Diethyl α,α′-diethyl-α,α′-dicarbethoxyadipate.[11]—One hundred and twenty-two g. (5.2 moles) of powdered sodium under 2.5 liters of xylene was placed in a five-liter three-necked flask provided with a mechanical stirrer, reflux condenser and dropping funnel. One kilogram of diethyl ethylmalonate was added gradually over a period of two hours, the mixture being cooled in an ice-bath. The mixture was then heated to the boiling point of xylene, whereupon it became a red colored homogeneous solution. Ethylene bromide (500 g., 2.65 moles) was then added during the course of one and one-half hours to the boiling solution. Refluxing was continued for ten hours. The mixture was cooled to room temperature and 1.5 liters of water added. After standing crystals of the desired ester separated at the xylene–water interface. The crystals were filtered out and the xylene layer fractionated through a Widmer column, first at 740 mm. pressure for the removal of xylene. Unreacted ester (250–300 g.) was obtained at 90–102°(7 mm.). After all material boiling below 165°(1 mm.) was removed the residue was allowed to cool and another crop of crystals obtained. After recrystallization from 95% alcohol, 230–250 g. of the desired ester, m. p. 95–96°, was obtained which corresponds to a yield of about 30%. The ester was characterized by conversion to the corresponding acid, m. p. 210–211° (with decomposition), and to the α,α′-diethyladipic acid, m. p. 129–131°.[11]

Summary

Five variously substituted glycols have been found to react with *n*-amylamine or phenethylamine to give 40–70% yields of the corresponding pyrrolidines, piperidines or hexahydroazepines. Heptane-1,6-diol gave only 17% yields of the 1-*n*-amyl or 1-phenethyl-2-methylhexahydroazepine.

MADISON, WISCONSIN RECEIVED FEBRUARY 25, 1938

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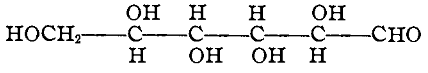
[11] Lean, *J. Chem. Soc.*, **65**, 1004 (1894).

[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF HEALTH, U. S. PUBLIC HEALTH SERVICE]

d-Alpha, Alpha-Galaoctose and Some of its Derivatives[1]

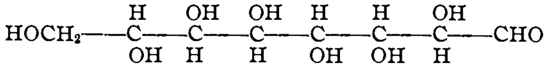
BY W. DAYTON MACLAY, RAYMOND M. HANN AND C. S. HUDSON

Study of the aldoheptoses[2,3] derived from *d*-galactose has supplied many data supporting the hypothesis that the physical and chemical properties of an aldose sugar and its ring derivatives are conditioned in first measure by the space configurations of carbon atoms one to five of the sugar molecule. In the present communication the properties of an eight carbon aldose, *d*-α,α-galaoctose, and some of its derivatives, will be described. This octose was obtained as a crystalline monohydrate by Fischer,[4] who, however, did not establish its configuration. This has now been accomplished by the preparation of the amide and the phenylhydrazide of the corresponding *d*-α,α-galaoctonic acid; their levorotations indicate by the amide and phenylhydrazide rules that the hydroxyl group on carbon atom two is to the left, when the carbon chain is written vertically with the carboxyl group at the top. The configuration of carbon atoms one to five in the octose, which is derived from *d*-α-galaheptose, is therefore the same as in *l*-galactose (see formulas) and it is to be expected that the magnitudes of the rotations of the octose and its ring derivatives will be near those of like substances in the *d*-galactose series but opposite in sign. This inference is well substantiated by the measurements (see Table I). The signs of rotation in all cases are as expected; the magnitudes of the molecular rotations of corresponding substances are near each other except in the case of the sugar acetates where they differ considerably.



$$\begin{array}{cccccc} & \text{OH} & \text{H} & \text{H} & \text{OH} & \\ \text{HOCH}_2\text{—} & \text{C—} & \text{C—} & \text{C—} & \text{C—} & \text{CHO} \\ & \text{H} & \text{OH} & \text{OH} & \text{H} & \end{array}$$

l-Galactose



$$\begin{array}{cccccccc} & \text{H} & \text{OH} & \text{OH} & \text{H} & \text{H} & \text{OH} & \\ \text{HOCH}_2\text{—} & \text{C—} & \text{C—} & \text{C—} & \text{C—} & \text{C—} & \text{C—} & \text{CHO} \\ & \text{OH} & \text{H} & \text{H} & \text{OH} & \text{OH} & \text{H} & \end{array}$$

d-α,α-Galaoctose

In addition to this parallelism of rotations there also exists in these series a parallelism of other physical properties and also of chemical

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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] Fischer, *Ann.*, **288**, 150 (1895).

TABLE I

COMPARISON OF ROTATIONS OF SUBSTANCES IN THE GALACTOSE AND α,α-GALAOCTOSE SERIES

	d-Galactose series rotation		*d*-α,α-Galaoctose series rotation	
	Sp. $[\alpha]_D$	Mol.	Sp. $[\alpha]_D$	Mol.
Sugar initial	(β) + 52.0	+ 9,360	(α) − 44.7	−10,700
Sugar final	+ 80.5	+14,500	− 61.7	−14,800
Aldonic acid initial	− 11.2	− 2,200	+ 5.6	+ 1,400
Aldonic acid final	− 57.6	−11,300	+ 47.1	+12,100
Aldonic acid amide	+ 30.2	+ 5,900	− 23.2	− 5,900
Aldonic acid phenylhydrazide	+ 10.4	+ 3,000	− 19.6[a]	− 6,700
Aldonic acid lactone	− 77.6	−13,800	+ 64.8	+15,400
Sugar acetate	(α) +107.0	+41,700	(β) − 61.4[b]	−32,800
	(β) + 23.0	+ 8,900	(α) − 0.9	− 480
Methyl glycoside	(α) +196.1	+38,100	(β) −147.7	−37,500
	(β) + 0.7	+ 140	(α) 0.0[c]	0
Methyl glycoside acetate	(α) +133.0	+48,200	(β) − 90.0	−45,600
	(β) − 14.0	− 5,100	(α) + 16.8	+ 8,500

[a] Specific rotation at 50°.

[b] Rotation from rearrangement solution.

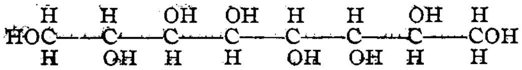
[c] From deacetylation of α-methyl-*d*-α,α-galaoctoside hexaacetate.

reactivity. Considering first the addition of hydrocyanic acid to sugars to form lactones of the galactonic acid type, it may be noted that *d*-α,α-galaoctonic lactone (*l*-galactonic type) is obtained in high yield from *d*-α-galaheptose (*l*-mannose type), very little of the isomeric lactone of *l*-talonic type being formed; this result conforms with the observation of Fischer and Ruff[5] that *d*-lyxose gives rise predominantly to *d*-galactonic lactone and to that of Peirce[6] that *d*-mannose yields 60 to 80% of the heptonic lactone possessing the *d*-galactonic configuration, but only 5 to 6% of the isomeric β-mannoheptonic acid of the *d*-talonic configuration. Free α,α-galaoctonic acid resembles galactonic acid in ease of isolation, in ready lactonization, and in the formation of similar crystallizable salts of cadmium, calcium, and sodium. The course of its lactonization in aqueous solution is similar to that of the hexonic acid in rate, and the differences between the initial and final molecular rotations of the two acids are not far apart (see Table I).

α-*d*-α,α-Galaoctose, upon solution in water, shows mutarotation of the complex type. The alpha-form of galactose shows a decreasing unimolecular reaction coefficient and the beta-form exhibits an increasing one.[7] The alpha-form of *d*-α,α-galaoctose is configurationally like the beta-form of galactose and it shows the like increase for its velocity coefficient (see Table IV). When the sugar is acetylated with sodium acetate and acetic anhydride it forms an α-heptaacetate in high yield, and rotational observations show this acetate to be readily rearranged to its β-isomer in acetylating mixtures catalyzed by sulfuric acid, a change comparable to that shown by β-*d*-galactose pentaacetate in passing to its alpha-form under the same experimental conditions, the alpha-form of the octose being the configurational analog of the beta-form of the hexose under the customary system of nomenclature. The *d*-α,α-galaoctonic amide resembles galactonic amide in its general properties. Its molecular rotation may be calculated by using the rotational values of the individual carbon atoms from the hexonic amide series,[8] the rotations of carbon atoms six and seven being assumed to be negligibly small, $(-\alpha + \beta + \gamma - \delta) = (-47.25 - 14.65 + 0.95 + 2.05)10^2 = -5890$, and its specific rotation as $-5890/255 = -23.1$, which agrees fully with the observed value -23.2.

The iso-rotation rules allow the calculation of the expected values of the rotations of some of the ring compounds of the octose (see Table II).

It is evident from the configuration of *d*-α,α-galaoctose that the corresponding alcohol and dibasic acid are not obtainable from any other



$$\underset{\mathrm{H}}{\overset{\mathrm{H}}{\mathrm{HOC}}}-\underset{\mathrm{OH}}{\overset{\mathrm{H}}{\mathrm{C}}}-\underset{\mathrm{H}}{\overset{\mathrm{OH}}{\mathrm{C}}}-\underset{\mathrm{H}}{\overset{\mathrm{OH}}{\mathrm{C}}}-\underset{\mathrm{OH}}{\overset{\mathrm{H}}{\mathrm{C}}}-\underset{\mathrm{OH}}{\overset{\mathrm{H}}{\mathrm{C}}}-\underset{\mathrm{H}}{\overset{\mathrm{OH}}{\mathrm{C}}}-\underset{\mathrm{H}}{\overset{\mathrm{H}}{\mathrm{COH}}}$$

d-α,α-Galaoctitol

aldooctose, just as *d*-mannitol is obtainable from only one aldohexose (*d*-mannose). The configuration shows that the octitol should be op-

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(5) Fischer and Ruff, *Ber.*, **33**, 2142 (1900).

(6) Peirce, *J. Biol. Chem.*, **23**, 330 (1915).

(7) Isbell and Pigman, *Bur. Standards J. Research*, **18**, 186 (1937).

(8) Hudson and Komatsu, THIS JOURNAL, **41**, 1141 (1919).

TABLE II

OBSERVED AND CALCULATED SPECIFIC ROTATIONS IN THE *d*-α,α-GALAOCTOSE SERIES

Substance	Calculated mol. rotation[a] $[M]^{20}_D \times 10^{-2}$	Molecular weight	Specific rotation Calcd.	Specific rotation Obsd.
β-Methyl-*d*-α,α-galaoctoside	$b - a_{Me} = b - 190 = -376$	254	[−148°]	**−148°**
α-Methyl-*d*-α,α-galaoctoside	$b + a_{Me} = -186 + 190 = +4$	254	+ 2	0
β-*d*-α,α-Galaoctose	$b - a_{OH} = -186 - 88 = -274$	240	−114	Unknown
α-*d*-α,α-Galaoctose	$b + a_{OH} = -186 + 88 = -98$	240	− 41	−45
β-Methyl-*d*-α,α-galaoctoside hexaacetate	$B - A_{Me} = B - 267 = -455$	506	[− 90.0]	−90
α-Methyl-*d*-α,α-galaoctoside hexaacetate	$B + A_{Me} = -188 + 267 = +79$	506	+ 16	+17
β-*d*-α,α-Galaoctose heptaacetate	$B - A_{Ac} = -188 - 164 = -352$	534	− 66	−61
α-*d*-α,α-Galaoctose heptaacetate	$B + A_{Ac} = -188 + 164 = -24$	534	− 4	− 1

[a] The value of a_{Me} is taken from the rotations of the α- and β-methyl-*d*-galactosides [Dale and Hudson, THIS JOURNAL, **52**, 2535 (1930)], that of a_{OH} from those of the α- and β-*d*-galactoses [53° for the β-form and 151° for the α-form] [Isbell and Pigman, *Bur. Standards J. Research*, **18**, 186 (1937)], that of A_{Me} from those of the α- and β-methyl-*d*-galactoside tetraacetates (Dale and Hudson, *loc. cit.*), and that of A_{Ac} from those of the first and second *d*-galactose pentaacetates [Hudson, *Bur. Standards Scientific Paper*, **553,** 378 (1926)]. The value of *b* is obtained by solving the first equation of the table, and that of *B* through the fifth equation.

tically active; no rotation could be detected in aqueous solution, and, therefore, following usual practice, observation was made in a saturated borax solution but the specific rotation[9] was found to be very low, namely, −0.5°, which is hardly beyond the limits of measurement. We therefore sought to decide the question of its possession of optical activity by preparation of its crystalline octaacetate as suggested by Hockett and Hudson[10] in the case of *d*-xylitol and *d*-arabitol; this octaacetate showed the strong specific rotation of +40°, proving that the octitol is optically active.[11]

We express our appreciation to Dr. W. T. Haskins for performing the micro-analyses in connection with this work.

Experimental

***d*-α,α-Galaoctonic Lactone from *d*-α-Galaheptose.**—To a solution of 100 g. of α-galaheptose monohydrate in 150 cc. of water cooled to 2°, 10 drops of concd. ammonia and 25 cc. of liquid hydrocyanic acid were added and the mixture allowed to stand in the refrigerator for three days, during which time it became semi-solid through crystallization of the heptonic cyanohydrin. The paste was thinned by addition of 500 cc. of water, the cyanohydrin hydrolyzed to the amide by heating at 60° for six hours, the amide suspension boiled with 100 g. of barium hydroxide octahydrate until free of ammonia, and the barium balanced out as sulfate. On standing the filtrate separated a crop of 35 g. of nearly pure *d*-α,α-galaoctonic acid having a specific rotation of +7.2° in water, and successive crops of crystals, 36 g. of rotation +22° and 15 g. of rotation +40°, progressively richer in lactone, were obtained on concentration. The mixed acid and lactone fractions readily lactonized to an equilibrium mixture containing about 90% lactone upon boiling their solutions in two parts of water under reflux for one hour. The average yield of crystalline material in three preparations was 87 g. (77% calculated as lactone), the final mother liquors containing non-crystallizable but titratable acid material indicating an over-all yield of 92%. Preliminary studies of this residuum show the presence of material giving a positively rotating phenylhydrazide, probably *d*-α,β-galaoctonic acid phenylhydrazide.

Pure *d*-α,α-galaoctonic lactone crystallizes from 200 parts of glacial acetic acid in small plates which decompose at 219–220° (corr.) and show an initial rotation of +64.8° in water (*c*, 0.8; *l*, 4) changing slowly at 20° to an equilibrium value of +57.4° in twenty days. Fischer[4] reports a specific rotation of 64.0° and a melting point of 225–228° (corr.).

Anal. Calcd. for $C_8H_{14}O_8$: C, 40.3; H, 5.9. Found: C, 40.3; H, 5.9.

***d*-α,α-Galaoctonic Acid.**—The method of Brackenbury and Upson[12] was employed to prepare the pure acid. The sodium salt which was prepared from 5 g. of lactone was suspended in 20 cc. of water, and three successive portions of 10 cc. of glacial acetic acid were added under vigorous shaking; the octonic acid separated as fine needles and after dissolving the sodium acetate by addition of 25 cc. of water they were filtered and dried; yield 5.0 g. (92%). The acid was recrystallized by solution in 50 parts of water at 70° and immediate cooling in an ice-bath. It melted at 221° (corr.) with decomposition. Due to its limited solubility, as well as its tendency to lactonize, the specific rotation was determined by dissolving the compound in water at 60°, immediately cooling, and measuring the rotation within four minutes. An average of five readings of samples prepared in this manner was +5.6° (range +5.2 to +6.0; *c*, 0.6; *l*, 4). The acid slowly mutarotated at 20° (see Table III).

Anal. Acid titration: 0.1615 g. neutralized 6.31 cc. of 0.1 *N* NaOH. Calcd. 6.24 cc. Calcd. for $C_8H_{16}O_9$: C, 37.5; H, 6.3. Found: C, 37.4; H, 6.2.

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[9] Unless otherwise stated 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.

[10] Hockett and Hudson, THIS JOURNAL, **57**, 1753 (1935).

[11] Since the acetates of the sugar alcohols prove to be of such value in questions of identification, we have prepared a considerable number of them and they will be described in a forthcoming publication.

[12] Brackenbury and Upson, THIS JOURNAL, **55**, 2512 (1933).

TABLE III

MUTAROTATION OF *d*-α,α-GALAOCTONIC ACID IN WATER

Concentration 0.1516 g. in 25 cc.; tube length 4 dm.; $T = 20 \pm 0.5°$ Initial reading +5.4°

Time, days	1	3	5	10
$[\alpha]^{20}_D$	+9.7	15.0	17.1	23.8
Time, days	21	31	70	6 months
$[\alpha]^{20}_D$	36.4	41.4	47.1	47.1

Salts of *d*-α,α-Galaoctonic Acid. 1.—The sodium salt was obtained as the dihydrate, crystallizing readily from 20 parts of 50% alcohol in small plates which exhibit a specific rotation of 4.3° in water (*c*, 4.0; *l*, 4).

Anal. Calcd. for $C_8H_{15}O_9Na{\cdot}2H_2O$: Na, 7.3. Found: Na, 7.3.

2.—The calcium salt was prepared by refluxing a solution of the acid with an excess of calcium oxide, filtering and evaporating the filtrate. The salt separates in rectangular plates as a monohydrate when recrystallized from 40 parts of water. A 1% solution of the substance in water failed to give a readable rotation in a 4-dm. tube. The air-dried salt retains all the water of crystallization, but becomes anhydrous after vacuum drying at 138° for four hours.

Anal. Calcd. for $C_{16}H_{30}O_{18}Ca{\cdot}9H_2O$: H_2O, 22.8; Ca, 5.6. Found: H_2O, 22.5; Ca, 5.6. Calcd. for anhydrous salt: Ca, 7.3. Found: Ca, 7.3.

3.—The cadmium salt was prepared by refluxing a solution of the acid with an equivalent amount of cadmium hydroxide. The salt crystallizes from 500 parts of water in the form of clusters of small needles. The salt was vacuum dried at 138° for seven hours.

Anal. Calcd. for $C_{16}H_{30}O_{18}Cd$: Cd, 18.0. Found: Cd, 17.9, 18.0.

4.—The brucine salt was prepared by refluxing a solution of 5.0 g. of the acid with 9.1 g. of brucine for one hour. The excess brucine was extracted with chloroform, the solution concentrated *in vacuo* to dryness, the dried residue taken up in 50 cc. of 70% methyl alcohol and crystallized; yield 9.6 g. (70%). The salt was recrystallized from 5 parts of 75% methyl alcohol, separating in plates melting at 157–158° (corr.) and showing a specific rotation of −18.8° in water (*c*, 1.24; *l*, 4).

Anal. Calcd. for $C_{31}H_{42}O_{13}N_2{\cdot}2.5H_2O$: C, 53.5; H, 6.8; N, 4.0. Found: C, 53.6; H, 6.8; N, 4.0.

5.—The quinine salt was similarly prepared; yield 50%. It was recrystallized from 10 parts of 70% methyl alcohol, separating in needles melting at 194° (corr.) and rotating −102.2° in water (*c*, 0.88; *l*, 4).

Anal. Calcd. for $C_{28}H_{40}O_{11}N_2{\cdot}H_2O$: C, 56.1; H, 7.1; N, 4.7. Found: C, 56.1; H, 7.1; N, 4.6.

Hexaacetyl-*d*-α,α-Galaoctonic Lactone.—Dry hydrochloric acid gas was bubbled through an ice cold suspension of 5.0 g. of *d*-α,α-galaoctonic lactone in 25 cc. of acetic anhydride. After the lactone had dissolved the solution was concentrated *in vacuo* at 80° to a sirup, the sirup dissolved in 10 cc. of chloroform and 10 cc. of petroleum ether added to bring about crystallization; yield 8.0 g. (78%). After recrystallization to constant properties from 10 parts of alcohol, the lactone hexaacetate was obtained in colorless needles melting at 137–139° (corr.) and exhibiting a specific rotation of +45.4° (*c*, 1.65; *l*, 4) in chloroform.

Anal. Calcd. for $C_{20}H_{27}O_{14}$: C, 49.0; H, 5.3; acetyl, 52.7. Found: C, 49.2; H, 5.3; acetyl, 52.8.

***d*-α,α-Galaoctonic Phenylhydrazide.**—A solution of 2 g. of *d*-α,α-galaoctonic lactone in 25 cc. of water was heated on the steam-bath with 1 cc. of phenylhydrazine and 0.5 cc. of acetic acid for three hours, the phenylhydrazide separating readily in a yield of 2.6 g. (93%). Recrystallized from 100 parts of boiling water, the substance melted at 223–225° and rotated −19.3° in water (*c*, 0.22; *l*, 4) at 50°. Fischer reports a melting point of 235° (corr.).

Anal. Calcd. for $C_{14}H_{22}O_8N_2$: C, 48.5; H, 6.4. Found: C, 48.5; H, 6.4.

***d*-α,α-Galaoctonic Amide.** 1.—A solution of 5 g. of lactone in liquid ammonia was allowed to evaporate at room temperature and the dry residue (5.35 g., quantitative) was recrystallized from 80 parts of boiling water. The properties of the amide agreed with those of the compound obtained by hydrolysis of the cyanohydrin.

2.—A portion of the hydrolyzed cyanohydrin was recrystallized repeatedly from 80 parts of boiling water, the pure amide separating as a white powder which upon microscopic examination was found to consist of square, thin plates. The substance decomposed at 228° (corr.) and its rotation in water at 42° was −23.2° (*c*, 0.4; *l*, 4).

Anal. Calcd. for $C_8H_{17}O_8N$: C, 37.6; H, 6.7; N, 5.5. Found: C, 37.9; H, 6.7; N, 5.5.

α-*d*-α,α-Galaoctose Monohydrate.—A solution of 20 g. of *d*-α,α-galaoctonic lactone in 400 cc. of water was reduced in the usual manner with 2000 g. of 2.5% sodium amalgam. Following removal of the sodium sulfate, the solution was freed of the sodium salt of the octonic acid by concentrating to 40 cc., adding 250 cc. of methyl alcohol and heating gently on the steam-bath for three hours with occasional stirring. The separated sodium salt was fil-

TABLE IV

MUTAROTATION OF α-*d*-α,α-GALAOCTOSE MONOHYDRATE IN WATER

Concentration 1.0029 g. in 25 cc. solution; tube length 4 dm.; $T = 20 \pm 0.5°$

Time after making soln., min.	$[\alpha]^{20}_D$ monohydrate	Time, min.	$K_1 + K_2$
5	−40.0°	0	——
15	40.9	10	0.0024
20	41.3	15	.0023
25	41.9	20	.0026
30	42.6	25	.0029
35	43.4	30	.0033
50	45.4	45	.0037
65	47.1	60	.0039
80	48.4	75	.0040
95	49.6	90	.0040
110	50.7	105	.0042
135	52.2	130	.0043
150	52.8	145	.0043
180	53.8	175	.0042
225	55.2	220	.0046
375	56.8(equil.)	370	——
24 hrs. (final)	56.8	∞	——

tered, the filtrate was concentrated to a thin sirup, ethyl alcohol added to turbidity, and crystallization of the octose monohydrate occurred on standing at 20° overnight; yield 12.5 g. (58%). The sugar may be recrystallized in a yield of 80% by solution in 2 parts of water and addition of 6 parts of alcohol. Upon heating in a capillary it sinters at 103°, giving off its water of crystallization, and melts to a clear sirup at 167–169° (corr.). Fischer reported a corrected melting point of 109–111° and stated that the specific rotation was greater than −40°. The course of the mutarotation of the monohydrate is recorded in Table IV. The octose is designated an alpha form since it is the more dextrorotatory form of a sugar of the *d*-series. The mutarotation is not unimolecular, a result which was anticipated because of its configurational resemblance to *l*-galactose.

Anal. Calcd. for $C_8H_{16}O_8 \cdot H_2O$: C, 37.2; H, 7.0; H_2O, 7.0. Found: C, 37.4; H, 7.2; H_2O, 6.9.

α-*d*-α,α-Galaoctose.—Upon heating the monohydrate at 100° *in vacuo* for four hours, its water of hydration is eliminated quantitatively. The anhydrous material melts at 167–169° (corr.) to a clear sirup. Its solution in water gave a rotation of −44.9° in three minutes and an equilibrium rotation of −61.7° (*c*, 0.8; *l*, 4). The course of its mutarotation paralleled that of the monohydrate. The octose was not fermented by either baker's or brewer's yeasts.

Anal. Calcd. for $C_8H_{16}O_8$: C, 40.0; H, 6.7. Found: C, 39.9; H, 6.8.

Heptaacetyl-α-*d*-α,α-galaoctose.—A suspension of 10 g. of the octose monohydrate and 2.5 g. of fused sodium acetate in 40 cc. of acetic anhydride was heated on the steam-bath for one and one-half hours, then refluxed gently for fifteen minutes and the cooled reaction mixture poured upon crushed ice. The acetylated product was extracted with chloroform, the extract concentrated to a dry sirup, taken up in 25 cc. of alcohol and, upon standing overnight, the galaoctose heptaacetate crystallized in a yield of 9.5 g. (46%). It was recrystallized from three parts of acetic acid, separating in prisms melting at 88–90° (corr.) and having a specific rotation of −0.9° (*c*, 2.15; *l*, 4) in chloroform.

Anal. Calcd. for $C_{22}H_{30}O_{15}$: C, 49.4; H, 5.7; acetyl, 56.4. Found: C, 49.6; H, 5.6; acetyl, 56.4.

Rearrangement of Heptaacetyl α-*d*-α,α-Galaoctose.—A solution of 0.5 g. of the α-heptaacetate in 25 cc. of a rearranging solution, prepared by adding 2 cc. of concentrated sulfuric acid dropwise to an ice-cold mixture of 70 cc. of acetic anhydride and 30 cc. of acetic acid, changed in rotation from 0.9 to −61.4° in the course of twenty-four hours. The change in molecular rotation was 32,400, a value in good agreement with such α,β-shifts among other sugar acetates. Since the specific rotation in the rearranging mixture is similar to that in chloroform, this result would indicate a nearly quantitative conversion to β-*d*-α,α-galaoctose heptaacetate, comparable to the change of the galactose acetates, the change in the hexose series being called β to α because of conventions of nomenclature. The rearranged acetate has been obtained as a colorless sirup, but has not been crystallized.

β-Methyl-*d*-α,α-galaoctoside.—Ten grams of the octose monohydrate was refluxed with 80 cc. of methyl alcohol containing 1.25% of dry hydrochloric acid for ten hours. The solution, which was devoid of reducing power, was treated with 12 g. of dry silver carbonate and the halogen-free filtrate concentrated to 35 cc. and placed in the refrigerator, when crystallization readily occurred; yield 4.7 g. (48%). The substance was recrystallized from 25 parts of absolute methyl alcohol, separating in plates melting at 186–187° (corr.) and rotating −147.7° (*c*, 0.64; *l*, 4) in water. Its rate of hydrolysis in 0.05 *N* hydrochloric acid was 0.0009 (expressed in minutes and decimal logarithms), proving that it is a glycoside of the stable type.

Anal. Calcd. for $C_9H_{18}O_8$: C, 42.5; H, 7.1; OCH_3, 12.2. Found: C, 42.3; H, 7.3; OCH_3, 12.4.

Hexaacetyl-α-methyl-*d*-α,α-galaoctoside.—The filtrate from which the 4.7 g. of β-methyl-*d*-α,α-galaoctoside had been crystallized failed to yield further crystalline material. It was therefore concentrated to a sirup and acetylated by heating on the steam-bath with 1.25 g. of fused sodium acetate and 20 cc. of acetic anhydride. The reaction mixture was poured upon crushed ice and crystalline material separated in a yield of 3.2 g. Recrystallized from 5 parts of 95% alcohol, the α-methyl-*d*-α,α-galaoctoside hexaacetate was obtained in the form of elongated rectangular plates melting at 162° (corr.) and exhibiting a rotation of +16.8° (*c*, 1.32; *l*, 4) in chloroform.

Anal. Calcd. for $C_{21}H_{30}O_{14}$: C, 49.8; H, 6.0; OCH_3, 6.1; acetyl, 51.0. Found: C, 49.8; H, 6.2; OCH_3, 6.0; acetyl, 51.0.

α-Methyl-*d*-α,α-galaoctoside.—A sample of 3.65 g. of the α-glycoside acetate was deacetylated in the usual manner with sodium methylate. The deacetylated material failed to crystallize; however, the colorless sirup had no measurable rotation, this result being in agreement with the rotation calculated by iso-rotation rules, namely, +2°.

Hexaacetyl-β-methyl-*d*-α,α-galaoctoside.—A suspension of 2.6 g. of the β-methylglycoside in 15 cc. of pyridine was treated with 15 cc. of acetic anhydride, allowed to stand overnight at room temperature, and poured over crushed ice. Following the decomposition of the anhydride the solution was extracted with carbon tetrachloride, the carbon tetrachloride removed by successive concentrations with absolute alcohol, and the residual sirup dissolved in 10 cc. of absolute alcohol, when crystallization took place; yield, 4.8 g. (93%). The acetate separated from 5 parts of 50% alcohol in clusters of needles, which melt at 118.5–119° (corr.) and give a rotation of −90° (*c*, 1.0; *l*, 4) in chloroform.

Anal. Calcd. for $C_{21}H_{30}O_{14}$: C, 49.8; H, 6.0; OCH_3, 6.1; acetyl, 51.0. Found: C, 49.6; H, 6.2; OCH_3, 6.3; acetyl, 51.2.

***d*-α,α-Galaoctitol.**—To a solution of 10 g. of galaoctose monohydrate in 70 cc. of water, 3 g. of Raney nickel was added and the sugar reduced at 98° for four hours under a hydrogen pressure of 2500 lb. (166 atm.). The alcohol (7.7 g.) which separated on cooling the reaction bomb was recrystallized from 10 parts of hot water, being obtained in needles melting at 230° (corr.). In agreement with Fischer, no measurable rotation could be obtained in a saturated aqueous solution, and in saturated borax solution the specific rotation was only −0.5° (*c*, 0.8; *l*, 4).

Anal. Calcd. for $C_8H_{18}O_8$: C, 39.6; H, 7.5. Found: C, 39.7; H, 7.6.

Octaacetyl-*d*-α,α-galaoctitol.—A mixture of 1.5 g. of *d*-α,α-galaoctitol, 1 g. of fused sodium acetate, and 15 cc. of acetic anhydride was heated gently and, following a vigorous exothermic reaction, refluxed for fifteen minutes. The reaction mixture was poured upon crushed ice and the octaacetate isolated in a yield of 2.4 g. (70%). It crystallized from 5 parts of 95% alcohol in rectangular elongated plates melting at 141° (corr.) and rotating +40.4° (*c*, 1.2; *l*, 4) in chloroform.

Anal. Calcd. for $C_{24}H_{34}O_{16}$: C, 49.8; H, 5.9; acetyl, 59.5. Found: C, 49.8; H, 6.0; acetyl, 59.6.

***d*-α,α-Galaoctose Benzyl Mercaptal.**—A solution of 1 g. of *d*-α,α-galaoctose monohydrate in 2 cc. of concentrated hydrochloric acid was shaken with 2 cc. of benzyl mercaptan, crystallization of the mercaptal occurring in ten minutes. The solid was filtered off, washed repeatedly with alcohol to remove excess mercaptan and recrystallized from 200 parts of 60% alcohol; yield 1.4 g. (78%). The mercaptal melts at 208–209° (corr.) and rotates +18.5° (*c*, 0.8; *l*, 4) in absolute pyridine.

Anal. Calcd. for $C_{22}H_{30}O_7S_2$: S, 13.6. Found: S, 13.4.

***d*-α,α-Galaoctose Benzyl Mercaptal Heptaacetate.**—One gram of the octose mercaptal was acetylated with pyridine and acetic anhydride in the usual manner. The mercaptal acetate was difficult to crystallize, finally being obtained in needles melting at 88–89° (corr.) and having a rotation of −29.6° (*c*, 0.84; *l*, 4) in chloroform.

Anal. Calcd. for $C_{36}H_{44}O_{14}S_2$: S, 8.4. Found: S, 8.2.

Summary

The configuration of the groups about carbon two of *d*-α,α-galaoctonic acid has been established by the preparation of a levorotating amide and phenylhydrazide; this observation completes the proof of the configuration of Fischer's *d*-α,α-galaoctose. The first five carbon atoms of the octose possess the configuration of the corresponding ones of *l*-galactose. A study of *d*-α,α-galaoctose and of many of its crystalline derivatives shows their properties to be closely similar to those of the corresponding substances of the *l*-galactose series, thus extending the view that the physical and chemical properties of lactonyl aldose compounds are conditioned by the spatial arrangement of carbons one to five, to an aldooctose.

The specific rotation of *d*-α,α-galaoctonic amide has been calculated, using numerical data previously established in studies of the hexonic amides and found to agree with the observed value, showing that optical superposition holds closely for such amides.

Comparison of the observed rotations of several pairs of *d*-α,α-galaoctose derivatives with those calculated by the iso-rotation rules shows good agreement.

Attention has been called to the value of preparation of the sugar alcohol acetates as an aid in determining the question of the optical activity or inactivity of sugar alcohols.

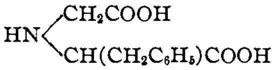
WASHINGTON, D. C. RECEIVED FEBRUARY 18, 1938

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF MOUNT HOLYOKE COLLEGE]

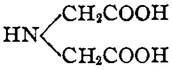
Salts and Hydantoin Derivatives of β-Phenylalanine-N-acetic Acid

BY DOROTHY A. HAHN AND MARGARET M. ENDICOTT

The preparation of β-phenylalanine-N-acetic acid already has been reported[1] but a modification of the method originally used in the hydrolysis of N-3-methyl-5-benzylhydantoin-N-1-acetic acid[2] has increased the yield to approximately 90% of the theoretical so that a detailed study of its derivatives is possible. Attention has been called to the close analogy which exists between this substance and iminodiacetic acid.[3]


$$HN\begin{cases}CH_2COOH\\CH(CH_2C_6H_5)COOH\end{cases}$$

and


$$HN\begin{cases}CH_2COOH\\CH_2COOH\end{cases}$$

It now appears that differences in the behavior of the two compounds are due mainly to differences in the symmetry of their respective molecules. And in this connection it should perhaps be noted that in the case of β-phenylalanine-N-acetic acid, it is not always possible to assign definite structural formulas to such of its derivatives as result from the replacement of only one of the two hydrogen atoms present in the carboxyl groups.

Both acids react with hydrochloric acid to form the corresponding salts. In the case of iminodiacetic acid the product is apparently a stable compound and can be prepared by dissolving the acid in dilute aqueous hydrochloric acid and then adding concentrated acid to precipitate it[3d] (p. 291). This method cannot be applied in the

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[1] Hahn and Litzinger, THIS JOURNAL, **54**, 4665 (1932).

[2] Litzinger, *ibid.*, **56**, 675 (1934).

[3] (a) Heintz, *Ann.*, **122**, 276 and **124**, 297 (1862); (b) Eschweiler, *ibid.*, **278**, 231 (1894); (c) Johnson and McCollum, *Am. Chem. J.*, **35**, 65 (1906); (d) Jongkees, *Rec. trav. chim.*, **27**, 287–326 (1908); (e) Bailey and Read, THIS JOURNAL, **36**, 1759 (1914); (f) Bailey and Snyder, *ibid.*, **37**, 938 (1915); (g) Treibs and Dinelli, *Ann.*, **517**, 170 (1935).