr.) and show a specific rotation of +16.7° (*c*, 1.03: *l*, 4) in purified chloroform.

*Anal.* Calcd. for $C_{20}H_{29}O_{13}N_3$: C, 46.22; H, 5.63; $COCH_3$, 49.71. Found: C, 46.06; H, 5.44; $COCH_3$, 49.89.

**Aldehydo-*d*-[α-galaheptose] Octaacetate.**—A solution of 3.0 g. of aldehydo-α-galaheptose hexaacetate in 50 cc. of a mixture of two parts of acetic anhydride and one part of acetic acid containing 2% of concentrated sulfuric acid by volume was allowed to stand overnight at 20°, then poured upon crushed ice, giving a clear solution from which needle-like crystals gradually separated in a yield of 2.8 g. The filtrate, upon extraction with chloroform, and concentration of the dried chloroform extract, yielded a further 0.9 g. of similar needles; total recovery 3.7 g. (quantitative).

Aldehydo-*d*-α-galaheptose octaacetate separates from 10 parts of 50% alcohol in thin square ended plates, 7 to 8 mm. long and about 0.5 mm. wide. It melts at 112°; (corr.) and has a specific rotation of +29.8° (*c*, 1.57: *l*, 4) in purified chloroform.

*Anal.* Calcd. for $C_{23}H_{32}O_{16}$: C, 48.91; H, 5.72; $COCH_3$, 60.99. Found: C, 48.80; H, 5.72; $COCH_3$, 60.97.

## Summary

A series of open chain derivatives of *d*-α-galaheptose has been prepared and described. These compounds, upon comparison with similar open chain derivatives of *l*-mannose, fail to show the parallelism of rotations noted in ring compounds in these two series.

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